From:	Cunningham, Meg
To:	alaptook@WIHRI.org; Bradley Yoder; Das, Abhik; Gantz, Marie; Higgins, Rosemary (NIH/NICHD) [E]; kurt.schibler@cchmc.org; mcw3@cwru.edu; nancy newman; nfiner@ucsd.edu; Roger.Faix@hsc.utah.edu; Wally Carlo, M.D.; wrich@ucsd.edu
Cc:	Zaterka-Baxter, Kristin; Archer, Stephanie (NIH/NICHD) [E]; Huitema, Carolyn Petrie; Brenda Vecchio; fmartinez@ucsd.edu; msumner@peds.uab.edu; Newman, Jamie
Subject:	SUPPORT Call - Canceled
Date:	Friday, December 19, 2008 10:27:33 AM

All

The SUPPORT call scheduled for Monday, December 22nd at 1 pm ET has been canceled.

Thanks,
Meg

From: Finer, Neil
To: Das, Abhik; Higgins, Rosemary (NIH/NICHD) [E]; Zaterka-Baxter, Kristin
Cc: Gantz, Marie
Subject: RE: SUPPORT CALL MONDAY
Date: Thursday, December 18, 2008 11:14:02 PM

I will include all of Marie's data in my report to the Steering Committee.
Thanks
Neil

From: Das, Abhik [mailto:adas@rti.org]
Sent: Thursday, December 18, 2008 11:39 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; Zaterka-Baxter, Kristin
Cc: Finer, Neil; Gantz, Marie
Subject: RE: SUPPORT CALL MONDAY

I dont have a problem with cancelling, but Marie was working on sending some routine updates to Neil tomorrow.

Thanks

Abhik

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, December 18, 2008 2:00 PM
To: Zaterka-Baxter, Kristin; Das, Abhik
Cc: Finer, Neil
Subject: SUPPORT CALL MONDAY

We don't have anything new for the support subcommittee - do you have any objection to cancelling??

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutesof Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20592
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Das, Abhik
To: Finer, Neil; Gantz, Marie
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT update for subcommittee meeting 9/12
Date: Tuesday, December 02, 2008 9:47:11 AM

Neil:

Marie is traveling back home from a project meeting today, so I am not sure she will be able to respond to you before the call.

Thanks

Abhik

From: Finer, Neil [mailto:nfiner@ucsd.edu]
Sent: Tuesday, December 02, 2008 9:46 AM
To: Gantz, Marie
Cc: Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik
Subject: RE: SUPPORT update for subcommittee meeting 9/12

Hi Marie
I think that I previously asked you to let me know the number of infants who were enrolled on both the Breathing Outcomes and the Neuroimaging secondary. I can't find that response. Could you resend that information to me and all the people on todays call for the longer follow-up of the breathing outcomes?
Many thanks
Neil

From:	Zaterka-Baxter, Kristin
To:	mcw3@cwru.edu; Pablo.Sanchez@UTSouthwestern.edu; sshankar@med.wayne.edu; [SCRN] Stoll, Barbara; kurt.schibler@cchmc.org; bpoindex@iupui.edu; richard.ehrenkranz@yale.edu; alaptook@WIHRI.org; vanmeurs@stanford.edu; wcarlo@peds.uab.edu; Kathleen.A.Kennedy@uth.tmc.edu; goldb008@mc.duke.edu; IFrantz@tufts-nemc.org; edward-bell@uiowa.edu; Roger.Faix@hsc.utah.edu; kwatterberg@salud.unm.edu; nxs5@cwru.edu; Nancy.Miller@UTSouthwestern.edu; melissa.leps@utsouthwestern.edu; ae5357@wayne.edu; ellen_hale@oz.ped.emory.edu; grisbyca@email.uc.edu; ldw@iupui.edu; monica.konstantino@yale.edu; ahensman@wihri.org; mbball@leland.stanford.edu; mcollins@peds.uab.edu; Georgia.E.McDavid@uth.tmc.edu; foy00004@mc.duke.edu; bmackinnon@tufts-nemc.org; karen-johnson@uiowa.edu; karen.osborne@hsc.utah.edu; CBackstrom@salud.unm.edu; Michael Cotten; susie.buchter@oz.ped.emory.edu; bradley.yoder@hsc.utah.edu; Brenda.H.Morris@uth.tmc.edu; vineet.bhandari@yale.edu
Cc:	Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik; nfiner@ucsd.edu; Wade Rich; Gantz, Marie; Auman, Jeanette O.; Pickett, James; Cunningham, Meg; Huitema, Carolyn Petrie; Archer, Stephanie (NIH/NICHD) [E]; Sunkara, Geeta S.
Subject:	SUPPORT DSMC Minutes and Notice of Study Continuation
Date:	Wednesday, November 19, 2008 4:50:24 PM
Attachments:	SUP15.pdf

Hi all,
The DSMC meet on Tuesday October 7, 2008 at RTI in Rockville MD to review the third planned SUPPORT trial interim analysis at 75% status. Please find attached Technical Memo SUP15 regarding the meeting minutes and the committees' recommendation that the Support study should continue as planned.

This memo will be posted to the NRN website shortly: https://neonatal.rti.org

Thanks,
Kris

Kris Zaterka-Baxter
Statistics and Epidemiology Division
RTI International
3040 Cornwallis Road
P.O. Box 12194
RTP, NC 27709-2194 USA
(tel) 919-485-7750
(fax) 919.485.7762
kzaterka@rti.org
www.rti.org

RTI INTERNATIONAL | **Memorandum**

November 19, 2008

SUPPORT TECHNICAL MEMO # 15

TO: Network Coordinators
Network PIs

FROM: The Data Coordinating Center

SUBJECT: SUPPORT Study DSMC Minutes and Notice of Study Continuation

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The Data Safety and Monitoring Committee for the NICHD Neonatal Research Network met in Rockville, MD on October 7, 2008 to review results from the 3rd planned interim monitoring look at the Surfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Study (SUPPORT). The DSMC members in attendance for this session were Drs. Avery (Chair), Boyle, Willinger, Clemons, Allen, Gleason, Blaisdell and Keszler. Drs. Thomson and Bangdiwala joined by phone. Drs. Das and Gantz, Ms. Zaterka Baxter, Cunningham and Huitema from the Network Data Coordinating Center were also present.

Dr. Avery began the meeting by reflecting upon the following questions and urged the committee to consider these questions when reviewing the trial data:

1) Is there an adverse effect that could be linked to one of the treatment modalities? As the advocate for the public and the research population, is there cause for us to intervene, raise a question or ask for additional data.
2) Is there evidence of a fatal flaw in the protocol and/or in the conduct of the trial that would make continuation of the study futile; that would no longer justify subject enrollment or trial cost .
3) Do we have significant data to already answer the research question and thus stop the trial?
4) Is the study statistically futile? Has is become clear that even with the remaining subjects the study outcome would not change from this point and thus would be futile to continue?

Dr. Das gave an overview of the SUPPORT study and Dr. Gantz continued with the presentation of the interim data from the 1136 infants who were enrolled as of August 11, 2008, the date when the analysis was performed.

After review and discussion of the data, the committee focused on answering the questions posed above and concluded that there were no apparent or significant safety or efficacy concerns and recommended that the study should continue as planned. However, they continue to note the importance of striving to achieve separation between the high and low oxygen groups in the oxygen saturation arm of the trial, so that the

questions posed for this arm of the study can be meaningfully answered upon conclusion of the trial.

Dr. Avery closed the meeting with the announcement of his retirement from the NRN DSMC as of October 7, 2008. Dr. Christine Gleason will serve as the new DSMC Chair and Dr. Martin Keszler will join as a new DSMC member.

Cc Rosemary Higgins, MD

From:	Finer, Neil
To:	Higgins, Rosemary (NIH/NICHD) [E]
Cc:	Martinez, Fernando
Subject:	RE: SUPPORT
Date:	Monday, November 10, 2008 5:20:57 PM

Hi Rose
How about 10:30 – 7:30 AM PT?
Neil

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, November 10, 2008 12:02 PM
To: Finer, Neil
Cc: Meg Cunningham
Subject: RE: SUPPORT

Ok
What time would you like to join the SC on Friday January 9?
Thanks
Rose

From: Finer, Neil [mailto:nfiner@ucsd.edu]
Sent: Monday, November 10, 2008 3:02 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT

I think a phone call in advance is easier and everyone is on their own phone system so they hear and are heard better.
Thanks Rose

Neil N. Finer, M.D.
Professor of Pediatrics
Director, Division of Neonatal-Perinatal Medicine
UC San Diego School of Medicine
UC San Diego Medical Center, Hillcrest
402 Dickinson St., MPF 1-140
San Diego, CA 92103-8774
Telephone: 619.543-3759
Facsimile: 619.543.3812

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, November 10, 2008 9:48 AM
To: Finer, Neil
Cc: Cunningham, Meg
Subject: SUPPORT

For the Jan 8-9, 2009 SC meeting – do you want the subcommittee to meet by phone in advance or at the meeting?
Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutesof Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20592
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Webb, Robin E.
To:	Higgins, Rosemary (NIH/NICHD) [E]
Subject:	PLEASE READ SUPPORT - School Age Breathing Outcomes Proposal 9-12-08
Date:	Friday, November 07, 2008 6:28:26 AM

Hi Rose,

Is this still ok to use? Please fill in you availability for the second week in December.

Thanks,
Robin

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, October 27, 2008 12:53 PM
To: Webb, Robin E.
Subject: RE: SUPPORT - School Age Breathing Outcomes Proposal 9-12-08

Mon 11/10 open except 11:30-12:30
Tues 11/11 No
Wed 11/12 open until 2 PM
Thurs 11/13 No
Fri 11/14 open except 2:30-4 PM

Mon 11/17 open until 3 pm
Tues 11/18 no
Wed 11/19 8-10 am
Thurs 11/20 no
Fri 11/21 no

Mon 11/24 open
Tues 11/25 open except 3-5 pm
Wed 11/26 open until 2 pm

Mon 12/1 open
Tues 12/2 open except for 2-3
Wed 12/3 open
Thurs 12/4 open except 1:30-3 PM
Fri 12/5 no

Mon 12/8
Tues 12/9
Wed 12/10
Thurs 12/11
Fri 12/12

From: Webb, Robin E. [mailto:rwebb@rti.org]
Sent: Monday, October 27, 2008 12:18 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; nfiner@ucsd.edu; Wally Carlo, M.D.; mcw3@cwru.edu; Bradley.yoder@hsc.utah.edu; Roger Faix; alaptook@WIHRI.org; kurt.schibler@cchmc.org; Das, Abhik; nancy newman; Rich, Wade; Gantz, Marie; Susan Hintz; Poole, W. Kenneth
Cc: Zaterka-Baxter, Kristin; Archer, Stephanie (NIH/NICHD) [E]; Cunningham, Meg; Huitema, Carolyn Petrie; Newman, Jamie; fmartinez@ucsd.edu; Carolyn.Grier@UHhospitals.org; bvecchio@careNE.org; msumner@peds.uab.edu
Subject: RE: SUPPORT - School Age Breathing Outcomes Proposal 9-12-08

Please send your availability for the days below, indicating time zone if other than ET.

Thanks,
Robin

Mon 11/10
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Thurs 12/4
Fri 12/5

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, October 22, 2008 3:17 PM
To: nfiner@ucsd.edu; Wally Carlo, M.D.; mcw3@cwru.edu; Bradley.yoder@hsc.utah.edu; Roger Faix; alaptook@WIHRI.org; kurt.schibler@cchmc.org; Das, Abhik; nancy newman; Rich, Wade; Gantz, Marie; Susan Hintz; Poole, W. Kenneth
Cc: Zaterka-Baxter, Kristin; Archer, Stephanie (NIH/NICHD) [E]; Cunningham, Meg; Huitema, Carolyn Petrie; Newman, Jamie; Webb, Robin E.
Subject: SUPPORT - School Age Breathing Outcomes Proposal 9-12-08

To the Support Subcommittee-
Attached is a proposal for school age breathing outcomes. I have also included Susan Hintz as the PI of the 6-7 year follow up.

We need to set up a call in the next 4-6 weeks for discussion.

Rose

From: Webb, Robin E.
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT - School Age Breathing Outcomes Proposal 9-12-08
Date: Wednesday, November 05, 2008 2:48:39 PM

Hi Rose,

Is this still ok to use? Please fill in you availability for the second week in December.

Thanks,
Robin

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, October 27, 2008 12:53 PM
To: Webb, Robin E.
Subject: RE: SUPPORT - School Age Breathing Outcomes Proposal 9-12-08

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Wed 12/3 open
Thurs 12/4 open except 1:30-3 PM
Fri 12/5 no

Mon 12/8
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Thurs 12/11
Fri 12/12

From: Webb, Robin E. [mailto:rwebb@rti.org]
Sent: Monday, October 27, 2008 12:18 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; nfiner@ucsd.edu; Wally Carlo, M.D.; mcw3@cwru.edu; Bradley.yoder@hsc.utah.edu; Roger Faix; alaptook@WIHRI.org; kurt.schibler@cchmc.org; Das, Abhik; nancy newman; Rich, Wade; Gantz, Marie; Susan Hintz; Poole, W. Kenneth
Cc: Zaterka-Baxter, Kristin; Archer, Stephanie (NIH/NICHD) [E]; Cunningham, Meg; Huitema, Carolyn Petrie; Newman, Jamie; fmartinez@ucsd.edu; Carolyn.Grier@UHhospitals.org; bvecchio@careNE.org; msumner@peds.uab.edu
Subject: RE: SUPPORT - School Age Breathing Outcomes Proposal 9-12-08

Please send your availability for the days below, indicating time zone if other than ET.

Thanks,
Robin

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From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, October 22, 2008 3:17 PM
To: nfiner@ucsd.edu; Wally Carlo, M.D.; mcw3@cwru.edu; Bradley.yoder@hsc.utah.edu; Roger Faix; alaptook@WIHRI.org; kurt.schibler@cchmc.org; Das, Abhik; nancy newman; Rich, Wade; Gantz, Marie; Susan Hintz; Poole, W. Kenneth
Cc: Zaterka-Baxter, Kristin; Archer, Stephanie (NIH/NICHD) [E]; Cunningham, Meg; Huitema, Carolyn Petrie; Newman, Jamie; Webb, Robin E.
Subject: SUPPORT - School Age Breathing Outcomes Proposal 9-12-08

To the Support Subcommittee-
Attached is a proposal for school age breathing outcomes. I have also included Susan Hintz as the PI of the 6-7 year follow up.

We need to set up a call in the next 4-6 weeks for discussion.

Rose

From:	Zaterka-Baxter, Kristin
To:	ahensman@wihri.org; mbball@leland.stanford.edu; grisbyca@email.uc.edu; ellen_hale@oz.ped.emory.edu; Georgia E McDavid; mcollins@peds.uab.edu; monica.konstantino@yale.edu; Nancy.Miller@UTSouthwestern.edu; Nancy Newman; ldw@iupui.edu; Mackinnon, Brenda; Johnson, Karen; Karen.Osborne@hsc.utah.edu; Conra Backstrom; Katherine A Foy; melissa.leps@utsouthwestern.edu; mproud@stanford.edu; rbara@med.wayne.edu; Shirley Cosby; VPhillips@peds.uab.edu
Cc:	wrich@ucsd.edu; Pickett, James; Auman, Jeanette O.; Gantz, Marie; Cunningham, Meg; Huitema, Carolyn Petrie; Das, Abhik; Higgins, Rosemary (NIH/NICHD) [E]
Subject:	SUPPORT Oximeters & Time Change
Date:	Monday, November 03, 2008 7:14:29 AM
Importance:	High

Hi all,

Here is a LATE reminder **ABOUT DAYLIGHT SAVINGS TIME AND THE MASIMO STUDY OXIMETERS:**

Daylight Savings Time Changes for Support:

1) Change all oximeters not in current use as soon as possible (if you have not already done so).

2) Do not change oximeters currently in use until they are put on another patient.

RTI will make any necessary back-corrections at their end.

Thanks.

Kris

Kris Zaterka-Baxter

Statistics and Epidemiology Division

RTI International

3040 Cornwallis Road

P.O. Box 12194

RTP, NC 27709-2194 USA

(tel) 919-485-7750

(fax) 919.485.7762

kzaterka@rti.org

www.rti.org

From: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT - School Age Breathing Outcomes Proposal 9-12-08
Date: Wednesday, October 29, 2008 3:34:21 PM

Finer, hintz, abhik, me + as many others as possible

From: Webb, Robin E. [mailto:rwebb@rti.org]
Sent: Wednesday, October 29, 2008 3:33 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT - School Age Breathing Outcomes Proposal 9-12-08

Hi Rose,

Who do you need on this call?

Thanks,
Robin

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, October 22, 2008 3:17 PM
To: nfiner@ucsd.edu; Wally Carlo, M.D.; mcw3@cwru.edu; Bradley.yoder@hsc.utah.edu; Roger Faix; alaptook@WIHRI.org; kurt.schibler@cchmc.org; Das, Abhik; nancy newman; Rich, Wade; Gantz, Marie; Susan Hintz; Poole, W. Kenneth
Cc: Zaterka-Baxter, Kristin; Archer, Stephanie (NIH/NICHD) [E]; Cunningham, Meg; Huitema, Carolyn Petrie; Newman, Jamie; Webb, Robin E.
Subject: SUPPORT - School Age Breathing Outcomes Proposal 9-12-08

To the Support Subcommittee-
Attached is a proposal for school age breathing outcomes. I have also included Susan Hintz as the PI of the 6-7 year follow up.

We need to set up a call in the next 4-6 weeks for discussion.

Rose

From: Das, Abhik
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: Miami Closure of the GDB Follow-Up study
Date: Monday, October 27, 2008 2:20:18 PM

FYI

From: Newman, Jamie
Sent: Monday, October 27, 2008 2:10 PM
To: Das, Abhik; Zaterka-Baxter, Kristin
Cc: Auman, Jeanette O.
Subject: RE: Miami Closure of the GDB Follow-Up study

I just spoke to Ruth Everett, the coordinator at Miami and got her onto the website and we went through edit reports/missing forms/discrepancy reports together– she had not been on since we shifted to user-specific passwords. I will send an email out to all collaborating centers momentarily to remind them to resolve all edits BEFORE they closeout study IRBs.

Her SUPPORT follow-up and Breathing Outcomes is under a separate IRB, so this only applies to GDB follow-up. She said she would contact her IRB to inform them that there remain some edits to resolve but did not anticipate this being a problem with their IRB.

Thanks, Jamie

From:	Webb, Robin E.
To:	Higgins, Rosemary (NIH/NICHD) [E]; nfiner@ucsd.edu; Wally Carlo, M.D.; mcw3@cwru.edu; Bradley.yoder@hsc.utah.edu; Roger Faix; alaptook@WIHRI.org; kurt.schibler@cchmc.org; Das, Abhik; nancy newman; Rich, Wade; Gantz, Marie; Susan Hintz; Poole, W. Kenneth
Cc:	Zaterka-Baxter, Kristin; Archer, Stephanie (NIH/NICHD) [E]; Cunningham, Meg; Huitema, Carolyn Petrie; Newman, Jamie; fmartinez@ucsd.edu; Carolyn.Grier@UHhospitals.org; bvecchio@careNE.org; msumner@peds.uab.edu
Subject:	RE: SUPPORT - School Age Breathing Outcomes Proposal 9-12-08
Date:	Monday, October 27, 2008 12:18:15 PM

Please send your availability for the days below, indicating time zone if other than ET.

Thanks,
Robin

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From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
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To: nfiner@ucsd.edu; Wally Carlo, M.D.; mcw3@cwru.edu; Bradley.yoder@hsc.utah.edu; Roger Faix; alaptook@WIHRI.org; kurt.schibler@cchmc.org; Das, Abhik; nancy newman; Rich, Wade; Gantz, Marie; Susan Hintz; Poole, W. Kenneth
Cc: Zaterka-Baxter, Kristin; Archer, Stephanie (NIH/NICHD) [E]; Cunningham, Meg; Huitema, Carolyn Petrie; Newman, Jamie; Webb, Robin E.
Subject: SUPPORT - School Age Breathing Outcomes Proposal 9-12-08

To the Support Subcommittee-
Attached is a proposal for school age breathing outcomes. I have also included Susan Hintz as the PI of the 6-7 year follow up.

We need to set up a call in the next 4-6 weeks for discussion.

Rose

From: Hensman, Angelita
To: Higgins, Rosemary (NIH/NICHD) [E]; Laptook, Abbot
Cc: Das, Abhik; Gantz, Marie
Subject: RE: SUPPORT OUTCOMES
Date: Monday, October 27, 2008 10:56:08 AM

Thanks Rose. We have a great team here.

By the way ....I attended the Fetus & Newborn Conference last week. Neil Finer did a talk on Hypothermia comparing head vs. whole body cooling and Av Fanaroff mentioned Hypothermia/cooling in his talk on "Hot topics". Even though questions were asked by the audience during the panel discussion about cooling at 6, 7 and 8 hours of age they were overlooked and no one mentioned the ongoing Late hypothermia trial. Felt like it was a missed opportunity. Maybe this is something the subcommittee could look into when network P.I's attend conferences.

There was also a lot of discussion on the outcomes calculator and whether it was dynamic. Questions were also asked on using GA in completed weeks vs. weeks and days.

Angelita

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, October 22, 2008 4:45 PM
To: Laptook, Abbot; Hensman, Angelita; Vohr, Betty
Cc: Das, Abhik; Gantz, Marie
Subject: SUPPORT OUTCOMES

To the dedicated NRN site at Brown:

As of last weeks data entry, your site has not missing SUPPORT primary or FU outcomes. This is amazing given the outstanding recruitment. Thanks for the hard work and dedication!!! Your efforts are much appreciated!

Best regards,
ROSE

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutesof Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20592
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

---

delete this message and any attachment(s) immediately. Thank you for your consideration in this matter.

From:	Vohr, Betty
To:	Higgins, Rosemary (NIH/NICHD) [E]; Laptook, Abbot; Hensman, Angelita
Cc:	Das, Abhik; Gantz, Marie; Alksninis, Barbara
Subject:	RE: SUPPORT OUTCOMES
Date:	Wednesday, October 22, 2008 4:48:21 PM

Thanks Rose. A lot of this is due to the hard work of our nurse practitioner, Barbara Alksninis !!!
Cangrats Barbara !

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, October 22, 2008 4:45 PM
To: Laptook, Abbot; Hensman, Angelita; Vohr, Betty
Cc: Das, Abhik; Gantz, Marie
Subject: SUPPORT OUTCOMES

To the dedicated NRN site at Brown:

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Best regards,
ROSE

Rosemary D. Higgins, MD
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For overnight delivery use Rockville, MD 20592
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301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Webb, Robin E.
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT - School Age Breathing Outcomes Proposal 9-12-08
Date: Wednesday, October 22, 2008 4:22:21 PM

Hi Rose,

I'll start working on this on Monday when I get back.

Thanks,
Robin

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, October 22, 2008 3:17 PM
To: nfiner@ucsd.edu; Wally Carlo, M.D.; mcw3@cwru.edu; Bradley.yoder@hsc.utah.edu; Roger Faix; alaptook@WIHRI.org; kurt.schibler@cchmc.org; Das, Abhik; nancy newman; Rich, Wade; Gantz, Marie; Susan Hintz; Poole, W. Kenneth
Cc: Zaterka-Baxter, Kristin; Archer, Stephanie (NIH/NICHD) [E]; Cunningham, Meg; Huitema, Carolyn Petrie; Newman, Jamie; Webb, Robin E.
Subject: SUPPORT - School Age Breathing Outcomes Proposal 9-12-08

To the Support Subcommittee-
Attached is a proposal for school age breathing outcomes. I have also included Susan Hintz as the PI of the 6-7 year follow up.

We need to set up a call in the next 4-6 weeks for discussion.

Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Zaterka-Baxter, Kristin"; "wrich@ucsd.edu"; "nfiner@ucsd.edu"
Subject: SUPPORT infant
Date: Monday, September 22, 2008 3:17:32 PM

Hi, the SUPPORT infant that I spoke to you about this am had the study oximeter placed this am – we will get deviation reports for no surf and delay in oximter placement.

Thanks for the help!
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutesof Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20592
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Richard Ehrenkranz"
Subject: RE: Concept reminder
Date: Monday, September 22, 2008 3:16:22 PM

Thanks, Meg will post this on the private website.

Good luck with the SUPPORT infant.

Rose

-----Original Message-----
From: Richard Ehrenkranz [mailto:richard.ehrenkranz@yale.edu]
Sent: Monday, September 22, 2008 3:04 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: Concept reminder

Rose:
I have attached our concept. With repect to the SUPPORT patient that I described this morning: the medical team and the parents agreed to starting the study oximeter and it was started at about 11 am.
Richard

Higgins, Rosemary (NIH/NICHD) [E] wrote:
>
> Hi,
>
> Just a reminder, your concepts for the upcoming steering committee
> meeting are due by September 24. We need to have them to post on the
> private website.
>
>
>
>
>
>
>
> Thanks
> Rose
>
>
>
> Rosemary D. Higgins, MD
>
> Program Scientist for the Neonatal Research Network
>
> Pregnancy and Perinatology Branch
>
> Center for Developmental Biology and Perinatal Medicine
>
> Eunice Kennedy Shriver National Institute of Child Health and Human
> Development
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> National Institutesof Health
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>
> 301-496-5575
>
> 301-496-3790 (FAX)
>
> higginsr@mail.nih.gov
>
>
>

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Richard A. Ehrenkranz, MD
Department of Pediatrics
Yale University School of Medicine
333 Cedar Street
PO Box 208064
New Haven, CT 06520-8064
tele: 203-688-2320
fax: 203-688-5426

From:	Webb, Robin E.
To:	Higgins, Rosemary (NIH/NICHD) [E]; alaptook@WIHRI.org; Bradley Yoder; Das, Abhik; Gantz, Marie; kurt.schibler@cchmc.org; mcw3@cwru.edu; nancy newman; nfiner@ucsd.edu; Roger.Faix@hsc.utah.edu; Wally Carlo, M.D.; wrich@ucsd.edu
Cc:	sharon.gough@hsc.utah.edu; Archer, Stephanie (NIH/NICHD) [E]; Brenda Vecchio; Cunningham, Meg; fmartinez@ucsd.edu; Huitema, Carolyn Petrie; msumner@peds.uab.edu; Zaterka-Baxter, Kristin; Webb, Robin E.; Carolyn.Grier@UHhospitals.org
Subject:	RE: SUPPORT Subcommittee for October
Date:	Tuesday, September 02, 2008 10:57:09 AM

We were unable to come up with a time on October 8th for this call, so this discussion will be added to the SUPPORT call that is scheduled for Friday, 9/12 at 1pm ET.

Thanks,
Robin

From: Webb, Robin E. [mailto:rwebb@rti.org]
Sent: Monday, August 25, 2008 2:03 PM
To: alaptook@WIHRI.org; Bradley Yoder; adas@rti.org; mgantz@rti.org; Higgins, Rosemary (NIH/NICHD) [E]; kurt.schibler@cchmc.org; mcw3@cwru.edu; nancy newman; nfiner@ucsd.edu; Roger.Faix@hsc.utah.edu; Wally Carlo, M.D.; wrich@ucsd.edu
Cc: Webb, Robin E.; sharon.gough@hsc.utah.edu; Archer, Stephanie (NIH/NICHD) [E]; Brenda Vecchio; Cunningham, Meg; fmartinez@ucsd.edu; Huitema, Carolyn Petrie; msumner@peds.uab.edu; Zaterka-Baxter, Kristin
Subject: FW: SUPPORT Subcommittee for October

We'd like to schedule a SUPPORT Subcommittee call prior to the SC meeting. Please let me know your availability for the days below, indicating time zone if other than ET.

Thanks,
Robin

Tues 10/7 3-5 PM
Wed 10/8

From: Zaterka-Baxter, Kristin
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Support AEs related to study
Date: Thursday, August 28, 2008 4:01:27 PM

After review of the Support data; Per Abhik, no news is good news! So you should fully enjoy your day off tomorrow!
Thanks,
Kris

From: Abbot Laptook
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT Subcommittee for October
Date: Monday, August 25, 2008 7:45:01 PM

Rose
Oct 7 3-5 if fine. Yom Kippur starts at sundown on Oct 8 and I will only be in for a few hours in the morning (need to leave by 10:30am). AL

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, August 25, 2008 2:18 PM
To: Webb, Robin E.; Abbot Laptook; Bradley Yoder; adas@rti.org; mgantz@rti.org; kurt.schibler@cchmc.org; mcw3@cwru.edu; nancy newman; nfiner@ucsd.edu; Roger.Faix@hsc.utah.edu; Wally Carlo, M.D.; wrich@ucsd.edu
Cc: sharon.gough@hsc.utah.edu; Archer, Stephanie (NIH/NICHD) [E]; Brenda Vecchio; Cunningham, Meg; fmartinez@ucsd.edu; Huitema, Carolyn Petrie; msumner@peds.uab.edu; Zaterka-Baxter, Kristin
Subject: RE: SUPPORT Subcommittee for October

The dates are wrong – PLEASE SEND ROBIN Availability for 10/8 (Not 9/8)

Sorry for the confusion

Rose

From: Webb, Robin E. [mailto:rwebb@rti.org]
Sent: Monday, August 25, 2008 2:03 PM
To: alaptook@WIHRI.org; Bradley Yoder; adas@rti.org; mgantz@rti.org; Higgins, Rosemary (NIH/NICHD) [E]; kurt.schibler@cchmc.org; mcw3@cwru.edu; nancy newman; nfiner@ucsd.edu; Roger.Faix@hsc.utah.edu; Wally Carlo, M.D.; wrich@ucsd.edu
Cc: Webb, Robin E.; sharon.gough@hsc.utah.edu; Archer, Stephanie (NIH/NICHD) [E]; Brenda Vecchio; Cunningham, Meg; fmartinez@ucsd.edu; Huitema, Carolyn Petrie; msumner@peds.uab.edu; Zaterka-Baxter, Kristin
Subject: FW: SUPPORT Subcommittee for October

We'd like to schedule a SUPPORT Subcommittee call prior to the SC meeting. Please let me know your availability for the days below, indicating time zone if other than ET.

Thanks,
Robin

Tues 9/7 3-5 PM
Wed 9/8

From: Marsha Sumner
To: rwebb@rti.org
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT Subcommittee for October
Date: Monday, August 25, 2008 3:31:06 PM

Dr. Carlo is not available 10/7 or 10/8. Dr. Carlo will be out of the country. Tks. marsha

---

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, August 25, 2008 1:18 PM
To: Webb, Robin E.; alaptook@WIHRI.org; Bradley Yoder; adas@rti.org; mgantz@rti.org; kurt.schibler@cchmc.org; mcw3@cwru.edu; nancy newman; nfiner@ucsd.edu; Roger.Faix@hsc.utah.edu; Wally Carlo, M.D.; wrich@ucsd.edu
Cc: sharon.gough@hsc.utah.edu; Archer, Stephanie (NIH/NICHD) [E]; Brenda Vecchio; Cunningham, Meg; fmartinez@ucsd.edu; Huitema, Carolyn Petrie; Marsha Sumner; Zaterka-Baxter, Kristin
Subject: RE: SUPPORT Subcommittee for October

The dates are wrong – PLEASE SEND ROBIN Availability for 10/8 (Not 9/8)

Sorry for the confusion

Rose

From: Webb, Robin E. [mailto:rwebb@rti.org]
Sent: Monday, August 25, 2008 2:03 PM
To: alaptook@WIHRI.org; Bradley Yoder; adas@rti.org; mgantz@rti.org; Higgins, Rosemary (NIH/NICHD) [E]; kurt.schibler@cchmc.org; mcw3@cwru.edu; nancy newman; nfiner@ucsd.edu; Roger.Faix@hsc.utah.edu; Wally Carlo, M.D.; wrich@ucsd.edu
Cc: Webb, Robin E.; sharon.gough@hsc.utah.edu; Archer, Stephanie (NIH/NICHD) [E]; Brenda Vecchio; Cunningham, Meg; fmartinez@ucsd.edu; Huitema, Carolyn Petrie; msumner@peds.uab.edu; Zaterka-Baxter, Kristin
Subject: FW: SUPPORT Subcommittee for October

We'd like to schedule a SUPPORT Subcommittee call prior to the SC meeting. Please let me know your availability for the days below, indicating time zone if other than ET.

Thanks,
Robin

Tues 9/7 3-5 PM
Wed 9/8

From: Bonnie Siner
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT - ROP outcomes
Date: Monday, August 25, 2008 2:43:33 PM

Rose,
Please direct these questions to me at bss5@case.edu since I do the tracking of ROP outcomes after discharge.

Bonnie

From: Das, Abhik
To: Higgins, Rosemary (NIH/NICHD) [E]; Zaterka-Baxter, Kristin; Webb, Robin E.
Subject: RE: SUPPORT Subcommittee for October
Date: Monday, August 25, 2008 2:15:52 PM

Maybe 10/8 or 10/9, since the meeting on the 7th can go on till 5 pm?

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, August 25, 2008 2:14 PM
To: Zaterka-Baxter, Kristin; Webb, Robin E.; Das, Abhik
Subject: RE: SUPPORT Subcommittee for October

This should be 10/7 and 10/8,
Sorry for the confusion
Rose

From: Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]
Sent: Monday, August 25, 2008 2:08 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT Subcommittee for October

The next Support DSMC mtg is Oct 7

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, August 25, 2008 2:06 PM
To: Webb, Robin E.; alaptook@WIHRI.org; Bradley Yoder; Das, Abhik; Gantz, Marie; kurt.schibler@cchmc.org; mcw3@cwru.edu; nancy newman; nfiner@ucsd.edu; Roger.Faix@hsc.utah.edu; Wally Carlo, M.D.; wrich@ucsd.edu
Cc: sharon.gough@hsc.utah.edu; Archer, Stephanie (NIH/NICHD) [E]; Brenda Vecchio; Cunningham, Meg; fmartinez@ucsd.edu; Huitema, Carolyn Petrie; msumner@peds.uab.edu; Zaterka-Baxter, Kristin
Subject: RE: SUPPORT Subcommittee for October

WE are asking for this narrow time range well in advance to meet asap after the DSMC meeting

Rose

From: Webb, Robin E. [mailto:rwebb@rti.org]
Sent: Monday, August 25, 2008 2:03 PM
To: alaptook@WIHRI.org; Bradley Yoder; adas@rti.org; mgantz@rti.org; Higgins, Rosemary (NIH/NICHD) [E]; kurt.schibler@cchmc.org; mcw3@cwru.edu; nancy newman; nfiner@ucsd.edu; Roger.Faix@hsc.utah.edu; Wally Carlo, M.D.; wrich@ucsd.edu
Cc: Webb, Robin E.; sharon.gough@hsc.utah.edu; Archer, Stephanie (NIH/NICHD) [E]; Brenda Vecchio; Cunningham, Meg; fmartinez@ucsd.edu; Huitema, Carolyn Petrie; msumner@peds.uab.edu; Zaterka-Baxter, Kristin
Subject: FW: SUPPORT Subcommittee for October

We'd like to schedule a SUPPORT Subcommittee call prior to the SC meeting. Please let me know your availability for the days below, indicating time zone if other than ET.

Thanks,

Robin

Tues 9/7 3-5 PM
Wed 9/8

From: Das, Abhik
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Webb, Robin E.
Subject: RE: SUPPORT Subcommittee for October
Date: Monday, August 25, 2008 2:14:47 PM

OK.

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, August 25, 2008 2:13 PM
To: Das, Abhik
Cc: Webb, Robin E.
Subject: RE: SUPPORT Subcommittee for October

The 9/12 one is for discussion of a secondary study from New Mexico. This call will be right before the SC and serve as the subcommittee meeting in advance of the SC.

Is this ok?
Thanks
Rose

From: Das, Abhik [mailto:adas@rti.org]
Sent: Monday, August 25, 2008 2:12 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Webb, Robin E.
Subject: RE: SUPPORT Subcommittee for October

Rose:

The DSMC meets Oct 7, and I already have a SUPPORT call on my calender on Sept 12.

Thanks

Abhik

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, August 25, 2008 2:06 PM
To: Webb, Robin E.; alaptook@WIHRI.org; Bradley Yoder; Das, Abhik; Gantz, Marie; kurt.schibler@cchmc.org; mcw3@cwru.edu; nancy newman; nfiner@ucsd.edu; Roger.Faix@hsc.utah.edu; Wally Carlo, M.D.; wrich@ucsd.edu
Cc: sharon.gough@hsc.utah.edu; Archer, Stephanie (NIH/NICHD) [E]; Brenda Vecchio; Cunningham, Meg; fmartinez@ucsd.edu; Huitema, Carolyn Petrie; msumner@peds.uab.edu; Zaterka-Baxter, Kristin
Subject: RE: SUPPORT Subcommittee for October

WE are asking for this narrow time range well in advance to meet asap after the DSMC meeting

Rose

From: Webb, Robin E. [mailto:rwebb@rti.org]

Sent: Monday, August 25, 2008 2:03 PM
To: alaptook@WIHRI.org; Bradley Yoder; adas@rti.org; mgantz@rti.org; Higgins, Rosemary (NIH/NICHD) [E]; kurt.schibler@cchmc.org; mcw3@cwru.edu; nancy newman; nfiner@ucsd.edu; Roger.Faix@hsc.utah.edu; Wally Carlo, M.D.; wrich@ucsd.edu
Cc: Webb, Robin E.; sharon.gough@hsc.utah.edu; Archer, Stephanie (NIH/NICHD) [E]; Brenda Vecchio; Cunningham, Meg; fmartinez@ucsd.edu; Huitema, Carolyn Petrie; msumner@peds.uab.edu; Zaterka-Baxter, Kristin
Subject: FW: SUPPORT Subcommittee for October

We'd like to schedule a SUPPORT Subcommittee call prior to the SC meeting. Please let me know your availability for the days below, indicating time zone if other than ET.

Thanks,
Robin

Tues 9/7 3-5 PM
Wed 9/8

From: Webb, Robin E.
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT Subcommittee for October
Date: Monday, August 25, 2008 2:15:36 PM

Sorry, my fault. I'll send out an email correcting the dates.

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, August 25, 2008 2:14 PM
To: Zaterka-Baxter, Kristin; Webb, Robin E.; Das, Abhik
Subject: RE: SUPPORT Subcommittee for October

This should be 10/7 and 10/8,
Sorry for the confusion
Rose

From: Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]
Sent: Monday, August 25, 2008 2:08 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT Subcommittee for October

The next Support DSMC mtg is Oct 7

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, August 25, 2008 2:06 PM
To: Webb, Robin E.; alaptook@WIHRI.org; Bradley Yoder; Das, Abhik; Gantz, Marie; kurt.schibler@cchmc.org; mcw3@cwru.edu; nancy newman; nfiner@ucsd.edu; Roger.Faix@hsc.utah.edu; Wally Carlo, M.D.; wrich@ucsd.edu
Cc: sharon.gough@hsc.utah.edu; Archer, Stephanie (NIH/NICHD) [E]; Brenda Vecchio; Cunningham, Meg; fmartinez@ucsd.edu; Huitema, Carolyn Petrie; msumner@peds.uab.edu; Zaterka-Baxter, Kristin
Subject: RE: SUPPORT Subcommittee for October

WE are asking for this narrow time range well in advance to meet asap after the DSMC meeting

Rose

From: Webb, Robin E. [mailto:rwebb@rti.org]
Sent: Monday, August 25, 2008 2:03 PM
To: alaptook@WIHRI.org; Bradley Yoder; adas@rti.org; mgantz@rti.org; Higgins, Rosemary (NIH/NICHD) [E]; kurt.schibler@cchmc.org; mcw3@cwru.edu; nancy newman; nfiner@ucsd.edu; Roger.Faix@hsc.utah.edu; Wally Carlo, M.D.; wrich@ucsd.edu
Cc: Webb, Robin E.; sharon.gough@hsc.utah.edu; Archer, Stephanie (NIH/NICHD) [E]; Brenda Vecchio; Cunningham, Meg; fmartinez@ucsd.edu; Huitema, Carolyn Petrie; msumner@peds.uab.edu; Zaterka-Baxter, Kristin
Subject: FW: SUPPORT Subcommittee for October

We'd like to schedule a SUPPORT Subcommittee call prior to the SC meeting. Please let me know your availability for the days below, indicating time zone if other than ET.

Thanks,

Robin

Tues 9/7 3-5 PM
Wed 9/8

From: Finer, Neil
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT Subcommittee for October
Date: Monday, August 25, 2008 1:45:22 PM

Hi Rose
I think a phone conference works better as everybody can hear better and the day after the DSMC is perfect.
Neil

Neil N. Finer, M.D.
Professor of Pediatrics
Director, Division of Neonatal-Perinatal Medicine
UC San Diego School of Medicine
UC San Diego Medical Center, Hillcrest
402 Dickinson St., MPF 1-140
San Diego, CA 92103-8774
Telephone: 619.543-3759
Facsimile: 619.543.3812

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, August 25, 2008 10:30 AM
To: Finer, Neil
Cc: Cunningham, Meg
Subject: SUPPORT Subcommittee for October

Neil
Do you want to have the SUPPORT Subcommittee meet in advance of the Steering committee meeting in October or at the SC meeting?

We could schedule a meeting for the day after the DSMC (or later that afternoon) – October 7 – let me know

Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
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Bethesda, MD 20892
For overnight delivery use Rockville, MD 20592
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "richard.ehrenkranz@yale.edu"; "monica.konstantino@yale.edu"; "Elaine Romano"
Cc: "adas@rti.org"; "Gantz, Marie"
Subject: SUPPORT
Date: Monday, August 25, 2008 12:27:11 PM

Congratulations – we are missing no SUPPORT primary outcome information from your site as of last week's data entry. Keep up the good work!!!
Thanks for all your efforts.

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutesof Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20592
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Yost, Patricia A.
To:	Auman, Jeanette O.; Newman, Jamie; drficmd@aol.com; bss5@cwru.edu; amt24@case.edu; Roy.Heyne@UTSouthwestern.edu; JANET.MORGAN@childrens.com; apappas@med.wayne.edu; sshankar@med.wayne.edu; Bara, Rebecca; du2744@wayne.edu; CBauer@med.miami.edu; reverett@med.miami.edu; MNeri@med.miami.edu; SEguaras@med.miami.edu; ira_adams-chapman@oz.ped.emory.edu; ellen_hale@oz.ped.emory.edu; steichji@email.uc.edu; Teresa.Gratton@uc.edu; Kimberly.Yolton@cchmc.org; adusick@iupui.edu; fahamer@iupui.edu; ldw@iupui.edu; ldrichar@iupui.edu; richard.ehrenkranz@yale.edu; Elaine.Romano@Yale.Edu; joanne.williams@yale.edu; BVohr@WIHRI.org; AHensman@WIHRI.org; sventura@wihri.org; srhintz@stanford.edu; mbball@leland.stanford.edu; MPeralta@peds.uab.edu; VPhillips@peds.uab.edu; jon.e.tyson@uth.tmc.edu; Brenda.H.Morris@uth.tmc.edu; Georgia.E.McDavid@uth.tmc.edu; Nora.I.Alaniz@uth.tmc.edu; Charles.Green@uth.tmc.edu; Patricia.W.Evans@uth.tmc.edu; Sharon.Wright@uth.tmc.edu; golds005@mc.duke.edu; lohme001@mc.duke.edu; foy00004@mc.duke.edu; rdillard@wfubmc.edu; npeters@wfubmc.edu; gary_myers@urmc.rochester.edu; diane_hust@urmc.rochester.edu; Rosemary_Jensen@URMC.Rochester.edu; dale_phelps@urmc.rochester.edu; yvaucher@ucsd.edu; wrich@ucsd.edu; mgfuller@ucsd.edu
Cc:	Das, Abhik; Higgins, Rosemary (NIH/NICHD) [E]; Zaterka-Baxter, Kristin; Cunningham, Meg; Huitema, Carolyn Petrie
Subject:	Center Specific Follow-up Monthly Reports Available on NRN website
Date:	Tuesday, August 12, 2008 11:52:15 AM

Sent on behalf of Jamie Newman:

The Follow-up center-specific monthly reports are currently available on the NRN Website. You can access them in the following manner:

Go to the Neonatal website at https://neonatal.rti.org
Log onto the private gateway using your username and password
Click on Administration
Click on Site Reports
An Adobe pdf version of the report will open when clicking on the report name. The following center-specific reports have been posted:

Follow-up Pending Report
Follow-up Missing Forms Report
Follow-up Discrepancy Report
SUPPORT Follow-up Pending Report
SUPPORT Follow-up Discrepancy Report
Hypothermia Extended Follow-up Pending Report

Please remember that if you do not have any missing forms, discrepancies, and/or pending visits this month, you will not see the corresponding report listed for you Center. If you have any questions about the reports, please contact Jenny Auman at joa@rti.org.

From:	Webb, Robin E.
To:	Higgins, Rosemary (NIH/NICHD) [E]; Neil_Finer" <; Rich, Wade; Michelle Walsh; wacarlo@uab.edu; Bradley.yoder@hsc.utah.edu; Roger Faix; Abbot Laptook; kurt.schibler@cchmc.org; Das, Abhik; Gantz, Marie; nancy newman
Cc:	Susan Hintz; Zaterka-Baxter, Kristin; Cunningham, Meg; Huitema, Carolyn Petrie; Newman, Jamie; msumner@peds.uab.edu; carolyn.grier@uhhospitals.org; bvecchio@careNE.org; fmartinez@ucsd.edu
Subject:	Ancillary to SUPPORT trial
Date:	Thursday, August 07, 2008 2:33:28 PM

Please send your availability for the days below indicating time zone if other than ET.

Thanks,
Robin

Tues 9/2
Wed 9/3
Thurs 9/4
Fri 9/5

Mon 9/8
Tues 9/9
Wed 9/10
Thurs 9/11
Fri 9/12

Mon 9/22
Tues 9/23
Wed 9/24
Thurs 9/25
Fri 9/26

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, August 06, 2008 5:08 PM
To: Neil_Finer" <; Rich, Wade; Michelle Walsh; wacarlo@uab.edu; Bradley.yoder@hsc.utah.edu; Roger Faix; Abbot Laptook; kurt.schibler@cchmc.org; Das, Abhik; Gantz, Marie; nancy newman
Cc: Susan Hintz; Webb, Robin E.; Zaterka-Baxter, Kristin; Cunningham, Meg; Huitema, Carolyn Petrie; Newman, Jamie
Subject: FW: ancillary to SUPPORT trial

Attached is a SUPPORT secondary study for consideration. We will have Robin set up a call.

Thanks
Rose

From: Kristi Watterberg [mailto:KWatterberg@salud.unm.edu]
Sent: Tuesday, August 05, 2008 1:31 PM

To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Janell Fuller; Jean Lowe; Susan Hintz
Subject: ancillary to SUPPORT trial

Hi, Rose. I am attaching a revised proposal for our ancillary study to SUPPORT, "Evaluation of early working memory in extremely preterm infants", and our responses to the reviewers of the first version. (I'm also happy to report that our manuscript on early working memory as assessed by object permanence has been accepted by the Journal of Child Neurology).

You will notice that Susan Hintz has been added to the protocol development group. She has reviewed our revisions, made several great suggestions, and is enthusiastic about the protocol. We would of course welcome others, if this is approved and goes forward.

Let me know if you need anything else, or have suggestions for us before sending on to the SUPPORT subcommittee.

Thanks, Kristi

From: Karen Osborne RN
To: Archer, Stephanie (NIH/NICHD) [E]; Higgins, Rosemary (NIH/NICHD) [E]; nfiner@ucsd.edu
Cc: Roger Faix; Bradley Yoder
Subject: RE: NCT00233324, NICHD-NRN-0031, Surfactant Positive Airway Pressure and Pulse Oximetry Trial
Date: Monday, July 14, 2008 1:01:56 PM

I hear what you are saying about the details and the constant changing! It's a big job to do both Network wise and locally.
Thanks for adding our site.

Karen

From: Archer, Stephanie (NIH/NICHD) [E] [mailto:archerst@mail.nih.gov]
Sent: Monday, July 14, 2008 7:32 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; Karen Osborne RN; nfiner@ucsd.edu
Cc: Roger Faix; Bradley Yoder
Subject: RE: NCT00233324, NICHD-NRN-0031, Surfactant Positive Airway Pressure and Pulse Oximetry Trial

Hi Karen,

Thanks for catching this. So many details in these records – and they keep changing the requested information on top of that!

I've made the changes and marked it as complete. I may be a week or two before it gets through the ClinicalTrials approval process.

Please let me know if I've missed anything on the other records, particularly the ongoing trials.

Thank you,

Stephanie

Stephanie Wilson Archer
The Eunice Kennedy Shriver
National Institute of Child Health and Human Development
Pregnancy & Perinatology Branch
6100 Executive Boulevard, Room 4B03
Rockville, MD 20852

Tel. 301-496-0430
Fax 301-496-3790
archerst@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Friday, July 11, 2008 5:07 PM
To: 'Karen Osborne RN'; nfiner@ucsd.edu; Archer, Stephanie (NIH/NICHD) [E]
Cc: Roger Faix; Bradley Yoder
Subject: RE: NCT00233324, NICHD-NRN-0031, Surfactant Positive Airway Pressure and Pulse Oximetry Trial

We will add your site

From: Karen Osborne RN [mailto:Karen.Osborne@hsc.utah.edu]
Sent: Friday, July 11, 2008 5:05 PM
To: nfiner@ucsd.edu
Cc: Higgins, Rosemary (NIH/NICHD) [E]; Roger Faix; Bradley Yoder
Subject: NCT00233324, NICHD-NRN-0031, Surfactant Positive Airway Pressure and Pulse Oximetry Trial

Hi Neil,

I have been dutifully going through the Network studies in Clinical Trials.gov to ensure that we are listed as appropriate and found that although Roger is listed as a Principle Investigator for the SUPPORT study, the U of Utah is not listed as a location. A simple oversight I'm sure, but one that I have to leave to you to remedy.

Thank you and have a good weekend!

Karen

Karen Osborne RN BSN CCRC
Project Manager
Neonatal Research Network
University of Utah
Dept of Pediatrics, Division of Neonatology
PO Box 581289
Salt Lake City, UT 84158
Phone # (801)213-3298
Pager # (801) 3393525
Fax # (801) 587-3618

From: Gantz, Marie
To: Higgins, Rosemary (NIH/NICHD) [E]; Auman, Jeanette O.
Cc: Das, Abhik
Subject: RE: Recruitment
Date: Wednesday, July 09, 2008 1:28:03 PM

As of last week we had 1107 in SUPPORT.

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, July 09, 2008 1:22 PM
To: Gantz, Marie; Auman, Jeanette O.
Cc: Das, Abhik
Subject: Recruitment

Can you tell me how many babies we have in each study as of this week's data entry?
SUPPORT
IPGE
6-24 hour hypothermia

Thanks
Rose

Sent from my BlackBerry Wireless Handheld

From: nancy newman
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Urgent Support Call Needed
Date: Thursday, June 19, 2008 9:20:30 AM

Hi- I am available in the morning on Tuesday, Monday I am off, tomorrow Friday I'm here all day.....Nancy

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, June 18, 2008 5:25 PM
To: mcunningham@rti.org; nfiner@ucsd.edu; adas@rti.org; mgantz@rti.org; wrich@ucsd.edu; wcarlo@peds.uab.edu; mcw3@cwru.edu; Bradley.yoder@hsc.utah.edu; Roger.Faix@hsc.utah.edu; alaptook@WIHRI.org; kurt.schibler@cchmc.org; nxs5@case.edu
Cc: Archer, Stephanie (NIH/NICHD) [E]; kzaterka@rti.org; fmartinez@ucsd.edu; msumner@peds.uab.edu; sharon.gough@hsc.utah.edu; BVecchio@WIHRI.org; petrie@rti.org
Subject: Re: Urgent Support Call Needed

All availability prior to and including tuesday is welcome.
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

----- Original Message -----
From: Cunningham, Meg <mcunningham@rti.org>
To: nfiner@ucsd.edu <nfiner@ucsd.edu>; Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik <adas@rti.org>; Gantz, Marie <mgantz@rti.org>; wrich@ucsd.edu <wrich@ucsd.edu>; wcarlo@peds.uab.edu <wcarlo@peds.uab.edu>; mcw3@cwru.edu <mcw3@cwru.edu>; Bradley Yoder <Bradley.Yoder@hsc.utah.edu>; Roger.Faix@hsc.utah.edu <Roger.Faix@hsc.utah.edu>; alaptook@WIHRI.org <alaptook@WIHRI.org>; kurt.schibler@cchmc.org <kurt.schibler@cchmc.org>; nancy newman <nxs5@case.edu>
Cc: Archer, Stephanie (NIH/NICHD) [E]; Zaterka-Baxter, Kristin <kzaterka@rti.org>; Martinez, Fernando <fmartinez@ucsd.edu>; msumner@peds.uab.edu <msumner@peds.uab.edu>; sharon.gough@hsc.utah.edu <sharon.gough@hsc.utah.edu>; Brenda Vecchio <BVecchio@WIHRI.org>; Huitema, Carolyn Petrie <petrie@rti.org>
Sent: Wed Jun 18 17:13:37 2008
Subject: Urgent Support Call Needed

All-

We need an urgent SUPPORT conference call to discuss oximeter skew this coming Tuesday. Please send your availability for Tuesday, June 24th, indicating time zone if other than ET as soon as possible. Rose will email around handouts prior to the call.

Thanks,

Meg

From: Cunningham, Meg
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Urgent Support Call Needed
Date: Wednesday, June 18, 2008 5:25:30 PM

Sorry, I thought you meant Tuesday.

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, June 18, 2008 5:25 PM
To: Cunningham, Meg; nfiner@ucsd.edu; Das, Abhik; Gantz, Marie; wrich@ucsd.edu; wcarlo@peds.uab.edu; mcw3@cwru.edu; Bradley.yoder@hsc.utah.edu; Roger.Faix@hsc.utah.edu; alaptook@WIHRI.org; kurt.schibler@cchmc.org; nxs5@case.edu
Cc: Archer, Stephanie (NIH/NICHD) [E]; Zaterka-Baxter, Kristin; fmartinez@ucsd.edu; msumner@peds.uab.edu; sharon.gough@hsc.utah.edu; BVecchio@WIHRI.org; Huitema, Carolyn Petrie
Subject: Re: Urgent Support Call Needed

All availability prior to and including tuesday is welcome.
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

----- Original Message -----
From: Cunningham, Meg <mcunningham@rti.org>
To: nfiner@ucsd.edu <nfiner@ucsd.edu>; Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik <adas@rti.org>; Gantz, Marie <mgantz@rti.org>; wrich@ucsd.edu <wrich@ucsd.edu>; wcarlo@peds.uab.edu <wcarlo@peds.uab.edu>; mcw3@cwru.edu <mcw3@cwru.edu>; Bradley Yoder <Bradley.Yoder@hsc.utah.edu>; Roger.Faix@hsc.utah.edu <Roger.Faix@hsc.utah.edu>; alaptook@WIHRI.org <alaptook@WIHRI.org>; kurt.schibler@cchmc.org <kurt.schibler@cchmc.org>; nancy newman <nxs5@case.edu>
Cc: Archer, Stephanie (NIH/NICHD) [E]; Zaterka-Baxter, Kristin <kzaterka@rti.org>; Martinez, Fernando <fmartinez@ucsd.edu>; msumner@peds.uab.edu <msumner@peds.uab.edu>; sharon.gough@hsc.utah.edu <sharon.gough@hsc.utah.edu>; Brenda Vecchio <BVecchio@WIHRI.org>; Huitema, Carolyn Petrie <petrie@rti.org>
Sent: Wed Jun 18 17:13:37 2008
Subject: Urgent Support Call Needed

All-

We need an urgent SUPPORT conference call to discuss oximeter skew this coming Tuesday. Please send your availability for Tuesday, June 24th, indicating time zone if other than ET as soon as possible. Rose will email around handouts prior to the call.

Thanks,

Meg

From: Zaterka-Baxter, Kristin
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Support DSMC review
Date: Monday, June 16, 2008 3:38:27 PM

Hi Rose, would you be available Tuesday October 7th for any questions that may come if we schedule the Support DSMC review then (in Rockville)?

Thanks,
Kris

Kris Zaterka-Baxter
RTI International
3040 Cornwallis Road
P.O. Box 12194
RTP, NC 27709-2194 USA
(tel) 919-485-7750
(fax) 919.485.7762
kzaterka@rti.org
www.rti.org

Federal Express/UPS/DHL Shipping Address:
Kris Zaterka-Baxter
RTI International
3040 Cornwallis Road
RTP, NC 27709 USA

From: Fernando Martinez
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re:
Date: Tuesday, June 03, 2008 12:57:17 PM

Thanks Dr. Higgins. I will print the e-mails for Neil and Wade.

Fernando

On Tuesday, June 03, 2008, at 09:32AM, "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> wrote:
>Fernando
>
>The UCSD email is still bouncing - I just sent something for the SUPPORT
>call - can you get it to Neil and Wade
>
>Rose
>
>
>
>Rosemary D. Higgins, MD
>
>Program Scientist for the Neonatal Research Network
>
>Pregnancy and Perinatology Branch
>
>Center for Developmental Biology and Perinatal Medicine
>
>Eunice Kennedy Shriver National Institute of Child Health and Human
>Development
>
>National Institutesof Health
>
>6100 Executive Blvd., Room 4B03
>
>MSC 7510
>
>Bethesda, MD 20892
>
>For overnight delivery use Rockville, MD 20592
>
>301-496-5575
>
>301-496-3790 (FAX)
>
>higginsr@mail.nih.gov
>
>
>
>

From:	Das, Abhik
To:	Higgins, Rosemary (NIH/NICHD) [E]; Zaterka-Baxter, Kristin; nfiner@ucsd.edu
Cc:	Cunningham, Meg; Monica Bocaner; Gantz, Marie
Subject:	RE: Support DSMC review at 75% status
Date:	Monday, June 02, 2008 4:23:37 PM

I am fine all these days.

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, June 02, 2008 12:22 PM
To: Zaterka-Baxter, Kristin; nfiner@ucsd.edu
Cc: Cunningham, Meg; Das, Abhik; Monica Bocaner; Gantz, Marie
Subject: RE: Support DSMC review at 75% status

August 27 -30 – Currently totally open
Sept 2-3 – open
Sept 4 – I need to give a talk at 8 am and would be available after 10 am
Sept 5 – available after 10 am

Rose

From: Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]
Sent: Monday, June 02, 2008 12:18 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; nfiner@ucsd.edu
Cc: Cunningham, Meg; Das, Abhik; Monica Bocaner; Gantz, Marie
Subject: Support DSMC review at 75% status

Hi all,
Marie looked at the Support study enrolled/status numbers and she estimates that the interim analysis at 75% status should be ready for review by the DSMC sometime between August 27 and Sept 5, 2008. Please let me know your availability around this time; this will most likely be a face-to-face meeting of the committee members in DC unless there are any other suggestions or objections.

Thanks,
Kris

Kris Zaterka-Baxter
RTI International
3040 Cornwallis Road
P.O. Box 12194
RTP, NC 27709-2194 USA
(tel) 919-485-7750
(fax) 919.485.7762
kzaterka@rti.org
www.rti.org

Federal Express/UPS/DHL Shipping Address:
Kris Zaterka-Baxter
RTI International
3040 Cornwallis Road
RTP, NC 27709 USA

From: Finer, Neil
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT AND STEERING COMMITTEE
Date: Monday, June 02, 2008 4:26:35 PM

Hi Rose
The phone works well and is cheap
Neil

Neil N. Finer, M.D.
Professor of Pediatrics
Director, Division of Neonatal-Perinatal Medicine
UC San Diego School of Medicine
UC San Diego Medical Center, Hillcrest
402 Dickinson St., MPF 1-140
San Diego, CA 92103-8774
Telephone: 619.543-3759
Facsimile: 619.543.3812

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, June 02, 2008 9:08 AM
To: Finer, Neil
Subject: SUPPORT AND STEERING COMMITTEE

Neil
DO you want to attend in person or by phone for the October meeting?
Let me know
Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutesof Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20592
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Finer, Neil
To:	Zaterka-Baxter, Kristin; Higgins, Rosemary (NIH/NICHD) [E]
Cc:	Cunningham, Meg; Das, Abhik; Monica Bocaner; Gantz, Marie
Subject:	RE: Support DSMC review at 75% status
Date:	Monday, June 02, 2008 4:25:54 PM

I will be available.
Neil

From: Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]
Sent: Monday, June 02, 2008 9:18 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; Finer, Neil
Cc: Cunningham, Meg; Das, Abhik; Monica Bocaner; Gantz, Marie
Subject: Support DSMC review at 75% status

Hi all,
Marie looked at the Support study enrolled/status numbers and she estimates that the interim analysis at 75% status should be ready for review by the DSMC sometime between August 27 and Sept 5, 2008. Please let me know your availability around this time; this will most likely be a face-to-face meeting of the committee members in DC unless there are any other suggestions or objections.

Thanks,
Kris

Kris Zaterka-Baxter
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RTP, NC 27709-2194 USA
(tel) 919-485-7750
(fax) 919.485.7762
kzaterka@rti.org
www.rti.org

Federal Express/UPS/DHL Shipping Address:
Kris Zaterka-Baxter
RTI International
3040 Cornwallis Road
RTP, NC 27709 USA

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Brad Yoder (Bradley.yoder@hsc.utah.edu)"; "Roger Faix"; "Karen.Osborne@hsc.utah.edu"
Cc: "Gantz, Marie"
Subject: SUPPORT PRIMARY OUTCOMES
Date: Thursday, May 29, 2008 2:23:34 PM

CONGRATULATIONS!!
As of the 5/21 data entry session, your site has all of the needed primary outcomes in for the SUPPORT TRIAL.
Thanks for all of the attention to detail, hard work, and effort!!!
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutesof Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20592
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Zaterka-Baxter, Kristin
To: vphillips@peds.uab.edu; Shirley Cosby; mcollins@peds.uab.edu
Cc: Cunningham, Meg; ahensman@wihri.org; karen.osborne@hsc.utah.edu; Higgins, Rosemary (NIH/NICHD) [E]
Subject: Oximeter delivery for SUPPORT study
Date: Thursday, May 22, 2008 5:37:13 PM

Hi Vivien, Shirley and Monica!

Vivien,
Could you please send Angelita one blue tomorrow for Saturday delivery at the following address:

Cheryl Cunha
Respiratory Therapy Department
Women & Infant's Hospital
101 Dudley Street
Providence, RI 02905
Ph: 401-274-1122 x 1623

Karen at Utah needs 2 blues as well sent tomorrow for Saturday delivery but am waiting for her to send that delivery address – will pass that along asap.

Thanks much!
Kris

From: Zaterka-Baxter, Kristin
Sent: Thursday, May 22, 2008 4:59 PM
To: 'Nancy Newman'
Cc: 'Angelita Hensman (ahensman@wihri.org)'
Subject: FW: Oximeter delivery for SUPPORT study

Hi Nancy,

Can you please send Angelita the extra blue and 2 oranges tomorrow for delivery on Saturday at the address below – thanks!!

Hi Angelita,
Georgia can not send another blue, that actually now would leave her short so I have left messages with several folks who will hopefully cam me back tomorrow and we'll have that one remaining blue sent fro Saturday delivery.
Thanks,
Kris

From: Angelita Hensman [mailto:AHensman@WIHRI.org]
Sent: Thursday, May 22, 2008 4:46 PM
To: Zaterka-Baxter, Kristin
Subject: RE: Oximeter delivery for SUPPORT study

Hi Kris,

Can you have the 2 blue pulse oximeters and 2 orange pulse oximeters FedEx'ed to:

Cheryl Cunha

Respiratory Therapy Department
Women & Infant's Hospital
101 Dudley Street
Providence, RI 02905
Ph: 401-274-1122 x 1623

Thanks
Angelita

From: Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]
Sent: Thursday, May 22, 2008 4:13 PM
To: Angelita Hensman
Subject: Oximeters
Importance: High

Hi Angelita,

Do you think you might need additional oximeters over the weekend (including Memorial Day)?
Thanks,
Kris

Kris Zaterka-Baxter
RTI International
3040 Cornwallis Road
P.O. Box 12194
RTP, NC 27709-2194 USA
(tel) 919-485-7750
(fax) 919.485.7762
kzaterka@rti.org
www.rti.org

Federal Express/UPS/DHL Shipping Address:
Kris Zaterka-Baxter
RTI International
3040 Cornwallis Road
RTP, NC 27709 USA

From: Webb, Robin E.
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: SUPPORT Conference Call
Date: Thursday, May 22, 2008 2:01:18 PM

Rose,

Do you want me to find some times and check with Carlo? Or poll for other days?

Thanks,
Robin

From: Walsh, Michele [mailto:Michele.Walsh@UHhospitals.org]
Sent: Thursday, May 22, 2008 1:54 PM
To: Webb, Robin E.
Cc: Higgins_Rosemary_" <
Subject: RE: SUPPORT Conference Call

I am on service that 2 week period.
It will be difficult for me to promise participation.
I can try to make a call at either 3p or 4pm
On the 28th, 29th, 30th, 3rd. 4th.
walsh

From: Webb, Robin E. [mailto:rwebb@rti.org]
Sent: Thursday, May 22, 2008 11:15 AM
To: mcw3@cwru.edu
Subject: FW: SUPPORT Conference Call
Importance: High

Please send you availability for the days below ASAP.

Thanks,
Robin

From: Webb, Robin E.
Sent: Friday, May 16, 2008 4:23 PM
To: higginsr@mail.nih.gov; Das, Abhik; kurt.schibler@cchmc.org; alaptook@WIHRI.org; mcw3@cwru.edu; wcarlo@peds.uab.edu; Roger.Faix@hsc.utah.edu; nfiner@ucsd.edu; Bradley.Yoder@hsc.utah.edu; Gantz, Marie; nxs5@cwru.edu; wrich@ucsd.edu; Zaterka-Baxter, Kristin
Cc: msumner@peds.uab.edu; fmartinez@ucsd.edu; Cunningham, Meg; 'Archer, Stephanie (NIH/NICHD) [E]'; Webb, Robin E.
Subject: SUPPORT Conference Call

We need to schedule a SUPPORT conference call. Please send your availability for the days below, indicating time zone if other than ET.

Thanks,
Robin

Tues 5/27
Wed 5/28

Thurs 5/29
Fri 530

Mon 6/2
Tues 6/3
Wed 6/4
Thurs 6/5
Fri 6/6

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Federal and Ohio law protect patient medical information, including psychiatric_disorders, (H.I.V) test results, A.I.Ds-related conditions, alcohol, and/or drug_dependence or abuse disclosed in this email. Federal regulation (42 CFR Part 2) and Ohio Revised Code section 5122.31 and 3701.243 prohibit disclosure of this information without the specific written consent of the person to whom it pertains, or as otherwise permitted by law.

From: Gantz, Marie
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Das, Abhik
Subject: RE: Missing SUPPORT outcomes
Date: Wednesday, May 21, 2008 2:46:45 PM

Yes, they do.

Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-6255

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, May 21, 2008 2:46 PM
To: Gantz, Marie
Cc: Das, Abhik
Subject: RE: Missing SUPPORT outcomes

Marie
Do these incorporate yesterday's data dump?
Thanks
Rose

From: Gantz, Marie [mailto:mgantz@rti.org]
Sent: Wednesday, May 21, 2008 2:45 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Das, Abhik
Subject: Missing SUPPORT outcomes

Rose,

Attached is the list of infants who are missing SUPPORT outcomes this month.

Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-6255

From:	Zaterka-Baxter, Kristin
To:	Nancy Miller; karen-johnson@uiowa.edu
Cc:	Michelle Tidwell; Ellen Hale; Higgins, Rosemary (NIH/NICHD) [E]; bmackinnon@tufts-nemc.org; Karen Osborne RN; ldw@iupui.edu; mcollins@peds.uab.edu; nancy newman; Bara, Rebecca; bbillian@wayne.edu; Mcdavid, Georgia E
Subject:	FW: SUPPORT study Masimos
Date:	Monday, May 12, 2008 1:18:25 PM

Hi Michelle,
Nancy Miller at Dallas will send 3 **orange** and Karen from Iowa will send 1 more to the address below:

Emory University Neonatal Medicine
Attn: Vicki Reid/Michelle Tidwell
49 Jesse Hill Jr. Drive
Atlanta, GA 30303
(404) 616-5397
michelle_tidwell@oz.ped.emory.edu

Hi Brenda,
Karen from Iowa will send you 1 **blue** oximeter to the address below:

Brenda MacKinnon, RNC
The Floating Hospital for Children
750 Washington Street
Tufts-NEMC #44 Boston, MA 02111
617-636-1218

bmackinnon@tufts-nemc.org

Thanks guys and thanks to everyone else I called; we now have the oximeters needed!
Kris

From:	Huitema, Carolyn Petrie
To:	Angelita Hensman; Higgins, Rosemary (NIH/NICHD) [E]; Archer, Stephanie (NIH/NICHD) [E]; [StatEpi] Neonatal Statisticians; [StatEpi] Neonatal Programmers; Zaterka-Baxter, Kristin; Das, Abhik; mbball@leland.stanford.edu; grisbyca@email.uc.edu; ellen_hale@oz.ped.emory.edu; Georgia E McDavid; linda_reubens@urmc.rochester.edu; mcollins@peds.uab.edu; monica.konstantino@yale.edu; Nancy.Miller@UTSouthwestern.edu; Nancy Newman; risa.demetrio@sharp.com; jyhall@stanford.edu; kathy.arnell@sharp.com; wrich@ucsd.edu; JANET.MORGAN@childrens.com; Ang, Jocelyn Y; Mperalta@peds.uab.edu; Roy.Heyne@utsouthwestern.edu; vphillips@peds.uab.edu; Brenda.H.Morris@uth.tmc.edu; vanmeurs@leland.stanford.edu; Abbot Laptook; [SCRN] Stoll, Barbara; bpoindex@iupui.edu; dale_phelps@urmc.rochester.edu; jon.e.tyson@uth.tmc.edu; nfiner@ucsd.edu; richard.ehrenkranz@yale.edu; goldb008@mc.duke.edu; sshankar@med.wayne.edu; wcarlo@peds.uab.edu; mcw3@cwru.edu; Barbara.Alexander@cchmc.org; Estelle E. Fischer; Holly Mincey; Jody Shively; Kate Bridges, MD; Lenora Jackson; Frantz, Ivan; Pablo.Sanchez@UTSouthwestern.edu; kurt.schibler@cchmc.org; Michael Cotten; Bell, Edward; Johnson, Karen; Kristi Watterberg; Roger Faix; Conra Backstrom; bradley.yoder@hsc.utah.edu; ira_adams-chapman@oz.ped.emory.edu; apappas@med.wayne.edu; srhintz@stanford.edu; yvaucher@ucsd.edu; golds005@mc.duke.edu; gary_myers@urmc.rochester.edu; Betty Vohr; adusick@iupui.edu; steichji@email.uc.edu; drfjcmd@aol.com; mgfuller@ucsd.edu; elaine.romano@yale.edu; Teresa.Gratton@uc.edu; Jackie.Hickman@Childrens.com; bss5@cwru.edu; lohme001@mc.duke.edu; Patricia.W.Evans@uth.tmc.edu; Kimberly.Yolton@cchmc.org; Sharon.Wright@uth.tmc.edu; ldw@iupui.edu; dhwilson@iupui.edu; Karen Osborne RN; Mackinnon, Brenda; Kennedy, Kathleen A; Katherine A Foy; melissa.leps@utsouthwestern.edu; Bara, Rebecca; bbillian@wayne.edu; Elizabeth Billian
Subject:	REVISION: Changes to GDB, Physiologic Definition of BPD, SUPPORT and EOS
Date:	Thursday, May 08, 2008 1:12:58 PM
Attachments:	PHY5 20080508.pdf

Dear All-

The revised technical memo is attached to this email. Below, changes are noted in red.

Thanks,
Carolyn

From: Huitema, Carolyn Petrie [mailto:petrie@rti.org]
Sent: Wednesday, April 30, 2008 8:28 PM
Subject: Changes to GDB, Physiologic Definition of BPD, SUPPORT and EOS

Dear All-

Please find attached to this email ***Technical Memo PHY5, GDB22, SUP14, EOS07***

Clean, revised forms will be posted to the website. Please hold keying the May 1, 2008 version of the NG07 until available in the DMS.

Physiologic Definition of BPD

The stand alone Physiologic Definition of Bronchopulmonary Dysplasia (BPD) study will become a subset of the GDB on May 1, 2008, per the decision of the Steering Committee at the January 2008 meeting. Data forms created for the Physiologic Definition of BPD (PHY01 and PHY02) will be used as worksheets for the revised NG07 and only entered into the data management system (DMS) when specified as necessary for individual studies.

Infants that are born before May 1, 2008 should complete the current PHY01 and PHY02 forms and NG07 form version date January 1, 2006. Infants born on or after May 1, 2008 are no longer required to enter the PHY01 and PHY02 forms and should complete the NG07 form version date May 1, 2008.

The following questions have been added on the May 1, 2008 version of the GDB study Respiratory Support form (NG07) to document whether or not an infant has BPD using the physiologic definition of BPD.

1. Is the infant eligible for the physiologic evaluation? Y N

If YES to question C.1

a. Was the evaluation performed? Y N

If YES to question C.1.a

b. Date of evaluation __ __ / __ __ / __ __ __ __
Month Day Year

c. Actual FiO2 being delivered at time of challenge For infants receiving blended supplemental oxygen via nasal cannula, record the blend in this field. __ . __ __

d. If on nasal cannula at time of challenge, record flow rate __ . __ __ __ *LPM*

e. Did the patient pass the evaluation? Y N

If NO to question C.1.a

f. If patient was eligible and evaluation not done, code reason.

1= Increased FiO2
2= Increased respiratory support (cpap or vent)
3= Instability (including Surgery/Sepsis)
4 = Parent/Physician Refusal
6 = Weaned to room air on/before day of evaluation
9 = Other- explain

SUPPORT Study

The physiologic evaluation for BPD will be completed on eligible SUPPORT study infants. The results of the evaluation will be recorded on the revised NG07. In addition to the NG07 data, the PHY01 and PHY02 forms will continue to be entered into the DMS for SUPPORT patients whenever section **C. Physiologic Evaluation** on the new NG07 is required to be completed.

EOS Study

Infants enrolled in the EOS study, outside of the GDB criteria will NOT have the physiologic definition of BPD performed for the purposes of the EOS study. Infants outside of the GDB criteria (a gestational age greater than or equal to 29 week and weighing 1001-1500g) will continue to have other relevant GDB data collected.

Thank you,
Carolyn Huitema

RTI INTERNATIONAL | **Memorandum**

April 30, 2008 *revised May 8, 2008*

Physiologic Definition of Bronchopulmonary Dysplasia
Physiologic Definition of BPD **Technical Memo # 5 (PHY5)**
Generic Database **Technical Memo #22 (GDB22)**
SUPPORT **Technical Memo #14 (SUP14)**
EOS **Technical Memo #07 (EOS07)**

TO: Network Coordinators
Network PIs

FROM: The Data Coordinating Center

SUBJECT: Physiologic Definition of Brochopulmonary Dysplasia Study

Physiologic Definition of BPD

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The following questions have been added on the May 1, 2008 version of the GDB study Respiratory Support form (NG07) to document whether or not an infant has BPD using the physiologic definition of BPD.

1. Is the infant eligible for the physiologic evaluation? Y N
If YES to question C.1
a. Was the evaluation performed? Y N
If YES to question C.1.a
b. Date of evaluation __ __ / __ __ / __ __ __ __ (Month / Day / Year)
c. Actual FiO2 being delivered at time of challenge For infants receiving blended supplemental oxygen via nasal cannula, record the blend in this field. __ . __ __
d. If on nasal cannula at time of challenge, record flow rate __ . __ __ __ *LPM*
e. Did the patient pass the evaluation? Y N
If NO to question C.1.a
f. If patient was eligible and evaluation not done, code reason.

1= Increased FiO2
2= Increased respiratory support (cpap or vent)
3= Instability (including Surgery/Sepsis)
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Cc. Rosemary Higgins, MD

Enclosed:

NG07 (May 1, 2008)
GDB Manual (May 1, 2008)

From:	Huitema, Carolyn Petrie
To:	ahensman@wihri.org; mbball@leland.stanford.edu; grisbyca@email.uc.edu; ellen_hale@oz.ped.emory.edu; Georgia E McDavid; linda_reubens@urmc.rochester.edu; mcollins@peds.uab.edu; monica.konstantino@yale.edu; Nancy.Miller@UTSouthwestern.edu; Nancy Newman; risa.demetrio@sharp.com; jyhall@stanford.edu; kathy.arnell@sharp.com; wrich@ucsd.edu; JANET.MORGAN@childrens.com; Ang, Jocelyn Y; Mperalta@peds.uab.edu; Roy.Heyne@utsouthwestern.edu; vphillips@peds.uab.edu; Brenda.H.Morris@uth.tmc.edu; vanmeurs@leland.stanford.edu; alaptook@wihri.org; [SCRN] Stoll, Barbara; bpoindex@iupui.edu; dale_phelps@urmc.rochester.edu; jon.e.tyson@uth.tmc.edu; nfiner@ucsd.edu; richard.ehrenkranz@yale.edu; goldb008@mc.duke.edu; sshankar@med.wayne.edu; wcarlo@peds.uab.edu; mcw3@cwru.edu; Barbara.Alexander@cchmc.org; Estelle E. Fischer; Holly Mincey; Jody Shively; Kate Bridges, MD; Lenora Jackson; Frantz, Ivan; Pablo.Sanchez@UTSouthwestern.edu; kurt.schibler@cchmc.org; Michael Cotten; Bell, Edward; Johnson, Karen; Kristi Watterberg; Roger Faix; Conra Backstrom; bradley.yoder@hsc.utah.edu; ira_adams-chapman@oz.ped.emory.edu; apappas@med.wayne.edu; srhintz@stanford.edu; yvaucher@ucsd.edu; golds005@mc.duke.edu; gary_myers@urmc.rochester.edu; bvohr@wihri.org; adusick@iupui.edu; steichji@email.uc.edu; drficmd@aol.com; mgfuller@ucsd.edu; elaine.romano@yale.edu; Teresa.Gratton@uc.edu; Jackie.Hickman@Childrens.com; bss5@cwru.edu; lohme001@mc.duke.edu; Patricia.W.Evans@uth.tmc.edu; Kimberly.Yolton@cchmc.org; Sharon.Wright@uth.tmc.edu; ldw@iupui.edu; dhwilson@iupui.edu; Karen Osborne RN; Mackinnon, Brenda; Kennedy, Kathleen A; Katherine A Foy; melissa.leps@utsouthwestern.edu; Bara, Rebecca; bbillian@wayne.edu; Elizabeth Billian
Cc:	Higgins, Rosemary (NIH/NICHD) [E]; Archer, Stephanie (NIH/NICHD) [E]; [StatEpi] Neonatal Statisticians; [StatEpi] Neonatal Programmers; Zaterka-Baxter, Kristin; Das, Abhik; Huitema, Carolyn Petrie
Subject:	Changes to GDB, Physiologic Definition of BPD, SUPPORT and EOS
Date:	Wednesday, April 30, 2008 8:28:55 PM
Attachments:	NG0720080501.doc 2008 GDB Manual 20080501uc.doc PHY5 20080430.doc

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Dear All-

Please find attached to this email ***Technical Memo PHY5, GDB22, SUP14, EOS07*** along with revised, with highlighted changes to the:

- ***GDB Manual (May 1, 2008)***
- ***NG07 (May 1, 2008)***

Clean, revised forms will be posted to the website. Please hold keying the May 1, 2008 version of the NG07 until available in the DMS.

Physiologic Definition of BPD

The stand alone Physiologic Definition of Bronchopulmonary Dysplasia (BPD) study will become a subset of the GDB on May 1, 2008, per the decision of the Steering Committee at the January 2008 meeting. Data forms created for the Physiologic Definition of BPD (PHY01 and PHY02) will be used as worksheets for the revised NG07 and only entered into the data management system (DMS) when specified as necessary for individual studies.

Infants that are 36 wks PMA and eligible for challenge before May 1, 2008 should complete the current PHY01 and PHY02 forms and NG07 form version date (January 1, 2006. Infants 36 wks PMA and eligible for challenge after May 1, 2008 are no longer required to enter the PHY01 and PHY02 forms and should complete the NG07 form version date May 1, 2008.

The following questions have been added on the May 1, 2008 version of the GDB study Respiratory Support form (NG07) to document whether or not an infant has BPD using the physiologic definition of BPD.

1. Is the infant eligible for the physiologic evaluation? Y N

If YES to question C.1

a. Was the evaluation performed? Y N

If YES to question C.1.a

b. Date of evaluation __ __ / __ __ / __ __ __ __
Month Day Year

c. Actual FiO2 being delivered at time of challenge For infants receiving

NICU Network

GENERIC DATABASE (GDB)
RESPIRATORY SUPPORT FORM (NG07)

NG07 Rel 1.0
May 1, 2008

Center: ___ Site: ___ Network No: _ _ _ _ Birth No: ___ Mother's Initials: _ _ _

A. SNAPSHOT	@24 HOURS		@ 36 WEEKS*		B. CUMULATIVE DATA	DAY 3	DAY 7	DAY 14	DAY 28	36 WEEKS	STATUS
1. On HFV?	Y	N	Y	N	1. Number days on HFV	__	__	__ __	__ __	__ __	__ __ __
2. On CV?	Y	N	Y	N	2. Number days on CV	__	__	__ __	__ __	__ __	__ __ __
3. On nasal SIMV?	Y	N	Y	N	3. Number of days on nasal SIMV	__	__	__ __	__ __	__ __	__ __ __
4. On CPAP?	Y	N	Y	N	4. Number days on CPAP	__	__	__ __	__ __	__ __	__ __ __
					5. Number of days on supplemental O_2	__	__	__ __	__ __	__ __	__ __ __
6. Highest FiO_2	__ . __ __		__ . __ __		6. Highest FiO_2 on day	__ . __ __	__ . __ __	__ . __ __	__ . __ __	[redacted]	__ . __ __
OR					OR						
7. Supplemental O_2 by nasal cannula?	Y		Y		7. Supplemental O_2 by nasal cannula?	Y	Y	Y	Y		Y
8. If FiO_2 = 0.21 (#6), by nasal cannula, [redacted]	Y	N	Y	N	8. If FiO_2 = 0.21 (#6), by nasal cannula, CPAP or vent?	Y N	Y N	Y N	Y N		Y N

If in section 'A', snapshot @36 weeks, questions 1-4 are answered NO and either question 6 FiO_2 > 0.21 or questions 7 or 8 are answered YES, complete section C :

C. Physiologic Evaluation

1. Is the infant eligible for the physiologic evaluation? Y N

If YES to question C.1

a. Was the evaluation performed? Y N

If YES to question C.1.a

b. Date of evaluation __ __ / __ __ / __ __ __ __
Month Day Year

[redacted]

e. Did the patient pass the evaluation? Y N

If NO to question C.1.a

f. If patient was eligible and evaluation not done, code reason: ____ If '9', explain_____

1= Increased FiO2	4 = Parent/Physician Refusal
2= Increased respiratory support (cpap or vent)	6 = Weaned to room air on/before day of evaluation
3= Instability (including Surgery/Sepsis)	9 = Other- explain

SURVEY OF MORBIDITY AND MORTALITY AMONG HIGH RISK PRETERM INFANTS (GDB)

NICHD Neonatal Research Network

Manual of Operations

January 1, 2006
Revised June19, 2006
Revised April 1, 2007
Revised June 7, 2007
Revised January 1, 2008
Revised May 1, 2008

TABLE OF CONTENTS

Chapter 1
Objectives and Study Designs

1.1 Introduction

This manual gives detailed instructions for the **Survey of Morbidity and Mortality Among High Risk Preterm Infants**. It is meant to serve as a reference guide for study staff, including investigators, coordinators, technicians and data managers. This study is being conducted by the NICHD Neonatal Research Network.

1.2 Survey of Morbidity and Mortality Among High Risk Preterm Infants

The purpose of this study is to provide a registry of baseline and outcome data for high risk preterm infants, based on data collected in a uniform manner from neonatal intensive care units (NICUs) at institutions participating in the NICHD Neonatal Research Network. These data, although not representative of a regional sample, do represent a number of major tertiary care academic centers. Although centers serve varying populations, they exemplify the neonatal morbidity problems of the 1980's through the 2000's. These data will be used to characterize the infants admitted to the units, to examine the relationships between certain entry characteristics and outcome, to measure trends in incidence of various disease entities, and to provide the basis for hypothesis formulation for Network multi-center studies.

Baseline and outcome data will be collected on all liveborn infants who are 1) Inborn and between 401 grams and 1000 grams inclusive birth weight and/or 2) Inborn and between 22 0/7 to 28 6/7 weeks (<29 weeks) inclusive gestational age Infants enrolled in a Network RCT or prospective observational study (inborn and transferred infants) may be included in the GDB dataset if requested by the study subcommittee and approved by the NRN Steering Committee. These may be otherwise premature and/or low birth weight infants outside the GDB gestational and birth weight criteria. In addition, infants who meet the above criteria with a heart rate at birth, who died in the delivery room will be included. These data will be obtained by review of the mother's and baby's charts. The data forms for the survey have been named **'generic data forms'** in recognition of the fact that the information collected is of universal interest and not specific to a particular disease or treatment. They provide a descriptive summary of the babies' background, perinatal and neonatal experience. Baseline data will be obtained soon after admission to the NICU and the outcome data will be obtained at the time of death or discharge from the hospital.

Chapter 2
Administration

2.1 Organizational Structure

The Survey of Morbidity and Mortality Among High Risk Preterm Infants is being conducted by the NICHD Neonatal Research Network. The NICHD Research Network was established by the Center for Research for Mothers and Children in 1986 to conduct multi-center clinical trials in neonatal medicine and management. The Network is funded as a cooperative agreement between the Clinical Centers, the Data Coordinating Center (DCC) and the NICHD. The Steering Committee for the Network is limited to the Principal Investigator from each Clinical Center, the Data Coordinating Center, and the NICHD Neonatal Research Program Official. Non-voting Steering Committee participants include the Director of the Center for Research for Mothers and Children (CRMC) and the Steering Committee Chairman, who is appointed by NICHD. The Steering Committee has the responsibility to develop study protocols and monitor their implementation.

2.1.1 Participating Centers

2.1.1.1 Clinical Centers

The Principal Investigators representing the Clinical Centers have agreed to abide by the study protocols and, in addition, to have comparable staff, facilities, and equipment. To ensure that centers meet standards for procedures, equipment and staffing, each center is certified prior to participation in Network studies.

2.1.1.2 Data Coordinating Center

The Data Coordinating Center (DCC) collaborates with the Steering Committee on protocol design, data management, data collection systems (including the final versions of protocols, forms and manual of operations), and analysis. The DCC conducts the interim and final statistical analyses and collaborates with the Steering Committee members in the preparation of publications based on the study results. The Principal Investigator of the DCC reports to the Steering Committee and the Data Monitoring and Safety Committee.

2.1.2 NICHD

In addition to its role as the funding agency, the NICHD participates as a voting member of the Steering Committee (the Program Official). NICHD staff also participates in the development of protocols and in assisting the Steering Committee in the coordination and publication of the studies conducted by the Network.

2.2 Committees

2.2.1 Steering Committee

This committee is comprised of the Principal Investigators from each of the Clinical Centers and the Data Coordinating Center, the NICHD Program Official, and the Chairman of the Steering Committee. The Steering Committee has the responsibility for identifying topics for network studies, designing study protocols, monitoring study implementation, and recruitment. The Steering Committee will also make recommendations for changes to study protocols if it deems necessary. This committee receives recommendations from the Data Monitoring and Safety Committee via NICHD.

2.2.2 Generic Database Subcommittee

The Generic Database Subcommittee is responsible for the design of the generic data forms and for monitoring the conduct of the study. This subcommittee reports to the Steering Committee.

2.2.3 Publication Committee

The Publication Committee is responsible for developing the publication policy for the NICHD Neonatal Research network and for writing the policy for the use of the Generic Data Base for publication.

Chapter 3
Survey of Morbidity and Mortality - Enrollment and Baseline Data

3.1 Enrollment

3.1.1 Eligibility

All infants who are 1) inborn and between 401 grams and 1000 grams inclusive birth weight and/or 2) inborn and between 22 0/7 to 28 6/7 weeks (<29 weeks) inclusive gestational age are eligible for the study. Infants enrolled in a Network RCT or prospective observational study (inborn and transferred infants) may be included in the GDB dataset if requested by the study subcommittee and approved by the NRN Steering Committee. These may be otherwise premature and/or low birth weight infants outside the GDB gestational and birth weight criteria. In addition, all inborn, liveborn infants who meet the above criteria and die prior to admission to the NICU are enrolled posthumously.

3.1.2 Screening Log Entry - Form NG01

The purpose of the Screening Log is to record all eligible infants.. It serves as a cross check for identification and ensures that no infants are forgotten for data collection. This form will not be entered into the center-based computer system.

3.1.2.1 NICU admissions

The Network Coordinator enters daily onto the log the baby's name, hospital record number, date of birth, birth weight, gestational age and whether or not enrolled in a study for every infant admitted to the NICU who meet the above eligibility criteria. In addition, the mother's initials may be recorded. For all births each sibling is assigned a birth number. For singleton or first born of a multiple birth, the code will be "1", "2", etc). **This log may be modified to meet the particular needs of individual centers.**

3.1.2.2 Deaths Prior to NICU Admission

The Network Coordinator checks the delivery room record at the beginning of every week, to identify liveborn infants in the weight range and gestational age range who expired prior to NICU admission. Name, hospital record number, date of birth, birth weight (measurement from the delivery room record), mother's initials and birth number (as above) should be recorded on the screening log.

3.1.3 Data Forms

If the baby meets GDB eligibility criteria, forms NG02 and NG03 should be obtained and placed in a file folder designated for that baby. If the infant dies in 12 hours or less then replace the NG03 with the NG03E.

3.1.4 Assignment of Network Number by Computer

The infant's identifying information should be entered into the Neonatal Research Network's data management computer system as soon as possible. This is known as the 'base' screen in the computer system and it does not, unlike the rest of the data to be entered, correspond to a paper form. However, the computer system uses the 'base' form and the NG01 interchangeably.

The following information is contained on the base record:

- **Date of Birth**

- **Birth Weight**

- **Mother's Initials:**
  The Mother's normal initials (first, middle and last). If there is **no** middle initial, record the two initials. **This information is optional.**

- **Birth Number [This information is required]**
  For a single birth or first born of a multiple birth enter '1. This code establishes a Family ID in the NICU. For the second born code '2' etc. It does not necessarily have to conform to strict birth order from a multiple birth, but must be kept consistent for each baby.

- **Gestational Age**

- **Infant enrolled in an NRN study requiring GDB forms**
  Infants enrolled in a Network RCT or prospective observational study (inborn and transferred infants) may be included in the GDB dataset if requested by the study subcommittee and approved by the NRN Steering Committee. These may be otherwise premature and/or low birth weight infants outside the GDB gestational and birth weight criteria.

- **Site [This information is required]**
  The center assigns these to their various hospitals. If applicable, any site letter or number is acceptable.

- **Network #:** The Network number is made up of a four digit Family (Pregnancy) Number plus the Birth Order Number. Therefore the Network Number is 5 digits.

It is important to enter a 'base' screen for an infant as soon as possible, since at the time of entering data on the 'base' screen that infant is assigned a Network Number. This number is the infant's unique identifying number and should be used for all subsequent data forms.

When entering test data, the computer assigns a 5-digit number starting at 'T1001'. When entering real data, the assigned network numbers start at '1'. Five spaces have been allotted to network number on all the forms.

3.1.5 Adding Network Number to NG01: Screening Log after Base Record Completion

After the base record is entered, put the network number on the screening log and all of the infant's generic forms.

3.2 Baseline Data Collection

When a baby has been enrolled in this study the coordinator should complete form NG02 with baseline information. Coding instructions are presented below. Most of the information required is standard in nature, and is to be obtained from the baby's chart and from the mother's medical record.

3.2.1 For Infants Participating in Clinical Trials

If an infant is in a study and is receiving either placebo or study drug, then answer 'T' (Trial) for any questions associated with this drug or medication. However, if the same infant receives the known medication at another time – not under the study protocol – the question regarding the medication would be "yes."

NG02: GENERIC BASELINE FORM

3.3 Coding Instructions for Form NG02

3.3.1 Heading

- **Mother's Initials: [Optional]**
  The Mother's normal initials (first, middle and last). If there is **no** middle initial, record the two initials. **This information is optional.**

- **Birth Number:**
  For a single birth or first born of a multiple birth enter '1'. This code establishes a Family ID in the NICU. For the second born code '2' etc. It does not necessarily have to conform to strict birth order from a multiple birth, but must be kept consistent for each baby.

- **Network Number:** The Network number is made up of a four digit Family (Pregnancy) Number plus the Birth Order Number. Therefore the Network Number will be 5 digits.

When the patient has been entered on the database for the first time, the computer assigns this unique identifier.

3.3.2 Section A - MATERNAL INFORMATION

The following information is to be obtained primarily from the mother's chart or any other reliable source.

1. **Mother's age:**
   Record the age in completed years at the time of delivery.

2. **Maternal Zip Code:**
   Record the first three digits of the zip code of the mother's current address as documented on the mother's chart. Code '000' if mother is homeless and/or in a shelter.

3. **Pregnancy history (include this pregnancy):**

   a. **Gravida:**
      The number of confirmed pregnancies, including this one.

   b. **Parity:**
      The number of products of conception delivered after 20 weeks gestation, resulting in the birth of a child, including this delivery. This includes live births only. Note that each infant of a multiple birth has the same parity. For example, if twins were born and it was the first delivery, then the parity for each twin would be 2. The parity for a singleton birth following these twins would be 3.

4. **Marital status**:
   Choose the appropriate marital status code. If mother is currently married but separated (including legal separations) use code '1' married. If the marital status is common law, use code '1' married. If she is single, divorced or widowed then use code '2' single. If marital status is unknown code '6'.

5. **Highest level of education achieved by the biological Mother:**
Record the highest level of education achieved by the biological mother at the time this delivery. If this is a surrogate pregnancy, record the highest education level of the surrogate mother at the time of delivery. This information should be obtained from the mother's or infant's medical record or other reliable source.

Code as follows:
1= <7th grade
2= 7th to 9th grade
3= 10th to 12th grade
4= High School degree
5= Partial college (include Jr. college and associates degree)
6= College degree (4 years)
7= Graduate degree
8= Unknown

6. **Mother's medical insurance:**
Record the type of medical insurance documented in the maternal medical record at the time of admission. This information may often be found on the admitting or face sheet in the hospital record.
Code as follows:
1= Medicaid- this may include Medicaid, Medicare, a state funded program, federally funded program
3= Private- This is traditional insurance, managed care, etc. (include CHAMPUS, Tricare or any insurance that may be tied to work).
5= Self-Pay/uninsured- if hospitalization is to be or has already been paid for by the mother or other responsible party
6= Unknown
9= Other

3.3.3 Section B - PREGNANCY COMPLICATIONS

The following information is to be obtained primarily from the mother's chart or any other reliable source. Items 4a and 5a may be coded as Yes, No or Unknown. Code 'Y' if the item is listed as a problem in the maternal or infant record. Code "UK" or 'N' otherwise.

1. **Multiple birth?**
Code 'Y' if there was a multiple birth.

If **YES**,
Complete only if this pregnancy is a multiple gestation. Do not include early (< 14 weeks) fetal reductions.

a. **Number of fetuses**:
Include all fetuses, live or stillborn.

2. **Mother has evidence of at least one prenatal care visit for this pregnancy?**
Code 'Y' if at least one prenatal care visit, prior to delivery is specifically documented. Code 'N' otherwise.

3. **Diabetes - insulin dependent?**
Record 'Y' if diabetes mellitus requiring insulin for control is diagnosed during or prior to present pregnancy.

a. If Yes, was insulin given prior to pregnancy?

4 **Hypertension?**
Record 'Y' if hypertension, chronic or pregnancy induced, is specifically recorded in the mother's chart. The standard definition of hypertension is maternal BP above 140 systolic or 90 diastolic was recorded prior to or during the present pregnancy on at least 2 occasions.
If Yes,
a. Hypertension existed prior to pregnancy?
Record 'Y' if patient had hypertension prior to this pregnancy documented in the chart and/or chronic hypertension.

5. **Antepartum hemorrhage?**
Record 'Y' if placenta previa, abruptio or threatened abortion resulting in bleeding, which can be external (vaginal bleeding) or occult (retroplacental clot), other than bloody show, is documented after 20 weeks of pregnancy.

6. **Was Chorioamnionitis documented in the Mother's medical record?**
Record 'Y' if Chorioamnionitis is specifically documented in the Mother's medical record.

7. **Was placental pathology performed?**
If Yes,
a. Was histologic chorioamnionitis documented?

3.3.4 Section C - LABOR AND DELIVERY

1. **Was there rupture of membranes prior to delivery?**
Note: If ROM at delivery this question should be answered 'No'.
For C-sections, if the date and time is not recorded, assume ROM at delivery and answer ''No'.
If Yes,
a. Date:
From labor and delivery sheet, admission notes or other reliable source

b. Time:
From labor and delivery sheet, admission notes, or other reliable source. Use a 24 hour clock with midnight coded as 00:00

c. If date and/or time unknown, were ROM estimated at > 18 hours?

2 Were steroids given prior to delivery to accelerate maturity?
Record 'Y' if corticosteroids (e.g. betamethasone, dexamethasone) were given during this pregnancy. Record 'N' if no steroids were given or 'UK' if unknown.

a. If **YES**, type of antenatal steroids given:
Record the type of corticosteroid given, or both as documented in the maternal medical record. Code 1= Betamethasone, 2= Dexamethasone, 3= Both or 4= If unknown

If the mother is in a study and is receiving either the placebo or the drug, then answer 'T' to any questions concerning mother being on the drug.

b. Was a complete course of steroids given prior to delivery?
Code 'Y' if bethamethasone [2 doses, 12 or 24 hours apart] or dexamethasone [4 doses, 6 hours apart] were given specifically to promote lung maturity and at least 12 hours from the second dose or 24 hours from the first dose has elapsed before delivery. If the time elapsed was less, this indicates that there was insufficient time for the drug to have an effect and would be considered incomplete. Information may be obtained from the maternal and/or infant chart. Count only doses that occurred prior to delivery. Code 'UK' if unknown.

3. Were maternal antibiotics used during the admission resulting in this delivery?
Code 'Y' if any maternal antibiotics were used during the admission resulting in this delivery.

a. If **Yes**, were antibiotics given by any systemic method (IV, IM or oral) within 72 hours prior to delivery?
b. If **Yes**, list antibiotics given:

4. Final mode of delivery:
As documented on labor/delivery sheet. If the final mode of delivery is unknown, code UK. Code NOS = not otherwise specified.

3.3.5 Section D - NEONATAL INFORMATION

1. Date and time of birth:

a. Date:
Record the date on which child was born (day begins at 00:00, ends at 23:59).

b. Time:
Use a 24-hour clock with midnight coded as 00:00.

2. Was the infant outborn?

Code 'N' if the infant was born within the walls of one of the designated Network hospitals.

Code 'Y' if the infant was born outside of a Network hospital.and was enrolled in an NRN trial (this should include anyone outside of the Network center hospital (s); could include other hospital, home delivery, taxi, etc).

If YES, date admitted to NICU

a. Date:
Day begins at 00:00, ends at 23:59.

3. Did the infant die ≤12 hours?

IF YES, COMPLETE FORM NG03E.

4. Sex:
Record the stated sex of the infant. To score '3', ambiguous, there must be confirmation of ambiguous genitalia by either a genetics consult at time of birth or pathology report if infant expires.

5. Ethnic Categories:
Code the mother's ethnicity as follows:

1= Hispanic or Latino: A person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race. The term, "Spanish origin," can be used in addition to "Hispanic or Latino."

2= Not Hispanic or Latino: None above.
3= Unknown or Not Reported: A person not knowing or not reporting ethnicity.

6. **Racial Categories:**
Code the mother's race as follows:

1= Black: A person having origins in any of the black racial groups of Africa. Terms such as "Haitian" or "Negro" can be used in addition to "Black or African American."
2= White: A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.
3= American Indian or Alaskan Native: A person having origins in any of the original peoples of North, Central, or South America, and who maintains tribal affiliation or community attachment.
4= Asian: A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam. (Note: Individuals from the Philippine Islands have been recorded as Pacific Islanders in previous data collection strategies.)
5= Native Hawaiian or Other Pacific Islander: A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.
6= More Than One Race: A person having origins in multiple racial designations.
7= Unknown or Not Reported: A person not knowing or not reporting Race

a. If coding option 6, record all races indicated (optional).

7. **Gestational age in weeks and days:**
Record the best estimate of gestational age using the following hierarchy:
1) Best OB estimate/Obstetrical measures based on last menstrual period, obstetrical parameters, and/or early prenatal ultrasound as recorded in the maternal chart.

2) Best Neonatologist estimate/Neonatologist's estimate based on physical criteria, neurologic examination, combined physical and gestational age exam (Ballard or Dubowitz), or examination of the lens.In instances when the gestational age in days is not recorded, enter "0" in the days field.

8. **Apgar score - 1 minute:**
Use the official one minute Apgar score as assigned in the delivery room from delivery chart.

9. **Apgar score - 5 minute:**
Use the official five minute Apgar score recorded as above.

10. Birth resuscitation/stabilization:
Record 'Y' for support provided to the infant at the time of birth.

a. Oxygen?
Supplemental O_2 (FiO_2 > .21) delivered to the infant via face mask, hood, CPAP, or ET tube.

b. Bagging and mask?
Positive pressure ventilation (breathing) with face mask and (anesthesia) bag. This includes Neopuff.

c. CPAP?
Continuous positive airway pressure delivered by CPAP device or mask.

d. Intubation?
Insertion of a tube (even if transiently) into the trachea to allow positive pressure ventilation for breathing. If intubation was done for suctioning or to give surfactant and immediately removed it should not be included here.

e. Chest compression?
External pressure over central chest to contract heart.

f. Epinephrine?
Epinephrine delivered intravenously or intratracheally for resuscitation.

11. Birth weight:
The birth weight in grams of the infant as recorded in one of the following places on the chart in order of preference (an individual center may employ a different ordering if it is deemed more reliable):

1) On the labor and delivery record.
2) On the nursery admission record.
3) On the admission physical examination form.
4) The pathology report when an infant expires.

12. Length:
The length in centimeters, as recorded on the admission physical (within 72 hours of birth).

13. Head circumference:
The head circumference in centimeters as recorded (within 72 hours of birth):

1) On the admission physical exam form.
2) On the nursery admission record.
3) The pathology report if the infant died.

14. **Was cord blood gas done**?
Record 'Y' if a cord gas was obtained at the time of delivery.
Record pH and base deficit values as documented on the delivery room record in the maternal and/or infant chart. If more than one vessel was sampled, record results from umbilical artery sample.
If Yes,
a. Cord pH (any vessel):
b. Base deficit (any vessel):

15. **Was Infant's first temperature in the NICU within 60 minutes of birth?**
If Yes,
Record the first temperature obtained on the infant after resuscitation and stabilization provided the temperature was recorded within 60 minutes of birth. For centers who admit infants to a holding area or a delivery room stabilization area, record the first temperature taken in this location. This applies for inborn and outborn infants. Record the temperature in centigrade or Fahrenheit.
a. Date:
b. Time:
c. Record the source of the temperature as:
1= Rectal
2= Axillary
3= Skin

Chapter 4
Survey of Morbidity and Mortality - Outcome Data Collection

4.0 Overview of Clinical Outcome Data Collection

4.1 Clinical Outcome - Forms NG03, NG03E and NG05

The outcome data form NG03 (to be completed from the baby's chart through day 120, discharge, transfer or death, whichever comes first) was designed to summarize each baby's clinical course. For infants who die in 12 hours or less, the early death form NG03E is completed in lieu of the NG03, as there are many questions on the NG03 which do not apply to infants who die early. In addition, because an infant's values for some items on NG03 could change after 120 days of hospitalization, form NG05 was created. This late clinical outcome form contains a subset of the items on NG03 and should be completed only for infants hospitalized greater than 120 days, after they have died, have been discharged or have been transferred.

It is very important that form NG03 or form NG03E be coded and entered on in computer system as soon as possible after the baby's discharge, transfer, death or as soon as possible after day 120. Special attention should be paid to obtaining the chart quickly. For example, it may be feasible to intercept the chart before it leaves the NICU for Medical Records.

It should be noted that form NG03 or form NG03E should not be held back for coding or entry into the computer system by waiting for the autopsy report. If the autopsy result for cause of death is to be included, it may be entered on the computer at a later date.

There are several different situations in which the baby leaves the NICU; in each case an effort should be made to obtain as complete data as possible.

4.1.1 Discharge from the NICU to Home

This is the straightforward case: The first date the baby is discharged to home, the baby's clinical data are all obtainable from the medical record in the NICU. If the baby is readmitted to the NICU from home, no further data will be collected.

4.1.2 Transfer to Another Location within the Center

When the baby is transferred from the NICU to a step down unit, another floor, or even another hospital within the same clinical center, the coordinator is still

expected to keep track of the baby and complete form NG03 when the baby finally leaves the clinical center.

4.1.3 Transfer to Another Hospital or to a Chronic Care Facility

The Network Coordinator should attempt to find out the final outcome (death or discharge) for each baby that is transferred out of the clinical center to another hospital. If an infant is transferred back within 7 days, do not count this as a discharge but rather as a continuous admission.

4.1.4 Death

The cause of death is to be recorded (descriptions and codes are listed in Appendix C). If possible, the coordinator should also try to ascertain cause of death for those babies who are transferred out to another hospital and die there.

NG03: GENERIC CLINICAL OUTCOME FORM

4.3 Coding Instructions for Form NG03

4.3.1 Heading

- **Mother's Initials:**
  The Mother's normal initials (first, middle and last). If there is **no** middle initial, record the two initials. **This information is optional.**

- **Birth Number:**
  For a single birth or first born of a multiple birth enter '1. This code establishes a Family ID in the NICU. For the second born code '2' etc. It does not necessarily have to conform to strict birth order from a multiple birth, but must be kept consistent for each baby.

- **Network Number:** The Network number is made up of a four digit Family (Pregnancy) Number plus the Birth Order Number .The Network Number will now be 5 digits.

  When the patient has been entered on the database for the first time, the computer assigns this unique identifier.

4.3.2 Section A - STATUS

1. Status of infant at time of completion of form:

- **Discharged to home**
  Record '1' if infant was discharged to home.

- **Still in hospital at 120 days**
  Record '2' if infant is still in the hospital at 120 days.

- **Transferred to another hospital**
  Record '3' if infant was transferred to another hospital without returning to a Network hospital within 7 days.

- **Transferred to chronic care facility**
  Record '4' if infant was transferred to a chronic care facility without returning in 7 days.

- **Death**
  Record '5' if the infant died.

2. Date of status:
Give date at status.

3. Weight at status:
Weight in grams on day of status (preferably), or within 7 days.

4. Length at status:
Length in centimeters on day of status (preferably), or within 7 days.

5. Head circumference at status:
Head circumference in centimeters on day of status (preferably), or within 7 days.

4.3.3 Section B - PULMONARY

1. Respiratory Distress:

a. Demonstrated clinical features of respiratory distress within the first 24 hours?
Record 'Y' if infant showed signs of grunting, flaring, retracting, paradoxical breathing, cyanosis and/or supplemental oxygen requirement within the first 24 hours.

b. Required oxygen or positive pressure support for more than 6 hours within the first 24 hours?
Record 'Y' for infants who required supplemental oxygen (FiO_2 > .21) and or positive pressure support continuously for more than 6 hours within the first 24 hours.
Note: Positive pressure is mechanical ventilation or CPAP.

2. **Did the baby receive surfactants?**
This includes any surfactant preparation used at any location (delivery room, NICU or at referring hospital).

a. If YES, date and time of first dose;

b. Total number of surfactant doses:
Record total number of doses received from birth to status, including any doses given at a referring center.

3. **Pneumothorax?**
Record 'Y' if pneumothorax is documented in the infant's chart. Pneumothorax is a collection of air in the pleural space where a lucency is identified in the pleural space with displacement of the lung away from the chest wall. Do not include a pneumothorax resulting from a thoracotomy during surgery (e.g. PDA ligation).

4. **Pulmonary hemorrhage?**
Record 'Y' if there was bright red blood per the ET tube associated with clinical deterioration.

5. **Steroids for BPD/CLD?**
Record 'Y' if the infant received any doses or courses of systemic steroids to prevent or treat bronchopulmonary dysplasia/chronic lung disease. Do not include inhaled steroids or doses of steroids given for extubation and/or stridor.

a. If **YES, Date of first dose:**
If 'Y' record the date the infant received the first dose of steroids.

6. **Did infant receive inhaled nitric oxide?**
a. If YES, Date of first exposure:

4.3.4 Section C - CARDIAC

1. **Patent ductus arteriosus (PDA)?**
Record 'Y' if clinical evidence of left to right PDA shunt documented by continuous murmur, hyperdynamic precordium, bounding pulses, wide

pulse pressure, congestive heart failure, increased pulmonary vasculature or cardiomegaly by CXR, and/or increased oxygen requirement or ECHO evidence of PDA with documentation of left to right ductal shunting.

If YES Treatment?

a. **Indomethacin?**
If YES, total number of courses:
A complete course is 3 doses. Some patients receive less than 3 doses because of adverse drug effects, decrease urine output, increased BUN/Cr, decreased platelets, etc. The intent is to give a complete course of 3 doses. If an infant received a partial course and then a second partial or complete course, this should be counted as 2 courses.

b. **Ibuprofin?**
If YES, total number of courses:
A complete course is 3 doses. Some patients receive less than 3 doses because of adverse drug effects, decrease urine output, increased BUN/Cr, decreased platelets, etc. The intent is to give a complete course of 3 doses. If an infant received a partial course and then a second partial or complete course, this should be counted as 2 courses.

c. **Surgery?**
Record 'Y' if surgical ligation was required to close the PDA.

4.3.5 Section D - NEUROLOGIC

1. **Was indomethacin given within the first 24 hours of life for any prophylaxis?**
If Yes,
   a. **Date**
   b. **Time**

2. **Were there seizures treated with an anti-convulsant for > 72 hours?**
Record 'Y' if seizures were treated with anti-convulsant for more than 72 hours.

3. **Were any cranial sonograms done within 28 days of birth?**
Record 'Y' if cranial sonograms were done within the first 28 days of life.

IF **NO**, GO TO QUESTION D5

a. **If YES, Were all studies without evidence of intracranial hemorrhage, peri-ventricular leukomalacia or ventriculomegaly?**

IF YES, GO TO QUESTION D5
If No, continue with question 3b.

b. **Date of sonogram with most severe findings:**
Record the date of the **cranial sonogram** with the most **severe findings** within the first 28 days. Determination of the most severe findings should be based on the following rank order from least severe to most severe. Least severe is blood/echo-density in the germinal matrix/sub-ependymal area followed by blood echo-density in the ventricle, ventricular dilatation and blood/echo-density in the parenchyma is the most severe. **Use the earliest scan of an infant in whom multiple scans have the same most severe findings.**

PLEASE NOTE: Document all the findings on the cranial imaging identified above. For all imaging studies (questions D3, D4 and D6) only record **definite** findings and do not record those that are interpreted as uncertain, probable or possible. **If it is unclear how to record the results of an image, discuss findings with the PI or his designee.** The documentation for items 3c-3g **does not** correspond to a grade of hemorrhage. Items 3c-3g should be considered independent of each other and therefore an infant may have more than one item recorded. For items d-g, indicate side of involvement by marking Y under right (R), left (L), or both.

c. **Blood/echodensity in germinal matrix/subependymal area?**
Record Y if blood/echo-density in the germinal matrix/sub-ependymal area is documented. **When blood echo-density is seen in the ventricle but NOT in the germinal matrix, record 'N' for germinal matrix hemorrhage.**

d. **Blood/echodensity in the ventricle?**
Record Y if blood/echo-density in the ventricle is documented. This finding should be recorded independent of the size of the ventricle. Indicate side of involvement.

e. **Ventricular size enlarged with concurrent or prior blood in the ventricles?**
Record Y if ventricular enlargement occurs in association with blood/echo-density in the ventricular system on any scan. Indicate side of involvement, right, left or both.

f **Ventricular size enlarged without concurrent or prior blood in the ventricles?**
Record Y if ventricular enlargement occurs without blood/echo-density in the ventricular system on any scans. Indicate side of involvement, right, left or both.

g. **Blood/echodensity in the parenchyma?**
Record Y if blood/echo-density in the parenchyma is documented. Intra-parenchymal echo-densities may or may not be accompanied by blood/echo-density in the ventricle. Intra-parenchymal echo-density differs from increased echogenicity. Indicate side of involvement, left, right or both.

NOTE: For sonographic reports that are limited to a grade of ICH (usually I-IV) without a description of the findings record as follows:
Grade I: record as 3c
Grade II: record as 3d
Grade III: record as 3d and 3e
Grade IV: record as 3g
For sonographic reports that are limited to isolated ventricular dilatation without other associated findings **(no blood/echo-density in ventricles)** record as 3f.

For sonographic reports that contain both a grade of ICH and a description, prioritize the descriptive findings over the assigned grade if the two pieces of information are not consistent. **Confirm the latter prioritization with the PI.**

4. **Cystic area(s) in the parenchyma within 28 days?**
If Yes, go to Question 4a.
If No, go to Question 5.

a. **Cystic Periventricular leukomalacia (cPVL)?**
Record as cPVL when this diagnosis is used. In the absence of a diagnosis of cystic PVL on sonographic reports, use cPVL when cysts (echo-lucencies) are described in the white matter around the ventricle. These cysts are most commonly dorsal and lateral to the external angle of the lateral ventricle. Echo-lucencies may be single or multiple, may be bilateral or unilateral, may vary in size, and may be diffuse or focal in distribution along the front to back axis of the head. **If PVL is reported and cysts or echolucencies within the brain parenchyma are not specified, review the scan with the PI or designee of the PI to verify the presence of this finding.** Indicate side of involvement by marking Y under right (R), left (L), or both.

b. Porencephalic cyst?
Porencephalic cyst will be used to lump all cystic disease other than cystic PVL. In the absence of a diagnosis on sonographic reports, use porencephalic cyst when there is a single unitary cyst within the cerebral hemisphere that may or may not communicate with the lateral ventricle. These cysts may be congenital and can be present on sonograms shortly after birth, or may evolve over time at the site of a previous parenchymal blood/echo-density (3g from above). These cysts may also be termed post-hemorrhagic cysts, or if multiple, multi-cystic encephalomalacia. Do not include subependymal cysts or choroids plexus cysts as part of this category. The latter two are minor cysts that will not be recorded. Indicate side of involvement by marking Y under right (R), left (L), or both.

5. Were any cranial imaging studies performed after 28 days of birth?
Record 'Y' if any cranial imaging was done after 28 days of life.

If No, Go to Section E.

6. Cranial imaging study performed closest to 36 weeks postmenstrual age and after 28 days of birth:

a. Type of imaging
Code Type: (1=MRI, 2= Sonogram, 3=CT scan). If the infant has more than one imaging modality within 7 days of the 36 week postmenstrual age date, record results based on the following hierarchy (highest to lowest) of MRI, sonogram, CT scan.

b. Date of imaging
Record the date of the imaging study closest to 36 weeks PCA.

c. Normal Study?
Record 'Y' if the results of the cranial imaging closest to 36 weeks postmenstrual age was reported to be normal.

If No,

d. Ventricle size enlarged?
Record 'Y' if ventricular size was documented to be enlarged. Indicate side of involvement if enlarged.

e. Cystic Periventricular leukomalacia (cPVL):
Record as cPVL when this diagnosis is used. In the absence of a diagnosis of cystic PVL on sonographic reports, use cPVL when cysts (echo-lucencies) are described in the white matter around the ventricle. These cysts are most commonly dorsal and lateral to the

external angle of the lateral ventricle. Echo-lucencies may be single or multiple, may be bilateral or unilateral, may vary in size, and may be diffuse or focal in distribution along the front to back axis of the head. **If PVL is reported and cysts or echolucencies within the brain parenchyma are not specified, review the scan with the PI or designee of the PI to verify the presence of this finding.** Indicate side of involvement by marking Y under right (R), left (L), or both.

f. Porencephalic cyst?
Porencephalic cyst will be used to lump all cystic disease other than cystic PVL. In the absence of a diagnosis on sonographic reports, use porencephalic cyst when there is a single unitary cyst within the cerebral hemisphere that may or may not communicate with the lateral ventricle. These cysts may be congenital and can be present on sonograms shortly after birth, or may evolve over time at the site of a previous parenchymal blood/echo-density (3g from above). These cysts may also be termed post-hemorrhagic cysts, or if more than one, multi-cystic encephalomalacia. Do not include subependymal cysts or choroids plexus cysts as part of this category. The latter two are minor cysts that will not be recorded. Indicate side of involvement by marking Y under right (R), left (L), or both

4.3.6 Section E - INFECTIONS

Organism codes for this section are listed in Appendix A. If the organism is not included in the list, code as '010' (to be assigned), and notify the DCC that a new code should be assigned. The DCC will issue new lists periodically.

1. Early onset septicemia/bacteremia (≤72 hrs)?
Record 'Y' if there was a positive blood culture drawn within the first 72 hours.

a. If YES, organism code(s):
Record the code(s) of organism(s) identified. If there were more than two organisms identified, list the organisms felt to be most important.

2. Did the infant receive antibiotics for ≥ 5 days, starting within the first 72 hours?
Code 'Y' if the infant was treated with antibiotics for five or more days beginning by 72 hours. Include cases where the infant died before an intended therapy of five or more days was completed.

3. **Number of episodes of late onset blood culture negative clinical infection (> 72 hours to status) treated with antibiotics for ≥ 5 days?**
An episode is defined as a blood culture obtained and antibiotics started. Record the number of culture negative episodes, occurring after 72 hours, treated with antibiotics for five or more days. Include cases where the infant died before an intended therapy of five or more days was completed.

4. **Late onset culture positive septicemia/bacteremia (> 72 hrs)?**
Record 'Y' if there was a positive culture of blood, obtained in the presence of compatible clinical signs of septicemia, occurring after 72 hours.

If YES,

a. **Number of episodes between day 3 and status that were treated with antibiotics for ≥ 5 days:**
Record the number of episodes of culture positive septicemia/bacteremia, occurring after 72 hours, treated with antibiotics for ≥ 5 days. Include positive episodes in which the infant dies before an intended therapy of five or more days is completed. A new organism cultured at any time is considered an additional episode. If the same bacterial organism is cultured, after 10 days of appropriate antibiotic therapy, this is considered a second episode.

b. **Organism code(s) and date of first positive culture for each of episodes for which the infant was treated with antibiotics for ≥ 5 days:**
Record the date and organism code(s) from positive blood culture(s) for which the infant was treated, or where there was intent to treat, for ≥ 5 days. If more than 3 organisms are identified, list the 3 organisms felt to be the most important. If the same organism is isolated under the circumstances described in a. (above), the code is repeated.

***For clarification on coding refer to Appendix I.**

5. **Meningitis?**
Record Y' if there was a positive cerebrospinal fluid (CSF) culture and treatment (or intent to treat) with antibiotics or antifungals for 7 or more days.

a. **If YES, organism code(s):**
Record the date and code(s) of organism(s) identified. If there were more than three organisms identified, list the three organisms felt to be most important

Use Appendix A to obtain code(s) for identified organism(s)

4.3.7 Section F – GASTROINTESTINAL

1. **Did weight ever fall below the birth weight during the first 10 days?**
Record 'Y' if the infant's weight recorded was below his/her birthweight.
If Yes,
   a. **Lowest weight in the first 10 days.**
   Record the lowest weight recorded in the first 10 days.
   b. **Date of lowest weight in the first 10 days.**
   Record the date of the lowest recorded weight for the infant during the first 10 days.
   c. **Was birth weight regained?**
   If Yes,
   d. **Date birth weight first regained.**
   Record the date when the infant first regained his/her birth weight.

2. **Did the baby receive parenteral alimentation?**

   If YES,
   a. **Date of first parenteral alimentation:**

   b. **Parenteral alimentation, total number of days:**
   Record the number of days in which the baby received parenteral alimentation including amino acids or lipid solution at some point during the day.

3. **Did the baby receive enteral feeds?**

   If YES,
   Record 'Y' if the infant was fed enterally. Feeds consist of formula or breast milk. Sterile water is not considered enteral feeding.

   a. **Date of first enteral feed:**

   b. **Did enteral feeds reach 120 ml/kg/day?**
   Calculate using the current weight.

   If YES, date first achieved?
   Record the date first achieved.

c. **Did the baby receive any breast milk in the first 28 days?**
Record 'Y' if medical record indicates that the infant received any breast milk in the first 28 days.

1) If YES, number of days baby received any breast milk in the first 28 days.

4. **Proven necrotizing enterocolitis (NEC) Diagnosis:**
Code the correct response using the Modified Bell's Staging Criteria for NEC in Appendix G. Also refer to Appendix I.

- Code '0' (Absent/Suspect) when there is no necrotizing enterocolitis present or in the presence Bell's Stage IA or IB.
- Code '2' (Proved, no surgery, Stages IIA, IIB or IIIA) or '3' (Proved, surgery, Stage IIIB) as appropriate.

a. **If proven NEC, record date of first episode**.

5. **Spontaneous gastrointestinal perforation without proven NEC?**
Record 'Y' if the infant has a spontaneous gastrointestinal perforation separate from necrotizing enterocolitis.

a. **If YES, Date of the first spontaneous gastrointestinal perforation:**
Record the date on which the first spontaneous gastrointestinal perforation occurred.

6 **Did the infant have GI surgery that resulted in short gut?**
Record 'Y' if the infant had surgery involving the GI that resulted in the diagnosis of short gut which includes malabsorption, severe diarrhea, gastric hypersecretion, secondary bacterial overgrowth and failure to thrive. Record surgical procedure in Section J.

4.3.8 Section G - HEARING

1. **Was a hearing screen performed?**
Record 'Y' if a hearing screen was performed to evaluate the infant's hearing while in the hospital.

a. **If 'Y'**, record the type of hearing screen protocol used:
1= OAE (otoacoustic emissions)
2= AABR (automated auditory brainstem responses)
3= ABR (auditory brainstem responses)
4= OAE + AABR
5= other protocol

b. Final screen results before status:
Record for each ear the results of the final screen before discharge as noted in hospital chart:
1= pass
2= fail
3= incomplete

c. If a failed screen in either ear, was a diagnostic ABR done prior to status?
If 'Y', record the results for each ear. If no result was recorded for either ear, enter *
1= pass
2= fail
3= incomplete

4.3.9 Section H – OPHTHALMOLOGIC

For your use, Appendix D contains a Retinopathy of Prematurity (ROP) Diagram.

1. Was an exam performed for Retinopathy of Prematurity (ROP)?
Review the medical record to determine if an examination was performed for ROP and flag all examinations found in order to answer the remainder of the questions. Record 'Y' if an ophthalmologist examined the infant's eyes for ROP. The exams usually begin at 4 to 6 weeks and continue until the retinal vasculature is mature.

If Yes,

a. Was ROP diagnosed in either eye?
Code 'Y' if ROP diagnosed prior to 'status' (any stage) in either eye in any of the examinations.

If Yes,

1. Did it reach stage 3 or worse in either eye?
Code 'Y' if it reached stage 3 or worse in either eye.

2. Did plus disease develop in either eye?
Plus disease is noted by the ophthalmologist separately from the stage and zone. It is recorded as present or not. Sometimes it is referred to as "posterior pole vascular dilation and tortuosity". Usually if this is present on any examination, it is close to the worst ROP time for the infant. Record 'Y' if plus disease was observed on the worst exam

recorded above for either eye. When the posterior veins of the retina are enlarged and the arterioles tortuous, then the designation "plus" is added to the ROP stage number. For example, Stage 2 with plus disease is sometimes written 2+.

b. Intervention therapies:

1. **Was retinal ablation performed in either eye (laser and/or cryotherapy?**

2. **Was any scleral buckle or vitrectomy performed in either eye?**

2. At the time of reaching status, indicate the most appropriate description as described below:

1= Determined, favorable in both eyes

EACH eye met one of the following criteria

- Vessels mature (aka fully vascularized)
- Vessels in zone III for two consecutive examinations
- Acute ROP of stage 1 or 2 in zone III for two consecutive examinations
- ROP in zone II or zone III but determined to be clearly regressing

2= Determined, severe ROP in either eye

Severe: EITHER eye met one of the following criteria

- Received surgery for ROP
- Retinal detachment from ROP

3= Undetermined ROP status in either eye (and neither had 'severe ROP")

EITHER eye met one of the following criteria:

- Immature vessels in zone I or zone II
- Immature vessels reaching zone III for only 1 consecutive examination
- Stage 1 or 2 ROP in zone III for only 1 consecutive examination
- Stage 3 ROP in zone III
- ROP in zone I or zone II
- plus disease

4.3.10 Section I - SYNDROMES

1. Syndromes and/or major malformations?

Record 'Y' if any syndromes and/or major malformations were observed, including Downs syndrome, chromosomal abnormalities, and other syndromes with multi-organ involvement.

a. If **YES, code:**
Record the code(s) of the syndromes and/or major malformations that were observed. The Syndrome/Major malformation codes are listed in Appendix H: Birth Defect Codes.

i) **If a syndrome is coded 699, specify**:
Write the specific name of the syndrome indicated.

4.3.11 Section J - MAJOR SURGERY

1. **Other major surgery not covered in previous sections?**
Record 'Y' if any surgery not mentioned in previous section occurred prior or on day 120.

a. If **YES, Code:**
See Appendix E for major surgery codes.

i) **If a major surgery is coded 999, specify**:
Write the specific name of the surgery performed.

4.3.12 Section K - 36 WEEK INFORMATION

If the infant has not been discharged by 36 weeks gestational age then record the following information at 36 weeks gestational age.

1. **Status at 36 weeks:**

- **Discharged to home**
  Record '1' if infant was discharged to home.

- **Still in hospital at 36 weeks Gestational Age**
  Record '2' if infant is still in the hospital at 36 weeks.

- **Transferred to another hospital**
  Record '3' if infant was transferred to another hospital without returning in 7 days.

- **Death**
  Record '5' if the infant died.

If 2 (In Hospital):

a. **Date of 36 week measurement:**
Record the actual date that this measurement was taken.

NOTE: The measurements may not be taken on the same calendar day but all should be within the window at 36 weeks (± 7 days). If all the measurements are not taken on the same day, then the date recorded should be that of the weight at 36 weeks ± 7 days.

b. Weight:
Record the weight in grams at 36 weeks (+-7 days) gestational age.

c. Length:
Record the length in centimeters at 36 weeks (+- 7 days) gestational age.

d. Head circumference:
Record the head circumference in centimeters at 36 weeks (+- 7 days) gestational age.

4.3.13 Section L - FEEDING STATUS

Complete this section if status of infant at time of completion of this form is Code '1' discharged to home.

1. Type of nutrition at discharge to home (*Do not complete for transfer patients). Complete for all that apply.*
Use following codes:
1= Breastmilk (Mother's milk, donor milk, fortified or not).
2= Formula
3= TPN

2. If enteral mode. Use following codes and code all that apply:
1= Breast
2= Bottle
3= NG/NJ tube
4= Gastrostomy tube
9= Unknown

4.3.14 Section M - TRANSFER

This section refers to when the infant is sent to another hospital or chronic care facility without returning in 7 days.

1. Date of transfer:
Record date of transfer.

2. Final outcome:
Code '1' if the baby died in hospital (informed via telephone contact or letter from the other hospital), Code '2' if the baby was discharged to home, Code '6' if the baby is still in hospital one year post natal age.

a. **If discharged to home, final weight at discharge:**
Enter final weight at discharge in grams.

4.3.15 Section N - DISCHARGE ALIVE

This refers to when the baby is finally discharged home.

1. **Date of discharge to home:**
Give date of discharge.

2. **Discharged home on continuous oxygen?**
Code 'Y' if discharged home on continuous oxygen.

3. **Discharged home on any of the following medications?**
Record 'Y' if infant is discharged home on any medication(s) listed below. If 'Y', record which medications the infant was to be receiving after discharge.
   a. **Diuretics** including but not limited to furosemide, spironolactone, chlorothiazide, or hydrochlorothiazide
   b. **Bronchodilators** including but not limited to albuterol.
   c. **Anticonvulsants** including but not limited to Phenobarbital, dilantin, valproic acid, depakane, carbamapepzine
   d. **Antireflux medications** including but not limited to ranitidine, famotidine, metaclopramide

4.3.16 Section O - DEATH

1. **Date of death:**

   a. Time of death:

2. **Autopsy performed?**
If an autopsy is performed the cause of death should not be coded until the results of the autopsy are known.

3. **Contributory cause of death:**
This should be the underlying, proximate disease which initiated the train of events leading to the cause of death. This underlying cause must be (1) etiologically specific and (2) antecedent to all other causes with respect to time and pathologic relationship. Without the underlying cause, death would not have occurred. The cause of death should be based on both clinical evidence and autopsy findings. In the absence of an autopsy, the clinical evidence will be used. Only one of the options is to be coded, after consultation with the PI or alternate PI.

A description of the causes of death is listed in Appendix C.

4. **If contributory cause of death is code 10 (Congenital malformation) or code 90 (Other), specify:**

5 **Was respiratory support withheld or withdrawn at any time after the first 24 hours and prior to death?**
Record 'Y' if a decision by made by the attending physician after discussion with the family to withhold or withdraw usual respiratory support therapies due to the extreme prematurity, severity of illness or congenital malformation with the expectation that the infant will expire imminently.

NG03E: GENERIC EARLY DEATH FORM

4.4 Coding Instructions for Form NG03E

4.4.1 Heading

- **Mother's Initials:**
  The Mother's normal initials (first, middle and last). If there is **no** middle initial, record the two initials. **This information is optional.**

- **Birth Number:**
  For a single birth or first born of a multiple birth enter '1. This code establishes a Family ID in the NICU. For the second born code '2' etc. It does not necessarily have to conform to strict birth order from a multiple birth, but must be kept consistent for each baby.

- **Network Number:** The Network number is made up of a four digit Family (Pregnancy) Number plus the Birth Order Number. Therefore the Network Number is 5 digits.

When the patient has been entered on the database for the first time, the computer assigns this unique identifier.

4.4.2 NG03E Form Questions

To be completed if the infant died at < 12 hours of age.

1. **Location of death:**
Code '1' if infant died in delivery room. Code '2' if infant died in the NICU. If the infant was treated in the NICU and died in the mother's room, code '2' NICU.

2. **Received ventilator support?**
Include all forms of support with a ventilator after initial resuscitation.

If YES, duration of ventilator support (to the nearest 1/4 hour)
Record duration in hours and minutes.

a. **Hours:**

b. **Minutes:**

3. **Received intravenous fluid therapy?**

4. **Medical therapy initiated**

a. **Antibiotics?**

b. **Surfactant replacement therapy?**

c. **Pressor support?**
This is to include Dopamine, Dobutamine, Epinephrine and Isuprel.

d. **Volume support?**
This is to include albumin 5% or 20%, blood transfusion, fresh frozen plasma, Plasmanate and Ringers Lactate.

5. **Autopsy performed?**
If an autopsy is performed the cause of death should not be coded until the results of the autopsy are known.

6. **Was respiratory support withheld or withdrawn at any time prior to death?**
Record 'Y' if a decision was made by the attending physician after discussion with the family, to withhold or withdraw usual respiratory therapies due to extreme prematurity, severity of illness or congenital malformation with the expectation that the infant will expire imminently.

7. **Contributory cause of death:**
This should be the underlying, proximate disease which initiated the train of events leading to the cause of death. This underlying cause must be (1) etiologically specific and (2) antecedent to all other causes with respect to time and pathologic relationship. Without the underlying cause, death would not have occurred. The cause of death should be based on

both clinical evidence and autopsy findings. In the absence of an autopsy, the clinical evidence will be used. Only one of options is to be coded, after consultation with the PI or alternate PI.

A description of the causes of death is listed in Appendix C.

8. **If contributory cause of death is code 10 (Congenital malformation) or code 90 (Other), specify:**

NG05: LATE CLINICAL OUTCOME FORM

4.5 Coding Instructions for Form NG05

The NG05 is to be completed for infants who are hospitalized greater than 120 days, after the infant dies, is discharged, is transferred, or reaches one year post-natal age. When completing questions on the NG05 consider only diagnoses and treatments made after day 120.

4.5.1 Section A STATUS

1. **Status of infant at time of completion of form:**

- **Discharged to home**
  Record '1' if infant was discharged to home.

- **Transferred to another hospital**
  Record '3' if infant was transferred to another hospital without returning in 7 days.

- **Transferred to chronic care facility**
  Record '4' if infant was transferred to a chronic care facility without returning in 7 days.

- **Death**
  Record '5' if the infant died.

- **Remains in hospital at one year**
  Record '6' if the infant is still in hospital after one year post-natal age.

2. **Date of status:**
   Give date at status.

3. **Weight at status:**
   Weight in grams at status (preferably), or within 7 days.

4. **Length at status:**
Length in centimeters at status (preferably), or within 7 days.

5. **Head circumference at status:**
Head circumference in centimeters at status (preferably), or within 7 days.

4.5.2 Section B - EXTENDED STAY INFORMATION

1. **What problem (s) caused hospitalization greater than 120 days:**
Answer 'Y' to all that apply.

   a. **Pulmonary?**
   b. **Cardiac?**
   c. **Neurologic?**
   d. **Gastrointestinal?**
   e. **Multiple Malformations?**
   f. **Social**
   g. **Ophthalmologic?**
   h. **Other? (If Yes, specify)**

2. **After reaching status, did either eye receive surgery for ROP?**

   a. **If Yes, List all surgeries done for either eye (Use codes below):**
   1= Laser treatment
   2= Cryotherapy
   3= Scleral buckle
   4= Vitrectomy
   5 = Other (specify for either eye)

3. **Was a hearing screen performed after 120 days?**
Record 'Y' if a hearing screen was performed to evaluate the infant's hearing while in the hospital.

   a. **If 'Y', record the type of hearing protocol used:**
   1= OAE (otoacoustic emissions)
   2= AABR (automated auditory brainstem responses)
   3= ABR (auditory brainstem responses)
   4= OAE + AABR
   5= other protocol

   b. **Final screen results before discharge**:
   Record for each ear the results of the final screen before discharge as noted in hospital chart:
   1= pass
   2= fail

3= incomplete

c. **If a failed screen in either ear, was a diagnostic ABR done prior to discharge**?
If 'Y', record the results for each ear. If no result was recorded for either ear, enter *

4.5.3 Section C - TRANSFER

This section refers to when the infant is sent to another hospital or chronic care facility without returning in 7 days.

1. **Date of transfer:**
Give date of transfer.

2. **Transferred on oxygen?**

3. **Transferred on ventilator and/or CPAP?**

4. **Final outcome:**
Code '1' if the baby died in hospital (informed via telephone contact or letter from the other hospital). Code '2' if the baby was discharged to home. Code '3' if the baby remains in the hospital at one year of age.

   a. **If Discharged to home, final weight:**

4.5.4 Section D - DISCHARGE ALIVE

This refers to when the baby is finally discharged home.

1. **Date of discharge to home:**
Give date of discharge.
2. **Discharged home on continuous oxygen?**
Code 'Y' if discharged home on continuous oxygen.
3. **Discharged home on any of the following medications?**
Record 'Y' if infant is discharged home on any medication(s) listed below. If 'Y', record which medications the infant was to be receiving after discharge.
   a. **Diuretics-** including but not limited to furosemide, spironolactone, chlorothiazide, or hydrochlorothiazide
   b. **Bronchodilators-** including but not limited to albuterol.
   c. **Anticonvulsants** including but not limited to phenobarbital, dilantin, valproic acid, depakane, carbamapepzine

d. **Antireflux medications-** including but not limited to ranitidine, famotidine, metaclopramide

4.5.5 Section E - DEATH

1. **Date of death:**

2. **Autopsy performed?**
If an autopsy is performed, the cause of death should not be coded until the results of the autopsy are known.

3. **Contributory cause of death:**
This should be the underlying, proximate disease which initiated the train of events leading to the cause of death. This underlying cause must be (1) etiologically specific and (2) antecedent to all other causes with respect to time and pathologic relationship. Without the underlying cause, death would not have occurred. The cause of death should be based on both clinical evidence and autopsy findings. In the absence of an autopsy, the clinical evidence will be used. Only one of the options is to be coded, after consultation with the PI or alternate PI.

   A description of the causes of death is listed in Appendix C.

4. **If cause of death is code 10 (Congenital malformation) or code 90 (Other), specify:**

Chapter 5
THE RESPIRATORY SUPPORT DATA

5.1 Respiratory Support Form NG07:

This form should be completed for all GDB infants who have survived for □12 hours who reach Status (death, discharge, transfer or 120 days). Document the support the infant received during the hospitalization at the time points noted. If infants survived □12 hours but death occurred < 24 hours, fill in data in Status column only. The PHY01 and PHY02 are used as the Physiologic Definition of BPD worksheets. The manual for the stand alone Physiologic Definition of BPD study is used as the Physiologic Definition of BPD workbook. Continue to use these documents for reference purposes. The worksheets will be retained in the site GDB study folders and will not be entered into the DMS. Requests to use data captured on the worksheets must be approved by the NICHD NRN Steering Committee and local IRBs.

The respiratory support box collects respiratory data in ~~two~~ three ways:

A) By SNAPSHOT- recording the respiratory support at exactly 24 hours and highest level of support on day of 36 weeks postmenstrual age. If the infant reaches Status (death, discharge, transfer) before any time point(s), no data is entered for the missed time point(s).

B) By CUMULATIVE DATA- recording the total number of days for each type of support (across a row) at each time point listed (day 3, 7, 14, 28, 36 wk and Status) cumulative over the hospitalization. If the infant reaches Status (death, discharge, transfer) before any time point(s), no data is entered for the missed time point(s).

C) By PHYSIOLOGIC EVALUATION – to conduct a physiologic monitored reduction of oxygen in eligible infants at 36 +1 weeks corrected age who are receiving oxygen to establish the definition of bronchopulmonary dysplasia. Infants are screened at exactly 36 weeks of age and, if eligible receive the challenge as close as possible to 36 weeks but no later than 37 weeks PMA

Section A- SNAPSHOT DATA

At 24 hours from birth:

For questions #1-4, record 'Y' for the type of support the infant is receiving at exactly 24 hours from birth. If the infant is not receiving the type of support, record 'N'.

Question #6 and #7- ONLY ONE QUESTION WILL BE ANSWERED.

Question #6- record the **highest** amount of oxygen the infant is receiving at exactly 24 hours from birth by ventilation (any mode), CPAP, nasal SIMV, Hood or isolette. If the infant is in room air record the FiO_2= 0.21.

OR

Question #7- record 'Y' if the infant is receiving supplemental oxygen (FiO_2 >0.21) by nasal cannula (any flow and oxygen concentration) at exactly 24 hours from birth.

Question #8- if the amount of oxygen in question #6 is recorded as 0.21, record 'Y' if the infant is receiving room air (FiO_2= 0.21) by nasal cannula, ~~CPAP or ventilation (any mode).~~ Otherwise record 'N'.

At 36 weeks postmenstrual age:

Questions #1-4- record 'Y' for the highest type of support the infant is receiving for the day of 36 weeks postmenstrual age (i.e. if the infant was receiving conventional ventilation (CV) and high frequency ventilation (HFV) on the day of 36 week postmenstrual age, count only the HFV for that day). The hierarchy for support will be HFV as highest, CV as next, nasal SIMV next, then CPAP as lowest type of support.

Question #6 and #7- ONLY ONE QUESTION WILL BE ANSWERED.

Question #6- record the highest amount of oxygen the infant is receiving on the day of 36 weeks postmenstrual age by ventilation (any mode), CPAP, nasal SIMV, Hood or isolette. If the infant is in room air record the FiO_2= 0.21.

OR

Question #7- record 'Y' if the infant is receiving supplemental oxygen (FiO_2 >0.21) by nasal cannula (any flow and oxygen concentration) on the day of 36 weeks postmenstrual age.

Question #8- if the amount of oxygen in question #6 is recorded as 0.21, record 'Y' if the infant is receiving room air (FiO_2= 0.21) by nasal cannula, ~~CPAP or ventilation (any mode).~~ Otherwise record 'N'.

If in section 'A', Snapshot @36 weeks, questions 1 - 4 ~~or 7 or 8 are~~ answered ~~"Yes"~~ NO ~~or~~ and in question 6 FiO_2 > 0.21% ~~or question~~ 7 or 8 are answered YES, the INFANT IS ELIGIBLE TO BE SCREENED *(refer to Physiologic Definition of BPD Workbook)*, then complete ~~the PHYS1 form~~ section C below.

Section B- CUMULATIVE DATA

Questions #1-5- For the columns Day 3 through STATUS, record the cumulative number of days the infants has received each type of support. The cumulative data will be calculated from birth (day of life 1) to Day 3, birth to Day 7, birth to Day 14, birth to Day 28, birth to day of 36 weeks postmenstrual age and birth to STATUS.

For each day the infant is in the hospital from birth, count only the highest type of respiratory support (including HFV, CV, Nasal SIMV and CPAP) for that day, i.e. if the infant was receiving conventional ventilation (CV) and high frequency ventilation (HFV) on the same calendar day , count only the HFV for that day.

The hierarchy for respiratory support will be HFV as highest, CV as next, Nasal SIMV next, then CPAP as lowest type of support.

The last entry is STATUS which will document the total number of days of HFV, CV (all modes of conventional ventilation including IMV, SIMV, and/or assist control where the infant has an endotracheal tube in place), Nasal SIMV (via nasal prong or cannula), CPAP (via nasal prongs or cannula) and supplemental oxygen (delivered by any method including ventilator, CPAP, hood, isolette, **or** cannula~~, or vapotherm~~).

Question #6 and #7- ONLY ONE QUESTION WILL BE ANSWERED
Question #6- Record the highest FiO2 for infants who are receiving oxygen (delivered by HFV, CV, Nasal SIMV, CPAP, hood or isolette) the infant has received on Day 3, Day 7, Day 14, Day 28, on day of 36 weeks postmenstrual age and on day of STATUS. When determining the highest FiO2 for the day, disregard any temporary increases in FiO2 for desaturation episodes, apnea, bradycardia or procedures, where the infant returns to his/her previous FiO2 in a reasonable amount of time **(< 2 hours)**. DO NOT include supplemental oxygen given **only** with feedings.

OR

Question#7- record 'Y' if the infant is receiving supplemental oxygen (FiO_2 >0.21) by nasal cannula (any flow and oxygen concentration) on Day 3, Day 7, Day 14, Day 28, on day of 36 weeks postmenstrual age and on day of STATUS. Supplemental oxygen by ~~Vapotherm~~ **high flow nasal cannula** is counted here.

Question #8- if the amount of oxygen in question #6 is recorded as 0.21, record 'Y' if the infant is receiving room air (FiO_2= 0.21) by nasal cannula, CPAP or ventilation (any mode). Otherwise record 'N'.

NOTE: Questions 6, 7and 8 in Section B @36 weeks postmenstrual age **will not be answered because this section is already recorded in Section A @ 36 weeks postmenstrual age.**

NOTE: If an infant is in a hood or flooded isolette, de-flood the isolette before infant is challenged.

Section C- PHYSIOLOGIC EVALUATION

Complete section C if in section 'A', Snapshot @36 weeks, questions 1 - 4 are answered 'N' and in question 6 FiO_2 > 0.21 or questions 7 or 8 are answered 'Y'.

Question #1. Is the infant eligible for the physiologic evaluation? Record 'Y' if the patient is eligible according to criteria in section B of the PHY01 worksheet.

Question #1.a. If Question #1 is answered 'Y', record 'Y' if the evaluation was performed. Otherwise, record 'N'.

IF YES to Question 1.a

If Question #1.a is answered 'Y', the evaluation was performed, record the date of the evaluation (month/day/year) in Question #1.b.

Record the actual FiO2 being delivered at time of challenge for Question #1.c. For infants receiving blended supplemental oxygen via nasal cannula, record the blend in this field

If the infant is on nasal cannula at time of challenge, record the flow rate in LPM for Question #1.d.

For Question #1.e, if the patient passed the challenge, record 'Y'. Otherwise record 'N'.

IF NO to Question 1.a

If Question #1.a is answered 'N', the evaluation was NOT performed, record the reason why the evaluation was not done for Question #1.f.

Codes:

1= Increased FiO_2
2= Increased respiratory support (cpap or vent)
3= Instability (including Surgery/Sepsis)
4 = Parent/Physician Refusal
6 = Weaned to room air on/before day of evaluation
9 = Other- explain

Chapter 6
Revisions/Additions to the GDB

6.0 Overview

It is recognized that changes (additions, deletions, revisions) to the GDB will be necessary periodically. Such changes may be: 1) permanent changes to the core GDB; or 2) time-limited data collection for studies which relate to areas of special interest. All proposed changes to the GDB must undergo thorough, prospective and formal review to determine whether the proposed changes are appropriate and acceptable.

The core GDB is a limited data set which represents important/essential information (which is expected to change over time) for all VLBW infants. The core GDB is not intended to include detailed data on areas of special interest in the VLBW population. Such data, in sufficient detail to provide meaningful information, can be collected as an addendum to the core GDB after appropriate approval.

It is the understanding of the GDB Subcommittee that areas of special interest generally lend themselves to data collection for a finite period of time; i.e. special interest data collection forms are not considered part of the core GDB. The process for proposing changes to the GDB, either permanent or temporary, is described in Section 6.1

6.1 Process of Proposing Revisions/Additions to the GDB

All proposed changes to the GDB must be submitted as a formal proposal to the Protocol Review Subcommittee (PR Subcommittee).

The Chair of the PR Subcommittee will determine whether the proposal is acceptable (contains all information required for review as identified by policies established by the Protocol Review Subcommittee). The Chair will also determine whether the proposal requires full review by the PR Subcommittee or whether it may be reviewed by the GDB Subcommittee (without prior full review by the PR Subcommittee).

If a proposal is reviewed and approved by either the PR or the GDB Subcommittee, the proposal will be reviewed by the Steering Committee for final approval prior to implementation.

APPENDIX A
ORGANISM CODES LIST

Code	Genus	Species
Bacteria		
310	Achromobacter	sp. [inc. Achromobacter xylosoxidans and others]
320	Acinetobacter	sp. [antiratus, baumannii calcoaceticus, haemolyticus, johnsonii, junii, lwoffii, radioresistens]
330	Aeromonas	sp.
340	Alcaligenes	sp. [Alcaligenes xylosoxidans and others]
140	Bacillus	sp.
410	Bacteroides	sp.
160	Bifidobacterium	sp. [Bifidum, lactis, infantis, thermophilum, and others]
350	Burkholderia	sp. [Burkholderia capecia and others]
360	Campylobacter	sp. [Campylobacter fetus, C. jejuni and others]
370	Chryseobacterium	sp.
226	Citrobacter	sp. [Citrobacter diversus, C. freundii, C. koseri and others]
420	Clostridia	sp.
500	Corynebacterium	sp.
240	Enterobacter	sp. [Enterobacter aerogenes, E. cloacae, and others]
380	Enterococcus	sp. [Enterococcus faecalis (a.k.a. Streptococcus faecalis and Streptococcus Group D), E faecium, and other Enterococcus species]
200	Escherichia	coli
390	Flavobacterium	sp.
590	Hemophilus	sp. [Haemophilus influenzae, H. vaginalis and others]
325	Herellea	vaginicola
230	Klebsiella	sp. [Klebsiella oxytoca, K. pneumoniae and others]

Code	Genus	Species
170	Lactobacillus	sp. [Acidophilus, casei, and others]
150	Listeria	sp. [Listeria monocytogenes]
105	Micrococcus	sp.
430	Moraxella	sp. [Moraxella catarrhalis (a.k.a. Branhamella catarrhalis) and others]
570	Neisseria	sp. [Neisseria meningitides, N. gonorrhoeae and others]
440	Pasteurella	sp.
460	Peptostreptococcus	sp.
480	Prevotella	sp.
470	Propionibacterium	sp.
260	Proteus	sp. [Proteus mirabilis, P. vulgaris and others]
300	Pseudomonas	sp.
301	Pseudomanas	aeruginosa
210	Salmonella	sp.
250	Serratia	sp. [Serratia liquefaciens, S. marcescens odorifera, ficara, plymuthica and others]
101*	Staphylococcus	aureus [coagulase positive]
104	Staphylococcus	coagulase negative (including S. epidermis, saprophyticus, haemolyticus, hominis, lugdunensis, simulans, cohnii, warnei, saccharolyticus)
510	Stenotrophomonas	maltophilia
111	Streptococcus	viridans
112	Streptococcus	Group A
113	Streptococcus	Group B

*Note- call lab if unclear whether staphylococcus is coagulase negative, coagulase positive, aureus or epi.

133	Streptococcus	pneumoniae
699	Other; Code to be assigned	

Code	Genus	Species
Fungi		
834	Aureobasidium	sp.
810	Candidia	sp.
811	Candidia	ablicans
813	Candida	krusei
816	Candidia	parapsilosis
817	Candidia	tropicalis
819	Candidia	glabrata
820	Candidia	guilliermondi
821	Candidia	lusitaniae
881	Malassezia	fur fur
872	Saccharomyces	sp. [yeast]
899	Other; Code to be assigned	
Resistant Organisms		
750	Methicillin resistant staphylococcus aureus (MRSA)	
760	Vancomycin resistant enterococci (VRE)	
Other Organism		
010	Other; Code to be assigned	

APPENDIX B
Drug Therapeutic Agent List

Penicillins

01= Ampicillin
02= Carbenicillin
03= Oxacillin
04= Penicillin G
05= Piperacillin
06= Ticarcillin
07= Mezlocillin
08= Methicillin
09= Nafcillin
10= Amoxicillin
11= Amoxicillin/clavulanate (Augmentin)

Cefalosporins

19= Cephalexin (Keflex)
20= Cephalothin
21= Cefazolin (Kefzol)
22= Cefotaxime (Claforan)
23= Cefoxitin
24= Moxalactam
25= Ceftazidime (Fortaz)
26= Ceftriaxone (Rocephin)
27= Ceftizoxime
28= Cefuroxime
29= Cefotetan
30= Cefixime

Aminoglycosides

31= Amikacin
32= Gentamicin
33= Kanamycin
34= Tobramycin

Other Antibiotics

44= Vancomycin
46= Bactrim
47= Chloramphenicol (Chloromycetin)
49= Clindamycin
50= Erythromycin

Other Antibiotics (continued)

91= Linezolid
62= Imipenem
63= Metronidazole
64= Aztreonam
67= Ampicilling + sulbactam (unasyn)
68= Azithromycin
70= Cefepime
75= Meropenem
76= Piperacillin + tazobactam (zosyn)
77= Rifampin
78= Ticarcillin + clavulanate
80= Ciprofloxacin
81= Clarithromycin (Biaxin)
82= Doxycycline
83= Trimethopin/sulfa (TMP/SMX)

Antifungals

43= Flucytosine (5FC)
48= Nystatin
61= Fluconazole
69= Caspofungin
92= Itraconazole
93= Posaconazole
94= Voriconazole
41= Amphotericin B
66= Amphotericin B Liposome (Ambisome)
95= Amphotericin B lipid complex (Abelcet)
97= Anidulafungin
98= Micafungin

Antivirals

45= Vidarabine
71= Acyclovir (Zovirax)
72= Ganciclovir
73= Nevarapine
74= Zidovuldine (AZT)
96= Valacyclovir hydrochloride (Valtrex)

Other Drugs Not Listed

99= Other

Appendix C
Causes of Death

Malformation

10 - Congenital malformation

Code '10' for major congenital malformations that are incompatible with life, or incompatible with life without drastic surgical or other measures to maintain life such as a chromosomal defect, inborn error of metabolism, neural tube defect, congenital heart disease, or renal abnormality. If an infant has respiratory distress syndrome or intracranial hemorrhage but is allowed to die because his/her main problem is the congenital malformation, then malformation should be coded as the cause of death.

Pulmonary

20 - RDS

Code '20', RDS, for severe respiratory insufficiency in the presence of RDS during the first 28 days of life where the infant dies of respiratory insufficiency, i.e., increasing oxygen and pressure requirements, pneumothorax, pneumopericardium, etc.

21 - RDS with severe intracranial hemorrhage

Code '21' for infants with severe respiratory insufficiency during the first 28 days of life with a severe (grade III-IV) intracranial hemorrhage. If an infant dies or is allowed to die because of or with the severe intracranial hemorrhage, the cause of death is really the respiratory insufficiency rather than the intracranial hemorrhage.

22 - RDS with infection

Code '22' for infants with severe respiratory distress during the first 28 days who have a fulminent pulmonary or other infection. For example, if an infant has group B strep sepsis with a clinical presentation of respiratory distress, or respiratory distress syndrome with an intercurrent bacterial infection then RDS with infection should be coded as the cause of death.

23 - RDS with massive pulmonary hemorrhage

Code '23' for infants with respiratory distress and massive pulmonary hemorrhage during the first 28 days of life.

25 - BPD

Code '25', for infants with chronic lung disease after 28 days of life who die of progressive respiratory insufficiency, with or without cor-pulmonale.

26 - BPD with infection

Code '26' for infants with chronic lung disease requiring oxygen for more than 28 days who develop a severe intercurrent infection. The combination of the chronic lung disease and infection usually predisposes the child to death.

27 - BPD with severe CNS insult

Code '27' for infants with chronic lung disease who have an oxygen requirement of more than 28 days where the lung disease is progressing and will most probably eventually cause death, but the infant is extubated prior to death because of severe brain atrophy, hydrocephalus, etc.

Infection

30 - Suspect sepsis/infection

Code '30' for infants with clinical presentation of septicemia or localized infection without positive cultures during life or on autopsy. The autopsy may reveal polymorph infiltrate of organs and other indications of infection, however cultures are negative.

31 - Proven sepsis/infection

Code '31' for septicemia or localized infection with positive blood or organ cultures. For example, septicemia, meningitis, pulmonary abscess etc.

NEC

40 - NEC

Code '40' for proven NEC, stage IIA or higher by Bell's criteria as shown in Appendix G.

41 - NEC with sepsis

Code '41' when the infant has proven NEC (stage IIA or higher by Bell's criteria in Appendix G.) together with positive blood or peritoneal fluid cultures. If the combination of the necrotizing enterocolitis with the documented septicemia or intestinal infection causes the death, then code "41" as the cause of death.

42 - Spontaneous perforation

Code '42' when the infant has an acute gastrointestinal perforation diagnosed by x-ray without classic radiographic findings of necrotizing enterocolitis or findings of necrotizing enterocolitis at surgery or autopsy, including pathologic specimens.

CNS insult

50 - Severe intracranial hemorrhage

Code '50' when the infant has severe intracranial hemorrhage (massive grade II-IV) with a clinical presentation of central nervous system decompensation including seizures, apneas, etc., in the absence of severe respiratory distress syndrome requiring high ventilator settings.

51 - Severe IVH with infection with culture proven or suspected

Code '51' when the infant has severe intracranial hemorrhage (grade III or IV) with documented blood/echo-density in the ventricle, ventricular size enlargement occurs in association with blood/echo-density in the ventricular system or blood/echo-density in the parenchyma.

Other

60 - Immaturity

Code '60' for infants < 24 weeks who die in the absence of infection, RDS, or massive IC bleed.

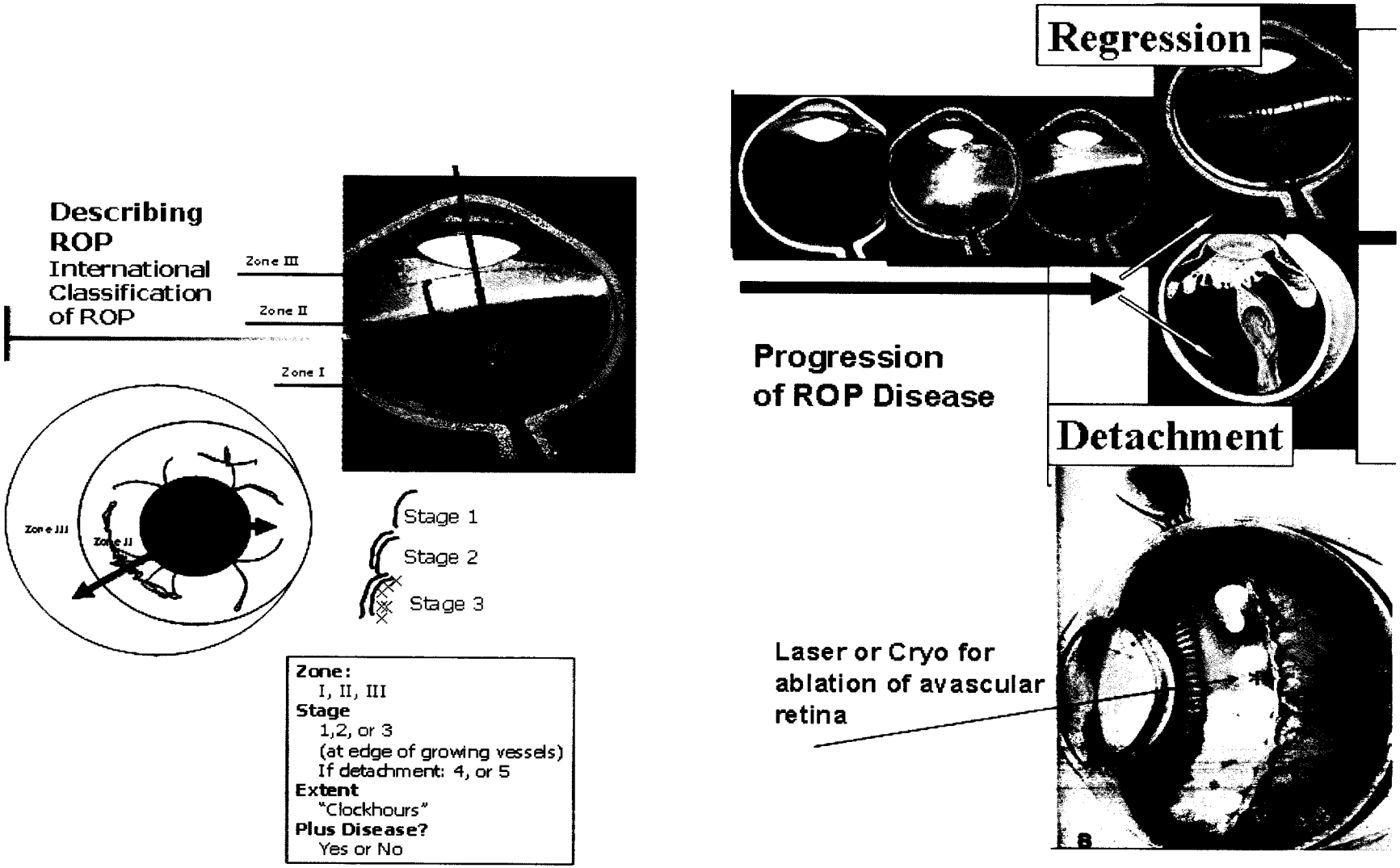
90 - Other

Code '90' for infants with other causes of death such as severe asphyxia with multi-system failure, severe metabolic disease, and severe trauma. Cardiorespiratory arrest is not to be used.

99 - Unknown

Code '99' only if the cause of death has been investigated but could not be established.

Appendix D
Retinopathy of Prematurity Diagram



Appendix E
Surgical Procedures

GI – 200 Series	
201	Laparotomy
202	Bowel resection (end to end anastomosis)
203	Jejunostomy/ileostomy/colostomy
204	Ostomy takedown/reanastomosis
205	Peritoneal drain
206	Gastrostomy
207	Appendectomy
208	Fundoplication
209	T-E fistula/esophageal atresia repair
210	Gastroschisis/omphalocele repair
211	Diaphragmatic hernia repair
212	Inguinal hernia repair
Pulmonary - 300 Series	
301	Tracheostomy
302	Anterior cricoid split
303	Resection of cystic adenomatoid malformation
GU – 400 Series	
401	Repair of extrophy of the bladder
402	Urinary diversion
Head & Neck - 500 Series	
501	Correction of choanal atresia
502	Repair of cleft lip/palate
CNS – 600 Series	
601	Shunt for hydrocephalus (post hemorrhagic)
602	Shunt for hydrocephalus (not post hemorrhagic)
603	Vent reservoir
Cardiac – 700 Series	
701	Repair of CHD
702	Cardiac shunt procedure
Other - 900 Series	
901	Central line placement (requiring anesthesia; not including umbilical or percutaneous central lines)
999	Other Surgeries not listed

Appendix F
Data Forms

The following pages contain the data forms for the Survey of Mortality Among Very Low Birth Weight Infants (401 to 1500 grams)

NGO1	SCREENING LOG
NGO2	GENERIC BASELINE FORM
NGO3	GENERIC CLINICAL OUTCOME FORM
NGO3E	GENERIC EARLY DEATH FORM
NGO5	GENERIC LATE CLINICAL OUTCOME FORM
NGO7	GENERIC RESPIRATORY SUPPORT FORM

Appendix G
Modified Bell's Staging Criteria for NEC

Stage	Systemic	Intestinal Signs	Radiologic Signs
IA - Suspected NEC	Temperature instability, apnea, bradycardia, lethargy	Elevated pre-gavage residuals, mild abdominal distension, emesis, guaiac. positive stool	Normal or intestinal dilation, mild ileus
IB - Suspected NEC	Same as above	Bright red blood from rectum	Same as above
IIA - Definite NEC Moderately ill	Same as above	Same as above, plus absent bowel sounds, ± abdominal tenderness	Intestinal dilation, ileus, pneumatosis intestinalis
IIB - Definite NEC	Same as above, plus mild metabolic acidosis, mild thrombocytopenia	Same as above, plus absent bowel sounds, definite abdominal tenderness, ± abdominal cellulitis or right lower quadrant mass	Same as IIA, plus portal vein gas, ± ascites
IIIA - Advanced NEC Severely ill Bowel intact	Same as IIB, plus hypotension, bradycardia, severe apnea, combined respiratory and metabolic acidosis, disseminated intravascular coagulation, neutropenia	Same as above, plus signs of generalized peritonitis marked tenderness, and distention of abdomen	Same as IIB, plus definite ascites
IIIB - Advanced NEC Severely ill Bowel perforated	Same as IIIA	Same as IIIA	Same as IIB, plus pneumoperitoneum

From: Ped. Clinics of North America, February 1986, Walsh, M., Kliegman, R., Necrotizing enterocolitis: Treatment based staging criteria.

Appendix H
Birth Defects Codes

CODE	TYPE OF DEFECT
Central Nervous System Defects - 100 Series	
101	Anencephaly
102	Meningomyelocele
103	Hydranencephaly
104	Congenital Hydrocephalus
105	Holoprosencephaly
199	**Other Central Nervous System Defects**
Congenital Heart Defects - 200 Series	
201	Truncus Arteriosus
202	Transposition of the Great Vessels
203	Tetralogy of Fallot
204	Single Ventricle
205	Double Outlet Right Ventricle
206	Complete Atrio-Ventricular Canal
207	Pulmonary Atresia
208	Tricuspid Atresia
209	Hypoplastic Left Heart Syndrome
210	Interrupted Aortic Arch
211	Total Anomalous Pulmonary Venous Return
299	**Other Congenital Heart Defects**

Gastro-Intestinal Defects - 300 Series

301	Cleft Palate
302	Tracheo-Esophageal Fistula
303	Esophageal Atresia
304	Duodenal Atresia
305	Jejunal Atresia
306	Ileal Atresia
307	Atresia of large bowel or rectum
308	Imperforate anus
309	Omphalocele
310	Gastroschisis
399	**Other Gastro-Intestinal Defects**

Genito-Urinary Defects - 400 Series

401	Bilateral Renal Agenesis
402	Bilateral polycystic, multicystic, or dysplastic kidneys
403	Obstructive Uropathy with Congenital Hydronephrosis
404	Exstrophy of the Urinary Bladder
499	**Other Genito-Urinary Defects**

Chromosomal Abnormalities – 500 Series

501	Trisomy 13
502	Trisomy 18
503	Trisomy 21
599	**Other Chromosomal Abnormality (DESCRIBE w/ Comment)**

Other Birth Defects – 600 Series

601	Skeletal Dysplasia (DESCRIBE w/ Comment)
602	Congenital Diaphragmatic Hernia
605	Inborn Error of Metabolism (DESCRIBE w/ Comment)
699	**Other Serious and/or Life-Threatening Birth Defect**

Pulmonary - 700 Series

701	Cystic Adenomatoid Malformation (CAM)
799	**Other Pulmonaary**

The following conditions should **NOT** be coded as a Major Birth Defect.

- Extreme Prematurity
- Intrauterine Growth Retardation
- Small Size for Gestational Age
- Fetal Alcohol Syndrome
- Hypothyroidism
- Intrauterine Infection
- Cleft Lip with out Cleft Palate
- Club Feet
- Congenital Dislocation of the Hips
- Limb Abnormalities
- Syndactyly
- Hypospadias
- Patent Ductus Arteriosus
- Pulmonary Hypoplasia (use code 401 for bilateral renal agenesis)

Appendix I
CLARIFICATION OF INFECTION/NEC

BLOOD CULTURE	NEC	ANTIBIOTICS	FINDINGS
Positive	Absent/suspect	≥ 5 days	Late onset sepsis
Positive	Proven	≥ 5 days	NEC and late onset sepsis
Negative	Absent/suspect	≥ 5 days	Blood culture negative
Negative	Proven	≥ 5 days	NEC

Appendix Ia
CHORIOAMNIONITIS – PATHOLOGIC FINDINGS

If "chorioamnionitis" is noted on the placental pathology report or if **any** of the following findings (as defined by the Stillbirth Collaborative Research Network {SCRN} Pathology Protocol) are documented on the placental pathology report, Code YES to histologic chorioamnionitis.

ACUTE CHORIOAMNIONITIS

Grade I — Acute subchorionitis – early acute chorionitis or both. Patchy-diffuse accumulations of neutrophils in the subchorionic plate fibrin and/or membranous chorionic trophoblast layer, (a few scattered neutrophils in the lower ½ of chorionic plate and/or the membranous chorionic connective tissue allowed)

Grade II — More than 10 PMNs per high power field scattered in the chorionic plate or membranous chorionic connective tissue and/or the amnion.

Grade III — Numerous PMNs present without necrosis of the amnion.

Grade IV — Necrotizing chorioamnionitis. Degenerating neutrophils (karyorrhexis), thickened eosinophilic amniotic basement membrane and at least focal amnionic epithelial degeneration/sloughing.

SUBACUTE CHORIOAMNIONITIS

More than occasional mononuclear cells (usually macrophages) in the placental membranes or chorionic plate. Neutrophils may be rare or abundant, but a coexistent acute chorioamnionitis should be present in at least one section. (Mononuclear cells are most frequent near the amnion).

CHRONIC CHORIONITIS

Mononuclear cell infiltrates in chorion without evidence of acute chorioamnionitis.

From SCRN Pathology Protocol, Manual of Operations

Appendix J
Overview of the Generic Database:

Information in this document was compiled from notebooks sent by George Washington University dated 1987-1997 that reside on RTI main campus, RTP, North Carolina.

Six major versions of the generic database manual were issued between 1987 and 1997. For each of these, documentation sent to RTI includes the manual of operations, the summary of changes from the previous version, the study forms, and a copy of the study forms showing the SAS variable names. The originals are available through RTI by request. Additionally, electronic versions have been made by scanning the originals into PDF form.

To make a request, please email Kristin Zaterka-Baxter, kzaterka@rti.org.

Variable Naming Convention

Variables on forms NG02, NG03, NG03E, NG05, and NG06 all start with a 3 character prefix. The prefixes are OBG for NG02, OCG for NG03, OZG for NG03E, OEG for NG05 and OFG for NG06. The variables on the form NG01 start with the letter A. No prefix is used for the few variables on the NG04.

Precautions in using the database

When analyzing data from the GDB, always check whether a version change occurred within the period of time covered by the analysis. If one or more changes occur within the period of time covered by the analysis, check that the variable you are using exist in all the relevant versions of the forms, and that they have identical or nearly identical definitions. The GDB contains many instances of questions being dropped, added, significantly modified, or replaced by groups of more detailed questions.

History of Changes

Introduction

The GDB was initiated in November 1987. Since then, over 700 changes were made to it, with a quarter of these being clarifications or minor modifications to the definitions in the manual. This brief overview describes some of the more significant changes instituted in each of the six revisions of the manual of operations.

November 1, 1987 (original release)

The original GDB included infants 501-1500 grams admitted within 30 days. There were 3 forms: the NG01 (screening log), the NG02 and the NG03 (which extended to discharge or death, and was not truncated at 120 days).

July 31, 1988

Major Changes: The NEC log (NG04) was added because of concerns about NEC during the IVIG trial. These concerns eventually led to the temporary suspension of the trial from June to September 1989. The NEC log recorded the basic information on all cases of suspected NEC. It was essentially abandoned when the IVIG study ended in April 1991 and was officially discontinued in 1993.

Form Changes: Information on high frequency ventilator use was added to the NG03, as were Bell's classification for NEC and information on the 5-7 day sonogram. The question on autopsy was expanded to include presence of IVH, cystic PVL and porencephaly.

Specific Changes made in the 1988 version of the GDB forms and Manual of Operations:

NG03
NEW QUESTIONS

A19a. High frequency ventilator?

A19b. High frequency ventilator, if yes, give type:
Code 1=oscillator 2=jet If another type occurs, contact the DCC to add to the code list.

C3a. 5-7 day sonogram results:
Grade I = PV area; Grade II = Mild IVH with no dilation; Grade III = with dilation; Grade IV = in parenchyma

C3c. 5-7 day sonogram: echodense lesions observed? Yes/No

C4n. Date of diagnosis for the most severe IVH
G4b. Necrotizing Enterocolitis – Bell's Classification
G4c. Date of diagnosis of NEC
J5. Autopsy performed?
J6a. Presence of intracranial bleeding on autopsy
J6b. Cystic periventricular Leukomalacia present?
J6c. Porencephaly?

September 22, 1989

Major Changes: The NG03 was limited to the first 120 days and a new form, NG05 was added to cover the period after 120 days. Before the split, information about morbidity such as NEC and IVH was not received until NG03 was completed, at death or discharge which, for some infants, would take a very long time.

Form Changes: On the NG02, the use of maternal drugs (cigarettes, narcotics, cocaine), of tocolytics and Phenobarbital was added.

On the NG03, surfactants and steroids for BPD were added to the pulmonary section. In the neurologic section, indomethacin for IVH, Phenobarbital were added. The question on feeding, NEC were also expanded, and intra-uterine infections were added.

Finally, note that this version did not include new NG01 and NG04 forms: the forms from the 1988 version were re-used.

Specific Changes made in the 1989 version of the GDB forms and Manual of Operations:

NG02
NEW QUESTIONS

A1. *The information in this section is from:* 1=mother's chart, 2=child's chart

A5a2. *If narcotics, specify.*
A5b2. *If Cocaine, source of information:* 1=history, 2=urine screen, 3=both

A5d1. *Cigarettes at anytime?*
A5d2. *Cigarettes during pregnancy?*
A5d3. *If cigarettes, average/day during pregnancy:*
C5. *Did the mother receive Phenobarbital within 7 days prior to delievery?*
C6a. *Tocolytic agents during labor?*
C6b. *If tocolytic agents, specify:*
D8: *Last menstrual period:* Date of first day of last menstrual period.

NG03
NEW QUESTIONS

Form Header: *Is the infant still in this hospital at 120 days?*
If yes, this form should be completed at this time. Complete NG05 when the infant dies or is discharged.
Form Header: *If infant in this hospital at 120 days, date form completed:*

A8a. *Steroids for bronchopulmonary dysplasia?*
A8b. *If steroids for bronchopulmonary dysplasia, give date started:*
A8c. *If steroids for bronchopulmonary dysplasia, give date stopped:*
A8d. *If steroids for bronchopulmonary dysplasia, give number of days:*
A20. *Conventional ventilation?*
A22. *Did the baby receive surfactant?*
C1a. *Neurologic, malformation?*
C5a. *IVH: Discharge sonogram grade:*
0=none, 1=grade I, 2=grade II, 3=grade III, 4=grade IV, 9=no ultrasound

C5b. *Date of last sonogram prior to 'Status':*
C10a. *Was idomethacin given for IVH?*
C10b. *If idomethacin given for IVH, first date given:*
C11a. *Was Phenobarbital given for any reason?*
C11b. *If Phenobarbital given, date first given:*
D1b. *If G.1. malformation, specify:*
D5: *Date of first enteral feed:*
D6: *Date of full enteral feeds first achieved:*
D8d. *More than one episode of proven NEC?*
E5a. *Intra-Uterine Infection?*
E5b. *If intra-uterine infection, describe:*
E6a. *Other infection?*
E6b. *If other infection, specify:*
15. *If transferred and then discharged home, give date of discharge:*
16a. *Discharged home on oxygen?*
16b. *If discharged home on oxygen, date finally weaned from oxygen*
J4. *If cause of death is RDS, further classify:*
1=respiratory insufficiency, 2=airl leak, 3=BPD after 28 days

J5. *If cause of death is malformation, specify:*

DELETED
The question "Persistent increase in ventricle size?" was dropped.

November 30, 1990

Major Changes: The NG06 was added to record information on the administration of surfactants. The cutoff for admissions was reduced from 30 days to 14 days. Also, infants are no longer counted as having been discharged or transferred if they are readmitted within 7 days.

Form Changes: On the NG02, maternal antibiotics and syndromes and/or major malformations were added. Tocolytics, Phenobarbital, alcohol, and several detail questions on cigarettes and narcotics were dropped. Several questions (such as mode of delivery) were simplified.

On NG03, 36 week measurements were added, as were PLUS disease details on BPD, NEC complications, feeding, and last sonogram, and on transfers and discharge. Information about Phenobarbital, and details about pneumonia and autopsy were dropped. Fluid restrictions for PDA were no longer recorded. Sepsis was split into early vs. late sepsis. Coding of death was altered significantly.

Specific Changes made in the 1990 version of the GDB forms and Manual of Operations:

ADDED/CHANGED
NG02

A3. *Marital Status*
Codes 2-5 were collapsed into one category called 'single'.

B6. *Hypertension/pre-eclampsia/eclampsia?*
The questions 'Hypertension' and 'Pre-eclampsia/eclampsia' were combined and the definition revised to read 'Hypertension, chronic or pregnancy induced, with or without edema and albuminaria, recorded in the mother's chart, or maternal blood pressure above 140 systolic or 90 diastolic starting prior to or during present pregnancy.'

C5. *Antibiotics given prior to delivery?* (new question coded as Y/N variable)

C7. *Mode of delivery*
Code 1 was changed from 'Vaginal spontaneous' to 'Vaginal vertex' and codes 2='Vaginal forceps' and 3='Vaginal vacuum' were deleted.

D6b. *Race* (new question added)
'If Hispanic, further classify as follows:'
1=white, 2=black, 3=unknown

D17a. *Syndromes and/or major malformations*
D17b. *If yes, specify:*

NG03

A8. *Pulmonary hemorrhage?*
A10. *Number of days of the first 28 the infant was in $FiO_2 > 0$*

A11. Chest X-ray consistent with chronic lung disease at any time during course? (Coded Y/N)
A12. Highest FiO_2 concentration at postconceptional age of 36 weeks:
B1. Was iddomethacin given prophylactically for PDA or IVH within the first 24 hours?
C5. Last sonogram prior to death/discharge (old question was deleted and modified)
C9f. Treatments for PHH – Other treatments (coded Y if other treatments used)
D8e. NEC complications – stricture S/P NEC requiring surgery?
D10a. Other G.I. conditions?
D10b. If yes, specify.
E1. Early onset septicemia/bacteremia (≤72 hours)
E1a. Early onset septicemia/bactermia?
E1b,c. If yes, organism codes (with two places for entries)
E1d. Did the infant receive antibiotics for ≥5 days (coded as Y/N)
G5. Plus disease? (to be coded for right and left eyes)
I1. 36 weeks information
I1a. Date
I1b. Weight
I1c. Length
I1d. Head circumference
Section J formerly section I
J5. Discharged home on monitor
Section K formerly section J

DELETED
NG02
A1. The information from this section is from.
A5a2. If yes, specify (specify narcotics used)
A5d1. Cigarettes at any time?
A5d3. If yes, packs/day during pregnancy.
B5. Did the mother receive Phenobarbital within 7 days prior to delievery?
B6. Tocolytic agents given?

NG03
A3b. Origin of pneumonia
A3c. If other, specify
B2e. Fluid restrictions, digoxin or diuretics for treatement of PDA
C10. Was indomethacin given for IVH?
C11. Was Phenobarbital given for any reason?
F3. Code 0=no information for zone of ROP
F5. Grade of cicatricial ROP
H8. Presence of intracranial bleed on autopsy.

February 16, 1993

Major Changes:

- The lower limit for birth weight was changed to 401 grams.
- The NG04 (NEC log) was officially discontinued. The NG06 was also discontinued, with most of its information incorporated into NG03.
- The NG03E, was added to capture specific information on infants who died within 12 hours.
- The NG05 was drastically shortened.

Form Changes: On NG02, tocolytics were brought back, and RPR/VDRL and Hepatitis B were added. Questions on maternal drugs (cocaine, cigarettes,

heroin/methadone, etc...), gestational diabetes, prolapsed cord and antenatal steroids were removed.

Several sections of the NG03 were substantially expanded and reorganized. In particular, the pulmonary section was expanded to include detailed pulmonary information on days 10 and 28, week 36, and at status. PIE, pneumoperitoneum, pneumomediastinum and details on RDS were also added. RIP, pneumonia and details about steroids for BPD were removed. The neurologic section was also modified to include more detailed information on sonograms, and the 5-7 day sonogram was changed to a 3-7 day sonogram. Other affected sections include those on PDA, ROP, catheters, status (weight, length and H.C. added), and infections (abscesses and cellulites, and culture negative sepsis were added).

Specific Changes made in the 1990 version of the GDB forms and Manual of Operations:

ADDED/CHANGED

NG02

Maternal Hepatitis B and RPR/VDRL
Use of tocolitics

NG03

Respiratory distress question now asks about specific symptoms.
Information on NG06 (surfactant administration) has been incorporated into the NG03.
Air leak
Use of flow interrupter ventilator
The date of administration of indomethacin, and of surgery for PDA are now recorded (Cardiac Section)
The 5-7 day sonogram information has been replaced by a 3-7 day sonogram (Neurologic Section)
Days on peripheral artery catheters are now recorded (Gastrointestinal Section)
Infection Section:
- *Culture negative infections*
- *Organisms for intra-uterine infections*
- *Abscesses and cellulites*

No longer asks number of days of phototherapy and the number of exchange transfusions, only whether the infant received any phototherapy and any exchange transfusions (Hematologic Section).
Syndromes and Malformations Section Added

NG05

Most of the information on NG05 ahs been deleted. Now it only contains the discharge/transfer/death in the same format as the NG03, and a question about which organ system caused hospitalization beyond 120 days.

DELETED

NG02

Maternal Drug Section
Gestational diabetes and prolapsed cord have been deleted from the pregnancy complication section.

NG03

Pneumonia no longer recorded
No longer records when steroids for BPD were started and stopped (still records if given)
GI conditions other than NEC and cholestatic jaundice are no longer recorded
Hearing test method no longer recorded

September 24, 1993

This was a minor update with a few changes to definitions. The most significant change was that antenatal steroids were brought back on the NG02. The antenatal steroids information was added retrospectively for infants whose NG02 was entered under the February 16 version (so there is no gap in antenatal steroids information). This effectively makes the September 1993 version a minor modification of the February version. For documentation purposes, both 1993 versions are treated as a single version dated September 1993.

June 4, 1994

The major changes to this version were the addition of the components CRIB score and the expansion of the question on tocolytics. A few sections on the NG03 were also re-organized.

Specific Changes made in the 1994 version of the GDB forms and Manual of Operations:

See "Specific GDB Changes 1994.pdf" in this same directory.

July 1, 1998

In April of 1998, RTI took over as the DCC for the Neonatal Network, and shortly after the following changes were made.

Several nutrition questions from the old NG03 (6/6/94 version) have been restored to the GDB form NG03. The following nutrition questions have been restored to the gastrointestinal section of the new NG03:

Old NG03 (6/6/94)	New NG03 (7/6/98)
D2	F1
D2a	F1a
D2a1	F1a1
D3	F2
D3a	F2a
D3b	F2b
D4	F3
D4a	F3a
D4b	F3b
D4b1	F3b1

Please begin to use the enclosed revised NG03 (7/6/98 version) for all infants reaching NG03 "status" after 7/1/98.

In addition to the revised NG03 form, there were also revisions of the NG01, NG02, NG03E, NG05 and the NG07. Please note that the only changes to these forms are formatting changes. These changes are as follows:

- **Form headers have been reformatted and a new field (Site No.) has been added.**
- **All date fields have now been changed to allow for a 4-digit year.**

February 14, 2002

See the following table.

SUMMARY OF UPDATES/CHANGES TO THE GDB MANUAL AND FORMS SINCE THE AUGUST 4, 1998 VERSION

Screening Log--NG01 (current version dated 2/14/02)

Reformatted: Placed the Mother's initial after the baby's hospital number. Changed Network Number to Family Number and placed the birth number after the Family Number.

Baseline Form--NG02 (current version dated 2/14/02)

A. MATERNAL INFORMATION

Added: Question 5. Highest level of education achieved by the Biological Mother.
Added: Question 6. Mother's medical insurance

B. PREGNANCY COMPLICATION

Added: Question 3. Was this pregnancy the product of artificial reproductive technology?

C. LABOR AND DELIVERY

Revised: Question 3 to read: Were steroids given prior to delivery to accelerate maturity?
Added: Type of antenatal steroid given: [1 = Betamethasone 2= Dexamethasone 3 =Both]

D. NEONATAL INFORMATION

Added: Question 13. Was cord blood gas done?
If Yes,
a. Cord arterial pH (if done)
b. Cord venous pH (if done)
c. Cord pH (unknown vessel)
d. Arterial base deficit (if done)
e. Venous base deficit (if done)
f. Base deficit (unknown vessel)

Added: Question 14. Infant's temperature on initial admission to the nursery from L & D
Added: Source: [1= Rectal 2 = Axillary 3= Skin]
Added: Date and Time:

Clinical Outcome Form--NG03 (current version dated 2/14/02)

Changed all occurrences of Chronic Lung Disease to BPD

B. PULMONARY

Changed: Question B. 5 changed to: Was a chest x-ray done after 21 days of age?
If Yes,
a. Was chest x-ray consistent with BPD/CLD?
b. Date of x-ray after day 21 and closest to day 28 used to meet criteria:

Changed: Question 6 changed to: Did baby require supplemental 0_2 at 36 weeks?
Changed: Question 7 changed to: Was x-ray done at 36 weeks?
If Yes,
a. Date of x-ray

D. NEUROLOGIC

Deleted: Old question 4- Cranial sonogram within 28 days of birth showing the most severe hemorrhage:

Revised: Question 3. Were any cranial sonograms done within 28 days of birth?

If No, go to Question D6

If Yes,

a. Were all studies normal?

If Yes, go to Question D6

b. Date of sonogram for most severe hemorrhage

E. INFECTION

Changed: Question 5.b to: Organism code(s) **and date of first positive culture for each** episode for which the infant was treated with antibiotics for ≥ 5 days. Added additional lines and dates for each episode.

Changed: Question 6. Infection of meninges/brain? If Yes, added additional lines and dates for each episode.

F. GASTROINTESTNAL

Changed: Question 1.a. **to:** If Yes, lowest weight?

Changed: 1.a.1) to: Date of lowest weight

Added: Question 1.b. If Yes, Did the infant regain birth weight?

Added: Question 1.b.1) If Yes, Date when first regained

Added: Question 6. Did the infant have GI surgery that resulted in short gut?

G. HEARING

Changed: Question 1 to: Was a hearing screen performed?

Added: If Yes, Hearing screen protocol used:

[1 = OAE 2 = AABR 3 = ABR 4= OAE +AABR 5= Other]

b. Final screen results before discharge:

i) Right ear

ii) Left ear:

Results: 1. Pass 2. Fail 3. Incomplete

c. If a failed screen in either ear, was a diagnostic ABR done prior to discharge?

1) If YES,

i) Right ear:

ii) Left ear:

Results: [1= Pass 2= Fail 3= Incomplete]

H. OPHTHALMOLOGY

Added: 1.a. 2) If ROP diagnosed, was threshold ROP diagnosed at any time?

I Right

ii Left

Changed: 3) Intervention Therapies:

Added: a. Was retinal ablation performed prior to a threshold diagnosis?

I Right, ii Left

b. Was any surgery performed?

I Right, ii Left

Codes:[0= None 1= Lasertherapy 2= Cryotherapy 3= Scleral buckle 4= Other]

Added: 4) If ROP diagnosed, were the ROP findings regressing at time of status?

a. Right

b. Left

K. 28 DAY ANTHROPOMETIRCS [This section was added]

1. Status at 28 Days:
   [1 = Discharged = 2 = In hospital 3 = Transferred 5 = Death]
   If "2", (In Hospital):
   a. Date at 28 Days
   b. Weight (g):
   c. Length (cm):
   d. Head circumference (cm):

N. DISCHARGE ALIVE

Deleted: Question 3. Discharged home on monitor?
Added: New Question 3: Discharged home on any of the following medications?
If YES,
a. Diuretics?
b. Bronchodilators?
c. Anticonvulsants?
d. Antireflux medications?

O. DEATH

Changed: Question 3. to :Autopsy requested?
Added: a. If YES, Was consent granted?
Changed: Old Question 3 to 4. Autopsy performed?

Early Death Form--NG03E (current version dated 2/14/02)

Changed Question 6. to :Autopsy requested?
Added: a. If YES, Was consent granted?
Changed: Old Question 6 to 7. Autopsy performed?

Late Clinical Outcome Form--NG05 (current version dated 2/14/02)

B. SYSTEM INFORMATION

Added: Question 2. Was a hearing screen performed after 120 days?
a. If Yes, Hearing screen protocol used:[1=OAE, 2=AABR, 3=ABR, 4=OAE+AABR 5=Other]
b. Final screen results before discharge
i) right ear, ii) left ear
c. If a failed screen in either ear, was a diagnostic ABR done prior to discharge:
1) If Yes, i) right ear, ii) left ear [Results: 1= Pass, 2= Fail, 3= Incomplete]

D. DISCHARGE ALIVE

Deleted: Question 3. Discharged home on monitor?
Added: New Question 3: Discharged home on any of the following medications?
If YES,
a. Diuretics?
b. Bronchodilators?
c. Anticonvulsants?
d. Antireflux medications?

E. DEATH

Changed Question 3. to: Autopsy requested?

Added: a. If YES, Was consent granted? **Changed old Question 3 to 4.** Autopsy performed?
Respiratory Support Form--NG07 (current version dated 2/14/02)
Changed: Question 3 to Number of Days on Nasal SIMV **Added:** New Question 6: Number of Days on Oxygen via Hood/Isolette **Added**: New Question 7: Number of Days on Oxygen by Nasal Cannula **Changed:** Old question 6 to 7: Highest FIO_2 **Changed:** Old question 7 to 9: Supplemental O_2 by Nasal Cannula? **Added:** New question 10: If in Room air, by Nasal Cannula or CPAP?
Infection Forms--NG08 **All of the infection Data Collection was terminated as of 1/1/2002**
Appendix I **Added: APPENDIX I CLARIFICATION OF INFECTION/NEC**

Appendix J

SUMMARY OF UPDATES/CHANGES TO THE GDB FORMS SINCE THE FEBRUARY 14, 2002 VERSION

Screening Log--NG01 (current version dated 1/1/06)

No changes since the February 14, 2002 version

Baseline Form--NG02 (current version dated 1/1/06)

A. MATERNAL INFORMATION

Changed: Question 6. Mother's medical insurance
Deleted: 2= Medicaid HMO, 4=Other HMO, 7= Both private and public (e.g. Medicaid; CHIPS) assistance and 8 = No insurance upon admission
Reworded: 3= Self-pay/uninsured, **added** 9= Other

B. PREGNANCY COMPLICATION

Revised: Question 2 to read: Mother has evidence of at least one prenatal visit in this pregnancy.
Deleted: Question 3. Was this pregnancy the product of artificial reproductive technology?
Changed: Old Question 4 to Question 3
Added: To New Question 3. If Yes, was insulin given prior to pregnancy. Added Yes/No/UK
Changed: Old Question 5 to Question 4
Revised: **New Question 4**. Hypertension/pre-eclampsia/eclampsia to read: Hypertension? Yes/No
Added: If Yes, a. Hypertension existed prior to pregnancy? Yes/No/UK
Changed: Old Question 6 to Question 5
Changed: Old Question 7 to Question 6
Added: New Question 6. Was Chorioamnionitis documented in the mother's medical record? Yes/No
Added: New Question 7. Was placental pathology performed? Yes/No.
Added: If Yes to question 7, a. Was histologic chorioamnionitis documented? Yes/No.

C. LABOR AND DELIVERY

Revised: Question 1 to read: Was there rupture of membranes prior to delivery?, Yes/No/UK
Added: If Yes, a. Date, b. Time, c. If date and time unknown, were ROM estimated at >18 hours? Yes/ No/UK
Deleted: Old Questions 2, 2a Date and 2b. time
Changed: Old Question 3 to Question 2, 2a and 2b. Added UK to response options.
Deleted: Old Questions 3c. Total number of courses given during this pregnancy.
Deleted: Old Question 4. Were tocolytics used during the admission resulting in this delivery?
Changed: Old Question 5 to Question 3 and reworded to read: Were maternal antibiotics used during the admission resulting in this delivery?, Yes/No/UK
Added: New Question 3a, If Yes, were antibiotics given within 72 hours prior to delivery?, Yes/No/UK
Added: New Question3b, If Yes, list antibiotics given.
Changed: Old Question 6 to Question 4
Added: To New Question 4 , Code 4= Unknown

Baseline Form--NG02 (current version dated 1/1/06) Continued

D. NEONATAL INFORMATION

Added: New Question 5. Ethnic Categories
Added: New Questions 6. Racial Categories
Changed: Old Question 9 (new question 10), Delivery room resuscitation to read "Birth resuscitation/stabilization
Added: New Questions 10c- CPAP and question 10f. Epinephrine
Deleted: Old Questions 9e, Drugs
Deleted: Old Questions 13a, 13b, 13d and 13e.
Changed: Old Question 13c was changed to 13a and 13f was changed to 13b.
Renumbered the remainder to the form.

Clinical Outcome Form--NG03 (current version dated 1/1/06)

A. STATUS:

Deleted: Question 6. Was respiratory support withheld and/or withdrawn at any time between birth and 24 hours after the infant was born?

B. PULMONARY

Changed: Question 1 to: Respiratory distress
Changed: Old Question 1b. to 1a. Demonstrated clinical features of respiratory distress within age 24 hours.
Changed: Old Question 1a. to 1b. **Reworded "New" 1b to:** Required oxygen or positive pressure support for more than 6 hours within the first 24 hours.
Deleted: Old Question 1c and 1d.
Added: New Question 2a. If Yes, date and time of first dose.
Deleted: Old Questions 5, 5a and 5b
Deleted: Old Question 6
Deleted: Old Question 7, 7a and 7b.
Changed: Old Questions 8 and 8a to Question 5 and 5a.
Added: New Question 6, Did infant receive inhaled nitric oxide? Yes/No.
Question 6a, If Yes, Date of first exposure.
Deleted: Old Questions 9 and 10.

C. CARDIAC

Changed: Question 1, If Yes, to If Yes, treatment.
Changed: Question 1a. Indomethacin for PDA to 1a. Indomethacin Yes/No
If Yes, total number of courses.
Added: New Question 1b. Ibuprofin, Yes/No. If Yes, total number of courses.
Changed: Old Question 1b. Surgery for PDA to 1c. Surgery, Yes/No

Clinical Outcome Form--NG03 (current version dated 1/1/06) Continued

D. NEUROLOGIC

Changed: Question 1 to read - Was indomethacin given within the first 24 hours of life for any prophylaxis?
Changed: Question 2 to read - Were there seizures treated with an anti-convulsant for > 72 hours?
Deleted: Question 2a.
Changed: Question 3a to read - If Yes, were all studies without evidence of intracranial hemorrhage, peri-ventricular leukomalacia or ventriclomegaly?
Changed: Question 3b to read - Date of sonogram with most severe findings.
Changed: Question 3d to collect Yes/No information for right/left side
Added: New Question 3e - Ventricular size enlarged with concurrent or prior blood in the ventricles? Yes/No for right/left side
Deleted: Old Question 3f. ventricles? Yes/No
Added: New Question 3f - Ventricular size enlarged without concurrent or prior blood in the ventricles? Yes/No for right/left side
Changed: Old Question 3e to Question 3g
Added: To Question 4, If Yes
4a. Cystic periventricular leukomalacia within 28 days? Yes/No for right/left side
4b. Porencephalic cyst within 28 days? Yes/No for right/left side
Deleted: Old Question 5
Changed: Old Question 6 to Question 5
Changed: Old Question 7 to **New Question 6.** Reworded: Cranial imaging study performed closest to 36 weeks postmenstrual age and after 28 days of birth.
Added: New Question 6a. Type of imaging (1= MRI, 2=Sonogram, 3=CT scan)
Changed: Old Question 7a to 6b. Date of sonogram changed to Date of image.
Changed: Old Question 7b to 6c Normal Study?
Deleted: Old Question 7d
Changed: Old Question 7c to 6d. **Added:** Yes/No for right/left side
Changed: Old Question 7e to 6e. **Added:** Yes/No for right/left side
Changed: Old Question 7f to 6f. **Added:** Yes/No for right/left side
Deleted: Old Question 8

E. INFECTION

Deleted: Old Question 1, 1a and 1b
Renumbered the remainder of Section E
Changed: Question 3 (old question 4) to: Number of episodes of late onset blood culture negative clinical infection.
Changed: Question 5 (old question 6) to: Meningitis?

Clinical Outcome Form--NG03 (current version dated 1/1/06) Continued

F. GASTROINTESTINAL

Changed: Question 1 to read: Did the weight ever fall below the birth weight during the first 10 days? If Yes,
Changed: Question 1a to read: Lowest weight in the first 10 days.
Changed: Question 1a1) to 1b: Reworded to read: Date of lowest weight in first 10 days.
Changed: Old Question 1b to Question 1c. Reworded to read: Was birth weight regained? If Yes,
Changed: Old Question 1b1) to Question 1d. Reworded to read: Date birth weight first regained.
Changed: Reworded Question 2b to read: Total number of days.
Changed: Reworded Question 3b to read: Did enteral feeds reach 120 ml/kg/day?
Added: New Question 3c. Did the baby receive any breast milk in the first 28 days? Yes/No/UK
Added: New Question 3c1). If Yes, number of days baby received any breast milk in the first 28 days.
Changed: Question 5 reworded to read: Spontaneous gastrointestinal perforation without proven NEC?

G. OPHTHALMOLOGY

Deleted: Old Questions 1a.1).i,ii, and iii
Deleted: Old Question 2), I and ii.
Deleted: Old Question 3)a, and b
Deleted: Old Question 4), a and b
Changed: Question 1a to read: If Yes, was ROP diagnosed in either eye?
Added: 1a.1) If yes, Did it reach stage 3 or worse in either eye? and 1a.2) Did plus disease develop in either eye?
Added: 1b and questions b1 and b2
Added: Question 2 and 1, 2, 3

K. 28 DAY ANTHROPOMETICS-- Deleted this entire section.

CHANGED OLD SECTION L TO: SECTION K. 36 WEEKS INFORMATION
All questions remained the same as the previous Section L.

L. FEEDING STATUS- This is a new section that has been added for January 1, 2006

M. TRANSFER

Deleted: Question 2
Changed: Old Question 3 to question 2

O. DEATH

Deleted: Question 2. Time of Death
Deleted: Question 3 and 3a. Autopsy Requested? If Yes, was consent granted?
Changed: Old Question 4 to Question 2
Changed: Old Question 5 to Question 3. Reworded to read: Contributory Cause of Death.
Changed: Old Question 6 to Question 4. Reworded to read: If contributory cause of death is code "10" (Congenital malformation), or code "90" (other), specify.
Changed Old Question 7 to Question 5. Reworded to read: Was respiratory support withheld or withdrawn at any time prior to death?

Early Death Form--NG03E (current version dated 1/1/06)

Deleted: Question 1, 1a and 1b. Date and time of Death.
Deleted: Question 6 and 6a. Autopsy requested? If yes, was consent granted?
Renumbered the remainder of the form.
Changed: New Question 7 to read: Contributory cause of death.
Changed: New Question 8 to read: If contributory cause of death is code "10" (Congenital malformation) or code "90" (other), specify.

Late Clinical Outcome Form--NG05 (current version dated 1/1/06)

B. EXTENDED STAY INFORMATION (Section was changed from System Information)

Changed: Question 1 to read: What problem(s) caused hospitalization greater than 120 days (answer all that apply)
Changed: Question 1f to Question 1h
Added: A new Question 1f. Social?
Added: New Question 1g. Ophthalmologic?
Changed: Old Question 1f to Question 1h
Added: New Question 2. After reaching status, did either eye receive surgery for ROP
2a. If Yes, list all surgeries done for either eye (use codes below)
2b. List codes (1= Laser Treatment, 2= Cryotherapy, 3= Scleral buckle, 4= Vitrectomy, = Other (specify) for either eye.
Changed: Old Question 2 to Question 3

C. TRANSFER
Changed: Question 3 to read: Transferred on ventilator and/or CPAP?
Deleted: Final Outcome Reason code 4= Remains in chronic Care facility at one year.

E. DEATH
Deleted: Question 2 time of death.
Deleted: Question 3 Autopsy requested? a. If yes, was consent granted?
Changed: Old Question 4 to Question 2
Changed Old Question 5 to Question 3: Reworded to read: Contributory Cause of Death
Added: Code 51 = Severe IVH with culture proven infection or suspected infection
Deleted: Code 60 = Immaturity

Respiratory Support Form--NG07 (current version dated 1/1/06)

This entire form has been revised

Appendix B
Updated with additional Drug Codes

SUMMARY OF UPDATES/CHANGES TO THE GDB STUDY MANUAL AND FORMS SINCE THE JANUARY 1, 2006 VERSION

Baseline Form--NG02 (version 3.1) (current version dated 06/19/06)

D. NEONATAL INFORMATION

Added: *Codes for question D.5 and D.6 (and question D.6.a) to reflect the current enrollment reports for NIH as follows (shades codes):*

5. Ethnic Categories: _____

1 = Hispanic or Latino
2 = Not Hispanic or Latino
3 = Unknown or Not Reported

6. Racial Categories: _____

1 = Black	5 = Native Hawaiian or Other Pacific Islander
2 = White	6 = More Than One Race
3 = American Indian or Alaskan Native	7 = Unknown or Not Reported
4 = Asian	

a. If coding option 6, record all races indicated (optional) ___, ___, ___,

Revised corresponding page 3-9, section 3.3.5 (item 5 and 6) in the study manual.

SUMMARY OF UPDATES/CHANGES TO THE GDB STUDY MANUAL AND FORMS SINCE THE JUNE 19, 2006 VERSION

Baseline Form--NG02 (version 3.2) (current version dated 04/01/07)

C. LABOR AND DELIVERY

Changed: Question C.2.b clarifying data is to be collected on completed courses 'of steroids' and deleting the 'within 7 days' time period in the question.

Revised corresponding page 3-7 in the study manual

Baseline Form--NG03 (version 1.3) (current version dated 04/01/07)

H. OPHTHALMOLOGY

Revised: Question H.1.a and H.1.a.1 to clarify which subsequent questions to answer if question H.1 is 'Yes' as follows:

H. OPHTHALMOLOGY

1. Was an exam performed for ROP? Y N

   If Yes,

   a. ~~If YES, w~~Was ROP diagnosed in either eye? Y N

      If Yes,

      1) ~~If Yes,~~ Did it reach stage 3 or worse in either eye? Y N

Revised corresponding page 4-14 in the study manual

Added: Question O.1.a "Time of Death" as follows:

Revised corresponding page 4-18 in the study manual

Appendix A

Updated: Appendix A: Organism Code list

Appendix B

Updated: Appendix B: Drug Therapeutic Agent List

Appendix Ia

Added: Appendix 1a: Chorioamnionitis – Pathologic Findings

Appendix B

Updated: Appendix B: Drug Therapeutic Agent List 06/01/07 with 'Valtex'

SUMMARY OF UPDATES/CHANGES TO THE GDB STUDY MANUAL AND FORMS FOR JANUARY 1, 2008 SINCE THE JUNE 19, 2006 VERSION

Title change "Survey of Morbidity and Mortality Among High Risk Preterm Infants:.

3.1.1 Eligibility

All infants who are 1) inborn and between 401 grams and 1000 grams inclusive birth weight and/or 2) inborn and between 22 0/7 to 28 6/7 weeks (<29 weeks) inclusive gestational age are eligible for the study. Infants enrolled in a Network RCT or prospective observational study (inborn and transferred infants) may be included in the GDB dataset if requested by the study subcommittee and approved by the NRN Steering Committee. These may be otherwise premature and/or low birth weight infants outside the GDB gestational and birth weight criteria. In addition, all inborn, liveborn infants who meet the above criteria and die prior to admission to the NICU are enrolled posthumously.

NG01
Added two columns on screening log:

Column Number 8	**Gestational Age (weeks)**
Column Number 9	**Infant enrolled in an NRN study requiring GDB forms (Y/N)**

May 1, 2008

Respiratory Support Form NG07:
In Chapter 5, the Respiratory Support Form NG07 includes questions from the physiologic definition of BPD. The following changes were added to the GDB manual.

The PHY01 and PHY02 are used as the Physiologic Definition of BPD worksheets. The manual for the stand alone Physiologic Definition of BPD study is used as the Physiologic Definition of BPD workbook. Continue to use these documents for reference purposes. The worksheets will be retained in the site GDB study folders and will not be entered into the DMS. Requests to use data captured on the worksheets must be approved by the NICHD NRN Steering Committee and local IRBs.

The respiratory support box collects respiratory data in one additional way:

C) By PHYSIOLOGIC EVALUATION *– to conduct a physiologic monitored reduction of oxygen in eligible infants at 36 +1 weeks corrected age who are receiving oxygen to establish the definition of bronchopulmonary dysplasia. Infants are screened at exactly 36 weeks of age and, if eligible receive the challenge as close as possible to 36 weeks but no later than 37 weeks PMA*

Section A- SNAPSHOT DATA At 24 hours from birth collects the *highest* amount of oxygen the infant is receiving at exactly 24 hours from birth by ventilation (any mode), CPAP, nasal SIMV, Hood or isolette for question 6.

Question #8 no longer specifies, *CPAP or ventilation (any mode).* This applies to at 24 hours and at 36 weeks postmenstrual age.

Section C is completed if *in section 'A', Snapshot @36 weeks, questions 1 - 4 ~~or 7 or 8~~ are answered ~~"Yes"~~ NO ~~or~~ and in question 6 FiO_2 > 0.21~~%~~ or questions 7 or 8 are answered YES, the INFANT IS ELIGIBLE TO BE SCREENED (refer to Physiologic Definition of BPD Workbook), then complete ~~the PHY01 form~~ section C below.*

In Section B- CUMULATIVE DATA, The last entry is STATUS, supplemental oxygen no longer includes *vapotherm.* For Question #7, *high flow nasal cannula* is counted here.

Special instructions for an infant in a hood or flooded isolette:

> ***NOTE: If an infant is in a hood or flooded isolette, de-flood the isolette before infant is challenged.***

Newly added Section C outlined below:

Section C- PHYSIOLOGIC EVALUATION

Complete section C if in section 'A', Snapshot @36 weeks, questions 1 - 4 are answered 'N' and in question 6 FiO_2 > 0.21 or questions 7 or 8 are answered 'Y'.

> *Question #1. Is the infant eligible for the physiologic evaluation? Record 'Y' if the patient is eligible according to criteria in section B of the PHY01 worksheet.*
>
> *Question #1.a. If Question #1 is answered 'Y', record 'Y' if the evaluation was performed. Otherwise, record 'N'.*
>
> ***IF YES to Question 1.a***
>
> > *If Question #1.a is answered 'Y', the evaluation was performed, record the date of the evaluation (month/day/year) in Question #1.b.*
> >
> > *Record the actual FiO2 being delivered at time of challenge for Question #1.c. For infants receiving blended supplemental oxygen via nasal cannula, record the blend in this field*
> >
> > *If the infant is on nasal cannula at time of challenge, record the flow rate in LPM for Question #1.d.*

For Question #1.e, if the patient passed the challenge, record 'Y'. Otherwise record 'N'.

IF NO to Question 1.a

If Question #1.a is answered 'N', the evaluation was NOT performed, record the reason why the evaluation was not done for Question #1.f.

Codes:

1= Increased FiO_2
2= Increased respiratory support (cpap or vent)
3= Instability (including Surgery/Sepsis)
4 = Parent/Physician Refusal
6 = Weaned to room air on/before day of evaluation
9 = Other- explain

blended supplemental oxygen via nasal cannula, record the blend in this field. __ .

__ __

d. If on nasal cannula at time of challenge, record flow rate__ . __ __ __ LPM

e. Did the patient pass the evaluation? Y N

If NO to question C.1.a

f. If patient was eligible and evaluation not done, code reason.

1= Increased FiO2
2= Increased respiratory support (cpap or vent)
3= Instability (including Surgery/Sepsis)
4 = Parent/Physician Refusal
6 = Weaned to room air on/before day of evaluation
9 = Other- explain

SUPPORT Study

The physiologic evaluation for BPD will be completed on eligible SUPPORT study infants. The results of the evaluation will be recorded on the revised NG07. In addition to the NG07 data, the PHY01 and PHY02 forms will continue to be entered into the DMS for SUPPORT patients whenever section **C. Physiologic Evaluation** on the new NG07 is required to be completed.

EOS Study

Infants enrolled in the EOS study, outside of the GDB criteria will NOT have the physiologic definition of BPD performed for the purposes of the EOS study. Infants outside of the GDB criteria (a gestational age greater than or equal to 29 week and weighing 1001-1500g) will continue to have other relevant GDB data collected.

Thank you,
Carolyn Huitema

From:	Zaterka-Baxter, Kristin
To:	Charlene Thornton
Cc:	Higgins, Rosemary (NIH/NICHD) [E]; Finer, Neil; Das, Abhik; Gantz, Marie; Archer, Stephanie (NIH/NICHD) [E]
Subject:	RE: NeOPRoM
Date:	Wednesday, April 30, 2008 8:21:49 AM

Thanks Charlene, based on the clarifications below, our numbers are correct on the spreadsheet sent yesterday. I'm assuming you did not get the updated spreadsheet in time to make the final addition? My apologies for the delay in getting that information to you; I am copying the folks from the Support trial so they are aware there may be an addendum to the info presented.
Thanks,
Kris

From: Charlene Thornton [mailto:cthornton@ctc.usyd.edu.au]
Sent: Wednesday, April 30, 2008 12:32 AM
To: Zaterka-Baxter, Kristin
Subject: RE: NeOPRoM

Hi Kris

Thanks for getting back to me. The pre-meeting doc was finalised ufoirtunatley last evening, but if your numbers are significantly different from what we have I will let Lisa know and she will advise all on the day with addendums.

What we were referring to was 1. % of patients recruited as a reflection of what your target recruitment was - so if you thought in your pre-trial plans that 100 babies would be recruited per month and only 70 were being recruited, then the % of anticipated recruitment would be 70%.

2. Yes anticipated recruitment was how many you thought would be recruited each month prior to trial commencement.

I hope this is clearer for you.

Thanks

Charlene

From: Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]
Sent: Wed 30/04/2008 1:49 AM
To: Charlene Thornton
Subject: RE: NeOPRoM

Hi Charlene,

I have the information you requested, as approved by out Steering Committee April 15th, but need clarification for two of the questions in order to give you the correct answers. Please clarify what you are looking for when you ask about the following items in the spreadsheet sent below:

1. % OF ANTICIPATED NO. 70% (is this the % on target for recruitment based on initial study design?)
2. ANTICIPATED RECRUITMENT (is this what we anticipated enrolling per month initially or how many, on average per month, we are actually enrolling?)

Thanks much,
Kris

From: Charlene Thornton [mailto:cthornton@ctc.usyd.edu.au]
Sent: Monday, April 14, 2008 4:55 PM
To: 'Neil Finer; Zaterka-Baxter, Kristin
Subject: FW: NeOPRoM

Dear Neil and Kris

Please find attached a summary of progress so far for your trial.

As previously mentioned - a report on each trial's progress will be emailed to all collaborators prior to the NeOProM collaborators meeting in May at PAS 2008. The aim of this report is to save time on the day of the collaborator's meeting for issues other than recruitment and progress updates.

I am emailing this to you for you to confirm the details herein. If there are any components of this information which you do not want to make available to the other collaborators, please indicate so on the spreadsheet. Similiarily, if you find any errors, please correct. If there are any fields left blank, can they please be filled if able to be.

The summary will be presented in a format more condusive to easy perusal for the official document, so please do not worry about any formatting issues at this time.

If you have any queries or concerns regarding this, please do not hesitate to contact either myself, or Lisa Askie.

Thanking you for your time and committment to this collaboration

Charlene Thornton
NeOProM

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From: Finer, Neil
To: Zaterka-Baxter, Kristin
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: NeOPRoM
Date: Tuesday, April 29, 2008 3:13:20 PM

Thanks Kris
This looks very complete
Neil

Neil N. Finer, M.D.
Professor of Pediatrics
Director, Division of Neonatal-Perinatal Medicine
UC San Diego School of Medicine
UC San Diego Medical Center, Hillcrest
402 Dickinson St., MPF 1-140
San Diego, CA 92103-8774
Telephone: 619.543-3759
Facsimile: 619.543.3812

From: Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]
Sent: Tuesday, April 29, 2008 10:39 AM
To: Charlene Thornton
Cc: Higgins, Rosemary (NIH/NICHD) [E]; Finer, Neil; Rich, Wade; Gantz, Marie
Subject: RE: NeOPRoM

Hi Charlene,
Attached are the documents and updated data (updates highlighted in yellow) you requested with two caveats:

1. I can not verify the answers listed for the two questions I sent in the previous email re. '*% of anticipated No.*' and '*anticipated recruitment*' until clarification is received regarding the details of the questions.
2. Please understand that the data from the imbedded secondary study *'Antenatal Consent'* i.e. the number of women screened, consented, and enrolled (presentation attached), represent only the data from those enrolled to the *secondary* and only up to the time of the presentation. It does not include *all* those enrolled in the main Support trial.

Thanks and please let me know if you have any questions
Kris

From: Charlene Thornton [mailto:cthornton@ctc.usyd.edu.au]
Sent: Monday, April 14, 2008 4:55 PM
To: 'Neil Finer; Zaterka-Baxter, Kristin
Subject: FW: NeOPRoM

Dear Neil and Kris

Please find attached a summary of progress so far for your trial.

As previously mentioned - a report on each trial's progress will be emailed to all collaborators prior to the NeOProM collaborators meeting in May at PAS 2008. The aim of this report is to save time on the day of the collaborator's meeting for issues other than recruitment and progress updates.

I am emailing this to you for you to confirm the details herein. If there are any components of this information which you do not want to make available to the other collaborators, please indicate so on the spreadsheet. Similiarily, if you find any errors, please correct. If there are any fields left blank, can they please be filled if able to be.

The summary will be presented in a format more condusive to easy perusal for the official document, so please do not worry about any formatting issues at this time.

If you have any queries or concerns regarding this, please do not hesitate to contact either myself, or Lisa Askie.

Thanking you for your time and committment to this collaboration

Charlene Thornton
NeOProM

From:	Gantz, Marie
To:	Higgins, Rosemary (NIH/NICHD) [E]
Cc:	Das, Abhik; Finer, Neil
Subject:	RE: SUPPORT
Date:	Friday, April 25, 2008 11:03:45 AM

Sure, that number is 1024.

Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-6255

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, April 25, 2008 10:52 AM
To: Gantz, Marie
Cc: Das, Abhik; Finer, Neil
Subject: SUPPORT

Marie
Can you send us the number of infants enrolled in SUPPORT as of the 4/22 data entry download? We would like it for the Meta analysis meeting at PAS. (Steering committee approved at last meeting)
Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutesof Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20592
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Susan Hintz
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT secondary update
Date: Friday, April 11, 2008 4:14:07 PM

So have I - I have the blood of trees in my hands.

Sent from my iPhone

On Apr 11, 2008, at 1:02 PM, "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov > wrote:

> We have just made copies
> Thanks
> Rose
>
> -----Original Message-----
> From: Susan Hintz [mailto:srhintz@stanford.edu]
> Sent: Friday, April 11, 2008 3:44 PM
> To: Higgins, Rosemary (NIH/NICHD) [E]
> Subject: SUPPORT secondary update
>
> Hi Rose
>
> I am bringing copies of these to the Steering Committee meeting.
> Just wanted you to have electronic copies. I sent also to Neil.
>
> Thanks
>
> susan

From: Gantz, Marie
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT FU
Date: Thursday, April 10, 2008 1:38:28 PM

Yes, I will do that.

Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-6255

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, April 10, 2008 1:31 PM
To: Gantz, Marie
Subject: RE: SUPPORT FU

When you do these, can you tell me when the windows closed by site and study number?
Thanks
Rose

-----Original Message-----
From: Gantz, Marie [mailto:mgantz@rti.org]
Sent: Tuesday, April 08, 2008 9:23 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; adas@rti.org
Subject: RE: SUPPORT FU

Yes, I will get you those numbers.

Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-6255

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, April 08, 2008 1:55 AM
To: Das, Abhik; Gantz, Marie
Subject: SUPPORT FU

Can you tell me how many and the study numbers of children with FU pending for SUPPORT from Miami, Rochester, Wake Forest?
Also, though with missing forms from those sites?
It can wait a few weeks.

Thanks
Rose

Sent from my BlackBerry Wireless Handheld

From:	Zaterka-Baxter, Kristin
To:	nxs5@cwru.edu; Nancy.Miller@UTSouthwestern.edu; melissa.leps@utsouthwestern.edu; ae5357@wayne.edu; du2744@wayne.edu; ellen_hale@oz.ped.emory.edu; grisbyca@email.uc.edu; ldw@iupui.edu; monica.konstantino@yale.edu; ahensman@wihri.org; mbball@leland.stanford.edu; mcollins@peds.uab.edu; Georgia.E.McDavid@uth.tmc.edu; foy00004@mc.duke.edu; bmackinnon@tufts-nemc.org; karen-johnson@uiowa.edu; karen.osborne@hsc.utah.edu; CBackstrom@salud.unm.edu; Rich, Wade
Cc:	Gantz, Marie; Das, Abhik; Higgins, Rosemary (NIH/NICHD) [E]; Auman, Jeanette O.
Subject:	Support Protocol "Other" Reports
Date:	Wednesday, April 09, 2008 10:53:33 AM

Hi all,
Please note we have posted the following reports to the NRN website (neonatal.rti.org >private gateway >administration >site reports > *your site* >support protocol ***other*** report:

"HFNC in CPAP group first 14 days Mar 08"
"PDs not reported on SUP5 Mar 08"
"Support Pulse Ox Gap Report"
"Support Study Oximeter Report"

Thanks and please let me know if you have any questions,
Kris

Kris Zaterka-Baxter
Statistics and Epidemiology Division
RTI International
3040 Cornwallis Road
P.O. Box 12194
RTP, NC 27709-2194 USA
(tel) 919-485-7750
(fax) 919.485.7762
kzaterka@rti.org
www.rti.org

Federal Express/UPS/DHL Shipping Address:
4426 South Miami Blvd
Durham, NC 27703 USA

From: Huitema, Carolyn Petrie
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: support call
Date: Tuesday, April 01, 2008 9:14:25 AM

Hi-

You suggested we discuss the physiologic definition on today's call.
Barbara Stoll will not be on the call (not on Subcommittee) so we are trying to schedule a separate time to finalize the phys def of BPD.

I think the main discussion needs to take place between you, Michele, Barbara, and Abhik.

Carolyn Huitema

Research Analyst
RTI International
(301) 270-6664
petrie@rti.org

From: Julie Rohr
Subject: oximeters
Date: Thursday, March 27, 2008 7:30:40 PM

I received the 4 study oximeters from Utah, got them through our clinical engineering department, and had the new oximeter on our study patient at 1655 our time.
Thanks to everyone for their help in getting oximeters to us.
Also, I will send the Alabama 5 to Masimo tomorrow.
Julie

Julie Rohr MSN RNC
Nurse/Clinical Trials Coordinator
Department of Pediatrics
UNM Hospital
2211 Lomas Blvd NE
Albuquerque, NM 87106
(505) 272-0363

From:	Zaterka-Baxter, Kristin
To:	Higgins, Rosemary (NIH/NICHD) [E]
Cc:	Das, Abhik
Subject:	FW: SUPPORT
Date:	Thursday, March 27, 2008 6:25:06 PM

Does this request also have to go through the Steering Committee; please see below.
Thanks,
Kris

From: Charlene Thornton [mailto:cthornton@ctc.usyd.edu.au]
Sent: Thursday, March 27, 2008 5:28 PM
To: Zaterka-Baxter, Kristin
Subject: SUPPORT

Dear Kris

I am looking for information regarding the DSMC for the SUPPORT trial.

I have the slides from a meeting held in January 2006. Can you please tell me who the members of the DSMC are? And if they have met since this time?

I am compiling a report on all of the trials prior to the NeOProM meeting at PAS in May.

Thanking you for your assistance.

Charlene Thornton
Systematic Reviews Officer
University of Sydney
NHMRC Clinical Trials Centre

From: Finer, Neil
To: Edmund Hey
Cc: Rich, Wade; Higgins, Rosemary (NIH/NICHD) [E]; Michael OReilly; Maribeth Sayre
Subject: RE: An incident with a recent UK BOOST trial baby I need to tell you about
Date: Thursday, March 27, 2008 11:54:56 AM

Hi Edmund

Centers in the SUPPORT study that use Sat Share – probably 2/3rds of the centers, are advised to disable the numeric display on the Masimo once the Sat Share is connected to the bedside monitor.

As a result, we would not have been able to replicate your observation.

It is important to understand that the Sat Share cable functions so that the Masimo acts as a patient sensor, and the bedside monitor then receives the SpO2 value as if it were the baby. The bedside monitor will have its own internal algorithms for motion artifact and sensitivity, and thus it is very possible that a low quality signal from the Masimo may be considered artifact by the bedside.

There are no doubt times when the displayed value of SpO2 may differ because of this and it was for that reason that we recommended that the Masimo numeric display be disabled. We realized that this could be a problem but felt that overall it reduced alarms and caretaker fatigue.

We noted that you indicated that the bedside monitor is displaying a relayed summary of the Masimo data. Do you set the bedside monitor to a trend mode? Our understanding is that the bedside monitor sees the Masimo as a patient ie a sensor, and the Masimo transmits the current SpO2 that it is reading to the bedside in the same way a sensor would.

We appreciate your concern. For our study, some centers do use the Masimo as the only oximeter.

I hope this helps and that Masimo can shed some light on this.

Neil

Neil N. Finer, M.D.

Professor of Pediatrics

Director, Division of Neonatal-Perinatal Medicine

UC San Diego School of Medicine

UC San Diego Medical Center, Hillcrest

402 Dickinson St., MPF 1-140

San Diego, CA 92103-8774

Telephone: 619.543-3759

Facsimile: 619.543.3812

From: Edmund Hey [mailto:shey@easynet.co.uk]
Sent: Thursday, March 27, 2008 2:31 AM

To: Finer, Neil
Cc: Rich, Wade
Subject: An incident with a recent UK BOOST trial baby I need to tell you about
Importance: High

Neil,

One more small set back for the UK BOOST trial I fear The incident I have been asked to tell you about concerns an occasion when the monitoring of saturation became misleading because staff were not looking at what the Masimo trial monitor was saying but at a relayed summary of this displayed on a multi-channel host monitor. I attach a copy of the formal 'alert' that has now gone out from Oxford to all UK centres. Whether this is of import to you I don't know, but I was under the impression that quite a lot of units recruiting into SUPPORT were using SatShare facilities. Has anything similar ever been reported in America either on a trial or a non-trial baby ? This is what the briefing statement sent round to UK trial centres said:

"Some recruiting centres in the UK BOOST Trial are planning to use the 'SatShare' facility to transfer saturation values from the BOOST study oximeter to a host monitor. This might be seen to carry the advantage of sticking with a familiar monitoring system. However, an incident that was identified in one unit last week caused serious concern. A study infant was having their saturation values sent to a host monitor using SatShare. The study oximeter had its alarms disabled as these were being set on the host monitor. A highly observant nurse noted that the host monitor was displaying a fixed high saturation value persistently when the BOOST oximeter was displaying a low value. An additional oximeter was used to check. The BOOST study oximeter was working normally but the values being displayed on the host monitor had become unreliable. Thankfully the infant remained well throughout. This incident is still being investigated with the help of the manufacturers. It is not yet clear whether this was a software compatibility issue between the two systems or one related to a loose connection. *In view of this epsiode we presently recommend strongly that the BOOST study oximeter should be used as the primary guide to clinical care in study infants, and that its alarms should not be disabled.* There are very many different combinations of host monitor and SatShare cable, and consequently we cannot guarantee to advise you fully on the safe use of the SatShare system until we have done further work with Massimo."

I am sure Peter Brocklehurst was right to conclude that this incident needed to be shared with the PIs of the other trials. Let me know if you need further back ground information. Given that you must have several years of experience of using Masimo monitors with link cables to other display devices by now, my colleagues in the UK really *would* be grateful for any feed-back or advice that you can give us.

Edmund

From:	Zaterka-Baxter, Kristin
To:	ahensman@wihri.org; mbball@leland.stanford.edu; grisbyca@email.uc.edu; ellen_hale@oz.ped.emory.edu; Georgia E McDavid; mcollins@peds.uab.edu; monica.konstantino@yale.edu; Nancy.Miller@UTSouthwestern.edu; Nancy Newman; ldw@iupui.edu; Mackinnon, Brenda; Johnson, Karen; Karen.Osborne@hsc.utah.edu; Conra Backstrom; Shankaran, Seetha; CATHY A. GRISBY; mbball@leland.stanford.edu; Katherine A Foy; melissa.leps@utsouthwestern.edu
Cc:	wrich@ucsd.edu; Pickett, James; Auman, Jeanette O.; Gantz, Marie; Cunningham, Meg; Huitema, Carolyn Petrie; Das, Abhik; Higgins, Rosemary (NIH/NICHD) [E]
Subject:	SUPPORT Oximeters & Time Change
Date:	Thursday, March 13, 2008 10:58:15 AM
Importance:	High

Hi all,

Here is a LATE reminder **ABOUT DAYLIGHT SAVINGS TIME AND THE MASIMO STUDY OXIMETERS:**

Daylight Savings Time Changes for Support:

1) Change all oximeters not in current use as soon as possible (if you have not already done so).

2) Do not change oximeters currently in use until they are put on another patient.

RTI will make any necessary back-corrections at their end.

Thanks.

Kris

Kris Zaterka-Baxter

Statistics and Epidemiology Division

RTI International

3040 Cornwallis Road

P.O. Box 12194

RTP, NC 27709-2194 USA

(tel) 919-485-7750

(fax) 919.485.7762

kzaterka@rti.org

www.rti.org

Federal Express/UPS/DHL Shipping Address:

4426 South Miami Blvd

Durham, NC 27703 USA

From: Finer, Neil
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Martinez, Fernando
Subject: RE: SUPPORT UPDATE FOR SC
Date: Monday, March 03, 2008 3:39:08 PM

That would be fine
Thanks Rose

Neil N. Finer, M.D.
Professor of Pediatrics
Director, Division of Neonatal-Perinatal Medicine
UC San Diego School of Medicine
UC San Diego Medical Center, Hillcrest
402 Dickinson St., MPF 1-140
San Diego, CA 92103-8774
Telephone: 619.543-3759
Facsimile: 619.543.3812

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, March 03, 2008 10:52 AM
To: Finer, Neil
Cc: Cunningham, Meg
Subject: SUPPORT UPDATE FOR SC

Neil
We have scheduled a support subcommittee call in advance of the SC meeting. Can we put you on the agenda for 11:05 am on Monday April 14 for up to an hour to update the Steering Committee? If the time doesn't work, let me know what time is good for you that day.

Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Finer, Neil
To:	Higgins, Rosemary (NIH/NICHD) [E]; Gantz, Marie; Das, Abhik
Cc:	Michael OReilly; Rich, Wade
Subject:	RE: Lost data vs misaligned data on Jan 1, 2008 on masked oximeters
Date:	Friday, February 22, 2008 11:09:56 AM

Hi Rose
I think that these numbers should be provided to Masimo. Ensure that we copy these to both Marybeth and to Michael OReilly
Neil

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, February 22, 2008 6:20 AM
To: Gantz, Marie; Das, Abhik; Finer, Neil
Subject: RE: Lost data vs misaligned data on Jan 1, 2008 on masked oximeters

Neil
Would this be helpful?
Rose

From: Gantz, Marie [mailto:mgantz@rti.org]
Sent: Friday, February 22, 2008 9:19 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik
Subject: RE: Lost data vs misaligned data on Jan 1, 2008 on masked oximeters

I can provide the serial numbers of the NRN oximeters that had this issue.

Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-6255

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, February 22, 2008 9:15 AM
To: Das, Abhik; Gantz, Marie
Subject: FW: Lost data vs misaligned data on Jan 1, 2008 on masked oximeters
Importance: High

FYI

From: Finer, Neil [mailto:nfiner@pedsmail.ucsd.edu]
Sent: Thursday, February 21, 2008 11:13 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; Wally Carlo, M.D.
Subject: FW: Lost data vs misaligned data on Jan 1, 2008 on masked oximeters
Importance: High

Hi Wally and Rose
Stay tuned!!
Neil

From: Maribeth Sayre [mailto:msayre@masimo.com]
Sent: Thursday, February 21, 2008 5:58 PM
To: Finer, Neil; Rich, Wade; williamtm@med.usyd.edu.au; Alpana Ghadge; Rikki Mills; Jim Litchfield; brian.darlow@otago.ac.nz; jan@promedtech.co.nz; barbara.schmidt@uphs.upenn.edu; Lorrie Costantini; Stacey Taggart; shey@easynet.co.uk; Breidge Boyle; Michelle Gabriel; Paul Cornick
Cc: Michael OReilly; Chris Novak; Stephen Taylor; Valerie Begnoche; Dave Baker; Phil Weber
Subject: Lost data vs misaligned data on Jan 1, 2008 on masked oximeters
Importance: High

Hello all,

There is a problem with the data from Jan 1, 2008 on the study masked oximeters. It was first noted by Dr Edmund Hey in the UK, and has subsequently been seen in SUPPORT babies in the US. The data on Jan 1, 2008 is repetition of a single bit of data for the whole 24 hours. The data on Jan 2, 2008 is a standard recording. There is some question as to whether the data recorded on Jan 2 is actually the data from Jan 1 (misaligned data/date) or whether the data from Jan 1, 2008 is lost. The problem seems to be related to Leap Year. Masimo has been trying to duplicate the problem, but has not been able to reproduce this error during testing of both standard and masked Radicals.

We have contacted UCSD, where they have found the problem in masked Radicals. Tomorrow, Feb 22, we will pick up one of the affected masked Radicals from UCSD, along with a standard Radical with the same problem. We will bring these Radicals back to Irvine for testing. As soon as we have results from these tests, I will send them to you. We are looking for answers to the following questions:

1. Is the data recorded on Jan 2, 2008 actually data from that date, or is it the data from Jan 1? (Misaligned data/date problem)

2. If the data recorded on Jan 2, 2008 is from Jan 2, what happened to the data from Jan 1, 2008? (Lost data)
3. If the data from Jan 1, 2008 is lost, is it recoverable?
4. If there is a Misalignment of data and date, how can it be corrected?
5. What will happen on Feb 29, 2008 and Mar 1, 2008?
6. What caused the problem? How can we fix it?

I apologize to all of you for this problem. I am very aware of how serious it is. We have 2 teams of technical and engineering people working on this. We will get information to you as soon as we have it.

I do have a request. Could all of you who have identified this problem in your NICUs please send me the serial numbers of the affected oximeters? We suspect that all of the masked oximeters may be involved, but don't know if this is true.

Please be assured we are working diligently to identify the error and correct it. And please accept my regrets for all the difficulty this has caused.

Please let me know if you have questions. Unfortunately I will be out of the office on sick leave for the next 5 days, but I will answer emails as soon as possible. For technical issues, please contact Chris Novak at: cnovak@Masimo.com

For all other issues, please contact Valerie Begnoche at: vbegnoche@Masimo.com
or Dave Baker at: dbaker@Masimo.com
Please copy me on all emails, as usual.

Thank you all for your patience and understanding.

Best regards,
Maribeth

****

From:	Gantz, Marie
To:	Das, Abhik
Cc:	Higgins, Rosemary (NIH/NICHD) [E]
Subject:	RE: Lost data vs misaligned data on Jan 1, 2008 on masked oximeters
Date:	Friday, February 22, 2008 9:23:27 AM

When I first looked at this on February 8, there were 7 infants on oximeters on January 1 and all had the issue.

Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-6255

From: Das, Abhik
Sent: Friday, February 22, 2008 9:20 AM
To: Gantz, Marie
Cc: 'Higgins, Rosemary (NIH/NICHD) [E]'
Subject: RE: Lost data vs misaligned data on Jan 1, 2008 on masked oximeters

Is it all of the ones we had active on Jan 1-2?

From: Gantz, Marie
Sent: Friday, February 22, 2008 9:19 AM
To: 'Higgins, Rosemary (NIH/NICHD) [E]'; Das, Abhik
Subject: RE: Lost data vs misaligned data on Jan 1, 2008 on masked oximeters

I can provide the serial numbers of the NRN oximeters that had this issue.

Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-6255

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, February 22, 2008 9:15 AM
To: Das, Abhik; Gantz, Marie
Subject: FW: Lost data vs misaligned data on Jan 1, 2008 on masked oximeters
Importance: High

FYI

From: Finer, Neil [mailto:nfiner@pedsmail.ucsd.edu]
Sent: Thursday, February 21, 2008 11:13 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; Wally Carlo, M.D.
Subject: FW: Lost data vs misaligned data on Jan 1, 2008 on masked oximeters
Importance: High

Hi Wally and Rose
Stay tuned!!
Neil

From: Maribeth Sayre [mailto:msayre@masimo.com]
Sent: Thursday, February 21, 2008 5:58 PM
To: Finer, Neil; Rich, Wade; williamtm@med.usyd.edu.au; Alpana Ghadge; Rikki Mills; Jim Litchfield; brian.darlow@otago.ac.nz; jan@promedtech.co.nz; barbara.schmidt@uphs.upenn.edu; Lorrie Costantini; Stacey Taggart; shey@easynet.co.uk; Breidge Boyle; Michelle Gabriel; Paul Cornick
Cc: Michael OReilly; Chris Novak; Stephen Taylor; Valerie Begnoche; Dave Baker; Phil Weber
Subject: Lost data vs misaligned data on Jan 1, 2008 on masked oximeters
Importance: High

Hello all,

There is a problem with the data from Jan 1, 2008 on the study masked oximeters. It was first noted by Dr Edmund Hey in the UK, and has subsequently been seen in SUPPORT babies in the US. The data on Jan 1, 2008 is repetition of a single bit of data for the whole 24 hours. The data on Jan 2, 2008 is a standard recording. There is some question as to whether the data recorded on Jan 2 is actually the data from Jan 1 (misaligned data/date) or whether the data from Jan 1, 2008 is lost. The problem seems to be related to Leap Year. Masimo has been trying to duplicate the problem, but has not been able to reproduce this error during testing of both standard and masked Radicals.

We have contacted UCSD, where they have found the problem in masked Radicals. Tomorrow, Feb 22, we will pick up one of the affected masked Radicals from UCSD, along with a standard Radical with the same problem. We will bring these Radicals back to Irvine for testing. As soon as we have results from these tests, I will send them to you. We are looking for answers to the following questions:

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Please be assured we are working diligently to identify the error and correct it. And please

accept my regrets for all the difficulty this has caused.

Please let me know if you have questions. Unfortunately I will be out of the office on sick leave for the next 5 days, but I will answer emails as soon as possible. For technical issues, please contact Chris Novak at: cnovak@Masimo.com

For all other issues, please contact Valerie Begnoche at: vbegnoche@Masimo.com
or Dave Baker at: dbaker@Masimo.com
Please copy me on all emails, as usual.

Thank you all for your patience and understanding.

Best regards,
Maribeth

From:	Finer, Neil
To:	Higgins, Rosemary (NIH/NICHD) [E]
Subject:	RE: SUPPORT
Date:	Tuesday, February 12, 2008 5:05:34 PM

Hi Rose
I would think a phone call in advance would work well and avoid any other meeting conflicts and potentially allow more time. I would suggest about 90 minutes and ask that you poll the group for times etc.
I will be in Hawaii – will the group meet there?
Thanks
Neil

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, February 12, 2008 11:59 AM
To: Finer, Neil
Subject: RE: SUPPORT

What ever you think would be most productive and effective – we can certainly do both –
Let me know
Rose

From: Finer, Neil [mailto:nfiner@pedsmail.ucsd.edu]
Sent: Tuesday, February 12, 2008 2:56 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT

Hi Rose
If we meet in advance by telephone, the only problem is the attendance by others – but the focus would be fine. Would me meet in advance and then again at the Steering Comm or only once?
Thanks
Neil

Neil N. Finer, M.D.
Professor of Pediatrics
Director, Division of Neonatal-Perinatal Medicine
UC San Diego School of Medicine
UC San Diego Medical Center, Hillcrest
402 Dickinson St., MPF 1-140
San Diego, CA 92103-8774
Telephone: 619.543-3759
Facsimile: 619.543.3812

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, February 12, 2008 11:26 AM
To: Finer, Neil
Cc: Cunningham, Meg
Subject: SUPPORT

Neil
Would you like the SUPPORT Subcommittee to meet in person or in advance of the steering committee meeting in April (Meeting is April 14-15). Let me know – we will have the phone lines available at the meeting regardless of the timing of the subcommittee meeting.

Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Finer, Neil
To:	Edmund Hey
Cc:	Rich, Wade; Higgins, Rosemary (NIH/NICHD) [E]; Wally Carlo, M.D.
Subject:	RE: Your message to Marybeth
Date:	Friday, February 08, 2008 5:34:18 PM

Hi Edmund
We will keep Masimo's feet to the fire.
Be well
Neil

From: Edmund Hey [mailto:shey@easynet.co.uk]
Sent: Friday, February 08, 2008 1:43 PM
To: Finer, Neil
Subject: Your message to Marybeth

Neil,

Thank you for copying me in to your e-mail to Marybeth. I gather the NPEU were landed with this new 'firmware' here in the UK three months ago just as our trial was about to start, but they were certainly not told that what was being installed was different from what the other trials were using. They were certainly not told that this would make it impossible to download data using all their current software programmes. The only thing they were told was that the alarms would now be triggered when the set value was passed rather than when it was reached. Nothing else. The people in Canada were not even told that and only finally discovered, after I alerted them, that they had actually been sent some trial monitors that functioned the old way and some that functioned the new way.

This lack of communication by Mariybeth has caused the computer programmer here in Oxford to spend the best part of two months trying to solve these problems in the misleading belief that they were due to problems with his software and not with the changes that Masimo had undertaken without explanation. It means, as you say, that we have not been able to monitor or audit ***any*** of the oximeter data coming on any of the trial babies since the trial opened three months ago. This has badly shaken everyone's confidence. It was hard enough to get clinicians to start using an oximeter with which they were not very familiar (Masimo oximeters are not at present widely used in the UK), and it has even started to make some clinicians uncertain about continuing to back the trial. None of this could have happened at a worse time. I find it even more amazing that none of this would have come to light even now had I not contacted Wade on my own initiative earlier today when I discovered that nobody on this side of the Atlantic could tell those managing this trial in the NPEU at Oxford why all the machines malfunctioned on New Years day.

We all clearly deserve a much more complete explanation of what has transpired over the last four months than has been forthcoming to date. Those running the UK trial here in the UK (I am only an unpaid advisor) did not even know that the new firmware would not work with any of the old customised software programmes for downloading data from the machine's memory. If you knew this why were the people in Oxford not told ? I find this all extremely disturbing. Do keep me posted with developments.

Edmund

From: Finer, Neil [mailto:nfiner@pedsmail.ucsd.edu]
Sent: 08 February 2008 20:33
To: Maribeth Sayre; shey@easynet.co.uk; Rich, Wade
Cc: Chris Novak; Mike Petterson; Daniel Draper; Valerie Begnoche; Walt Weber; Ammar Al-Ali; williamtm@med.usyd.edu.au; alpana.ghadge@ctc.usyd.edu.au; Rikki Mills; Jim Litchfield;

brian.darlow@chmeds.ac.nz; jan@promedtech.co.nz; barbara.schmidt@uphs.upenn.edu; costan@mcmaster.ca; Stacey Taggart; Paul Cornick; Breidge Boyle
Subject: RE: Masimo moasked oximeters

Hello Marybeth
I am concerned regarding the tone of your email. If Masimo made a change in the firmware and was aware as you should be, that we and others are conducting research during which we are using the actual download which is keyed to the infants care on the day, hour and minute in question, we would have expected that Masimo would have informed all the users both for clinical use and research that as of Jan 1 2008, there would be a misalignment of the stored oximetry data. .As you are aware, we are using the old firmware because the new generation of firmware made changes to the serial data output stream, also never communicated to us, which would have made our data analysis software obsolete. Masimo did not inform any of us at that time, nor have they informed us about this potentially very significant issue. Masimo has created a very problematic situation regarding the interpretation of the data. It is surprising that you are upset that the users want to fix this issue as quickly and efficiently as possible, as Masimo as noted, did not inform the current users of oximeters with the old firmware of these circumstances. Wade actually called your cell to inform you of this problem.
I would hope that any future communications will be appropriate and respectful of everyone's position, and be mindful that we are using these oximeters on a large population of fragile infants to determine the optimal SpO2 ranges for their care.
Lets also set the record straight that everyone working on these studies is also very busy, mostly caring for fragile and compromised infants.
Respectfully
Neil Finer

From: Maribeth Sayre [mailto:msayre@masimo.com]
Sent: Friday, February 08, 2008 11:26 AM
To: shey@easynet.co.uk; Rich, Wade; Finer, Neil
Cc: Chris Novak; Mike Petterson; Daniel Draper; Valerie Begnoche; Walt Weber; Ammar Al-Ali; williamtm@med.usyd.edu.au; alpana.ghadge@ctc.usyd.edu.au; Rikki Mills; Jim Litchfield; brian.darlow@chmeds.ac.nz; jan@promedtech.co.nz; barbara.schmidt@uphs.upenn.edu; costan@mcmaster.ca; Stacey Taggart; Paul Cornick; Breidge Boyle
Subject: Masimo moasked oximeters

Hi Gentlemen:

I must again insist that when you have problems or questions relating to the masked oximeters used in the NeoPROM trials that you notify me as the liaison person at Masimo. PLEASE DO NOT SEND QUERIES OR PROBLEMS TO WALT WEBER OR ANY OTHER OF THE ENGINEERS! By all means, send technical problems to Tech Support, and copy me, or vice versa. If there is a problem needing the expertise of any of our engineers, I, or Tech Support, will direct it to them. There are 2 reasons for this policy: (1) As liasion person for Masimo, I need to be aware of any problems. (2) Our engineers are extremely busy working on other projects, and we do not want them side-tracked. I hope it will not be necessary for Masimo to take steps to block your messages to engineers.

To the current problem of data labeled January 1 being repetetive, and the actual data for January 1 being the data listed for January 2: This is apparently related to 2008 being a Leap Year.

I am trying to ascertain the options for correcting the date on the data collected after Jan 1. I will send out an email to all the NewPROM participants as soon as I have options to offer. I will include what to expect on February 29.

I apologize for this inconvenience and will get some options to you as soon as possible.

Thanks,
Maribeth

****

Blansfield, Earl (NIH/NICHD) [E]

From: Gantz, Marie <mgantz@rti.org>
Sent: Wednesday, November 21, 2007 2:55 PM
To: REverett@med.miami.edu; SDuara@med.miami.edu
Cc: Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik; Auman, Jeanette O.
Subject: Missing ROP outcomes for SUPPORT

Follow Up Flag: For Your Information
Flag Status: Flagged

Sometime in the next week or so, Rose will be sending out reminders to enter data for infants whose ROP outcomes for SUPPORT are currently missing. Last month, you had four such infants whose acute ROP status had not been obtained and probably will not be obtained in the future. It was determined through conversations between RTI and Dale Phelps that it made the most sense to let you mark the outcomes as permanently missing using the new questions on SUPP10. Jenny is currently working on getting those questions into the DMS. So, I just wanted to let you know that those 4 infants will still appear on your missing outcomes reminder this month, but as soon as the new SUPP10 questions are available, you will be able to mark them as permanently missing and the reminders will stop.

Thanks, and have a great Thanksgiving!

Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-6255

From:	Finer, Neil
To:	Charlene Thornton; Higgins, Rosemary (NIH/NICHD) [E]
Cc:	Rich, Wade; Wally Carlo, M.D.
Subject:	RE: NeOProM
Date:	Thursday, January 31, 2008 8:10:17 PM

Hi Charlene
Welcome to your new position.
I would like to receive correspondence about any issues, and would want you to include Wade Rich (wrich@ucsd.edu) The Study Coordinator in any such information. I will ask that Rose indicate her preferences and list any additional contacts. In addition Rose would need to approve providing you with any of the requested documents. It is my understanding that Lisa has been given all of this. Do you need additional information other than what Lisa has?
I will be in Hawaii and have a Resuscitation meeting to follow the PAS. It would be great to arrange a meeting there. I would also want to include Dr Wally Carlo in any such meeting and include him as an additional individual to be included in all correspondence.
Regards
Neil Finer

From: Charlene Thornton [mailto:cthornton@ctc.usyd.edu.au]
Sent: Thursday, January 31, 2008 4:30 PM
To: Finer, Neil; higginsr@mail.nih.gov
Subject: NeOProM

Dear Neil and Rosemary

I am the new co-ordinator for the NeOProm – neonatal oxygenation prospective meta-analysis – working with Lisa Askie at the Clinical Trails Centre in Sydney, Australia.

My position involves organising matters for this collaboration.

To assist me in this role I request some information from you.

Would you like all contact for this collaboration to go through you or do you have an assistant you would like for me to cc in on all emails?

Can you please provide for me the key people working on SUPPORT ie Trial Co-ordinator etc and their email addresses so I can contact them re information about the trial. I would like a copy of the latest SUPPORT protocol and/or handbook and copies of the data collection forms. As you are aware, we are trying to collect similar data to allow for the PMA to occur and this would assist me in aligning data if I knew what each trial was collecting.

The final matter is the collaborators meeting I am trying to organise at PAS in May 2008 in Hawaii. Will you be attending PAS? And if so, are you interested in attending the NeOProM satellite meeting? I will be in contact again shortly if would like to attend with potential meeting times.

Thanking you for your assistance

Charlene Thornton
Systematic Reviews Officer
University of Sydney
NHMRC Clinical Trials Centre

From: Susan Hintz
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT ANCILLARY STUDY
Date: Thursday, January 24, 2008 1:20:51 PM

No - haven't heard from her.

Susan

Sent from my iPhone

On Jan 24, 2008, at 8:32 AM, "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov
> wrote:

> Did Ricki Goldstein get in touch with you regarding grade III-IV IVH?
> Thanks
> Rose
> ----------
> Sent from my BlackBerry Wireless Handheld
>
>
> ----- Original Message -----
> From: Susan Hintz <srhintz@stanford.edu>
> To: Higgins, Rosemary (NIH/NICHD) [E]
> Sent: Thu Jan 24 10:41:14 2008
> Subject: Re: SUPPORT ANCILLARY STUDY
>
> No big deal. I will call you next week
>
> Susan
>
> Sent from my iPhone
>
> On Jan 24, 2008, at 2:56 AM, "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov
>> wrote:
>
>> I will be at council all day-is there a time you had in mind??
>> ----------
>> Sent from my BlackBerry Wireless Handheld
>>
>>
>> ----- Original Message -----
>> From: Susan Hintz <srhintz@stanford.edu>
>> To: Higgins, Rosemary (NIH/NICHD) [E]
>> Sent: Thu Jan 24 01:16:45 2008
>> Subject: Re: SUPPORT ANCILLARY STUDY
>>
>> Hi Rose
>>
>> I would like to ask you something about this. I am out of town
>> speaking at a conference, but I may try to call you tomorrow.
>>
>> Thanks
>>
>> S

>>
>> Sent from my iPhone
>>
>> On Jan 23, 2008, at 12:34 PM, "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov
>>> wrote:
>>
>>
>>
>> Hi
>>
>> Attached is a secondary to SUPPORT for FU and potential 6-7 year
>> FU. Let me know if you would like to have a call to discuss. I
>> have included Susan Hintz on the email as this relates to the MRI/FU
>> and the potential 6-7 year FU protocol.
>>
>> Thanks
>> Rose
>>
>>
>>
>> Rosemary D. Higgins, M.D.
>>
>> Program Scientist for the Neonatal Research Network
>>
>> Pregnancy and Perinatology Branch
>>
>> Center for Developmental Biology and Perinatal Medicine
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>> NICHD, NIH
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>> 6100 Executive Blvd., Room 4B03B
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>> MSC 7510
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>> Bethesda, MD 20892
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>> (For overnight delivery, use Rockville, MD 20852)
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>> 301-435-7909
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>> 301-496-3790 (FAX)
>>
>> <mailto:higginsr@mail.nih.gov> higginsr@mail.nih.gov
>>
>>
>>
>> <Proposal for ancillary study to Support Trial (2).doc>
>>
>> <Working_Memory_in_ELBW_12-1-07 (2).doc>
>>

From:	Huitema, Carolyn Petrie
To:	mcw3@cwru.edu; Pablo.Sanchez@UTSouthwestern.edu; sshankar@med.wayne.edu; [SCRN] Stoll, Barbara; kurt.schibler@cchmc.org; bpoindex@iupui.edu; richard.ehrenkranz@yale.edu; alaptook@WIHRI.org; vanmeurs@stanford.edu; wcarlo@peds.uab.edu; Kathleen.A.Kennedy@uth.tmc.edu; goldb008@mc.duke.edu; IFrantz@tufts-nemc.org; edward-bell@uiowa.edu; Roger.Faix@hsc.utah.edu; kwatterberg@salud.unm.edu; nxs5@cwru.edu; Nancy.Miller@UTSouthwestern.edu; melissa.leps@utsouthwestern.edu; Bara, Rebecca; du2744@wayne.edu; ellen_hale@oz.ped.emory.edu; grisbyca@email.uc.edu; ldw@iupui.edu; monica.konstantino@yale.edu; ahensman@wihri.org; mbball@leland.stanford.edu; mcollins@peds.uab.edu; Georgia.E.McDavid@uth.tmc.edu; foy00004@mc.duke.edu; bmackinnon@tufts-nemc.org; karen-johnson@uiowa.edu; karen.osborne@hsc.utah.edu; CBackstrom@salud.unm.edu; bbillian@wayne.edu
Cc:	Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik; nfiner@ucsd.edu; Wade Rich; Gantz, Marie; Auman, Jeanette O.; Pickett, James; Cunningham, Meg; Archer, Stephanie (NIH/NICHD) [E]; Zaterka-Baxter, Kristin; Huitema, Carolyn Petrie
Subject:	The use of High Flow Nasal Cannual (HFNC) in the CPAP arm of the SUPPORT Trial (SUP13)
Date:	Wednesday, January 23, 2008 4:54:23 PM
Attachments:	SUP13.pdf

Dear All-

Attached is the SUPPORT Study Technical Memo #13.
This technical memo outlines the use of High Flow Nasal Cannual (HFNC) in the CPAP arm of the SUPPORT Trial

- The use of HFNC is not a protocol deviation and a SUPP06 should not be completed.
- However, the use of HFNC is strongly discouraged during the first 14 days in CPAP infants, especially those who have not been intubated.
- HFNC as it pertains to SUPPORT is nasal cannula with flow >.5L (per SUPPORT Technical Memo #4).
- The Data Coordinating Center will continue to monitor use of HFNC through the SUPP05.

Thank you,
Carolyn Huitema

Research Analyst
RTI International
(301) 270-6664
petrie@rti.org

RTI INTERNATIONAL | **Memorandum**

January 23, 2008

SUPPORT TECHNICAL MEMO # 13

TO: Network Coordinators
Network PIs

FROM: The Data Coordinating Center

SUBJECT: High Flow Nasal Cannula (HFNC)

This technical memo outlines the use of High Flow Nasal Cannual (HFNC) in the CPAP arm of the SUPPORT Trial

- The use of HFNC is not a protocol deviation and a SUPP06 should not be completed.
- However, the use of HFNC is strongly discouraged during the first 14 days in CPAP infants, especially those who have not been intubated.
- HFNC as it pertains to SUPPORT is nasal cannula with flow >.5L (per SUPPORT Technical Memo #4).
- The Data Coordinating Center will continue to monitor use of HFNC through the SUPP05.

The reason for this is as follows:

The use of High Flow Nasal Cannula (HFNC) has been monitored to discourage its use in the first 14 days for infants assigned to CPAP due to the fact that the level of potential CPAP achieved is not measured. HFNC as it pertains to SUPPORT is defined as nasal cannula with flow >.5L (per SUPPORT technical memo #4). The use of HFNC was NOT a pre-specified protocol violation for this trial, thus, centers are not expected to report it as a protocol deviation on form SUPP06. However, the Data Coordinating Center will continue to monitor and provide feedback to the centers on the use of HFNC based on data collected on form SUPP05. Please also note that many of the items that are collected and provided to the centers were not pre-specified protocol violations as indicated in Section 4.3 of the protocol. The goal of tracking the additional items is to ensure that those suggestions which have been included in the Manual of Operations or in technical memos since the protocol was finalized are being followed. NRN centers should continue the proscription of HFNC in the first 14 days in the CPAP infants, especially those who have not been intubated.

Cc Rosemary Higgins, MD

From: Susan Hintz, via an autoresponder
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Away from the office [Re: SUPPORT ANCILLARY STUDY]
Date: Wednesday, January 23, 2008 3:34:10 PM

I will be speaking at a conference out of town from Wednesday 1/23/08 through Friday 1/25/08. Your email regarding SUPPORT ANCILLARY STUDY will be read when I return. Should you need to contact me urgently, please call my office 650-723-5711.

From:	Huitema, Carolyn Petrie
To:	Higgins, Rosemary (NIH/NICHD) [E]; Archer, Stephanie (NIH/NICHD) [E]; Das, Abhik
Cc:	Zaterka-Baxter, Kristin; Cunningham, Meg
Subject:	FW: SUPPORT Oximeter shipping list
Date:	Tuesday, January 22, 2008 9:50:20 AM
Attachments:	SUPPORTCoordinators20080122.pdf

SUPPORT Oximeter Shipping List attached.

From: Huitema, Carolyn Petrie
Sent: Tuesday, January 22, 2008 9:47 AM
To: Huitema, Carolyn Petrie; 'Angelita Hensman'; 'Nancy Newman'; 'Katherine A Foy'; 'Ellen Hale'; 'ldw@iupui.edu'; 'mbball@leland.stanford.edu'; 'Mackinnon, Brenda'; 'mcollins@peds.uab.edu'; 'Wade Rich'; 'grisbyca@email.uc.edu'; 'Johnson, Karen'; 'Conra Lacy'; 'Nancy Miller'; 'Georgia.E.McDavid@uth.tmc.edu'; 'Karen Osborne'; 'Bara, Rebecca'; 'Monica Bocaner'
Cc: Zaterka-Baxter, Kristin; Cunningham, Meg
Subject: RE: SUPPORT Oximeter shipping list

Thank you for your time! Attached is the final SUPPORT study oximeter shipping list.
This will be posted on the private NRN website under Protocols\SUPPORT\Oximeter Shipping List

Carolyn

From: Huitema, Carolyn Petrie
Sent: Thursday, January 17, 2008 4:32 PM
To: Angelita Hensman; 'Nancy Newman'; 'Katherine A Foy'; 'Ellen Hale'; 'ldw@iupui.edu'; 'mbball@leland.stanford.edu'; Mackinnon, Brenda; mcollins@peds.uab.edu; Wade Rich; 'grisbyca@email.uc.edu'; 'Johnson, Karen'; 'Conra Lacy'; Nancy Miller; 'Georgia.E.McDavid@uth.tmc.edu'; 'Karen Osborne'; Bara, Rebecca; 'Monica Bocaner'
Cc: Zaterka-Baxter, Kristin; Cunningham, Meg; Huitema, Carolyn Petrie
Subject: SUPPORT Oximeter shipping list

Dear All-

Attached is the requested document (contact information to ship SUPPORT study oximeters).
I pulled these from the NRN website however, please send me any changes.

This will be posted next Tuesday on our NRN website and emailed to you as a final copy.

Have a pleasant weekend-

Carolyn Huitema

Research Analyst
RTI International
(301) 270-6664
petrie@rti.org

Research Coordinators at the NICHD Neonatal Network Sites for The SUPPORT Study	
Name of Center	**Network Coordinator Contact Information**
Brown University	Angelita Hensman, R.N.C. Department of Pediatrics Women & Infant's Hospital 101 Dudley Street, Room 1136 Providence, RI 02905 ahensman@wihri.org (401) 274-1100 ext. 1730
Case Western Reserve University	Nancy Newman, R.N. University Hospitals Case Medical Center Rainbow Babies & Children's Hospital 11100 Euclid Ave., Room 3100 Cleveland, OH 44106-6010 nxs5@cwru.edu (216) 368-3084
Duke University	Kathy Foy, Division of Neonatology Duke University Medical Center 204 Bell Building, Rm 141 Durham, NC 27710 foy00004@mc.duke.edu (919) 668-3360
Emory University	Ellen Hale, R.N.C., B.S. Room D-1506 80 Jesse Hill, Jr. Dr. Atlanta GA 30303 ellen_hale@oz.ped.emory.edu (404) 616-4218
Indiana University	Leslie Dawn Wilson, RN, BSN Research Manager Neonatal Network Coordinator Riley Hospital RR 208 699 West Dr Indianapolis, IN 46202 ldw@iupui.edu (317) 274-8255

Research Coordinators at the NICHD Neonatal Network Sites for The SUPPORT Study	
Name of Center	**Network Coordinator Contact Information**
NICHD	Stephanie Wilson Archer NICHD-NRN 6100 Executive Boulevard, Room 4B03 (MSC 7510) Bethesda, MD 20892 archerst@mail.nih.gov 301-496-0430
RTI	Kris Zaterka-Baxter, R.N. RTI International 4426 South Miami Blvd Durham, NC 27703 kzaterka@rti.org 919-485-7750
Stanford University	M. Bethany Ball Stanford University Division of Neonatology 750 Welch Road, Suite 315 Palo Alto, CA 94304 mbball@stanford.edu (650) 725-8342
Tufts University	Brenda MacKinnon, RNC NICHD Neonatal Research Network Coordinator The Floating Hospital for Children 750 Washington Street, Tufts-NEMC #44 Boston, MA 02111 bmackinnon@tufts-nemc.org 617-636-1218
University of Alabama	Monica Collins, RN, MaEd Division of Neonatology University of Alabama at Birmingham 525 New Hillman Building 619 South 19th St Birmingham, AL 35233 mcollins@peds.uab.edu (205) 934-5771
University of California, San Diego	Wade Rich University of California--San Diego 402 Dickerson St MPF 1-140 San Diego, CA 92103 wrich@ucsd.edu (619) 543-3759

Research Coordinators at the NICHD Neonatal Network Sites for The SUPPORT Study	
Name of Center	**Network Coordinator Contact Information**
University of Cincinnati	Cathy Grisby, R.N. Cincinnati Children's Hospital (S Building) 9th Floor/Room S9.303 240 Albert Sabin Way Cincinnati 45229-2842 grisbyca@email.uc.edu (513) 803-0950
University of Iowa	Karen J. Johnson, R.N. Department of Pediatrics University of Iowa 200 Hawkins Drive, 8900 JPP Iowa City, IA 52242 karen-johnson@uiowa.edu 319-356-2924
University of New Mexico	Conra Backstrom Lacy Department of Pediatrics 915 Camino de Salud NE Albuquerque NM 87131 cbackstrom@salud.unm.edu 505-272-0367
University of Texas – Dallas	Nancy Miller, R.N. and Melissa H. Leps, R.N. (Co-Coordinator) Department of Pediatrics University of Texas Southwestern Medical Center 5323 Harry Hines Blvd., E3 404 Dallas, TX 75235-9063 Nancy.Miller@utsouthwestern.edu melissa.leps@utsouthwestern.edu (214) 648-3780
University of Texas – Houston	Georgia McDavid, R.N. Department of Pediatrics University of Texas-Houston 6431 Fannin, Suite 3.252, Medical Sciences Building Houston, TX 77030-1501 Georgia.E.McDavid@uth.tmc.edu (713) 500-5734

Research Coordinators at the NICHD Neonatal Network Sites for The SUPPORT Study	
Name of Center	**Network Coordinator Contact Information**
University of Utah	Karen Osborne, RN BSN Neonatal Research Network University of Utah The Williams Building Dept of Pediatrics, Division of Neonatology Salt Lake City, UT 84158 karen.osborne@hsc.utah.edu (801) 213-3298
Wayne State University	Becky Bara, RN, BSN or Elizabeth Billian, RN, BSN (Co-Coordinator) Division of Neonatal & Perinatal Medicine Children's Hospital of Michigan Dept. of Neonatology, #4C19 3901 Beaubien Blvd. Detroit, MI 48201 rbara@med.wayne.edu bbillian@wayne.edu (313) 745-1436
Yale University	Monica Konstantino, R.N. Yale-New Haven Children's Hospital 20 York St. WP493 New Haven, CT 06504 monica.konstantino@yale.edu (203)688-7987

From: Nancy Miller
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Kris Zaterka-Baxter; Melissa Leps
Subject: Re: Masimos
Date: Tuesday, January 15, 2008 6:29:58 PM

Rose,
We've consented more Moms for SUPPORT and need more pulse oximeters. We need 3 of each color.
They can be sent to this address.
Thanks,
Nancy

Nancy A. Miller, R.N.
Clinical Research Coordinator
Department of Pediatrics
Division of Neonatal-Perinatal Medicine
UT Southwestern Medical Center at Dallas
5323 Harry Hines Blvd. E3-404B
Dallas, Texas 75390-9063
214-648-3780
pager 972-206-9151

From: Cunningham, Meg
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: so no SUPPORT update today?
Date: Friday, January 11, 2008 8:16:13 AM

Also the coordinators do not want to give an update, they said nothing happened worth talking about yesterday.

Meg Cunningham
RTI International
701 13th St. NW, Ste. 750
Washington, DC 20005
tel: 202-974-7837
fax: 202-728-2095
www.rti.org

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Sharing SUPPORT Pulmonary data
Date: Thursday, January 10, 2008 11:56:25 AM

We have 9 votes with 9 yeses, plus Neil's yes vote.

From: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: Dr. Stevens" update for Breathing Outcomes
Date: Thursday, January 10, 2008 7:21:19 AM

Thanks
He will join the support sybcommittee this am. You are welcome to join also
Rose

Sent from my BlackBerry Wireless Handheld

----- Original Message -----
From: Newman, Jamie <newman@rti.org>
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thu Jan 10 07:19:49 2008
Subject: Dr. Stevens' update for Breathing Outcomes

Rose,

I have sent Dr. Stevens' update for Breathing Outcomes to Meg, Monica, Kris and Carolyn and Monica has already responded indicating that she will print the update as a handout.

Thanks, Jamie

From: Stevens, Timothy [mailto:Timothy_Stevens@URMC.Rochester.edu]
Sent: Wednesday, January 09, 2008 9:51 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; Newman, Jamie
Subject: RE: Conf Call

Hi Rose and Jamie,

Attached is my update of the Breathing Outcomes Study.

Thanks and I'll talk with you tomorrow.

Tim

From: Stevens, Timothy
Sent: Wednesday, January 09, 2008 4:57 PM
To: 'Higgins, Rosemary (NIH/NICHD) [E]'; 'Newman, Jamie'
Subject: Conf Call

Hi Rose and Jamie,

Some time ago, you asked whether I was free to be on a conference call tomorrow between 11am and noon. I have not received contact info for the call. Do you still need me?

Thanks

Tim

From: Cunningham, Meg
To: nfiner@ucsd.edu; wrich@ucsd.edu
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT Materials for the meeting
Date: Monday, January 07, 2008 2:43:56 PM

Hi Dr. Finer,

Please send us any materials for the subcommittee meeting by the end of the day.

Thanks!
Meg

Meg Cunningham
RTI International
701 13th St. NW, Ste. 750
Washington, DC 20005
tel: 202-974-7837
fax: 202-728-2095
www.rti.org

From:	Gantz, Marie
To:	Finer, Neil
Cc:	Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik
Subject:	RE:
Date:	Thursday, December 27, 2007 3:51:24 PM

Hi Neil,

We showed the DSMC some data comparing infants enrolled in SUPPORT to eligible infants who were not enrolled that we could share. I will include that information when I send you the SUPPORT updates next week.

Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-6255

From: Finer, Neil [mailto:nfiner@ucsd.edu]
Sent: Thursday, December 27, 2007 1:14 PM
To: Gantz, Marie
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject:

Hi Marie and Rose
Hope that you both had a wonderful Holiday and all the best for the New Year
I know that you are probably already preparing the reports for the Steering Committee meeting.
Is there any data from the DSMC meeting that was blinded that we can/could share??
Be well
Neil N. Finer, M.D.
Professor of Pediatrics
Director, Division of Neonatal-Perinatal Medicine
UC San Diego School of Medicine
UC San Diego Medical Center, Hillcrest
402 Dickinson St., MPF 1-140
San Diego, CA 92103-8774
Telephone: 619.543-3759
Facsimile: 619.543.3812

From:	Michael O`Shea
To:	Higgins, Rosemary (NIH/NICHD) [E]
Subject:	RE: SUPPORT
Date:	Friday, December 21, 2007 9:51:40 AM

Excellent - thanks very much.

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, December 21, 2007 9:47 AM
To: Michael O`Shea
Subject: RE: SUPPORT

We had just over 860 out of 1300+ as of the end of November – so 2/3's of the way there!
Thanks
Rose

From: Michael O`Shea [mailto:moshea@wfubmc.edu]
Sent: Friday, December 21, 2007 9:46 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT

Thanks for this good news - how close is the trial to reaching target sample size?

Mike

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, December 21, 2007 9:10 AM
To: Michael O`Shea; Nancy Peters
Cc: Gantz, Marie; Das, Abhik
Subject: SUPPORT

Hi,
As of the latest tally for SUPPORT, we are missing no primary outcome information at this time from your site. Thanks for all the effort!!!
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Zaterka-Baxter, Kristin
To:	mcw3@cwru.edu; Pablo.Sanchez@UTSouthwestern.edu; sshankar@med.wayne.edu; [SCRN] Stoll, Barbara; kurt.schibler@cchmc.org; bpoindex@iupui.edu; richard.ehrenkranz@yale.edu; alaptook@WIHRI.org; vanmeurs@stanford.edu; wcarlo@peds.uab.edu; Kathleen.A.Kennedy@uth.tmc.edu; goldb008@mc.duke.edu; IFrantz@tufts-nemc.org; edward-bell@uiowa.edu; Roger.Faix@hsc.utah.edu; kwatterberg@salud.unm.edu; nxs5@cwru.edu; Nancy.Miller@UTSouthwestern.edu; melissa.leps@utsouthwestern.edu; ae5357@wayne.edu; du2744@wayne.edu; ellen_hale@oz.ped.emory.edu; grisbyca@email.uc.edu; ldw@iupui.edu; monica.konstantino@yale.edu; ahensman@wihri.org; mbball@leland.stanford.edu; mcollins@peds.uab.edu; Georgia.E.McDavid@uth.tmc.edu; foy00004@mc.duke.edu; bmackinnon@tufts-nemc.org; karen-johnson@uiowa.edu; karen.osborne@hsc.utah.edu; CBackstrom@salud.unm.edu
Cc:	Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik; nfiner@ucsd.edu; Wade Rich; Gantz, Marie; Auman, Jeanette O.; Pickett, James; Cunningham, Meg; Huitema, Carolyn Petrie; Nancy.Miller@UTSouthwestern.edu; Archer, Stephanie (NIH/NICHD) [E]
Subject:	SUPPORT DSMC Memo re. Study continuation
Date:	Monday, December 17, 2007 4:47:32 PM
Attachments:	SUPPORT DSMC Site Memo.pdf

Hi all,
The DSMC meet on Tuesday December 11, 2007 via teleconference to review the second planned SUPPORT trial interim analysis at 50% status. Please find attached Technical Memo SUP12 regarding the committees' recommendation that the Support study should continue as planned. Official minutes are forthcoming.

Thanks,
Kris

Kris Zaterka-Baxter
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RTI International
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P.O. Box 12194
RTP, NC 27709-2194 USA
(tel) 919-485-7750
(fax) 919.485.7762
kzaterka@rti.org
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Federal Express/UPS/DHL Shipping Address:
4426 South Miami Blvd
Durham, NC 27703 USA

RTI INTERNATIONAL | **Memorandum**

December 14, 2007

SUPPORT TECHNICAL MEMO # 12

TO: Network Coordinators
Network PIs

FROM: The Data Coordinating Center

SUBJECT: DSMC Notice of Study Continuation

The NICHD Neonatal Research Network Data Safety and Monitoring Committee convened on December 11, 2007 to review the second planned interim analysis of the NICHD NRN study titled "The SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants (SUPPORT Trial)". Upon reviewing the data, the committee concluded that the trial was on course and they had no significant safety concerns. However, the high use of high flow nasal cannula in study infants was noted. The DSMC also noted the need for continued monitoring of the degree of separation between the high and low oxygen groups in the oxygen saturation arm of the trial. The final recommendation of the committee is that the study should continue as planned.

The official minutes of this meeting are pending and will be forwarded to you by the NRN Data Coordinating Center once finalized.

From: Betty Vohr
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: BITSEA AND SUPPORT FU
Date: Wednesday, December 12, 2007 3:28:18 PM

Restricted group.
Betty

From: Abbot Laptook
Sent: Wednesday, December 12, 2007 3:19 PM
To: Betty Vohr
Subject: FW: BITSEA AND SUPPORT FU

Betty,
Did you respond to this? Tx, AL

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, December 12, 2007 1:17 PM
Subject: FW: BITSEA AND SUPPORT FU

I am missing several votes on the BITSEA. Please send a response ASAP.
Thanks
Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wednesday, November 14, 2007 10:13 AM
To: (rohls@unm.edu); Abbot Laptook (alaptook@WIHRI.org); 'Abhik Das'; Ambal (ambal@uab.edu); Av Fanaroff (aaf2@po.cwru.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); 'Brenda Poindexter'; 'Carlo Waldemar (E-mail)'; 'Ed Bell'; 'Ed Donovan'; 'Ehrenkranz Richard (E-mail)'; 'Ivan Frantz'; Kennedy, Kathleen A; Krisa VanMeurs (VanMeurs, Krisa); 'Kristi Watterberg'; Kurt Schibler (Kurt Schibler [kurt.schibler@cchmc.org]); Michael Cotten (cotte010@mc.duke.edu); 'Michelle Walsh'; 'MIckey Caplan'; 'Oh William (E-mail)'; 'Pablo Sanchez'; 'Poole Kenneth (E-mail)'; 'Roger Faix'; 'Ronald GOldberg'; 'Seetha Shankaran'; 'Stevenson David (E-mail)'; 'Stoll Barbara (E-mail)'; 'Tyson Jon (E-mail)'
Cc: Cunningham, Meg; Archer, Stephanie (NIH/NICHD) [E]; 'Newman, Jamie'; Zaterka-Baxter, Kristin
Subject: BITSEA AND SUPPORT FU

Hi,
I need a vote as to whether or not folks would like to administer the BITSEA on all FU infants (including trial infants) as opposed to generic FU infants (< 27 weeks) to avoid confusion with SUPPORT FU infants (and other trial infants in the future).

Please respond by November 19:

BITSEA ON ALL INFANTS _____

BITSEA ON < 27 week INFANTS ONLY __x____

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine

NICHD, NIH
6100 Executive Blvd., Room 4B03B
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301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Michael Cotten
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT STUDY
Date: Tuesday, December 11, 2007 6:11:11 PM

---

understood....nothing huge to report from here.....Ambal and I will have dinner with Joe Neu tonight...
mc

"Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov>

12/11/2007 05:44 PM

To <cotte010@mc.duke.edu>
cc
Subject Re: SUPPORT STUDY

I am in the office - couldn't miss the support dsmc update!!

Sent from my BlackBerry Wireless Handheld

----- Original Message -----
From: Michael Cotten <cotte010@mc.duke.edu>
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Tue Dec 11 17:42:44 2007
Subject: Re: SUPPORT STUDY

thanks Rose. Ambal and I are looking for you at the probiotics meeting....

mc

"Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov>

12/11/2007 05:31 PM
To
"Finer, Neil" <nfiner@ucsd.edu>, <rohls@unm.edu>, <alaptook@WIHRI.org>, "Abhik Das" <adas@rti.org>, <ambal@uab.edu>, <aaf2@po.cwru.edu>, <Bradley.yoder@hsc.utah.edu>, "Brenda Poindexter" <bpoindex@iupui.edu>, "Carlo Waldemar (E-mail)" <wcarlo@peds.uab.edu>, "Ed Bell" <Edward-bell@uiowa.edu>, "Ed Donovan" <edward.donovan@cchmc.org>, "Ehrenkranz Richard (E-mail)" <richard.ehrenkranz@yale.edu>, "Ivan Frantz" <IFrantz@Tufts-NEMC.org>, "Kennedy, Kathleen A" <Kathleen.A.Kennedy@uth.tmc.edu>, "Krisa VanMeurs (VanMeurs, Krisa)" <vanmeurs@leland.stanford.edu>, "Kristi Watterberg" <kwatterberg@salud.unm.edu>, <kurt.schibler@cchmc.org>, <cotte010@mc.duke.edu>, "Michelle Walsh" <mcw3@po.cwru.edu>, "MIckey Caplan" <mcal13@Northwestern.edu>, "Oh William (E-mail)" <william_oh@brown.edu>, "Pablo Sanchez" <Pablo.Sanchez@UTSouthwestern.edu>, "Poole Kenneth (E-mail)" <poo@rti.org>, "Roger Faix" <Roger.Faix@hsc.utah.edu>, "Ronald GOldberg" <goldb008@mc.duke.edu>, "Seetha Shankaran" <sshankar@med.wayne.edu>, "Stevenson David (E-mail)" <dstevenson@stanford.edu>, "Stoll Barbara (E-mail)" <barbara_stoll@oz.ped.emory.edu>, "Tyson Jon (E-mail)" <Jon.E.Tyson@uth.tmc.edu>, <Karen.Osborne@hsc.utah.edu>, <melissa.leps@UTSouthwestern.edu>, "Angelita Hensman" <ahensman@WIHRI.org>, "Becky bara" <ae5357@wayne.edu>, "Bethany Ball" <mbball@leland.stanford.edu>, "Brenda MacKinnon" <BMacKinnon@Tufts-NEMC.org>, "Cathy Grisby" <grisbyca@email.uc.edu>, "Conra Backstrom" <CBackstrom@salud.unm.edu>, "Diane Wilson" <dhwilson@iupui.edu>, "Ellen Hale" <ellen_hale@oz.ped.emory.edu>, "Georgia McDavid" <Georgia.E.McDavid@uth.tmc.edu>, <karen-johnson@uiowa.edu>, "Katherine A Foy" <foy00004@mc.duke.edu>, "Kathy Auten" <auten002@mc.duke.edu>, "Leslie Wilson" <ldw@iupui.edu>, "Monica Collins" <mcollins@peds.uab.edu>, <monica.konstantino@yale.edu>, "Nancy Miller" <Nancy.Miller@UTSouthwestern.edu>, "Nancy Newman" <nxs5@cwru.edu>, <susan.tepper@hsc.utah.edu>
cc
"Archer, Stephanie (NIH/NICHD) [E]" <archerst@mail.nih.gov>, "Zaterka-Baxter, Kristin" <kzaterka@rti.org>, "Cunningham, Meg" <mcunningham@rti.org>, "Newman, Jamie" <newman@rti.org>, "Huitema, Carolyn Petrie" <petrie@rti.org>
Subject
SUPPORT STUDY

Hi,
The DSMC met late this afternoon and reviewed interim data from the SUPPORT Study. The trial is on course and will proceed as planned. A report for your IRB will be forthcoming from RTI.

Thanks to everyone for the continued effort and commitment to the trial!!! KEEP UP THE EXCELLENT

WORK!!!

Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
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301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov <mailto:higginsr@mail.nih.gov>

From: Avroy A. Fanaroff
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT STUDY
Date: Tuesday, December 11, 2007 6:08:34 PM

---

congratulations
look forward to completion of another successful network trial and eagerly anticipate the results
Happy holidays
Av

-------*Original Message*-------

From: Higgins, Rosemary (NIH/NICHD) [E]
Date: 12/11/07 17:33:03
To: Finer, Neil; rohls@unm.edu; alaptook@WIHRI.org; Abhik Das; ambal@uab.edu; aaf2@po.cwru.edu; Bradley.yoder@hsc.utah.edu; Brenda Poindexter; Carlo Waldemar (E-mail); Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz; Kennedy, Kathleen A; Krisa VanMeurs (VanMeurs, Krisa); Kristi Watterberg; kurt.schibler@cchmc.org; cotte010@mc.duke.edu; Michelle Walsh; MIckey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald GOldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); Karen.Osborne@hsc.utah.edu; melissa.leps@utsouthwestern.edu; Angelita Hensman; Becky bara; Bethany Ball; Brenda MacKinnon; Cathy Grisby; Conra Backstrom; Diane Wilson; Ellen Hale; Georgia McDavid; karen-johnson@uiowa.edu; Katherine A Foy; Kathy Auten; Leslie Wilson; Monica Collins; monica.konstantino@yale.edu; Nancy Miller; Nancy Newman; susan.tepper@hsc.utah.edu
Cc: Archer, Stephanie (NIH/NICHD) [E]; Zaterka-Baxter, Kristin; Cunningham, Meg; Newman, Jamie; Huitema, Carolyn Petrie
Subject: SUPPORT STUDY

Hi,

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Thanks to everyone for the continued effort and commitment to the trial!!! KEEP UP THE EXCELLENT WORK!!!

Rose

Rosemary D. Higgins, M.D.

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

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301-496-3790 (FAX)

higginsr@mail.nih.gov

From: Barbara Stoll
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT STUDY
Date: Tuesday, December 11, 2007 5:41:10 PM

Delighted to hear this-- always a little on edge when you get these DSMC emails until you read to the end
Regards
BJS

Barbara J. Stoll, MD
George W. Brumley, Jr., Professor and Chair, Department of Pediatrics
Medical Director, Children's Healthcare of Atlanta at Egleston
2015 Uppergate Dr
Atlanta GA 30022
Office: 404-727-2456 Fax: 404-727-5737
barbara_stoll@oz.ped.emory.edu

From:	Abbot Laptook
To:	Higgins, Rosemary (NIH/NICHD) [E]
Cc:	Das, Abhik
Subject:	RE: DSMC Agenda for the SUPPORT and Late Hypothermia teleconference 12/11/07
Date:	Tuesday, December 04, 2007 9:14:32 PM

Rose
Were we going to have Jon on the call in case there are issues re Bayesian analysis? AL

From: Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]
Sent: Tuesday, December 04, 2007 5:01 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; Abbot Laptook; Neil Finer
Cc: Das, Abhik
Subject: DSMC Agenda for the SUPPORT and Late Hypothermia teleconference 12/11/07

Hi all,
Please find attached the agenda for the DSMC review of the studies listed above to be held on 12/11/07 from 3:00 to 6:00 p.m. via teleconference.

Rose, if you could possibly be available just in case during these three hours that would be wonderful; if that's ok, we'll call/email you if there is anything requested.

Neil, we have scheduled the Support study review from 3:00 to 5:00 p.m. with discussion of the interim analysis to begin around 3:50; if possible could you please be available between 3:30 and 5:00 in case the committee has any questions?

Abbot, we have you scheduled from 5:00 to 5:20 p.m. for a presentation of the Late Hypothermia study; if possible could you please be available a bit before hand if the Support review finishes earlier; I can either call you or send you an email if that is indeed the case. Otherwise, the call in numbers are listed on the agenda.

Thanks and please let me know if you have any questions.
Kris

Kris Zaterka-Baxter
Statistics and Epidemiology Division
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Federal Express/UPS/DHL Shipping Address:
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Durham, NC 27703 USA

From: Finer, Neil
To: Rich, Wade; shey@easynet.co.uk
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Defining common NeOProM collaboration outcomes
Date: Tuesday, December 04, 2007 6:11:50 PM

Hi Edmund
See below for the answers.
Regards
Neil

From: Edmund Hey [mailto:shey@easynet.co.uk]
Sent: Sunday, December 02, 2007 4:13 AM
To: Finer, Neil
Cc: Rich, Wade
Subject: Defining common NeOProM collaboration outcomes

Neil and Wade,

The UK BOOST trial is *finally* on the move at last and we hope to have at least a dozen centres recruiting by Christmas. Just five quick queries about SUPPORT if I may so that I have things clear in my mind when I meet up with Lisa Askie over the proposed prospective NeOMroM collaboration while she is briefly in the UK in two weeks time.

[1] Can you confirm that SUPPORT is doing a Walsh test at 36 weeks pma in order to have an *objective* way of defining which babies have 'BPD' ? The Canadian COT trial had also originally planned to do this but I think they found it hard to get everyone to sign up to this. The UK trial will, however, be doing something similar. Yes, we will use a "Walsh Test".

[2] I see you have a simple "respiratory support after 14 days" report form from which you can identify how many days the baby spent ventilated, on CPAP, or in oxygen, and how old the baby was when this was last used. All these six things were agreed data items for the proposed collaborative NeOProiM data set. Do I take it that people are left to use their common sense in completing this form and that if this support was given for long enough to be considered significant by the person completing the form it counted as a day's support. During the first 14 days, we gather data every 2 hours, and what is written down is the data at the exact time it is charted. It is possible that a status change can occur between documented data points. Since we also document all intubations and extubations, we would know about them. Changes from CPAP to NSIMV and back, for instance, would not be noted.

[3] I see that one of your pre-defined short term secondary outcomes was when the baby was "last in oxygen" [Protocol 5.3.2 bullet point 14]. How are you collecting this information if the child went home in oxygen, and what is then your working definition of "last in oxygen" ? The pragmatic definition used in the first Australian BOOST trial was "last in oxygen for four hours a day". Dale Phelps told me they had something a little more complex than this in STOP-ROP to make people realise that they should ignore a brief return to use for 1-2 days after the child had been off such support for a significant time, but I failed to keep a note of what she said. Do you know what that guideline said ? Has anything comparable been included in the guideline as to how people should go about saying when oxygen was last used in your current study ? Status for this trial is defined as Death, Discharge, or 120 days of life. The actual SUPPORT study will not determine when home oxygen use stops.

[4] Are you attempting to collect the information that would be needed to be able to classify the babies, retrospectively, as having had BPD using the NICH definition (Jobe and Bancalari, 2001) or do you feel that the Walsh definition makes this older definition redundant ? The challenge of that definition is to know whether a baby had been in oxygen for at least half the day on a cumulative total of 28 days by the time the baby reaches 36 weeks pma, and I was not clear whether the information that was being collected made it possible to say whether those criteria had been met . We are using the Walsh

definition, and by extension oxygen at 36 wks.
We will be able to calculate the other durations from our GDB data sheets.

[5] All the Masimo monitors being used in the UK trial were modified by the company without warning just before the trial opened so that the alarm setting is now only triggered when the set value is passed rather than when it is reached. That is not, as I understand it, how the monitors you are using in the SUPPORT trial originally worked. I presume the company have not tried to alter the machines you currently have in use in your trial. However, I did just wonder if a similar change was now being made to all the new machines that the company has on sale and whether that was going to leave units with alarms on some Masimo monitors that work one way and some that work another. In speaking with Steve Taylor at Masimo I learned that they have in fact changed their "philosophy" toward alarms such that all new devices will alarm when the set values is passed, not when it is reached, as is the case on SUPPORT oximeters. I have asked Maribeth Sayre, who is their research liaison, to make sure that we know which type of monitor is being used for each trial, so that there is no confusion. In terms of trial design, I do not see that it will make a big difference as long as everyone knows how their alarm functions.

Edmund

From: Pablo Sanchez
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT!!!!
Date: Wednesday, November 28, 2007 7:09:21 PM

---

thanks, Rose--pablo

>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> 11/28/07 12:00 PM >>>
Hi,

As of last week, your site had NO missing SUPPORT primary or FU outcomes
- congratulations and keep up the excellent work!!
Rose

Rosemary D. Higgins, M.D.

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

NICHD, NIH

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Bethesda, MD 20892

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301-435-7909

301-496-3790 (FAX)

higginsr@mail.nih.gov

From: Roy Heyne
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT!!!!
Date: Wednesday, November 28, 2007 2:10:10 PM

---

thanks for the feedback.

>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> 11/28/2007 12:00 PM >>>
Hi,

As of last week, your site had NO missing SUPPORT primary or FU outcomes
- congratulations and keep up the excellent work!!
Rose

Rosemary D. Higgins, M.D.

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

NICHD, NIH

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301-435-7909

301-496-3790 (FAX)

higginsr@mail.nih.gov

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: BITSEA AND SUPPORT FU
Date: Wednesday, November 14, 2007 2:06:10 PM

You can send the votes to me.

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wednesday, November 14, 2007 10:13 AM
To: (rohls@unm.edu); Abbot Laptook (alaptook@WIHRI.org); Abhik Das; Ambal (ambal@uab.edu); Av Fanaroff (aaf2@po.cwru.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz; Kennedy, Kathleen A; Krisa VanMeurs (VanMeurs, Krisa); Kristi Watterberg; Kurt Schibler (Kurt Schibler [kurt.schibler@cchmc.org]); Michael Cotten (cotte010@mc.duke.edu); Michelle Walsh; MIckey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald GOldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail)
Cc: Cunningham, Meg; Archer, Stephanie (NIH/NICHD) [E]; Newman, Jamie; Zaterka-Baxter, Kristin
Subject: BITSEA AND SUPPORT FU

Hi,
I need a vote as to whether or not folks would like to administer the BITSEA on all FU infants (including trial infants) as opposed to generic FU infants (< 27 weeks) to avoid confusion with SUPPORT FU infants (and other trial infants in the future).

Please respond by November 19:

BITSEA ON ALL INFANTS _____

BITSEA ON < 27 week INFANTS ONLY _____

Rosemary D. Higgins, M.D.
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From: CATHY A. GRISBY
To: Kristin Zaterka-Baxter; Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT AE
Date: Wednesday, November 14, 2007 11:14:38 AM

Hi,

I'm sending you an AE from last week that did not go through on our fax machine. Sorry for not picking up on it sooner.

Cathy

From:	Zaterka-Baxter, Kristin
To:	Gordon Avery; rjb6j@hscmail.mcc.virginia.edu; cgleason@u.washington.edu; Willinger, Marian (NIH/NICHD) [E]; Clemons, Traci (NIH/NICHD); mikeross@ucla.edu; kant@unc.edu; merran.thomson@ic.ac.uk; mcallen@jhmi.edu; GailD@nih.gov
Cc:	Das, Abhik; Poole, W. Kenneth; bprice@obgyn.humc.edu; milhil@u.washington.edu; meganhb@u.washington.edu; Higgins, Rosemary (NIH/NICHD) [E]; alaptook@WIHRI.org; Cunningham, Meg
Subject:	RE: NICHD NRN DSMC Support Trial Review 12/11/07
Date:	Tuesday, November 13, 2007 5:22:49 PM
Attachments:	HypothermiaProtocolAfter6hrs0731072.pdf lilfordBMJ 1995.pdf

Hi all,

Please find attached the protocol for the new NRN Study titled *"Evaluation of Systemic Hypothermia Initiated After 6 Hours of Age in Infants = 36 Weeks Gestation with Hypoxic-Ischemic Encephalopathy: A Bayesian Evaluation"*. In addition, please also find attached an article regarding the issues of sample size for rare conditions as background information for your review of this study prior to the next DSMC teleconference on December 11, 2007 from 3:00 pm to 6:00 pm (EST).

Please note the conference agenda and NRN Support Study interim analysis report at 50% status will be sent one week prior to the meeting (i.e., on or before Tuesday Dec. 4th) for your review.

Thanks and please let me know if you have any questions.
Kris

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From: Zaterka-Baxter, Kristin
Sent: Monday, September 17, 2007 3:27 PM
To: Zaterka-Baxter, Kristin; 'Gordon Avery'; 'rjb6j@hscmail.mcc.virginia.edu'; 'cgleason@u.washington.edu'; [SCRN] Willinger, Marian; 'tclemons@emmes.com'; 'mikeross@ucla.edu'; 'kant@unc.edu'; 'merran.thomson@ic.ac.uk'; 'mcallen@jhmi.edu'; 'GailD@nih.gov'
Cc: Das, Abhik; Gantz, Marie; Poole, W. Kenneth; Auman, Jeanette O.; 'bprice@obgyn.humc.edu'; 'milhil@u.washington.edu'; 'meganhb@u.washington.edu'
Subject: NICHD NRN DSMC Support Trial Review 12/11/07

Hi all,
We have scheduled the next NICHD NRN DSMC conference call for **Tuesday December 11, 2007 from 3:00 pm to 6:00 pm (EST)**. This call will be to:

1. Review the Support Trial Interim analysis at 50% infant status (3:00 – 5:00 pm EST)
2. Review a new NRN Study titled *"Evaluation of Systemic Hypothermia Initiated After 6 Hours of Age in Infants = 36 Weeks Gestation with Hypoxic-Ischemic Encephalopathy: A Bayesian Evaluation"*

(5:00 – 6:00 pm EST)

The meeting agenda and **new** study materials will be distributed mid November and the Support Trial safety report will be distributed one week prior to the conference call.

Thanks and please let me know if you have any questions at all.
Kris

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From: Zaterka-Baxter, Kristin
Sent: Tuesday, September 11, 2007 12:45 PM
To: 'Gordon Avery'; 'rjb6j@hscmail.mcc.virginia.edu'; 'cgleason@u.washington.edu'; [SCRN] Willinger, Marian; 'tclemons@emmes.com'; 'mikeross@ucla.edu'; 'kant@unc.edu'; 'merran.thomson@ic.ac.uk'; 'mcallen@jhmi.edu'; 'GailD@nih.gov'
Cc: Das, Abhik; Gantz, Marie; Poole, W. Kenneth; Auman, Jeanette O.; 'bprice@obgyn.humc.edu'; 'milhil@u.washington.edu'
Subject: RE: NICHD NRN Support DSMC Review at 50%

Hi all,
Based on the previous request for availability, we've narrowed down a few dates to conduct a 2 – 3 hour teleconference for the next review of the Support trials interim analyses. Please let me know your availability for these dates.

November 2007:

Tuesday 11/06/07
Wednesday 11/07/07

Tuesday 11/13/07

December 2007:

Tuesday 12/11/07
Friday 12/14/07

Please let me know if you have any questions.
Thanks,
Kris

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From: Zaterka-Baxter, Kristin

Sent: Monday, June 18, 2007 2:23 PM
To: 'Gordon Avery'; rjb6j@hscmail.mcc.virginia.edu; cgleason@u.washington.edu; [SCRN] Willinger, Marian; tclemons@emmes.com; mikeross@ucla.edu; kant@unc.edu; merran.thomson@ic.ac.uk; mcallen@jhmi.edu; GailD@nih.gov
Cc: Das, Abhik; Gantz, Marie; Poole, W. Kenneth; Auman, Jeanette O.
Subject: NICHD NRN Support DSMC Review at 50%

Dear DSMC Members,

We estimate that the NICHD NRN SUPPORT study will meet 50% accrual status sometime between mid October 2007 and mid December 2007. We would like query for your availability between these dates to meet by teleconference for review of the study data as planned per protocol. Please send me your availability.

Thanks, and please let me know if you have any questions.

Kris

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Evaluation of Systemic Hypothermia Initiated After 6 Hours of Age in Infants ≥ 36 Weeks Gestation with Hypoxic-Ischemic Encephalopathy: A Bayesian Evaluation (Late Hypothermia Study for HIE)

Principal Investigator: Abbot Laptook

Final
July 31, 2007

Version: 1.0

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Evaluation of Systemic Hypothermia Initiated After 6 Hours of Age in Infants ≥ 36 Weeks Gestation with Hypoxic-Ischemic Encephalopathy: A Bayesian Evaluation (Late Hypothermia Study for HIE)

Principal Investigator
Abbot Laptook

NICHD Network Subcommittee Members

Jon Tyson, M.D.	Joseph Lucke, M.D.
Seetha Shankaran, M.D.	Claudia Petroza, MD
Ed Bell, MD.	Abhik Das, Ph.D
Richard Ehrenkranz, MD	Rosemary Higgins, MD
Ronald Goldberg, MD	Angelita Hensman, RN
Namasivayam Ambalavanan, MD	Karen Osborne, RN

Objective: Evaluate whether induced hypothermia with body cooling initiated between 6-24 hours of age and continued for 96 hours in infants ≥ 36 weeks gestation with hypoxic-ischemic encephalopathy will reduce the incidence of death or disability at 18 months of age.

Study Design: Multicenter, randomized trial. The intervention of hypothermia will be unmasked.

Sample size: 168 infants

Eligibility criteria: Infants ≥ 36 weeks gestation with a pH (cord or neonatal) ≤ 7.0 or base deficit ≥ 16 mEq/L, **or** an acute perinatal event and either a 10 minute Apgar ≤ 5 or continued need for ventilation. All infants must have signs of encephalopathy at an age between 6-24 hours at the time of enrollment.

Study intervention: Infant will be randomized between 6-24 hours of age to either hypothermia or a non-cooled control group. Hypothermia will be achieved with whole body cooling to an esophageal temperature of 33.5°C using a Cincinnati Sub-Zero Hyper/Hypothermia device for 96 hours. Infants in the control group will have their core temperature using the esophageal site maintained at 37°C by appropriate servo control of the skin temperature. Cardio-respiratory, renal, metabolic, hematological and neurological status will be monitored along with esophageal, skin, and axilla temperatures during 96 hours of the intervention.

Primary outcome: The primary outcome will be death or moderate/severe disability at 18 months of age.

Sample size estimates: It is estimated that 168 infants (84 per group) can be enrolled within 3 years. This represents the largest number of infants anticipated to be enrolled in the longest time feasible for conducting the study

(3 years for enrollment and 1.5 years for follow-up). Hypoxia-ischemia severe enough to warrant a brain specific therapy such as therapeutic hypothermia is uncommon. Conventional levels of statistical precision typically used to test a hypothesis in clinical trials are unlikely to be obtained in rare conditions. Given the small sample size a Bayesian analysis will be used to provide a systematic analysis of the available data. The first year of the trial will be considered a pilot phase in view of the uncertainty of enrollment; if enrollment is excessively low, the trail will be discontinued. If enrollment is adequate the study will continue and additional infants will be recruited during the final two years of enrollment.

1.1 Hypothesis

The risk for death or disability among infants with perinatal hypoxia-ischemia and moderate or severe encephalopathy is reduced if systemic hypothermia (esophageal temperature of 33.5°C) is initiated after 6 hours of age and continued for 96 hours compared to infants with esophageal temperature maintained at 37.0°C.

2.1 Background

Perinatal hypoxia-ischemia represents the etiology for newborn encephalopathy in up to 30% of affected infants, and can result in death, CP, mental impairment and seizures.[1, 2] Management of infants with HIE has been limited to supportive intensive care without any brain oriented specific therapy. This approach is changing based upon laboratory and clinical trials of brain cooling. A small reduction in brain temperature of neonatal animals (as little as 2°C) favorably affects multiple processes involved in the pathogenesis of brain injury (energy state, excitotoxins, nitric oxide, apoptosis, etc.) and attenuates the extent of clinical and histological brain injury.[3] In two subsequent large randomized clinical trials using a cooling cap or cooling blanket to achieve brain hypothermia there was either a strong favorable direction of effect[4] or improvement in outcome with a cooling regimen.[5]

During the design of these two trials the time of initiation, depth, and duration of hypothermia were extrapolated from animal studies. The best studied parameter of hypothermia regimens among perinatal animals was the time to initiate cooling; brain hypothermia was effective in reducing brain injury when started at 1.5 hrs following ischemia, was less effective at 5.5 hrs and was not effective at 8.5 hrs following brain ischemia in fetal sheep.[6-8] Two subsequent reports have demonstrated that neuroprotection can be achieved when brain hypothermia is initiated beyond the window of 5.5 hours. Hypothermia initiated at 6 hours in 14 day rats undergoing hypoxia-ischemia and continued for 6 hours had lower infarct volume and better cerebral energy metabolite ratios compared to hypothermia of the same duration and initiated immediately, 2 or 4 hours following hypoxia-ischemia.[9] Hypothermia initiated at 12 hours in adult rats undergoing cerebral ischemia and continued for 5 hours mitigated the extent of necrosis in the lateral CA-1 hippocampus.[10] The majority of the literature however supports greater efficacy of hypothermia when initiated sooner rather than later following a hypoxic-ischemic event. Observations from adult animals suggest that extending the duration of hypothermia may offset delays in initiating cooling and result in neuroprotection.[11-13] It is unknown if the duration of the therapeutic window in human neonates is similar to fetal sheep and if a longer duration of hypothermia can widen the window. Although the latter remains in question, the pathogenesis of brain injury evolves over an extended interval of days to weeks. Evidence of a prolonged inflammatory response following hypoxia-ischemia supports this contention. IL-1β stimulates the synthesis of other cytokines, induces leukocyte infiltration, influences glial gene expression, and stimulates production of trophic factors.[14] Following hypoxia-ischemia in neonatal rats IL-1 activity increases transiently and reaches a peak at 6 hours.[15] The initial rise in IL-1β is followed by a secondary rise starting at 3 days and extends to 14 days after hypoxia-ischemia.[16] Similar prolonged expression of other inflammatory mediators such as intercellular

adhesion molecule 1 (ICAM-1) is detectable in adult animals. The latter is an endothelial ligand for the β-2 integrins on leukocytes. Post-ischemic influx of leukocytes into ischemic tissue may exacerbate injury and antibody to ICAM-1 reduces the extent of brain damage after middle cerebral artery occlusion (MCAO) in rats.[17] The temporal profile of ICAM-1 protein and mRNA expression after transient MCAO in adult rats peak at 12 hours and persists to one week of reperfusion.[18] Other potential endogenous repair mechanisms have a prolonged temporal profile after hypoxia-ischemia. For example the subventricular zone provides a progeny of reparative cells that appear to be stimulated by hypoxia-ischemia in 10 day old mice and is expanded for at least 2 weeks following hypoxia-ischemia.[19]

There also is an emerging body of animal investigations that demonstrate exacerbated neuronal injury with modest increases in brain temperature during ischemia (3°C).[20, 21] Even small, clinically relevant changes in temperature of only 1-2°C adversely affected post-ischemic neurological function and neuronal injury of adult dogs.[22] In adult gerbils a transient hyperthermia occurs during the early recirculation phase following brain ischemia and suppression of the hyperthermia by anesthetics attenuated injury to the hippocampus.[23] These findings were independent of the anesthetic effects. Of greater concern is that 3 hours of hyperthermia (39-40°C) initiated at 24 hours following brain ischemia increased ischemic neurons of the CA-1 sector by 2.5 fold compared to 38°C in adult rats.[24] Similar effects of elevated temperature are observed in neonatal animals. In 7 day rat pups an increase in brain temperature of 1-2°C during hypoxia-ischemia aggravated behavioral deficits and neuronal injury compared to normothermic animals.[25] In 10 day rat pups an increase in core body temperature (37.5°C compared to 36.0°C) for four hours immediately following hypoxia-ischemia increased the extent of neuronal injury.[26]

Hyperthermia acts through several mechanisms to worsen cerebral hypoxia-ischemia including enhanced release of neurotransmitters, exaggerated oxygen radical production, greater blood-brain barrier breakdown, impaired recovery of energy metabolism and protein synthesis and worsening of cyto-skeletal proteolysis.[27] The interest in elevated temperature of the fetus and newborn is reflected in associations reported between maternal fever and outcomes such as need for resuscitation, encephalopathy, seizures and cerebral palsy based on observational and case-control studies.[28-33] Recognition of the adverse effects of hyperthermia has prompted analysis of fever in adult stroke patients. A meta-analysis of 9 studies (3,790 patients) demonstrated an association between hyperthermia after stroke onset and an increase in morbidity and mortality (a test of heterogeneity was non-significant for mortality).[34] These studies have not rigorously excluded the possibility that larger strokes result in fever. Nevertheless, the effects of hyperthermia in adults is sufficiently concerning that it is recommended to vigorously minimize fever in patients with ischemia even if the extent of temperature elevation is considered minor or delayed in onset.[27] Only an interventional trial can determine if this association is causal.

2.1.1 Preliminary Data

Observations from the recently completed NICHD whole body hypothermia trial suggests that elevated body temperature is a frequent finding among infants with HIE cared for in the usual care group. Temperature regulation in the usual care group was initially servo control of abdominal wall skin temperature between 36.5-37.0°C with subsequent adjustments of the servo set point based on local practice of individual units (most commonly based on axillary temperatures). Each infant in the usual care group had esophageal temperatures recorded at 4 hour intervals during the 72 hour intervention period (total 19 values). Esophageal temperatures were not used in the management of infants in the usual care group.

The mean (± sd) esophageal temperature for infants in the usual care group was 37.2 ± 0.6°C over the 72 hour intervention. The distribution of all esophageal temperatures (n = 1839, 173 missing values) is listed in the table. Sixty-four percent of all esophageal temperature values in the usual care group were > 37°C. Of the 106 infants randomized to the usual care group, 4 had missing esophageal temperatures and 40 infants had a maximum esophageal temperature ≥ 38°C (the maximum temperature was 41.1°C). Even for the 52 infants with a maximum esophageal temperature < 38°C (n=970 values), the percent distribution for esophageal temperatures ≤ 36.5, 36.6-37, 37.1-37.5, and 37.6-38.0°C were 11.3, 31.1, 46.6, and 10.9%, respectively.

Esophageal Temperature (°C)	% of all Temperature Values
≤ 36	2.6
36.1 – 36.5	7.3
36.6 – 37.0	25.9
37.1 – 37.5	41.5
37.6 – 38.0	15.5
38.1 – 38.5	4.2
>38.5	3.0

The relationship between elevated temperature in the usual care group and the risk of an adverse outcome (death or disability) was examined in an observational study and presented at the May 2006 PAS meeting.[35] Logistic regressions were used to relate death or disability to measures of temperature for each infant adjusting for the level of encephalopathy, gender, race and gestational age. Separate regressions were created for measures of the highest and median temperature of esophageal or skin temperature and results were expressed as an odds ratio and 95% confidence interval. The measure of the highest temperature of each infant was represented by the average of the highest quartile of temperature collected during the 72 hour intervention period. The results indicated that an increase of only 1°C in the average of the highest quartile of skin or esophageal temperature was associated with a 3.6-4 fold increase in the odds of death or disability. The odds of death were increased 5.9 fold for each centigrade increase in the median esophageal temperature. There was no relation between the median skin temperature and outcome.

Given the observational study design, a casual inference between elevated temperature and outcome cannot be distinguished from elevated temperature secondary to brain injury. However the results suggest that evaluation of neuroprotection associated with brain hypothermia or any other intervention should be compared to study patients in whom increases in temperature are avoided.

2.1.2 Study Rationale and Need to Conduct the Study in the NRN

The NRN trial of systemic hypothermia[5] is limited to infants that qualify in the first 6 hours following birth and it is unknown if systemic hypothermia is of benefit when initiated at a later age. The parameters of the cooling regimen were based on the best available animal data at the time of trial design and do not imply that these are optimal. There are three important scientific justifications to conduct this study: 1) animal data suggests that brain injury evolves over a prolonged time (days to weeks) following hypoxia-ischemia, 2) temperature modulation may have prominent effects on brain outcome even remote from the time of injury, and 3) prolongation of treatment with hypothermia may offset later initiation of the reduction in temperature. The relative importance of time of initiation and duration of hypothermia for the extent of neuroprotection is not known. The efficacy of brain cooling initiated at < 6 hours of age is based on controlled laboratory observations in the sheep fetus.[8] Given the uncertainty in determining the timing of a "hypoxic-ischemic event" for many infants in the prior Hypothermia trial, it is plausible that hypothermia was initiated more than 6 hours from the "event". If the results of the study are positive, more infants can be offered the therapy and outcomes can be improved. If the results do not demonstrate benefit, important information is provided that should limit the inappropriate use of this therapy.

This investigation will address a population of patients that could not previously be studied due to geographic considerations (inability to transport eligible infants within 6 hours), late recognition of encephalopathy, or progression of an encephalopathy beyond mild degrees of involvement.[36] Thus continued investigation of systemic hypothermia beyond its present use addresses gaps in knowledge concerning potential broader application of this therapy.

There are compelling reasons why this investigation should be conducted in the NRN. The NRN has an established follow-up program for the primary outcome with certified examiners trained to reliability, low attrition, and standardized assessments. Many of the present Network centers participated in the prior trial of systemic hypothermia and the subsequent free standing evaluation of the amplitude integrated EEG. This experience has provided an infrastructure for screening, identification and examination of infants, and familiarity with the intervention of systemic hypothermia. No other network is positioned to initiate this type of study with minimal resource investment as the NRN.

3.1 Inclusion Criteria

All infants with a gestational age ≥ 36 weeks will be screened for study entry if they are admitted to the NICU with an admitting diagnosis of neonatal depression, perinatal asphyxia or encephalopathy. Infants will be evaluated in two sequential steps; evaluation by clinical and biochemical criteria (Step A) followed by a neurological exam (Step B). Details are as follows:

Step A: All infants between 6 and 24 hours of age will be evaluated for the following:

1. History of an acute perinatal event (abruptio placenta, cord prolapse, severe FHR abnormality, e.g., variable or late decelerations).
2. An Apgar score ≤ 5 at 10 minutes.
3. Continued need for ventilation initiated at birth and continued for at least 10 minutes.
4. Cord pH or first postnatal blood gas pH at ≤ 1 hour ≤ 7.0.
5. Base deficit on cord gas or first postnatal blood gas at ≤ 1 hour ≥ 16 mEq/L.

The above criteria are intended to screen for infants with a high probability of acute hemodynamic compromise around the time of birth. All of the above criteria do not need to be fulfilled in each patient. Two different pathways will be used as an indication of an acute event for the fetus/newborn. If a profound fetal acidemia is present category A1 (see below) is followed, and if either a blood gas is not available or the fetal acidemia on a blood gas is more modest, category A2 is followed.

IF BLOOD GAS IS AVAILABLE:	**IF BLOOD GAS IS NOT AVAILABLE OR pH between 7.01 and 7.15, BASE DEFICIT 10 to 15.9mEq/L**
A1	A2
Infant should have: (4 or 5 from above)	Infant should have: (1 and 2 or 3 from above)
	• Acute perinatal event and either
• Cord pH or first postnatal blood gas within 1 hour with pH ≤ 7.0	• An Apgar score ≤ 5 at 10 minutes
OR	**OR**
• Base deficit on cord gas or first postnatal blood gas within 1 hour at ≥ 16 mEq/L	• Continued need for ventilation initiated at birth and continued for at least 10 minutes

If the criteria in A1 or A2 are met, the infant qualifies for a neurological examination (Step B).

Step B. An abnormal neurological exam will be the presence of moderate or severe encephalopathy defined as seizures OR the presence of abnormality in at least 3 of the 6 categories in Table 1.

Table 1

Category	Moderate Encephalopathy	Severe Encephalopathy
1. Level of consciousness	Lethargic	Stupor/coma
2. Spontaneous activity	Decreased	No activity
3. Posture	Distal flexion	Decerebrate
4. Tone	Hypotonia (focal, general)	Flaccid
5. Primitive reflexes		
Suck	Weak	Absent
Moro	Incomplete	Absent
6. Autonomic system		
Pupils	Constricted	Skew deviation or dilated, non-reactive to light
Heart rate	Bradycardia	Variable HR
Respirations	Periodic breathing	Apnea

The neurological examination will be performed by a physician examiner. To ensure compliance with the defined entry criteria and achieve consistency among examiners, all physician examiners will meet a standardized certification process. To facilitate the accuracy of the neurological examination, every attempt should be made to withhold the administration of medications that may alter the examination (e.g., versed, fentanyl etc) until after the exam is completed unless imperative for clinical care.

These criteria are identical to the completed Network Hypothermia trial[5] except for the time of entry (6-24 hrs vs < 6hrs of age). The amplitude integrated EEG will not be used as inclusion criteria since it remains uncertain whether the aEEG improves selection of infants at risk for death/disability compared to the above criteria. In addition use of the same entry criteria allows comparison with the completed Network Hypothermia trial. This study will recruit infants that qualify for brain hypothermia, but are not cooled either because they were not transferred to a center at less than 6 hours of age, the neurological status progressed to moderate/severe encephalopathy after 6 hours of age, their neurological findings were not recognized at < 6 hours of age, the equipment was not immediately available, or it was not feasible to examine the infant, obtain consent, and randomize before 6 hours.

4.1 Exclusion Criteria

1) presence of a known anomaly or chromosomal aberration, 2) birth weight <1800 gms, 3) infant in extremis, 4) refusal of parents or attending physician.

5.1 Randomization and Stratification

After informed consent is obtained, infants will be randomized to either an esophageal temperature of 37.0°C or 33.5°C for 96 hours. Enrolled infants will be stratified by age of enrollment (≤ 12 and > 12 hours) and stage of encephalopathy (moderate or severe). It is anticipated that the majority of infants who will qualify for this study will fall within the 6-12 hour age range.

6.1 Intervention

Infants randomized to cooling will be placed on a cooling/heating blanket which will be coupled to a Cincinnati Sub-Zero Hyper-Hypothermia Blanketrol System. Blankets can be positioned on radiant warmers, cribs, or isolettes. An esophageal temperature probe will be placed in the lower third of the esophagus and the probe will be interfaced with the Blanketrol System. The esophageal temperature will be controlled in the automatic control mode ("servo") at 33.5°C for 96 hours. No other heating mechanism will be used during this interval (all external heat sources must be off). At the completion of 96 hours, the control set point will be increased 0.5°C per hour until the esophageal temperature is 37.0°C. Once achieved, the esophageal probe will be removed, the infant will be taken off the cooling/heating blanket, and temperature control will be changed to the standards of the participating NICU.

Infants randomized to the non-cooled control group will have an esophageal temperature probe placed in the lower third of the esophagus and temperature monitored with either a Blanketrol system or a Mon-A-Therm dual input thermometer. Esophageal temperature will be controlled at 37.0°C by servo control of the abdominal skin temperature using an initial servo set point of 36.0°C. There will be an acceptable range of temperatures above and below 37.0°C beyond which a simple algorithm will be provided to respond to potential elevated temperatures. Following 108 hours of observations (to mirrored the cooled group), the esophageal temperature probe will be removed and temperature control will be changed to the standards of the participating NICU.

7.1 Discontinuation of Induced Hypothermia

Infants in the cooled group will have hypothermia discontinued if any of the following occur: parents withdraw consent, Neonatologist withdraws consent, infant needs ECMO therapy, or a serious adverse event requiring therapy (one or more of the following: cardiac arrhythmia, persistent acidosis, major thrombosis or bleeding, skin breakdown or equipment malfunction).

8.1 Post Randomization Exclusion of Infants

The study is designed as intent-to-treat, and therefore infants will not be excluded after randomization.

9.1 Safety Monitoring of Control and Experimental Infants

a. Skin, esophageal, axilla, and servo set point temperature will be monitored hourly until 12 hours and every 4 hours thereafter during the 96 hour intervention interval and subsequent 12 hours (total of 108 hr). For infants undergoing hypothermia, temperature will be recorded every 15 minutes for the first 3 hours of cooling, then hourly until 12 hours and then every 4 hours thereafter.
b. Metabolic status: serum electrolytes will be monitored as per clinical routine.
c. Respiratory status: blood gases will be monitored as per clinical routine.
d. Cardiovascular: heart rate, blood pressure and use of inotropic agents will be recorded at baseline and every 4 hours for 96 hours.

e. Renal status: urine output and body weight will be recorded daily during the intervention interval. Serum BUN and creatinine will be monitored as per clinical routine.
f. Neurological status: at baseline, at 96 hours and at discharge (performed by certified examiner).
g. Hematological: PT/PTT will be acquired only if bleeding is suspected based upon clinical symptoms or an unexplained fall in hematocrit by more than 10%. Complete blood counts will be monitored as per clinical routine.
h. Infectious Disease: Results of blood cultures will be recorded.

10.1 Sedation/Analgesia/Anti-convulsants

The use of sedative, hypnotic and analgesic agents and anti-convulsants will be at the discretion of the Attending physician.

11.1 Data Collection

Data will be collected on maternal labor events (including presumed chorioamnionitis and antibiotic use), mode of delivery, infant characteristics and demographics, delivery room events, Sarnat stage at randomization, and after 96 hours of age, occurrence of seizures, evidence of other organ dysfunction, use of anti-convulsants and sedative-hypnotic agents, results of CNS imaging and EEG studies and neurological exam at discharge. Determination of the stage of encephalopathy will be based on a modified Sarnat stage by scoring the presence of moderate or severe abnormalities in 6 categories. The number of moderate or severe signs determines the extent of encephalopathy and if signs are equally distributed the designation of moderate or severe encephalopathy is based on the level of consciousness. Esophageal, skin, axillary, blanket and control set point temperature will be recorded at 15 min intervals during the first 3 hours of the intervention, hourly for 9 hours and then at 4 hour intervals during 96 hours of "treatment" and 12 hours of "rewarming". Orders for "do not resuscitate" and withdrawal of support will be recorded.

12.1 Follow-up

All surviving infants will be followed in the Neonatal Research Network follow-up program with a compliance rate maintained at 95%. Tracking information will be recorded at the time of discharge from the NICU. An attempt will be made to obtain an autopsy in case of death occurring prior to and following NICU discharge.

Growth parameters, a neurological examination, psychometric testing, and vision and audiometric evaluations will be performed as part of the follow-up evaluations. In addition, the family's socio-economic and educational status will be assessed. Infants will be tracked and undergo follow-up at Network centers with evaluations at 18-22 months of age by personnel trained to reliability and blinded to treatment assignment group. If an infant is not evaluated at the 18-22 month clinic visit because of acute illness, behavior problems, or "other" reasons, appointments will be re-scheduled until the evaluation is complete.

13.1 Primary Outcome

The primary outcome will be death or disability (either moderate or severe in extent). Severe disability will be defined by any of the following: a Bayley MDI < 70, Gross Motor Functional (GMF) Level of 3-5, blindness or profound hearing loss requiring amplification. Moderate disability will be defined as a Bayley MDI between 70-84 and either a GMF level of 2, a seizure disorder, or a hearing deficit.

Infants without the primary outcome will be categorized as normal or mildly impaired. Normal will be defined by an MDI ≥ 85, GMF level 1, and absence of any neurosensory deficits. Mild impairment will be defined by either an MDI of 70-84 alone, or an MDI ≥ 85 and any of the following (presence of a GMF level 2, seizure disorder or hearing loss not requiring amplification).

14.1 Secondary Outcomes

- Number of deaths in the NICU and following discharge
- Number of infants with moderate and severe disability
- Number of infants with mild, moderate and severe disability
- Number of infants with any disability based on level of encephalopathy at randomization
- Number of infants with non-CNS organ system dysfunction
- Number of infants with a DNR order
- Number of infants with a DNR order and support is withdrawn
- Number of infants with a DNR order and either die or survive
- Number of infants with neonatal seizures, with and without EEG abnormalities

15.1 Estimated Available Number of Patients

Estimates of the number of available patients for conducting this trial within the Network include 1) infants who do not develop seizures or moderate/severe HIE until after 6 hours age and 2) infants who cannot be randomized by 6 hours of age (late time of referral, unavailability of study personnel).

An estimate of the number of patients in the first category can be extrapolated from a study performed at UT-Southwestern comparing the Amplitude Integrated EEG and the neurological examination.[36] Entry criteria for this study was similar to the inclusion criteria stated above and infants (n=50) were categorized in the first 6 hours as normal or demonstrating features of encephalopathy (modified Sarnat stages I, II or III). There were 15 normal, 3 stage I, 17 stage II, and 2 stage III; 13 infants had features of both Sarnat stage I and II and could not be categorized definitively as either stage; 3 of these 13 progressed to a stage II with an abnormal short term outcome. Based on these data 9.7% (3/31) of infants who would not qualify for entry into the Network Hypothermia study during the first 6 hours (normal, Stage I, and those with features of both Stage I and II) may progress after 6 hours of age. If this is extrapolated to the screened (n=798) but not eligible infants (798-238 = 560) in the Network Hypothermia trial (conducted over 35 months) there are 54 potential candidate infants for a study conducted over 35 months.

An estimate of the number of patients in the second category can be extrapolated from the screening log and eligibility forms (IHO1 and IHO2) from the prior NRN systemic hypothermia trial.[5] Of the 798 infants in the screening log 78 infants (9.7%) were excluded based on unable to randomize by 6 hours of age. If this is extrapolated to the screened but not eligible infants in the NRN Hypothermia trial (n=560) another 54 infants may be eligible (35 month study). The latter figure should be considered an underestimate since some infants that may qualify were probably never referred to Network centers for the Hypothermia study given the age constraints (< 6 hours of age). If it is estimated conservatively that one infant per center per year is recruited based on the time of entry criteria (6-24 hours) beyond that of the screening/eligibility forms of the prior study, another 47 infants may be eligible for a 35 month study conducted in 16 centers.

These two sources of patients provide an estimate of 155 patients over 35 months or 160 patients extrapolated to a 3 year interval. Given the limited number of patients within the Network a randomized study could be done with the explicit purpose to obtain the most precise and unbiased estimate of the relative risk for death or disability that is reasonably feasible. The longest trial that has been considered reasonably feasible in the Network has been approximately five years. We propose to enroll 168 infants in a trial that would require approximately 3 years for enrollment and two years for follow-up. This provides 160 infants for analysis assuming a lost to follow-up of no greater than 5%. Conducting a longer trial (or incurring the additional expense, effort, and uncertainty inherent in involving Centers outside the Network) is unlikely to be acceptable to the Steering Committee.

This approach to sample size—assessment of the largest number of patients that is reasonably feasible in order to obtain the most precise and unbiased estimate of treatment effects—differs from the conventional (frequentist) approach to determining sample size. Frequentist statisticians ordinarily recommend against conducting a randomized trial when it is not feasible to achieve conventional sample size estimates. However, the alternative in this circumstance is to conduct no trial and to allow the use of hypothermia beyond 6 hours to creep into clinical practice based on anecdotal experience or at best observational studies. As Schulz and Grimes have emphasized, assertions that trials should not be conducted "unless an arbitrarily defined level of statistical power can be assured make no sense if the alternative is acquiescence in ignorance of the effects of healthcare interventions...Unbiased trials with no results trump no results at all.[37]

Based on the largest feasible randomized trial, conventional statistical analyses may be used to provide an unbiased estimate of treatment effect with a 95% confidence interval. As discussed below, we propose Bayesian methods of analysis to indicate the probability of a clinically important effect.

16.1 Data Analysis

The use of Bayesian methods in clinical trials is rapidly increasing, and these methods have particular advantages for small or medium size trials.[38] For these reasons, a brief description of Bayesian methods is provided below.

16.1.1 Introduction to Bayesian methods (A technical summary of the Bayesian statistical model for this proposal is included as an Appendix 1)

16.1.1.1 Differences Between Frequentist and Bayesian Statistics

Conventional frequentist inference uses objective probabilities for the assessing the relative frequency that a statistical procedure is correct in an infinite sequence of replications. Bayesian inference uses subjective probabilities as logic for maintaining coherent beliefs. Frequentist inference focuses on the probability that the observed or more extreme data would be obtained assuming that the null hypothesis is true. Bayesian inference focuses on the probability that a hypothesis is true given the observed data. For example, suppose a clinical trial identified an excess of infants with death among control infants compared to infants receiving the intervention under investigation. Frequentist statistics would address the question: What is the likelihood that this excess or a larger difference between groups would have occurred if the null hypothesis—e.g., that treatment has no effect on mortality—is correct (i.e., Pr (observed or more extreme data $|$ H_o)? Bayesian statistics addresses a fundamentally different question that addresses more directly what physicians want to learn from the trial: What is the probability that the intervention has no effect on mortality (or conversely, the probability that it does), given the data obtained in the trial (i.e.,Pr(H_o $|$ data).

16.1.1.2 Consideration of Prior Evidence

Any Bayesian analysis consists of combining prior evidence (represented as a *prior* distribution) with data (represented as a likelihood) obtained from the current study. The result is a *posterior distribution* from which all inference is derived. Thus a Bayesian statistician must quantify prior evidence in the form of a prior distribution. This is in contrast with the frequentist approach where the analysis of a clinical study does not involve consideration of the evidence from other relevant studies. The frequentist statistician leaves it to the reader to consider the results from other studies in interpreting the current study results and reaching a conclusion or making a treatment recommendation. In contrast, Bayesian analyses involve formal consideration of prior evidence (before seeing the results of the trial) to estimate the posterior likelihood of the null hypothesis (after reviewing trial results). As an example, the posterior probability that an intervention reduced mortality as determined after completing a new trial may be assessed in a cumulative meta-analysis in which the prior probability is based on the results of all prior trials of the intervention. This approach to assessing treatment effect considering all prior and current evidence has been adopted by clinicians who use cumulative meta-analyses. Bayesian inference uses subjective probabilities with objective learning; classical inference uses objective probabilities with subjective learning.

16.1.1.3 Resolving Controversy about Bayesian Methods

Bayesian analyses have been criticized for the possibility of producing posterior probabilities that may hinge on excessively dogmatic or highly idiosyncratic beliefs about the phenomena under investigation or on widely varying beliefs among different investigators. This criticism has been largely addressed by the following kinds of responses from Bayesian statisticians:

1. The investigator's prior is open to public scrutiny, forcing him to make explicit his beliefs, justifiable or speculative, about the phenomenon under study, and thereby promoting honesty in the analysis.[39]
2. Accordingly, one's prior probability should be justified by the relevant evidence over speculation. Wherever possible, the prior probability should be based on standardized assessments of high quality studies, e.g. effects obtained from a well-performed meta-analysis of randomized trials.
3. One's prior may be *tempered* to take into account the beliefs of the scientific community and specialists in the field.[40]
4. There exist *reference* priors that have little influence on the data.[41] These may be used to obtain standard analyses relatively free of prior beliefs.
5. Bayesian analyses can be conducted using skeptical values for prior probabilities to determine whether the study results are sufficiently compelling to be persuasive even to skeptics.

Whether or not large trials have been performed, Bayesian statistics provides a formal quantitative method to assess the range of treatment effect compatible with the best available evidence and to estimate the probability of a clinically important benefit, considering all relevant prior evidence as viewed from the perspective of skeptics, enthusiasts, or physicians in equipoise. For these and other reasons, including the development of Bayesian software, the use of Bayesian methods in the design, monitoring, and analysis of clinical trials is progressively increasing For example, the FDA recently encouraged the use of adaptive study designs based on Bayesian techniques in Phase I and Phase II trials.[38] Whatever the phase or sample size for a trial, Bayesian approaches provide a method to assess the range of treatment effect compatible with the data and to estimate the probability of a clinically important effect.

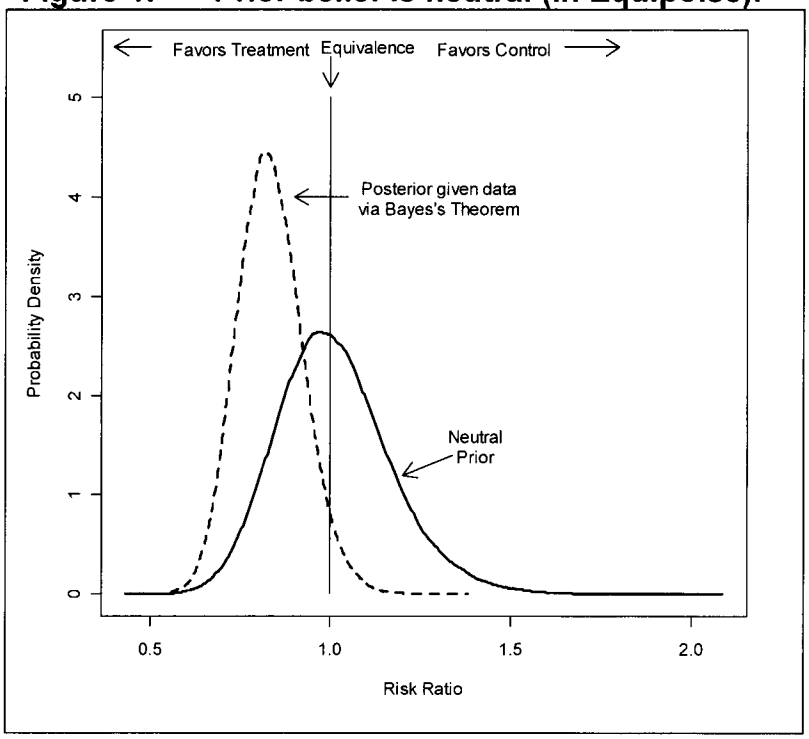
16.1.2 Analytic Approach for the Proposed Trial

The following is presented to illustrate the application of Bayesian methods to the kind of results that may be obtained in the proposed trial (n =160). Treatment effect is expressed as relative risk for death or impairment in the hypothermia group relative to that in the control group. Bayesian analyses are discussed below for circumstances in which the findings are compatible with moderate benefit (relative risk = 0.72), major benefit (relative risk = 0.64), no benefit (RR = 1.00) or harm (RR =1.10).

1. A relative risk of 0.72 is identified in the trial.[1] This relative risk would be identical to that in the prior trial, as could occur if the increased effectiveness due to a longer treatment period completely offset a reduction in effectiveness due to a delay in initiating therapy.

As indicated above, the posterior probability computed in a Bayesian analysis would depend on the prior probability, and the prior probability will vary depending on whether the viewpoint adopted is neutral (in equipoise), skeptical, or enthusiastic. The neutral prior would be that the relative risk would be 1.00. A skeptical prior would be that overall effect of hypothermia is actually harmful in this setting with a relative risk of 1.10. An enthusiastic prior would be that the relative risk would be 0.72 as in the prior trial.[5] To reflect the range of values that would be considered plausible from each perspective, the 95% credible intervals are.73 – 1.36 for the neutral prior,.83 – 1.48 for the skeptical prior, and.48 – 1.03 for the enthusiastic prior. Shown below are three figures indicating the values for the posterior probability that would be obtained for each of the 3 perspectives.[42] These figures correspond to Figures 1, 2 and 3 of reference 42 by Lilford and colleagues.

Figure 1. Prior belief is neutral (in Equipoise).



[1]This relative risk would be obtained if death or impairment occurred in 36 of 80 hypothermia infants and 50 of 80 control infants.

Figure 2. Prior belief is skeptical.

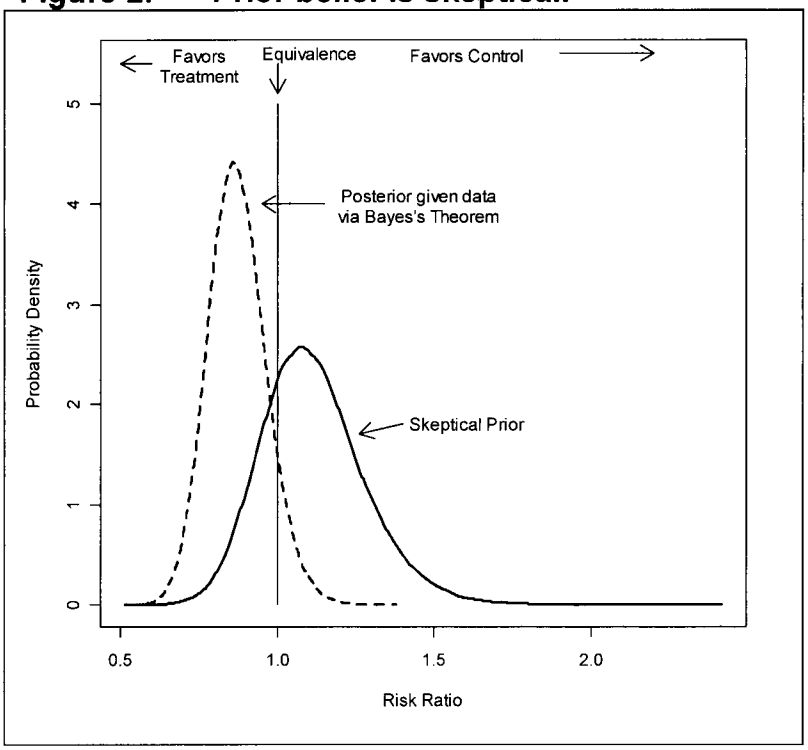


Figure 3. Prior belief is enthusiastic.

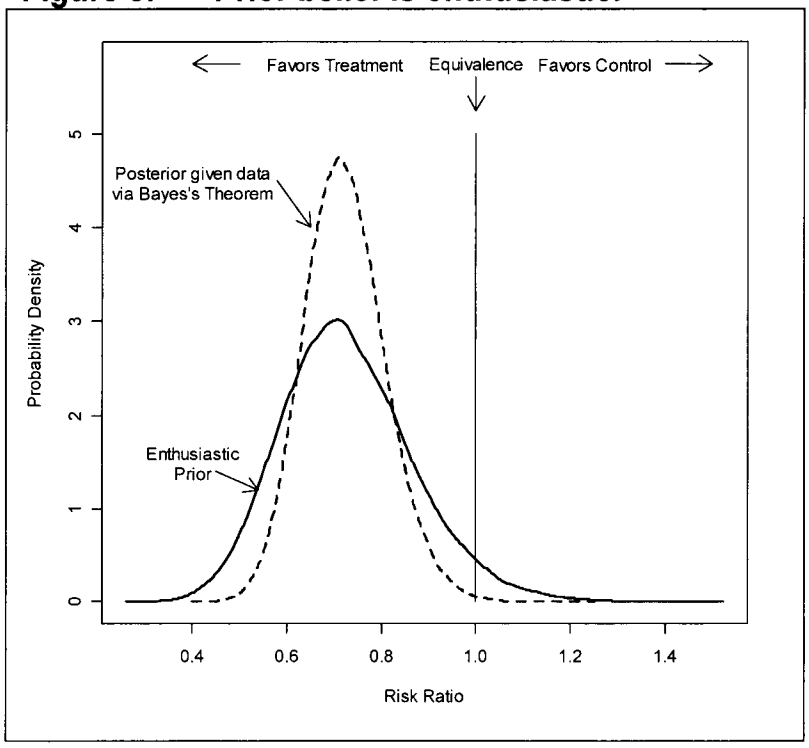


Table 2 below reflects the findings shown in the figures and provides the posterior probability of benefit reducing death or impairment exceeding 0%, 10%, or 20% (i.e, a true relative risk <1.0, <0.9, or <0.80).

Table 2

	Posterior Probability of Benefit					
	>0% reduction in death or impairment		**>10% reduction in death or impairment**		**>20% reduction in death or impairment**	
Perspective	Prior	Posterior	Prior	Posterior	Prior	Posterior
Neutral	**.50**	**.96**	**.25**	**.78**	**.07**	**.37**
Skeptical	**.25**	**.91**	**.08**	**.64**	**.01**	**.22**
Enthusiastic	**.96**	**.99**	**.89**	**.97**	**.71**	**.82**

Thus, if a neutral perspective is adopted in analyzing the trial, the posterior probability of at least some benefit would be **96%**, a 10% reduction in death or impairment would be **78%**, and the posterior probability of a 20% reduction would be **37%**. Even if a skeptical perspective is adopted, the corresponding posterior probability of at least some benefit would be **91%**; the value for a 10% benefit would be **64%**, and the value for a 20% probability would be **22%**.

2. A relative risk of 0.64 is identified.[2] Such a benefit could occur if the delay in treatment beyond 6 hours does not appreciably affect the benefits of therapy and/or the increase in duration of therapy has strong beneficial benefits. For the sake of brevity, figures are not displayed. However, as shown in Table 3 below, a high probability is obtained for all levels of benefit, even if a skeptical perspective is adopted.

Table 3

	Posterior Probability of Benefit					
	>0% reduction in death or impairment		**>10% reduction in death or impairment**		**>20% reduction in death or impairment**	
Perspective	Prior	Posterior	Prior	Posterior	Prior	Posterior
Neutral	**.50**	**.99**	**.25**	**.90**	**.07**	**.59**
Skeptical	**.25**	**.97**	**.08**	**.81**	**.01**	**.41**
Enthusiastic	**.96**	**.99**	**.89**	**.99**	**.71**	**.93**

Thus, if a neutral perspective is adopted in analyzing the trial, the posterior probability of at least some benefit would be **99%**; a10% reduction in death or impairment would

[2]This relative risk would be obtained if death or impairment occurred in 32 of 80 infants in the hypothermia group and 50 of 80 infants in the control group.

be **90%**, and the posterior probability of a 20% reduction would be **59%**. Even if a skeptical perspective is adopted, the corresponding posterior probability of at least some benefit would be **97%**; the value for a 10% benefit would be **81%**, and the value for a 20% probability would be **41%**.

3. A relative risk of 1.0 is identified. Such a value could be obtained if there was no benefit from hypothermia initiated after 6 hours age or if the harm from extended use completely offset the benefit. As shown in Table 4 below, the value for the posterior probability would not justify administration of hypothermia even if an enthusiastic prior were adopted.

Table 4

	Posterior Probability of Benefit					
	>0% reduction in death or impairment		**>10% reduction in death or impairment**		**>20% reduction in death or impairment**	
Perspective	Prior	Posterior	Prior	Posterior	Prior	Posterior
Neutral	**.50**	**.50**	**.25**	**.14**	**.07**	**.01**
Skeptical	**.25**	**.34**	**.08**	**.06**	**.01**	**.003**
Enthusiastic	**.96**	**.87**	**.89**	**.54**	**.71**	**.15**

Thus, if a neutral perspective is adopted in analyzing the trial, the posterior probability of at least some benefit is **50%**; 10% reduction in death or impairment would be **14%**, and the posterior probability of a 20% reduction would be **1%**. If a skeptical perspective is adopted, the corresponding posterior probability of at least some benefit would be **34%**; the value for a 10% benefit would be **6%**, and the value for a 20% probability would be **0.3%**. If an enthusiastic perspective is adopted, the corresponding posterior probability of at least some benefit is **87%**; 10% reduction in death or impairment would be **54%** and the value for a 20% probability would be **15%**.

1. A relative risk of 1.10 is identified. [3] Such a value could be obtained if the harm from extended use was greater than any benefit.

Thus, if a neutral perspective is adopted in analyzing the trial, the posterior probability of any benefit is **26%**; a 10% reduction in death or impairment would be **4%**, and the posterior probability of a 20% reduction would be **0.1%**. If a skeptical perspective is adopted, the corresponding posterior probability of at least some benefit would be **14%**; the value for a 10% would be **1%**, and the value for a 20% probability would be **0.02%**. If an enthusiastic perspective is adopted, the corresponding posterior probability of at least some benefit would be **69%**; the corresponding posterior probability of a 10% reduction in death or impairment would be **29%** and the value for a 20% probability would be **4%**.

[3]This relative risk would be identified if death or impairment occurred in 55 of 80 infants in the hypothermia group and 50 in the control group.

One might view the above results with concern that a clinician with an enthusiastic viewpoint may interpret the posterior probabilities as an indication to adopt the treatment even if the relative risk for a reduction in death or impairment is 1.0 or 1.1. However the viewpoint of the enthusiast is not advocated and is presented for sake of completeness. With a relative risk of 1.0, the enthusiast may want to adopt the treatment given an 87% probability of some reduction in death or impairment; however the likelihood of finding a > 10% benefit is not much better than 50:50 and the investment of time, cost and the possibility of harm in using the treatment may temper even the enthusiast. With a relative risk of 1.1 there is a dramatic reduction in the enthusiasts' belief that the treatment would yield some benefit; before observing the data the enthusiast was 96% sure of at least some effect and after performing the trial he/she is only 69% sure. The results have considerable impact even on the enthusiast. If one were to adopt the treatment that has a relative risk of 1.1, they would be doing so in the face of a 31% (1 – 0.69) chance of no benefit or harm, and a 71% chance of not having a 10% reduction in death or disability.

Results of the Bayesian analysis will be adjusted for center and gender.[43, 44]

For comparison, the frequentist required sample size for a trial with an alpha error of 0.05, 80% power and a relative risk of 0.64, 0.72, 0.9 and 1.1 are 80, 134, 1054 and 991 subjects per group, respectively.

17.1 Phases of the Study

The study will be initiated as a pilot for 12 months given the uncertainty about the number of patients available for enrollment. A 12 month interval should provide a long enough time to determine the ability to recruit for this trial given the variability in start time among centers (IRB issues, in-services, education of referring centers etc). A commitment to complete the entire study will not be made until the end of the pilot period. This decision will be made by the DSMC along with review of the data for any unexpected toxicity associated with a longer interval of systemic hypothermia. Outcomes (death/disability) for infants in the pilot phase are not required for continuation of the study. All infants enrolled in the pilot phase will be used as patients in the main trial since the protocol is identical.

18.1 Monitoring of Safety for the Trial

- The protocol will be reviewed by the Institutional Review Board of each participating institution.
- Adverse events will be reported on the MedWatch form to the Data Center of the NICHD Neonatal Network, Research Triangle Institute (RTI), Chapel Hill, North Carolina. Adverse events will be compared between the two groups using sequential analysis methods (the statistic is computed after the adverse event information of each sequential pair of hypothermia intervention/control is available). The computed statistic is compared to boundaries that are constructed so that an overall alpha level is maintained. This alpha level will be set at 10% to guard against false negatives. A Bross "wedge" type set of boundaries and a real time plot of the statistic will be used for this monitoring. RTI will be responsible for

reporting adverse events to the Data Safety Monitoring Committee (DSMC) of the Network.

- All protocol deviations will be monitored by RTI.
- RTI will prepare reports for presentation to the DSMC at periodic intervals.
- DSMC will be responsible for monitoring the safety and efficacy of the trial.

19.1 Budget and Justification

Table 6 shows an estimated budget is provided for the entire trial assuming enrollment of 168 patients with outcomes available for 95% of the patients (160 patients).

	Cost ($ per patient, device or center)	**Number of patients, device or centers**	**Total cost - $**
Research time	1,500/patient	168	252,000
Medical Supplies	60/patient	168	10,080
Follow up	1,200/patient	160	192,000
Blanketrol II machine for new centers	4,100/device estimated	4 sites, 6 devices	24,600
Training meeting	500	16	8,000
Start up costs	1500/center	16	24,000
Total			***510,680***

Research time: Costs will cover time to screen and determine eligibility of patients, data collection, initiating and monitoring of the cooling intervention, and transmission of all data items. There may be further discussion needed regarding dedicated funds for being on-call.

Medical supplies: Costs will cover supplies for the Cincinnati Sub-Zero Blanketrol including temperature probes, thermal blankets, and temperature probe adaptors.

Follow-up: Costs will cover tracking infants, incentives to participate in Follow-up and performance of follow-up at Network sites. The higher costs of follow-up for this study are based upon a) this group of patients are not routinely followed by the Network, b) poor outcomes may be common and require higher incentives for participation, and c) the absence of a brain specific treatment for infants in this age group (after 6 hours of age) may result in infants transported from very far distances and require higher follow-up costs.

Blanketrol devices: Each new network center will require Cincinnati Sub-Zero Hyperthermia-Hypothermia Blanketrol II devices and the costs listed are based on a price estimate from the company. The University of Utah is planning on enrolling at 3 different hospitals. Cincinnati Sub-Zero now makes a Blanketrol III device and has given a price quote of $7,350 per unit. The relative merits of this device compared to the Blanketrol II are unclear at present but may deserve discussion.

Training meeting: The study PI from each Network site will be required to attend one training session in conjunction with the Steering Committee prior to initiation of the trial. Funds are required to cover the cost of travel and lodging assuming this would occur following a Steering Committee meeting.

Start-up costs: Funds are required for the time to train personnel and implement the study within sites.

Appendix 1

Bayesian Statistical Model for Hypothermia Study

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1 Introduction

The following is a technical report explicating the proposed Bayesian statistical model for *Evaluation of Systemic Hypothermia Initiated after 6 Hours of Age in Infants Greater than 36 Weeks Gestation with Hypoxic-Ischemic Encephalopathy* with Dr. A. Laptook, Principal Investigator.

2 Primary Outcome

The primary outcome is the composite of death or survival moderate to severe impairment versus the composite survival with mild to no impairment at 18–22 months.

3 Treatment and Stratification

The treatment will be hypothermia versus standard care. Prognostic stratification variables will be *age* at enrollment (age $\leq$ 12 hrs versus age $>$ 12 hrs), and *stage* of encephalopathy (moderate versus severe), and their interaction. Infants will be randomly assigned to treatment within stratification by *age* and *stage*. Infants will be stratified by, but not randomized within, site.

4 Model for Data Generation Process

A Bayesian model comprises three components: a model for the *data generating process* or *likelihood*, the *prior* distribution of beliefs regarding the parameters before the data are observed, and the *posterior* distribution of beliefs regarding the parameters after the data are observed. The first two components together with the data determine the last. Here the data generating process is presented.

Let N denote the number of HIE infants in the study, and let S denote the number of sites from which observations will be collected. (Currently N is anticipated to be about 160 and S is 16) Let $y_i \in \{0, 1\}$ denote the binary outcome:

$$y_i = \begin{cases} 0 & \text{for survival with no to mild disability} \\ 1 & \text{for death or survival with moderate to severe disability} \end{cases}$$

for infant i, $i = 1, \ldots, N$. Also for infant i, let s_i denote the site number, z_i the treatment, and $\mathbf{x}_i$ the p-vector ($p = 3$) of prognostic covariates, where

$$s_i \in \{1, \ldots, S\},$$

$$z_i = \begin{cases} 0 & \text{for standard care} \\ 1 & \text{for hypothermia treatment;} \end{cases}$$

$$x_{1i} = \begin{cases} 0 & \text{for age} \leq 12 \text{ hrs} \\ 1 & \text{for age} > 12 \text{ hrs;} \end{cases}$$

$$x_{2i} = \begin{cases} 0 & \text{for moderate encephalopathy} \\ 1 & \text{for severe encephalopathy;} \end{cases}$$

and

$$x_{3i} = x_{1i}x_{2i} = \begin{cases} 0 & \text{for age} \leq 12 \text{ hrs or moderate encephalopathy} \\ 1 & \text{for age} > 12 \text{ hrs and severe encephalopathy.} \end{cases}$$

We make the standard assumption that a treatment for any particular infant has no effect on the outcome of any other infant and that the process of measuring an outcome has not effect on the outcome (Gelman, Carlin, Stern, & Rubin, 2004). We also assume the infants' outcomes are mutually independent. Therefore, the outcome y_i follows a Bernoulli distribution whose probability parameter π is a function of the site, treatment, and predictors associated with the infant:

$$y_i \mid (s_i, z_i, \mathbf{x}_i) \sim \text{Bernoulli}\left[\pi\left(s_i, z_i, \mathbf{x}_i\right)\right].$$

The effects of site, treatment, and covariates are modeled as a logistic regression:

$$\text{logit}\left[\pi\left(s_i, z_i, x_i\right)\right] = \alpha_{s_i} + \theta z_i + \mathbf{x}_i'\boldsymbol{\beta} \tag{1}$$

The parameter θ represents the (randomized) treatment effect, expressed as log-odds, with $\theta < 0$ favoring treatment. The treatment is assumed to be fixed and modified neither by site nor by the covariates.

The parameter $\boldsymbol{\beta}$ represents the prognostic covariate effects. These effects are assumed to be fixed and modified neither by site nor by treatment. These covariates are included to increase the precision of the treatment effect.

The influence of the sites on outcomes can be modeled in one of three different ways: complete pooling, no pooling, or partial pooling (Gelman & Hill, 2007). *Complete pooling* regards the sites as homogeneous, having no differential effects, but serving merely as independent replications within the overall study. In this case, all the site effects are presumed equal so that $\alpha_s = \alpha$ for all s. *No pooling* regards the sites as separate studies such that the outcomes from any one site provide no information regarding those from any other site. Each site would thus require its own parameter α_s. *Partial pooling* regards the sites as having heterogeneous effects, but without any additional information as to which site would exhibit which effect.

Partial pooling is assumed here and is modeled as *exchangeability* among sites (Gelman et al., 2004). From the exchangeability assumption, the effect of any site can be modeled as arising from a super-population of site effects. Here we assume

$$\alpha_s \sim \text{normal}(\mu_\alpha, \sigma_\alpha^2). \tag{2}$$

The site effects are assumed to be modified neither by treatment nor by the covariates.

Thus, the model for the data generating process, i.e. the likelihood, is a *multilevel logistic regression with a varying intercept* (Gelman & Hill, 2007). This model is a extension of the model in the proposal to include sites and prognostic covariates.

5 Prior Densities

The second component is the *prior* distribution or density regarding the parameters. In general, th elicitation of prior densities can be difficult (Garthwaite, Kadane, & O'Hagan, 2005), but in our case, the elicitation of priors is considerably simplified. Except for the treatment parameter θ, the priors for the site and covariate effects will be *diffuse*, *vague*, or *weakly informative* so that they have little influence on the observations.

The priors for μ_α and σ_α^2 in Equation 2

$$\mu_\alpha \sim \text{normal}(0, 10^2);$$
$$\sigma_\alpha \sim \text{uniform}(0, 10).$$

The priors for the covariate coefficients in Equation 1 will be

$$\boldsymbol{\beta} \sim \text{normal}\left(\mathbf{0}, 10^2\mathbf{I}\right).$$

The prior density for θ will be informative because previous evidence gives some idea of the size of the effect (Eicher et al., 2005; Gluckman et al., 2005; Shankaran et al., 2005). The parameter θ will reflect neutral, enthusiastic, and skeptical priors (D. Spiegelhalter, Abrams, & Myles, 2004). The prior density will be

$$\theta \sim \text{normal}(\mu_\theta, 0.5^2),$$

where

$$\mu_\theta = \begin{cases} 0.0 & \text{for the neutral prior;} \\ -0.7 & \text{for the enthusiastic prior;} \\ 0.3 & \text{for the skeptical prior.} \end{cases}$$

These values for μ_θ approximate the risk ratios and their 95% credible intervals of the proposal.

6 Posterior Density

The third component is the posterior density, which is determined by the likelihood and the prior. For notational convenience, stack the y_i and s_i into N-vectors y and s and the $\mathbf{x}_i'$ into an $N \times p$ matrix $\mathbf{X}$. Also stack the α_s into the S-vector $\boldsymbol{\alpha}$. In an obvious abuse of notation, let normal$(\cdot \mid \mu, \sigma^2)$ denote the normal density function with mean μ and variance σ^2, and uniform$(\cdot \mid a, b)$ denote the uniform density with bounds a and b. Given the observed outcomes y and associated

sites s and covariates **X**, Bayes's Theorem yields

$$\begin{aligned}
&\text{pr}\left(\theta, \boldsymbol{\beta}, \boldsymbol{\alpha}, \mu_\alpha, \sigma_\alpha^2 \mid \mathbf{y}, \mathbf{s}, \mathbf{X}\right) \\
&\quad \propto \prod_{i=1}^{N} \text{pr}\left(y_i \mid \theta, \boldsymbol{\beta}, \alpha_{s_i}, \mathbf{x}_i\right) \text{pr}\left(\theta\right) \text{pr}\left(\boldsymbol{\beta}\right) \text{pr}\left(\alpha_{s_i} \mid \mu_\alpha, \sigma_\alpha^2\right) \text{pr}\left(\mu_\alpha\right) \text{pr}\left(\sigma_\alpha^2\right) \\
&\quad \propto \prod_{i=1}^{N} \exp\left[y_i \left(\alpha_{s_i} + \theta z_i + \mathbf{x}_i' \boldsymbol{\beta}\right)\right] \left[1 + \exp\left(\alpha_{s_i} + \theta z_i + \mathbf{x}_i' \boldsymbol{\beta}\right)\right]^{-1} \\
&\qquad \times \text{normal}\left(\theta \mid \mu_\theta, 0.5^2\right) \times \text{normal}\left(\boldsymbol{\beta} \mid \mathbf{0}, 10^2 \mathbf{I}\right) \times \text{normal}\left(\alpha_{s_i} \mid \mu_\alpha, \sigma_\alpha^2\right) \\
&\qquad \times \text{normal}\left(\mu_\alpha \mid 0, 10^2\right) \times \text{uniform}\left(\sigma_\alpha \mid 0, 10\right).
\end{aligned}$$

The posterior distribution is analytically intractable, but can be calculated by modern Bayesian computational methods. The posterior *marginal* densities of the parameters can be approximated to a high degree of accuracy by Markov chain Monte Carlo (MCMC) methods (Gelman et al., 2004). In essence, MCMC methods produce the marginal densities of each parameter by sampling in a round-robin fashion from the marginal density of each parameter conditional on the values of the other parameters until convergence is achieved. In addition to their posterior densities, all parameters will be summarized by their posterior means, standard deviations, and their 95% credible intervals.

7 Derived Parameters

The posterior density of the adjusted odds ratio comparing treatment to control

$$\omega = \exp(\theta) \tag{3}$$

is obtained by sampling from the posterior density of $\theta \mid \mathbf{y}$.

The posterior density for the proportions of outcomes for either treatment z and any combination of covariates $\mathbf{x}$ and averaged over sites can be obtained as

$$\text{logit}\left[\pi\left(z, \mathbf{x}\right)\right] = \mu_\alpha + \theta z + \boldsymbol{\beta}' \mathbf{x}$$

by sampling from the posterior densities of $\mu_\alpha \mid \mathbf{y}$, $\theta \mid \mathbf{y}$, and $\boldsymbol{\beta} \mid \mathbf{y}$. The posterior densities of the adjusted risk difference

$$\delta(\mathbf{x}) = \pi\left(1, \mathbf{x}\right) - \pi\left(0, \mathbf{x}\right)$$

and the adjusted risk ratio

$$\rho(\mathbf{x}) = \frac{\pi\left(1, \mathbf{x}\right)}{\pi\left(0, \mathbf{x}\right)}$$

for any combination of predictors can then be readily obtained. Again, these derived parameters will be summarized by their posterior means, standard deviations, and their 95% credible intervals.

8 Hypothesis Testing

Adapting the categories provided by D. Spiegelhalter et al. (2004). The primary hypotheses to be tested are whether hypothermia treatment is *beneficial*, *equivalent*, or *harmful* relative to standard care. In addition to the above mutually exclusive categories, hypothermia may be not harmful but nonetheless *nonbeneficial* or not beneficial but nonetheless *nonharmful*. And finally,

hypothermia may be neither beneficial, harmful, nor equivalent, but *equivocal* with respect to standard care.

Let ω be the posterior odds ratio as in Equation 3. Let c_b and c_h with $c_b < c_h$ be clinical thresholds for hypothermia treatment being beneficial or harmful relative to standard care, and let η be a probability level such as .95 or .99. The choice of c_b is based on how large a benefit is required to produce a clinically meaningful result, taking into account the cost and concomitant risks of treatment. The threshold c_h reflects how much harm is allowed before the treatment is deemed clinically inappropriate. The parameter η reflects the uncertainty allowed for each hypothesis. Using odds ratio and these clinical thresholds, hypothermia treatment would be

- beneficial if $\Pr(\omega < c_b) > \eta$,
- equivalent if $\Pr(c_b \leq \omega \leq c_h) > \eta$, or
- harmful if $\Pr(\omega > c_h) > \eta$.

If none of the hypotheses obtain, then hypothermia treatment would be

- nonharmful, i.e., probably equivalent or beneficial, if $\Pr(\omega < c_h) > \eta$, or
- nonbeneficial, i.e., probably equivalent or harmful, if $\Pr(\omega > c_b) > \eta$.

If neither of the hypotheses obtain, then hypothermia treatment would be

- equivocal

with respect to standard care. Multiple choices of clinically relevant criteria can be examined, without requiring statistical adjustments for multiple hypotheses. Similar hypotheses can be tested with $\rho(\mathbf{x})$ and $\delta(\mathbf{x})$.

9 Software

The MCMC analyses will be conducted in WinBUGS (D. J. Spiegelhalter, Thomas, Best, & Lunn, 2002). The WinBUGS program code, provided in the appendix, has already been written and tested. Convergence diagnostics will be conducted by using multiple start values with the potential scale reduction estimator. Artificial data sets resembling the data to be expected have been generated and successfully analyzed. Subsidiary analyses and graphics production will be conducted in R (R Development Core Team, 2006). Connections between R and WinBUGS is provided by the R package `R2WinBUGS` (Sturtz, Ligges, & Gelman, 2005).

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Education and debate

Clinical trials and rare diseases: a way out of a conundrum

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Currently, clinical trials tend to be individually funded and applicants must include a power calculation in their grant request. However, conventional levels of statistical precision are unlikely to be obtainable prospectively if the trial is required to evaluate treatment of a rare disease. This means that clinicians treating such diseases remain in ignorance and must form their judgments solely on the basis of (potentially biased) observational studies, experience, and anecdote. Since some unbiased evidence is clearly better than none, this state of affairs should not continue. However, conventional (frequentist) confidence limits are unlikely to exclude a null result, even when treatments differ substantially. Bayesian methods utilise all available data to calculate probabilities that may be extrapolated directly to clinical practice. Funding bodies should therefore fund a repertoire of small trials, which need have no predetermined end, alongside standard larger studies.

Introduction

: the problem

Randomised clinical trials have become the standard method to assess clinical effectiveness when benefits are modest but worth while. They are more reliable than other methods[1] and have solved some clinical questions conclusively--for example, the effectiveness of adjuvant treatment in early breast cancer. Clinical questions are most easily answered when a disease is fairly common and the outcome of interest has a high risk of occurring. It is not surprising that randomised controlled trials have provided fairly conclusive results about the treatment of such conditions as acute myocardial infarction and the common cancers and that these results have formed the basis of clinical guidelines and audit standards. When diseases are rare and benefits modest, however, clinical trials, as currently conceived, have little to contribute. This is because they cannot be expected to provide a "definitive" answer--that is, they cannot be expected to detect or exclude clinically worthwhile differences between

treatments with standard levels of statistical confidence. Hence they are not funded by grant giving bodies.

In this article we argue that randomised trials can be expected to provide useful information, even when a definitive answer is unlikely in prospect. Standard (so called frequentist) statistical techniques are not, however, suitable in these circumstances, but bayesian methods provide a much clearer guide to action.

An example of the problem

The evaluation of treatments applicable to congenitally abnormal fetuses (fetal surgery) is an example. The conditions for which this surgery may be contemplated are, individually, rare. For example, fetal hydrothorax, suitable for drainage, has an incidence of 1 in 10000 pregnancies. Current clinical trials are usually designed to give a chance of a false positive answer (P value) of 5%. Provided that the trial is designed to detect a clinical effect that would justify its use in practice, the chance of a false negative result in a trial (the beta or type two error) should also, logically, be 5%.[2] Six hundred participants would be needed in each arm of a trial to show that intervention could reduce mortality from 40% to, say, 30%. Access to 12000000 pregnancies would be required to recruit sufficient participants, assuming 100% compliance. Clearly, a grant request designed to look at this problem is likely to fail: there have indeed been no randomised studies of fetal surgery.

The same problem applies to many other rare diseases. Clinicians are forced to rely on observational studies, anecdotal information, (limited) clinical experience, and perception of biological plausibility. When a disease is uniformly and rapidly fatal such non-randomised case series may prove extremely valuable--for example, the use of penicillin to treat meningococcal meningitis. Most rare diseases, however, have a variable prognosis, and bias in allocating treatment in observational studies might be large in relation to the effects of treatment.

Current practice

Studies of rare diseases will remain vulnerable to this bias unless randomised trials are though of in a different way. Currently, they are highly stylised. Clinicians formulate a clinical question--preferably one that applies to a well circumscribed group of patients. They then decide on a worthwhile clinical effect--the size of effect that would make one treatment worth while (allowing for other desirable or undesirable facets of treatment)--either by seeking subjective opinion or by means of decision analysis.[3] The necessary sample size is then calculated on the basis of this worthwhile clinical effect and the acceptable risk for a false negative or false positive result.

In the case of rare diseases clinical scientists are likely to find that a trial of sufficient size to provide a definitive answer is virtually impossible because of the

difficulty of recruiting sufficient patients (fig **1**). A study of sufficient size would need to recruit from very large areas over long periods. Such studies are expensive and difficult to organise. If different doctors have different areas of clinical uncertainty then the problem will be compounded because power will be lower still in the various prognostic subgroups. For example, it may be deemed necessary in the case of fetal hydrothorax to analyse results separately according to whether the hydrothorax is unilateral or bilateral or whether fetal ascites is present. The factor limiting obtaining unbiased evidence for treatment of rare diseases is the concept that trials should provide a definitive answer as defined above. Since clinically useful effects are unlikely to be seen at the standard level of statistical precision, clinicians are locked out: they remain in complete ignorance (or at least having to rely on evidence that is subject to treatment allocation bias).

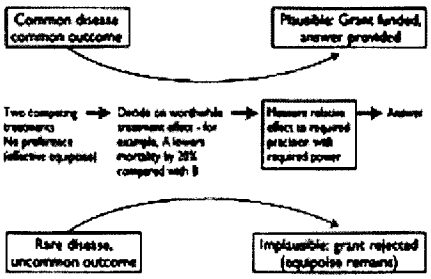

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Fig 1--Current conception of clinical trials. Doctors who treat rare diseases are locked out. Instead of improving their knowledge through an imprecise but unbiased estimate they gain no knowledge--the ideal is the enemy of the desirable

Confronting the problem: bayesian methods

We suggest an alternative: carry out trials of treatments for rare diseases, even though a definitive answer is unlikely to result in practice. The idea is simply to change the level of certainty.

But how should the results be analysed, given that conventional (frequentist) confidence limits are unlikely to exclude a null result, even when treatments differ substantially? We suggest that the bayesian perspective is particularly useful in such circumstances.[4 5 6] The bayesian approach can give probabilities that the clinical effect lies in a particular range (and also the size of the most likely effect). This is in stark contrast to the often misinterpreted P value produced by the usual (frequentist) approach. The frequentist P value is the probability of the observations (or something more extreme) occurring were the null hypothesis true--a difficult concept to grasp and one that does not provide what is wanted. The bayesian approach, by contrast, provides probabilities of treatment effects

that apply directly to the next patient who is similar to those treated in any completed or ongoing trial. Put another way, the bayesian approach provides probabilities that can be used in formal decision analysis, or extrapolated to clinical practice. Thus, the conclusion of the bayesian trial might be that the probabilities that the drainage of fetal hydrothorax reduces mortality by at least 50%, by 25%, or not at all are 0.2, 0.5, and 0.2 respectively.

These probabilities are calculated on the basis of the observed data and a prior distribution of probabilities. In this case the prior distribution usually represents the expectations of clinicians (or a clinician) before the trial. The purpose of the trial is to alter that belief according to the strength of the evidence. A null hypothesis would suggest a prior distribution of probabilities based on no effect--that is, the most likely effect perceived before observation of the data is no difference. The further a hypothesised result deviates from this the less likely it is to happen. A typical prior expectation would be that the probability of relative risks differing by more than twofold is extremely unlikely--having a probability of 0.025 (2.5%) in each direction. The crucial point is that the bigger the trial the greater the relative effect of data on the prior distribution and the less will be the difference between conventional confidence limits and the equivalent bayesian interval. The particular strength of the bayesian approach is that it produces a probability distribution which may guide clinical action even when a "definitive" answer is not available--the expected result of clinical trials of rare diseases.

Because the bayesian approach attempts simply to enumerate the probabilities of effects of different sizes, the trial can be analysed as data accumulate--a so called open trial.[5 7 8 9] The traditional (so called frequentist) method, by contrast, is based on hypothesis testing, and the probability of getting a false positive answer is affected by how often the data are tested statistically. This is a further argument for the bayesian approach for trials of treatment for rare diseases, since such studies are unlikely ever to be complete and the rate of recruitment is difficult to predict in advance.

Of course, small trials will sometimes mislead. Thus, in the example given above, a small trial may suggest that there is a probability of 0.5 (50%) that draining a fetal hydrothorax reduces mortality by 25% or more. However, the distribution of probabilities might be such that there is, say, a probability of 0.2 that this intervention does not reduce the risk of death or increases it. Clearly, there is a substantial risk of getting the wrong answer. If, however, we had an equipoised prior expectation--that is, we thought it equally likely at the start of the trial that the intervention (or non-intervention) would improve or diminish the chances of the desired outcome--then we have achieved something. Instead of an equal chance of benefit and harm, we now have an 80% chance of benefit and a 20% chance of harm. Clinicians are familiar with the need to make decisions under uncertainty and recommend the treatment which seems to have the best chance of maximising benefit (expected utility).

The alternative is to eschew clinical trials for rare diseases, and thereby to remain in ignorance and subject to bias. The point is that clinicians must make management decisions and clinical science should aim to provide the best possible information. The individual rare diseases are, by definition, not a big public health problem. There are, however, many rare diseases, so that, taken together, they represent a substantial health burden. Small trials might mislead us on, say, 20% of topics, but they would then suggest the correct treatment on the remaining 80%. Assuming that in each case clinicians were in justifiable collective equipoise[10] before the trial began--that is, they were split 50:50--then if clinicians follow trial recommendations 20% of people overall would get the wrong treatment if such trials were done compared with 50% if they were not done.

Ethics and bayesian trials

The bayesian approach is ethically sound; it makes prior belief explicit. Trials are ethical when prior belief is in equipoise[10 11 12]--that is, randomisation occurs only when the doctor or doctor and patient expect utility to be the same with each treatment.[12 13 14] Although randomisation will reduce the chance of treatment allocation bias, different doctors and doctor and patient pairs will be in equipoise at different levels of basic risk.[15] Therefore, in the analysis it may be desirable to stratify for risk. This was done in the Medical Research Council's cervical cerclage trial.[16] The entry criterion was clinical uncertainty, but the prognostic features producing such uncertainty varied considerably from clinician to clinician. Stratified analysis, however, showed that this treatment was effective for certain women--namely, those who had suffered two previous mid-trimester miscarriages. We suggest that the same principle of equipoise and a stratified analysis should apply to rare disease but that the trial should be analysed along bayesian lines, since this would allow the results to be scrutinised whenever deemed appropriate and it would not be essential to provide convincing evidence of likely recruitment to gain funding.

How the approach may work in practice

To illustrate this approach, consider a category of patient with fairly advanced (say, stage 3) primary biliary cirrhosis for whom a new drug (perhaps a biological modifier) is proposed as an alternative to conventional ursodeoxycholic treatment. The prevalence is so low that improvement in death and transplantation rates "cannot be subject to controlled trials."[17]

This conclusion comes from thinking of trials as a black box to be used only when the chances are high that a clinically worthwhile effect can be seen at classic levels of statistical significance. Let us say that five year mortality among patients with this stage of primary ciliary cirrhosis is 30% with current treatment. Standard (frequentist) power calculations suggest a study size of 320 in each arm to show even a large (10 percentage points) improvement in mortality from 30% to 20%.

Let us imagine that a bayesian trial is started using an open access (see below) trials facility. Suppose further that after five years 50 patients have been randomly allocated to each treatment and that 15 patients given conventional treatment and 10 given the new treatment have died--that is, an improvement of 10 percentage points as proposed in the above power calculation. However, the 95% confidence interval for the true difference ranges from a 7 percentage point increase to a 27 percentage point decrease in mortality (fig **2**). The result is not significant, and a traditionalist (frequentist) would say that the new treatment was still unproved and that it may even be wrong to use this expensive and possibly harmful medicine until further studies had been carried out. However, the bayesian would ask: "how have these data impacted on my prior belief?" Such prior belief would be based on biological plausibility, the results of other (perhaps open) studies, and clinical experience.

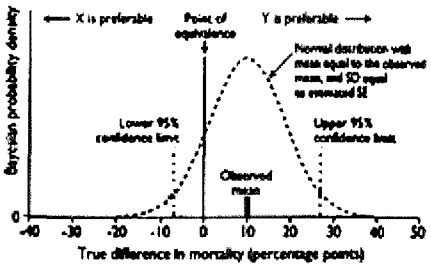

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Fig 2--Fifty patients have been randomly allocated two treatments. At the end of five years 15 of those allocated conventional treatment (treatment X) and 10 allocated new treatment (treatment Y) have died. This is a 10 percentage point difference in mortality, but the 95% confidence limits are wide, -7 percentage points to 27 percentage points. The results are clearly not significant (P=0.25). However, clinicians need to know which treatment effect has the greatest probability of occurring when they treat the next apparently similar patient and how the lesser probabilities are distributed around this greatest probability. From a bayesian viewpoint, the distribution shown is the posterior belief in the value of the true difference in mortality that arises from the data and a completely uninformative prior belief. Such a prior belief means that not only is the observer in equipoise but all sizes of treatment effect (difference in mortality) are regarded as equally likely--that is, a difference in mortality of 40 percentage points is regarded as likely as a 20 percentage point difference or no difference at all. This is clearly completely implausible in a clinical context.

Nevertheless, it does represent the information arising just from the data. In this case the probability that the new treatment is preferable is 0.88

Figure **3** shows the effect of the above data on an observer who previously considered a decrease and increase in mortality to be equally likely (in equipoise) and that a result more extreme than a 20 percentage point improvement or worsening in mortality was implausible. Calculation based on Bayes's theorem now shows that the most likely treatment effect is a 3.3 percentage point improvement in mortality, and there is a probability of 0.75 that the new treatment is better as far as mortality is concerned. In addition, both a reduction in mortality of more than 15 percentage points and an increase in mortality of more than 8.5 percentage points are highly unlikely (1% chance each).

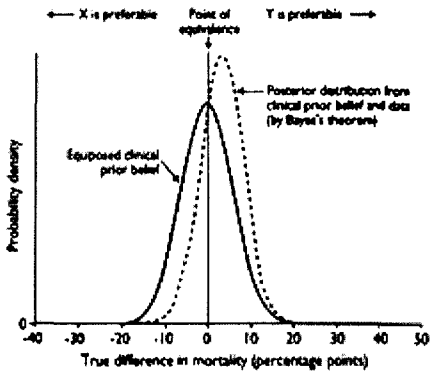

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Fig 3--This clinician has a prior belief that is in equipoise and reflects a belief that large effects (a difference in mortality of more than 20 percentage points) either way are unlikely. The posterior distribution is shifted towards the right, so that the posterior belief that the new treatment is preferable (or at least more likely to lower mortality) is 0.75 and the probability with the greatest chance of occurring is in an improvement of 3.3 percentage points

The clinician in figure **4**, however, was sceptical about the chances of the new treatment being better than no treatment and is rather vague about where the true difference lies. This clinician would find very large increases or smaller decreases in mortality plausible. Calculation of the posterior probabilities in the light of the data produced in the trial, now means that this clinician is in equipoise. Such a clinician, if previously unwilling to offer randomised treatment to patients, could now do so against personal equipoise.

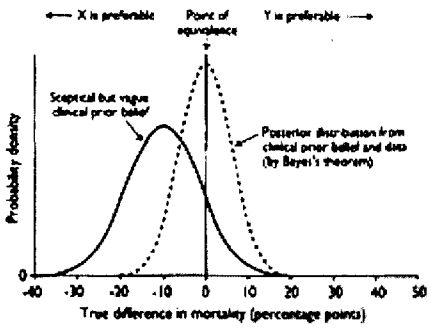

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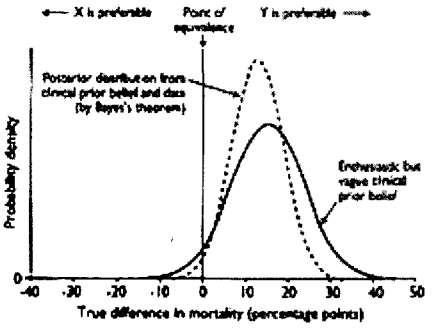
Fig 4--This clinician is sceptical about the chances of the new treatment being better than the conventional treatment but is otherwise vague about where the true difference lies. The prior belief that Y is better is just 0.12. The posterior distribution is in equipoise, given that side effects, short term benefits, and costs are similar for both treatments

Figure **5** shows an enthusiastic clinician who thinks that the new treatment is likely to improve mortality but is otherwise vague about where the true difference lies. The posterior probabilities, which take account of the data, are centred on a 12.5 percentage point reduction in mortality. The probability that the new treatment improves mortality is 0.98. Such a clinician may have been (and would remain) unwilling to offer randomised treatment to patients unless such improvements in mortality were necessary to justify side effects or costs, or both.[18] The clinician's overenthusiasm has also been curbed: the clinician's prior probability of 0.12 that the new treatment produces a huge 25 percentage point reduction in mortality is reduced to just 0.02 in the light of the data.



View larger version (19K):
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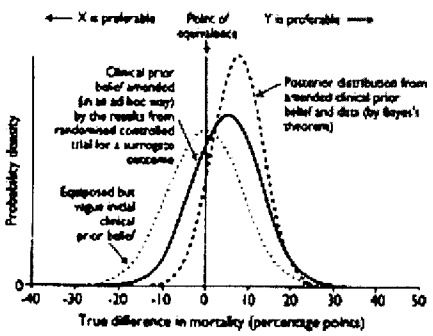
Fig 5--This clinician is enthusiastic about the chances of the new treatment being better than the old but is otherwise vague about where the true difference lies. The prior belief is that the most likely effect of the new treatment is a 15 percentage point reduction in mortality compared with the old treatment and that the probability that Y, the new treatment, is better than the old in reducing mortality is 0.96 (96%). The posterior distribution is centred on 12.5 percentage points. The probability of the new treatment being better has improved to 0.98 (98%), but the probability of a huge advantage (25 percentage points) has shrunk from 0.12 to just 0.02

Making use of all knowledge

The results of non-randomised studies should not be discarded--rather they should be incorporated into prior beliefs with due caution (scepticism). Furthermore, randomised controlled trials of treatments for rare diseases have the potential to produce relatively precise information on surrogate outcomes; and the effect of this information on clinical opinion can be incorporated in bayesian calculations as shown in figure **6**. Clinical trials capable of measuring improvements in mortality at classic significance levels are difficult to mount. Eleven small trials of UDCA00 have been done for primary ciliary cirrhosis, but only four mention time to transplantation or survival.[19] They do, however, show that results in liver function tests are improved by this treatment in comparison with placebo or colchicine. (Fewer patients are required to show a significant change in a continuous variable, such as alkaline phosphatase concentrations, than in a rate, such as death rate.) Although an improvement in mortality cannot necessarily be inferred from improvement in such surrogate outcomes, such results would increase our confidence that death rates are indeed improved. Thus similar data on liver function tests of survivors in this hypothetical trial would increase the likelihood of an improvement in mortality and clinicians might wish to amend their prior expectations accordingly. This might move an initially equipoised prior belief in the direction of benefit (fig **6**). The randomised results on improved mortality can then be combined formally with the amended prior beliefs to calculate the probabilities of different sizes of treatment effect. This shows that the greatest probability is a 7.3 percentage point reduction in mortality, and the probability of the new treatment being superior is 0.90. Of course, all randomised controlled trials can by chance produce an incorrect result--that the treatment which is really worse is better--and this is much more likely in small trials. Nevertheless, a decision taken on the basis of a posterior belief that includes evidence from a randomised controlled trial, however small, is more likely to be correct than a decision based simply on a prior belief with no evidence from such a trial. Any randomised evidence is better than none.



View larger version (20K):
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Fig 6--Interaction between prior beliefs, surrogate outcomes, and mortality data from a bayesian viewpoint. An example based on the medical treatment of primary biliary cirrhosis. The clinical prior belief in equipoise is first amended on the basis of liver function results in an ad hoc way so that the probability of the new treatment (Y) being preferable is 0.74. Mortality results in figure **2** show fewer deaths at five years in treatment group, but results are not significant at conventional level (P=0.25). These data combined with the amended

prior belief produce the posterior distribution shown; and the probability of the new treatment being preferable is 0.90

Implications for science policy

The concept of randomisation when the beliefs of clinicians treating rare diseases are in equipoise has implications for science policy. Rather than fund individual trials, funding bodies should fund the capacity to undertake rolling trials on a continuous basis--this would include a trials office that deals with a wide range of issues, is knowledgeable, has facilities for 24 hour randomisation, and can follow up patients over time. Such facilities would allow responsible investigators to offer randomised treatment to the first patient treated by a new method or to randomise when the treatment in question might be completely supplanted at some time in the future. This would be a substantial change in how research commissioners think about trials, and we suggest that it may complement, but not supplant, the existing methods, which should remain the standard for common diseases.

Ethics committees sometimes include scientific review and reject randomised controlled trials of treatments showing worthwhile effects that have little chance of producing a result at classic levels of significance. If thereby they encourage a larger trial, then some good has been done. However, if the disease is rare and no patients are randomly allocated treatment (instead of a small number) science, and people who suffer from rare diseases, have been badly served. If this effect is unwittingly replicated over the world, then trials which could contribute to a structured review and meta-analysis will be thwarted, thereby compounding the error. When diseases are rare, or potentially supplantable in the short term, then some unbiased information is better than none. This philosophy might result in replication of the trial elsewhere, thereby providing an unexpected scientific bonus.

We thank Dr David Spiegelhalter for his advice and inspiration.

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(Accepted 8 September 1995)

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From: Barbara Stoll
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Ellen Hale
Subject: MRI secondary-- SUPPORT
Date: Tuesday, November 13, 2007 4:06:54 PM

Rose

After IRB approval, can we enroll infants into the MRI secondary eventhough we are not budgeted this year to enter patients.

Thanks

BJS

Barbara J. Stoll, MD
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Atlanta GA 30022
Office: 404-727-2456 Fax: 404-727-5737
barbara_stoll@oz.ped.emory.edu

From: Duara, Shahnaz
To: Higgins, Rosemary (NIH/NICHD) [E]; Navarrete, Cristina
Subject: RE: SUPPORT GROWTH SECONDARY
Date: Friday, November 02, 2007 12:07:19 PM

Yes, we could – let us know time and other calling info.
Hope the ROP-SUPPORT babies get sorted out soon – we have limited info on some and need to find a way to get them of the edits list. Dale's email was evry helpful.

Best
Shahnaz

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, November 02, 2007 11:47 AM
To: Duara, Shahnaz; Navarrete, Cristina
Subject: SUPPORT GROWTH SECONDARY

Hi,
Recruitment continues in the growth secondary study.

Can you join the SUPPORT subcommittee by phone on Jan 10 for an update (probably going to occur around 11 am ET).
Let me know
Thanks
Rose

Rosemary D. Higgins, M.D.
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From:	Zaterka-Baxter, Kristin
To:	ahensman@wihri.org; mbball@leland.stanford.edu; grisbyca@email.uc.edu; ellen_hale@oz.ped.emory.edu; gaynelle.hensley@utsouthwestern.edu; Georgia E McDavid; auten002@mc.duke.edu; mcollins@peds.uab.edu; monica.konstantino@yale.edu; Nancy.Miller@UTSouthwestern.edu; Nancy Newman; ldw@iupui.edu; Mackinnon, Brenda; Johnson, Karen; Karen.Osborne@hsc.utah.edu; Conra Backstrom; Shankaran, Seetha; KATHLEEN F ABRAMCZYK; CATHY A. GRISBY; mbball@leland.stanford.edu; Katherine A Foy
Cc:	wrich@ucsd.edu; Schaefer, Scott E.; Pickett, James; Auman, Jeanette O.; Gantz, Marie; Cunningham, Meg; Huitema, Carolyn Petrie; Das, Abhik; Higgins, Rosemary (NIH/NICHD) [E]
Subject:	SUPPORT Oximeters & Time Change
Date:	Friday, November 02, 2007 10:46:19 AM
Importance:	High

JUST A REMINDER ABOUT DAYLIGHT SAVINGS TIME AND THE MASIMO STUDY OXIMETERS:

Daylight Savings Time Changes for Support:

1) Change all oximeters not in current use on Monday.

2) Do not change oximeters currently in use until they are put on another patient.

RTI will make any necessary back-corrections at their end.

Thanks.

Kris

Kris Zaterka-Baxter, RN, CCRP

RTI International

4426 South Miami Blvd.

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From:	Zaterka-Baxter, Kristin
To:	nxs5@cwru.edu; Nancy.Miller@UTSouthwestern.edu; melissa.leps@utsouthwestern.edu; ae5357@wayne.edu; crosman@med.wayne.edu; ellen_hale@oz.ped.emory.edu; grisbyca@email.uc.edu; ldw@iupui.edu; monica.konstantino@yale.edu; ahensman@wihri.org; mbball@leland.stanford.edu; mcollins@peds.uab.edu; Georgia.E.McDavid@uth.tmc.edu; auten002@mc.duke.edu; bmackinnon@tufts-nemc.org; karen-johnson@uiowa.edu; karen.osborne@hsc.utah.edu; CBackstrom@salud.unm.edu; Katherine A Foy; mcw3@cwru.edu; Pablo.Sanchez@UTSouthwestern.edu; sshankar@med.wayne.edu; [SCRN] Stoll, Barbara; kurt.schibler@cchmc.org; bpoindex@iupui.edu; richard.ehrenkranz@yale.edu; alaptook@WIHRI.org; vanmeurs@stanford.edu; wcarlo@peds.uab.edu; Kathleen.A.Kennedy@uth.tmc.edu; goldb008@mc.duke.edu; IFrantz@tufts-nemc.org; edward-bell@uiowa.edu; Roger.Faix@hsc.utah.edu; kwatterberg@salud.unm.edu; Das, Abhik; Higgins, Rosemary (NIH/NICHD) [E]; Brenda.H.Morris@uth.tmc.edu; susie.buchter@oz.ped.emory.edu; bradley.yoder@hsc.utah.edu
Cc:	Finer, Neil; Rich, Wade; Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik; Gantz, Marie; Auman, Jeanette O.; Pickett, James; Price, Jeffrey M.; Cunningham, Meg; Newman, Jamie; Huitema, Carolyn Petrie
Subject:	Support Study Revisions 10/15/2007
Date:	Tuesday, October 30, 2007 6:48:44 PM
Attachments:	SUP1120071015.doc SUPPORTManual[uc]20071015.doc SUPP04NICUAdmission_uc_20071015.doc SUPP04aSurfDoses20071015.doc SUPP05SafetyMonitor_uc_20071015.doc SUPP08Adverse Event_uc_20071015.doc SUPP09OutcomeForm_uc_20071015.doc SUPP10 ROP_uc_20071015.doc SUPP11SupportAfter14Days_uc_20071015 .doc

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Hi all,

Please find attached a Technical Memo (SUP11) and Support study revisions to the following study documents. These revisions were based on several past discussions and finalized during the last Steering Committee meeting on October 15, 2007:

1. The Study Manual (version dated 10/15/07)
2. Form SUPP04 (version dated 10/15/07)
3. Form SUPP04a (new form) (version dated 10/15/07)
4. Form SUPP05 (version dated 10/15/07)
5. Form SUPP08 (version dated 10/15/07)
6. Form SUPP09 (version dated 10/15/07)
7. Form SUPP10 (version dated 10/15/07)
8. Form SUPP11 (version dated 10/15/07)

Please note these are highlighted copies only; the clean and final versions will be posted on the NRN website shortly. Please note an email notification will be sent when the new versions of the forms are available in the DMS. Data collection will be ***prospective only.***

Thanks and please let me know if you have any questions.
Kris

Kris Zaterka-Baxter
RTI International
4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
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RTI INTERNATIONAL | **Memorandum**

October 26, 2007

SUPPORT TECHNICAL MEMO # 11

TO: Network Coordinators
Network PIs

FROM: The Data Coordinating Center

SUBJECT: Manual of Procedures and Forms revisions (SUPP04, {new Supp04a}, 05, 08, 09, 10, and 11). Version Date October 15, 2007.

Please find below an outline of revisions made to the Manual (version date 10/15/2007). All corresponding revised forms are enclosed. Please note all added text appears underlined and all ~~deleted~~ text appears stricken through.

1. Chapter 1, Overview and Trial Design, Forms descriptions (page 1-3)

NICU Admission and Procedures Form (SUPP04a- Surfactant Doses)

This form is to be completed if more that 4 surfactant doses are given between the first dose in the NICU and day 14 of study.

2. Chapter 2, Administration (page 2-2)

PARTICIPATING CENTERS	NRN PI	SUPPORT STUDY PI
Case Western Reserve Univ. (3) Rainbow Babies and Children's Hospital	Michele Walsh, MD	Michele Walsh, MD
University of Texas-Dallas (4)	Pablo Sanchez	Pablo Sanchez
Wayne State University (5) Children's Hospital of Michigan	Seetha Shankaran, MD	Seetha Shankaran, MD
~~University of Miami (8)~~ ~~Jackson Memorial Hospital~~	~~Shahnaz Duara, MD~~	~~Shahnaz Duara, MD~~
Emory University (9) Grady Memorial Hospital	Barbara J. Stoll, MD	Susie Buchter, MD
University of Cincinnati (11) University of Cincinnati Hospital	Kurt Schibler, MD	Vivek Narendran, MD
Indiana University (12)	Brenda Poindexter, MD	Brenda Poindexter, MD
Yale University (13) The Children's Hospital at Yale – New Haven	Richard A. Ehrenkranz, MD	Vineet Bhandari, MD

Brown University (14) Women and Infant's Hospital	Abbot Laptook, MD	Abbot Laptook, MD
Stanford University (15) Stanford University Med Center	Krisa Van Meurs, MD	Krisa Van Meurs, MD
University of Alabama (16) University of Alabama at Birmingham	Waldemar A. Carlo, MD	Waldemar A. Carlo, MD
University of Texas- Houston (18)	Kathleen Kennedy MD	Brenda Morris, MD
Duke University (19)	Ronald Goldberg, MD	C. Michael Cotten, MD
~~Wake Forest University (20)~~	~~Michael O'Shea, MD~~	~~Michael O'Shea, MD~~
~~Children's Hospital at Strong (21)~~	~~Dale L. Phelps, MD~~	~~Nirupama Laroia, MD~~
University of California-San Diego (22)	Neil Finer, MD	Neil Finer, MD
Tufts NEMC (23)	Ivan Frantz, MD	Ivan Frantz, MD
University of Iowa (24)	Edward Bell, MD	Edward Bell, MD
University of Utah (25)	Roger Faix, MD	Bradley, Yoder, MD
University of New Mexico (26)	Kristi Watterberg, MD	Kristi Watterberg, MD

3. Chapter 9, Admission to NICU (page 9-3). New form SUPP04a and revised from SUPP04 enclosed (version date 10/15/07)

3. Was Surfactant given in the NICU?
   If Yes, Record the following for each dose: If more than 4 doses given see form SUPP04a
a. Date: Record the date the infant received the first dose of surfactant in the NICU and for the first 14 days. Day begins at 00:00, ends at 23:59
b. Time: Record the time the infant received the first dose of surfactant in the NICU using using the 24-hour clock with midnight coded as 00:00
c. Type: Record the type:
   1= Infasurf
   2= Curosurf
   3= Survanta
   4= Exosurf
   5 = Other, If other, specify type.

Note: If more than 4 doses were given record each additional dose on form Supp04a..

4. Chapter 10, Safety Monitoring Forms SUPP05(page 10-2 {Q.3 Fi02} and 10-3 {Q.4 Blood Gas}). Revised form SUPP05 enclosed (version date 10/15/07)

h. Mode of Support
Record the respiratory support as:
1 = HFV
2 = CV
3 = Nasal SIMV
4 = CPAP
5 = NC
6 = Hood
7 = No Support
8 = Infant temporarily out of unit

9= No Support all day and off Study oximeter

5. Chapter 13, Serious Adverse Experience, Form SUPP08 (page 13-1 and 13-2). Revised form SUPP08 enclosed (version date 10/15/07)

13.2 Adverse Event Form (SUPP08)

1. Air leak

a. Pnemothorax
Record 'Y' if pneumothorax is documented in the infant's chart. Pneumothorax is a collection of air in the pleural space where a lucency is identified in the pleural space with displacement of the lung away from the chest wall. Do not include a pneumothorax resulting from a thoracotomy during surgery (e.g. PDA ligation). Otherwise code 'N'

b. Pulmonary Interstitial Emphysema (PIE)
Record 'Y' if pulmonary interstitial emphysema (PIE) is documented in a radiographic report in the infant's chart. PIE is a radiographic and pathologic diagnosis made when air ruptures from alveoli or small airways into the perivascular tissues of the lung. This diagnosis will only be documented if from the radiographic reports. Do not include PIE documented in patient notes unless there is radiographic documentation to support this diagnosis. Otherwise code 'N'

c. Pneumopericardium
Record 'Y' if pneumopericardium is documented in the infant's chart. This documentation may be found in a radiographic report, echocardiogram report or patient progress notes. Pneumopericardium is an extrapulmonary collection of air in which the air completely surrounds the heart, including its inferior border. Otherwise code 'N'.

If coding 'Y' to question 1.a, b or c above, code most proximate mode of ventilatory support for each occurrence as follows:

1 = HFV
2= CV3 = Nasal SIMV
4 = CPAP
5= NC
6= Hood
7= No Support
8 = Infant temporarily out of unit
9= No Support all day and off Study oximeter

Record 'Date of Onset" and 'Attribution to SUPPORT study' for each occurrence.

6. Chapter 14, Outcome Status, From SUPP09 (page 14-3). Revised SUPP09 enclosed (version date 10/15/07)

14.1.4 Section C – Ophthalmology

1. Was an exam performed for Retinopathy of Prematurity (ROP)?
Review the medical record to determine if an examination was performed for ROP.

If Yes, complete the **SUPP10 Form** (ROP Outcomes And Tracking Summary).
If No, and the infant survived, complete the **SUPP10** (ROP) form based on subsequent exams (including back-transfer hospital and/or outpatient visits)

7. Chapter 15, ROP Outcomes and Tracking Summary SUPP10 (page 15-3 and 15-4)

10. Final Acute Status Lost to Follow-up at 55 weeks PMA
Complete this question **only** for the final eye exam entered.

Record 'N' if the last examination meets criteria for final acute status reached (see section 15.2 below).

Record 'Y' if the final 'acute' ROP status is permanently missing because the infant is lost-to-follow up. For example, the last exam is not yet mature, or not yet in zone III for the second time in a row, or the baby still has ROP, but had not reached criteria for surgery. All attempts must have been made to capture this data from the follow up exams, and it is coded 'Y' as missing only when there was no final exam done (parents did not bring infant in).

By the time an infant has reached 55 weeks PMA, the eye disease will have reached final status, whether we know about it from an examination or not. That is why we make this determination at this time. If it is later learned that examinations actually were done, the results can be entered on the form with a late correction/edit.

Therefore, if you know the infant is less than 55 weeks PMA and has not had an exam that meets the final/acute criteria, you are still trying to get the family to bring the baby in for exams because it is clinically important and also will give you a primary study outcome. If it is now past 55 weeks, you may give up trying to get them to come in because it's too late to identify disease that could be treated, and the time for the clinical outcome for the study is also past. Late outcomes will be collected at the 18-22 month follow up examination.

Potential merit of later exams: Most likely, they will reassure the infant that the eyes have healed. They may detect an important need for glasses at 6-9 months after birth. If the outcome is retinal detachments, the parents will learn the baby is not going to see and needs to be referred for early intervention. In either event, late exams that show retinal detachments will confirm that once upon a time, the baby did have bad ROP. Late exams that show good outcomes will NOT tell us if they once had ROP that has now regressed (healed).

Note: even in these circumstances where we have given up, the infant will still be tracked down for the 18-22 month follow up visit. At that time they are asked if any eye surgery was done after discharge / status. If yes, what surgery. If it was for ROP, then that will become a final status revision. Also, even if no surgery was done, but the child has experienced vision loss *from ROP*, this would also be a final outcome.

Note that some infants have vision loss that is not from ROP. This is usually "cortical vision loss" and is from brain injury.

11. Final ROP Status determined at 18 Moth Follow Up
Complete this question **only** for the final eye exam entered.

Answer this question as 'N' if the final acute status was already determined before 55 weeks PMA. That is, "no, we did not determine the final outcome based on the 18-22 month exam."

Also, answer this question as 'N' if the final status was not determined by 55 weeks PMA, AND it was not determined at the 18-22 month visit either. This would happen if there were no 18-22 month examination. It would also happen if there were an 18-22 month examination, but the parents report no eye surgery and no other eye exams so we don't know what happened to the ROP.

You can record 'Y' for the final ROP status obtained during the 18-22 month follow up visit only if the parents are now reporting to you eye surgery for ROP that you had not learned about before, or they are telling you about eye exams that you have not learned about before (or else you would have recorded it before). If this is the case, reports from the exam(s) and/or surgery should be obtained to determine what has happened. These data will likely require ophthalmology input to determine if the primary ROP outcome was reached. Examples: A. ROP can be assumed (imputed) to have reached surgical criteria if the infant's subsequent surgery is vitrectomy for retinal detachment, or is an exam under anesthesia with a diagnosis of ROP stage 4A, 4B or stage 5 ROP, or retinal fold crossing the macula. B. ROP may not have met laser/CRYO criteria if the surgery was for strabismus (crossed eye), plugged tear duct, or only examination under anesthesia, for example to rule out glaucoma.

8. Chapter 16, Respiratory Support after 14 Days SUPP11(page 16-1). Revised SUPP11 enclosed (version date 10/15/07)

- Highest Level of Support
Record the highest level of support the infant is in on at the scheduled time points during this STUDY day.
Enter: 1= HFV, 2=CV, 3= Nasal SIMV, 4= CPAP, 5= NC, 6= Hood,
7= No Support, 8= Infant temporarily out of unit 9= No Support all day and off the study oximeter*.

9. Minor editorial changes in the Table of Contents chapter 2 (corrected section numbers 2.3 through 2.6)

Cc Rosemary Higgins, MD

Enclosed: Forms SUPP04, SUPP04a, SUPP05, SUPP08, SUPP09, SUPP10 and SUPP11 in addition to the Manual of Procedures (highlighted revisions)

The SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants (SUPPORT Trial)

NICHD Neonatal Research Network

Final

Manual of Operations

January 4, 2005
Revised March 10, 2005
Revised May 16, 2005
Revised June 27, 2005
Revised October 3, 2005
Revised March 7, 2006
Revised March 23, 2006
Revised June 5, 2006
Revised November 1, 2006
Revised October 15, 2007

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Chapter 1

Overview and Trial Design

1.1 Introduction

This manual provides detailed instructions for study procedures related to The SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants (SUPPORT Study): The manual is meant to serve as a reference guide for study staff including investigators, coordinators, technicians, and data managers. The trial objectives and design are summarized briefly below. For further discussion to the study background and design, please refer to the protocol dated August 28, 2004.

1.2 Study Design

This will be a prospective, randomized, factorial 2X2 design multi-center trial conducted by the NICHD Neonatal Research Network. The individual factors to be tested will be:

1) A prospective comparison of CPAP and a permissive ventilatory strategy begun in the delivery room and continuing in the NICU with early (≤ 1 hour) surfactant and mechanical ventilation.
2) A prospective comparison of a lower SpO2 range (85% to 89%) with a higher more conventional SpO2 range (91% to 95%) until the infant is no longer requiring ventilatory support or oxygen.

The oxygen saturation monitoring portion of this study will be designed to parallel the planned POST-ROP trial, a multi-center, multinational prospective trial to evaluate different SpO2 levels from birth. The methodology described under oxygen monitoring (**Section 4.1B**) was developed for the current protocol to allow a blinded comparison of 2 different SpO2 levels using specially designed pulse oximeters. These devices will be developed by the Masimo Corporation (Irvine Ca) and tested prior to initiation of this trial, and the POST-ROP study group has agreed to use the ranges described in this protocol, and the methodology that will allow the oximeters to provide actual SpO2 values when the SpO2 is < 85% and > 95% (Personal communication, Cynthia Cole 2004). This methodology will provide the clinicians and caretakers with the infants' actual SpO2 values during hypoxia and hyperoxia, within the current parameters of clinically accepted practice.

Please refer to **Section 8.2** of the Protocol for further Tables describing details regarding the projected outcomes relative to the study interventions

Randomized Intervention	Low SpO2 85% to 89%	High SpO2 91 to 95%
Treatment **Early CPAP**	Early CPAP + Low SpO2	Early CPAP + High SpO2
Control **Prophylactic/Early Surfactant**	Control + Low SpO2	Control + High SpO2

1.4 Primary Hypothesis

1) We hypothesize that relative to infants managed with prophylactic/early surfactant and conventional ventilation that the use of early CPAP and a permissive ventilatory strategy in infants of less than 28 weeks gestation with continuing CPAP in the NICU will result in an increased survival without BPD at 36 weeks.

2) We hypothesize that that relative to infants managed with a higher SpO2 range that the use of a lower SpO2 range (85% to 89%) will result in an increase in survival without the occurrence of threshold ROP and/or the need for surgical intervention.

1.5 Secondary Hypotheses

We hypothesize that the use of continuous positive airway pressure (CPAP) with a permissive ventilator strategy and/or a lower SpO2 range starting at birth in the delivery room will result in the following:

- A decreased Mortality/NDI at 18-22 months corrected age.
- A decreased frequency of endotracheal intubation before 10 minutes of age
- A decrease of the total duration of mechanical ventilation during the entire NICU stay
- A decreased incidence of surfactant treatment
- A decreased incidence of air leaks on admission and overall
- A decreased duration of intubation
- A decreased duration of mechanical ventilation
- A decreased duration of oxygen supplementation
- A decreased duration of the percentage of pulse oximetry values > 90%
- A decreased incidence of blindness of at least one eye at 18-22 month follow-up
- A decrease in the percentage of infants who receive postnatal steroids to prevent or treat BPD
- A decreased incidence of BPD at 36 weeks using the physiologic definition of BPD

- A decreased incidence of ROP or Stage 3 ROP
- A decreased incidence of necrotizing enterocolitis (NEC)
- A decreased incidence of IVH and severe IVH
- A decreased incidence of periventricular leukomalacia
- A decreased incidence of neurodevelopmental impairment at 18-22 month follow-up
- A decreased incidence of cerebral palsy at 18-22 month follow-up

1.6 Summary of Data Forms

The following is a summary of the data forms used in this study. Further details on each form are provided in subsequent chapters. A complete set of forms can be found in Appendix A.

Screening Log (SUPP01)
A Screening Log (SUPP01) is provided to facilitate the tracking of infants with gestational age 27 6/7 weeks or less for whom a decision has been made to provide full resuscitation as necessary in the Network centers.

Eligibility Form (SUPP02)
This form will be completed for all inborn infants with a minimal gestational age of 24 weeks 0 days to 27 6/7 completed weeks by best obstetrical estimates and who are to receive full resuscitation as necessary.

Delivery Room Form (SUPP03)
Data for this form will be collected in the delivery room and will be completed on all infants.

NICU Admission and Procedures Form (SUPP04)
This form is to be completed on all infants enrolled in the study upon admission to the NICU.

NICU Admission and Procedures Form (SUPP04a- Surfactant Doses)
This form is to be completed if more that 4 surfactant doses are given between the first dose in the NICU and day 14 of study.

Safety Monitoring Form (SUPP05)
This form is to be completed each day starting with Study day 1 until Study day 14 or outcome status, whichever comes first.

Safety Monitoring Form (SUPP05A)
This form is to be completed each time an intubation/extubation occurs after admission to the NICU through day of life 14.

Replacement Oximeter Form (SUPP05B)
This form is to be completed each time a study oximeter is replaced from study initiation to 36 weeks or status (whichever comes first).

Protocol Deviation Form (SUPP06)
This form will be completed for all randomized patients whenever a protocol deviation/violation is encountered.

Reintubation Form (SUPP07)
This form will be completed for all intubation/extubations after 14 days.

Adverse Event Form (SUPP08)
This form will be completed for the adverse events, as specified in the protocol, occurring during the initial 14 days of life.

MedWatch Form (SUPP08A)
This form is to be completed in the event of a serious adverse event. It should be faxed to Ken Poole (919) 485-7762 and Rosemary Higgins (301) 496-3790 within 24 hours or the next working day.

Outcome Status Form (SUPP09)
This form will be completed when the infant is discharged home, transferred, if hospitalized at 120 days, death or withdrawn (whichever comes first).

ROP Outcomes and Tracking Summary (SUPP10)
The form will be used to record data for each eye examination (in or outpatient) until both eyes are acute/final.

Respiratory Support After 14 Days (SUPP11)
This form is to be completed daily from study day 15 through 36 weeks or status, whichever comes first.

Chapter 2

Administration

2.1 Organizational Structure

The NICHD Neonatal Research Network is conducting this study. The Network is funded by the NICHD under cooperative agreements with seventeen institutions comprised of sixteen clinical centers and a data coordinating center. The Steering committee for the Network consists of the Principal Investigator from each clinical center, the data center, and the NICHD project officer. The Steering Committee Chairman is appointed by NICHD and is not a Principal Investigator from any of the Clinical Centers.

2.2 SUPPORT Trial Subcommittee

The SUPPORT Protocol Subcommittee is responsible for the preparation and maintenance of the protocol, data forms, and manual of operations. This subcommittee will monitor the overall study performance (including protocol compliance) and will report the progress of the trial to the Steering Committee. SUPPORT Subcommittee members are:

Neil Finer, MD

Waldemar A. Carlo, MD,

Michele Walsh, MD

Abbot Laptook, MD

Kurt Schibler, MD

Bradley Yoder, MD

Roger Faix, MD

Rosemary D. Higgins, MD

Abhik Das, PhD

Marie Gantz, PhD

Nancy Newman, RN

Wade Rich, RRT

2.3 Participating NICHD Neonatal Research Network Centers

Centers from the NICHD Neonatal Research Network participating in the trial are listed below. The NICHD center number is indicated in parentheses next to the name of each center and the principal investigator is located in the second column.

PARTICIPATING CENTERS	NRN PI	SUPPORT STUDY PI
Case Western Reserve Univ. (3) Rainbow Babies and Children's Hospital	Michele Walsh, MD	Michele Walsh, MD
University of Texas-Dallas (4)	Pablo Sanchez	Pablo Sanchez
Wayne State University (5) Children's Hospital of Michigan	Seetha Shankaran, MD	Seetha Shankaran, MD
~~University of Miami (8)~~ ~~Jackson Memorial Hospital~~	~~Shahnaz Duara, MD~~	~~Shahnaz Duara, MD~~
Emory University (9) Grady Memorial Hospital	Barbara J. Stoll, MD	Susie Buchter, MD
University of Cincinnati (11) University of Cincinnati Hospital	Kurt Schibler, MD	Vivek Narendran, MD
Indiana University (12)	Brenda Poindexter, MD	Brenda Poindexter, MD
Yale University (13) The Children's Hospital at Yale – New Haven	Richard A. Ehrenkranz, MD	Vineet Bhandari, MD
Brown University (14) Women and Infant's Hospital	Abbot Laptook, MD	Abbot Laptook, MD
Stanford University (15) Stanford University Med Center	Krisa Van Meurs, MD	Krisa Van Meurs, MD
University of Alabama (16) University of Alabama at Birmingham	Waldemar A. Carlo, MD	Waldemar A. Carlo, MD
University of Texas- Houston (18)	Kathleen Kennedy MD	Brenda Morris, MD
Duke University (19)	Ronald Goldberg, MD	C. Michael Cotten, MD
~~Wake Forest University (20)~~	~~Michael O'Shea, MD~~	~~Michael O'Shea, MD~~
~~Children's Hospital at Strong (21)~~	~~Dale L. Phelps, MD~~	~~Nirupama Laroia, MD~~
University of California-San Diego (22)	Neil Finer, MD	Neil Finer, MD
Tufts NEMC (23)	Ivan Frantz, MD	Ivan Frantz, MD
University of Iowa (24)	Edward Bell, MD	Edward Bell, MD
University of Utah (25)	Roger Faix, MD	Bradley, Yoder, MD
University of New Mexico (26)	Kristi Watterberg, MD	Kristi Watterberg, MD

2.4 Responsibilities of the Clinical Centers

The minimum staff required for network participation at each clinical center is the physician Principal Investigator (PI), the Research Coordinator, and a small number of unmasked personnel who will provide 24 hour coverage to monitor study equipment.. The responsibilities of these individuals are described briefly in this chapter and in more detail in subsequent chapters.

The PI or designee is responsible for ensuring the proper conduct of the trial at his or her clinical center (including recruitment and treatment of patients as specified in the protocol), accurate collection of data and transmission of information to the Data Coordinating Center (DCC). Other specific duties include the following:

- Presenting an in-service to the other physicians
- Applying for IRB approval
- Introducing the study to the parents of prospective patients, and obtaining signed informed consent from the parents of eligible infants (in some centers this responsibility may be delegated)
- Reviewing all infants for whom informed consent has been obtained to confirm their eligibility
- Informing the IRB of the study progress.

The Research Coordinator will be responsible for the day-to-day operations of the study at the clinical center, including data collection and management. This responsibility includes the following:

- Presenting an in-service to the appropriate nursing and ancillary staff detailing the study protocol
- Collecting information necessary to complete the data collection forms, and coordinating data entry
- Training and certifying the staff in the use of the network microcomputer
- Controlling access to the network microcomputer and ensuring that required back-up, security and confidentiality are maintained
- Responding to edit messages and other communications from the data center
- Distributing updates of the protocol and of the manual of operations to clinical center staff
- Achieving and maintaining fluency with the procedures for obtaining the treatment group assignment from the data center
- reporting deviations to the data center within 24 hours of occurrence

2.5 Responsibilities of the Data Coordinating Center

The DCC is responsible for all aspects of statistical design and analysis as well as data management of the study. In particular, this includes:

- Processing, updating and distributing the protocol and manual of operations
- Developing, printing and distributing the data forms, including periodic updates as necessary
- Developing, testing and implementing the database and other software. Ensuring that data are correct and complete by implementing editing and auditing procedures
- Monitoring the progress and quality of the study
- Preparing interim and final analyses and reports
- Participating in the preparation of presentations and publications relating to the study.

2.6 Responsibilities of NICHD

In addition to its role as a funding agency, the NICHD participates in the activities of the cooperative agreement by being represented on the Steering Committee. The Program Official also participates in the development of protocol and in assisting the Steering committee in the coordination of the studies conducted by the Network. The NICHD Program Official, in conjunction with the RTI Principal Investigator is responsible for monitoring site performance of all participating centers. The Program Official has the following responsibilities:

- Assistance in the development of the study protocol.
- Assistance in the development of capitation-based budgets, including the identification of study costs and special institutional needs.
- Allocation of network resources to meet study needs including pharmacies, study drug supply, and other special requirements of the study.
- Facilitation of training meetings, site visits, and subcommittee meetings.
- Participating in preparation of publications.

Chapter 3

Screening, Eligibility, Consent

3.1 Study Population

Study subjects are inborn infants of 24 0/7ths to 27 6/7th weeks at birth for which a decision has been made to provide full resuscitation as required. Infants 27 weeks or less gestation (completed weeks by best obstetric estimate) will be enrolled.

3.2 Inclusion Criteria

- Infants with a minimal gestational age of 24 weeks 0 days to 27 completed weeks (up to 27 6/7ths) by best obstetrical estimate
- Infants who will receive full resuscitation as necessary, i.e., no parental request or physician decision to forego resuscitation
- Infants without known major congenital malformations

3.3 Exclusion Criteria

- Any infant transported to the center after delivery
- Infants born during a time when the research apparatus/study personnel are not available

3.4 Informed Consent

Infants will be recruited for this study by approaching one or both parents at the time of admission to the hospital at risk for premature delivery at 27 weeks or less. It is anticipated that, whenever possible, the parents will be approached by study personnel to discuss the trial and obtain an informed consent for the participation of the infant at delivery. As discussed in Section 4.1, randomization will be by family, thus all offspring will be randomized to the same trial arms, provided adequate equipment and personnel are available at the time of delivery.

3.5 Screening Procedures

All admissions for threatened premature delivery will be screened on a daily basis to ensure that eligible patients can be enrolled. Obstetrical colleagues at each participating institution will be informed of the nature of this study and encouraged to discuss this study with their patients at risk of premature delivery. The study coordinator at each site will maintain a screening log of potentially eligible patients. In addition the usual practice of neonatal consultation for all such at risk deliveries will provide a second opportunity to approach mothers with fetuses at risk of preterm delivery.

Chapter 4

Randomization

4.1 Randomization Procedures

Randomization will be stratified by gestational age group (24 - 25 6/7 and 26 - 27 6/7) and will occur prior to delivery for consented deliveries. The randomizations will be performed by **utilizing specially prepared envelopes**. The Data Center will prepare brown sealed envelopes which will contain the identity of the treatment combination to be assigned the infants enrolled into the study. **Deliveries will be randomized as a unit, thus multiples, twins, triplets etc will be randomized to the same arm of the trial.** One envelope will correspond to the delivery of a consenting mother regardless of the number of babies delivered so that all babies from a given delivery will receive the same treatment combination.

4.1.1 Randomization and Masking, Storing and Assigning Oximeters

Two sets of envelopes will be used; one for the gestational age group 24 -25 6/7 weeks and one for the 26 - 27 6/7 week gestational age group. These should be kept in separate boxes or drawers with the group clearly indicated **(this will be noted on the label on the front of the envelope).** The envelopes will be sequentially numbered with a randomization number on the outside of the envelope so they can be selected in the order of use to maintain a balancing of the treatment assignments. These envelopes are to be stored in a secure place in or near the delivery for quick accessibility.

The envelope should be selected, from the appropriate group, and opened at the time of delivery by a study staff member only when the delivery is imminent. Inside the sealed envelope will be a white card which will contain the randomization number and treatment assignments. The card will indicate which of the Early CPAP/Early Surfactant treatments is selected and will indicate a color code for the High/Low SpO2 arm of the study. They will be specified as one of the following:

- **Treatment Group** (EARLY CPAP and permissive ventilation management) with an **Oximeter code** of either **Blue or Orange**
  OR
- **Control Group** (Early SURFACTANT and conventional ventilator management) with an **Oximeter code** of either **Blue or Orange.**

The **Blue/Orange codes** will designate an assignment to either the **Low (85% - 89%)** or **High (91% - 95%)** SpO2 group. The oximeters will be shipped directly to the clinical sites from Masimo. The Data Center will supply the sites with the **Blue and Orange** labels and these color coded labels will correspond to the serial numbers on the oximeter(s). The serial number(s) will need to be recorded on the appropriate data form (**SUPP04 Form**).
Note: The oximeters should be stored in such a manner that the individual who will be obtaining them and returning them to their original location can easily identify which oximeters belong to which color-coded randomization group. It is not recommended that the oximeters be

identified with the blue or orange colored labels. A system whereby the serial numbers for each color group are identified at the storage sight, along with a list of which infants have been placed on which serial numbers, makes it possible to track oximeters without using the color coded labels on the devices themselves.

The person opening the envelope should announce to the team the assignment of the Early CPAP/Early Surfactant arm of the study. Someone should then take the opened envelope to the secure area where the oximeters are stored and select the oximeter (s) whose color code is specified in the randomization envelope. **Once the envelope is opened, it should be stored in a secure location only accessible to staff with "a need to know".** Randomization should be done only if sufficient numbers of oximeters of both types (i.e. high and low SpO2) are available to accommodate the delivery.

Once the use of an oximeter has been completed, it should be returned to the color coded location for storing the inventory of oximeters (e.g., a color coded shelf) checking to be sure that the serial numbers match. A log should be maintained to record the date and time the particular oximeter is returned to this location.

Chapter 5

Study Interventions

5.1 Study Intervention A

5.1.1 Mode of Ventilatory Support

The intervention will begin after birth when the infant is given to the resuscitation team. The conduct of the resuscitation will follow usual guidelines. Once stabilized:

- All **Control infants** in both strata will receive prophylactic/early surfactant (within 1 hour of age).
- All **Treatment infants** will be placed on CPAP/PEEP following stabilization, and will be intubated only for resuscitation indications.

The assignment to either a high or low SpO2 by **Study Oximeter Assignment** will be performed immediately following NICU admission, with a maximum allowable delay of 2 hours following NICU admission.

Treatment Groups

5.1.2 CPAP Group: Early Extubation and CPAP – Both Strata

5.1.3 Delivery Room Management

1) FiO2:
Standard of care

2) CPAP:
CPAP or ventilation with PEEP will be utilized if the infant requires positive pressure during resuscitation. CPAP will be continued until admission to the NICU using the Neopuff or equivalent device and a face mask or nasal prongs. Initial PPV will be at a PIP of 15-25 cm H_2O and a PEEP/CPAP of 5 cm cmH_2O. High flow nasal cannula (e.g. Vapotherm) may not be used as the primary mode of therapy for infants randomized to Early CPAP in the first 14 days.

3) Intubation:
Infants may not be intubated for surfactant only in the DR. Infants who require intubation for resuscitation will receive surfactant within 60 minutes of birth. Intubation will be performed only for the standard NRP indications including failure to respond to PPV with evidence of continuing cyanosis or bradycardia, the need for chest compressions, the need to administer intratracheal medications, or other situations in which the resuscitation team determines that surfactant is urgently required.

Intubation may be performed at any time for the occurrence of repetitive apnea requiring bag and mask ventilation, clinical shock, sepsis, and/or the need for surgery

The other aspects of the resuscitation will be managed according to the NRP guidelines and follow current center practice.

5.1.4. NICU Management

These infants will be managed on nasal CPAP and intubation is never required by protocol. They ***MAY*** be intubated if they meet ***ANY*** of the criteria listed below. If intubated within the first 48 hours of life they should receive surfactant.

1. **Intubation:**
   - An FiO_2 >.50 required to maintain an indicated SpO2 $\geq$ 88% (using the altered Pulse Oximeters) for one hour
   - A $PaCO_2$ > 65 torr (arterial or capillary samples, if venous PvCO2 > 70 torr) documented on a single blood gas
   - Hemodynamic instability defined as a low blood pressure for gestational age and/or poor perfusion, requiring volume and/or pressor support for a period of 4 hours or more. (Note that clinically defined shock is an accepted indication for intubation.)

Intubation may be performed at any time for the occurrence of repetitive apnea requiring bag and mask ventilation, clinical shock, sepsis, and/or the need for surgery

These criteria will continue in effect for a minimum of 14 days of life.

Intubation performed without meeting any of the above criteria will be considered a study protocol violation unless extenuating circumstances are noted.
(e.g. - Upper airway obstruction (choanal atresia, micrognathia/glossoptosis)).

2. **Extubation:**

An intubated CPAP-Treatment infant ***MUST*** have extubation attempted within 24 hours if ***ALL*** of the following criteria are met and documented on a single blood gas:

- $PaCO_2$ < 65 torr with a pH > 7.20 (arterial or capillary samples)
- An indicated SpO2 $\geq$ 88% with an FiO2 $\leq$ 50%
- A mean airway pressure (MAP) < 10 cm H_2O, ventilator rate $\leq$ 20 bpm, an amplitude < 2X MAP if on high frequency ventilation (HFV)
- Hemodynamically stable (Defined as an infant with clinically acceptable blood pressure and perfusion in the opinion of the clinical team – such an infant may be receiving ionotropic/vasopressor agents, but should not require ongoing volume infusions to stabilize the circulation and the doses of any continuously infused medications for circulatory stabilization should not have increased within 1 hour of any planned extubation).
- Absence of clinically significant PDA

These criteria will continue in effect for the first 14 days of life.

*Failure to extubate an infant meeting all of the above criteria will be recorded as a study protocol violation (**on the SUPP06 Form**) unless extenuating circumstances are noted (e.g. PIE, airleak).*

3. Reintubation

If a Treatment infant is extubated as per Protocol Criteria, and requires re-intubation for any indication, any further attempt at extubation may be delayed for 24 – 48 hrs based on the clinician's decision.

Re-intubation criteria are the same as those for Intubation for the CPAP infants. Thus, intubation is not required, but these infants ***MAY*** be reintubated if they meet ***ANY*** of the following:

4. Re-Intubation Criteria:

- An FiO_2 >.50 required to maintain an indicated SpO2 $\geq$ 88% (using the altered Pulse Oximeters) for one hour
- A $PaCO_2$ > 65 torr (arterial or capillary samples, if venous PvCO2 > 70 torr) on a single blood gas
- Hemodynamic instability defined as a low blood pressure for gestational age and/or poor perfusion, requiring volume and/or pressor support for a period of 4 hours or more. Note that clinically defined shock is an accepted indication for intubation.

Intubation may be performed at any time for the occurrence of repetitive apnea requiring bag and mask ventilation, clinical shock, sepsis, and/or the need for surgery.

Re-intubation performed without meeting any of the above criteria will be considered a study protocol violation unless extenuating circumstances are noted.

5. D/C CPAP

Treated infants who remain in Room Air for at least 1 hour may have their CPAP discontinued. CPAP may be discontinued earlier and follow unit Standard of Care. May be restarted at any time in such infants.

CPAP infants who require intubation three times, for any criteria, will have all subsequent treatment including subsequent extubations and any further re-intubations performed using unit Standard of Care. This addition is to prevent such infants from being exposed to further protocol driven intubations and extubations.

6. Surfactant

Infants intubated in the first 48 hours for respiratory distress should be given a minimum of one dose of surfactant. Up to 4 surfactant administrations may be given if the FiO2 is greater than 50% following manufacturers' recommendations for dose and dosing interval.

5.1.5 Explanation:

The purpose of the above criteria is to minimize the duration of intubation of Treatment infants. The Criteria for extubation are more severe than those of the Control Group infants, and extubation must be attempted for any infant who fulfills the stated criteria.

The criteria for re-intubation recognize that intubation is traumatic, and is designed to avoid frequent attempts at extubation for infants who fail.

5.1.6 Control Group- Prophylactic/Early Surfactant and Ventilation

5.1.7 Delivery Room Management:

Infants will be intubated in the delivery room and given surfactant or receive surfactant within 60 min minutes of birth. The other aspects of the resuscitation will be managed according to the NRP guidelines and follow current center practice.

5.1.8 NICU Management:

1. Extubation:

An intubated Surfactant-Control infant will continue to receive mechanical ventilation until extubation criteria are satisfied, but **MUST** have extubation attempted within 24 hours of fulfilling ***ALL*** of the following criteria documented on a single blood gas:

- $PaCO_2$ < 50 torr and pH > 7.30 (arterial or capillary samples)
- An FiO2 ≤.35 with a SpO2 ≥ 88% using the study pulse oximeters with
- A mean airway pressure (MAP) < 8 cm H_2O, ventilator rate ≤ 20 bpm, an amplitude < 2X MAP if on high frequency ventilation (HFO)
- Hemodynamically stable (Defined as an infant with clinically acceptable blood pressure and perfusion in the opinion of the clinical team – such an infant may be receiving ionotropic / vasopressor agents, but should not require ongoing volume infusions to stabilize the circulation and the doses of any continuously infused medications for circulatory stabilization should not have increased within 1 hour of any planned extubation).
- Absence of clinically significant PDA (Defined as bounding pulses, audible murmur and Echo confirmation of L-R shunting with increased LA/Ao size

These criteria will continue in effect for a minimum of 14 days for all infants.

Failure to attempt to extubate an infant meeting all of the above criteria, or extubation prior to reaching criteria, will be recorded as a study protocol violation ***(on Form SUPP06)*** *unless extenuating circumstances are noted.*

2. Weaning

This protocol will not define strict weaning criteria for the Control infants, but it is to be understood that reasonable attempts should be made to extubate these infants. While it is understood that some centers may be using somewhat more severe FiO2 and PaCO2 criteria than those listed here as current practice, these Criteria are thought to reflect current Network practice and practice at 2 of the 3 Best practice centers.

3. Reintubation:

- Control Infants may be reintubated using Standard of Care. Any subsequent extubations will also follow standard practice.

5.1.9 Explanation:

Control infants are to be treated using an approach considered similar to current standards of care. Apparatus for resuscitation for Control Infants at each center will represent their usual equipment for the resuscitation of an ELBW infant. The Neopuff may be utilized for such infants

as above, but this is not mandatory. It is anticipated that the majority of these infants will be intubated and receive surfactant in the delivery room.

5.2 Study Intervention B

5.2.1 Low versus High SpO2 Range:

There will be 2 ranges of SpO2 utilized during this trial. The Low target range will be 85% to 89% and the High target range will be 91% to 95%. The altered Pulse Oximeters (PO) as described below will display a range of 88% to 92% when the SpO2 ranges are in the Target ranges indicated above. Thus a Low range PO will read 88% when the actual SpO2 is approximately 86%, and 92% when the actual SpO2 is 89%. Similarly the High range PO will display 88% when the actual SpO2 is 91% and indicate 92% when the actual SpO2 is approximately 95%. As an added safety feature, the POs used in this trial will gradually revert to the actual SpO2 values and allow the caretakers to be aware of actual SpO2 values < 85% and > 95%.

5.2.2 Low Range Infants:

These infants will be monitored with a target SpO2 range of 85% -89% with suggested indicated alarm limits of 85% and 95%, representing approximately a 10% span for alarms as long as the infants are receiving any ventilatory support, CPAP, and/or supplemental oxygen.

The study pulse oximeters will be applied to the infant within two hours following NICU admission. The assigned PO will remain on the infant and will be removed once the infant has been in room air and off ventilatory support or CPAP for 72 hours, and if oxygen is subsequently required a similar altered pulse oximeter providing the same SpO2 range will be used until 36 weeks PCA.

5.2.3 High Range Infants:

These infants will be monitored with a target SpO2 range of 91% -95% with suggested indicated alarm limits of 85% to 95% representing approximately 10% span for alarms as long as they are receiving any ventilatory support, CPAP and/or supplemental oxygen.

The study pulse oximeters will be removed once the infant has been in room air for 72 hours, and if oxygen is subsequently required a similar altered pulse oximeter providing the same SpO2 range will be used until discharge 36 weeks PCA.

These interventions will be delivered using specially developed pulse oximeters whose displays will be adjusted so that the randomized range of SpO2 (either 85%-89%, or 91%-95%) will be indicated by a range of 88%-92%. These POs will be able to display trend plots of the SpO2 display for a preceding interval to allow the caretakers to receive feedback regarding the actual SpO2 ranges of their baby.

The suggested alarms limits will be 84% to 96% for both groups. All values outside of alarm limits will be unaltered values.

The target oxygen saturation (88-92%) of the display will be the same in both groups as indicated in Table 1 below.

Table 1

Output and Actual SpO2 Targets and Alarms

Group	Display Target	Actual Target	Alarm Values
Low SpO2 range	88-92%	85-89%	<85 and >95%
High SpO2 range	88-92%	91-95%	<85 and >95%

Every 30 days until 36 weeks PCA, or until the infant is no longer receiving ventilatory support or oxygen, the stored actual SpO2 values (one value per 10 seconds of monitoring) will be downloaded and transmitted to RTI for subsequent analyses to determine that were are within the desired ranges. (This interval of sampling may change to a less frequent interval for the convenience of the study personnel, without loosing significant data). These data points will be used to confirm that the infants were managed at the target ranges and provide objective confirmation of the SpO2 Group assignments. The technology for downloading and interpreting this data was used in the DR CPAP Pilot trial, but recent technology utilizing a software program (Profox, Profox Inc, Escondido, Ca) which has been written to facilitate this process, will dramatically simplify this procedure.

All ventilatory care after 14 days of age will follow the standard of care for each unit. Each unit will provide guidelines for their approach to continuing mechanical ventilation.

See Flow of Study Intervention on page 5.7:

Flow of Study Intervention

	Early Extubation and CPAP	Prophylactic/Early Surfactant and Ventilation
Delivery Room Management:	• Resuscitate using CPAP. If necessary, initial PPV settings PIP 15-25, PEEP 5. • Transport on CPAP **If intubated for resuscitation** • Give surfactant within 1 hour of age. Do not intubate unless indicated by NRP guidelines	• Intubate and give surfactant within 1 hour of age • Transport with PPV according to SOC
Upon NICU Admission:	Randomize within 2 hours to Pulse Oximeter	Randomize within 2 hours to Pulse Oximeter
Intubation Criteria:	**May intubate for ANY of these criteria** • FiO_2 >.50 required to maintain indicated SpO2 ≥ 88% (using the altered Pulse Oximeters) for one hour • $PaCO_2$ > 65 torr (art. or cap. samples, if venous $PaCO_2$ > 70 torr) documented on a single blood gas • Hemodynamic instability defined as a low blood pressure for gestational age and/or poor perfusion, requiring volume and/or pressor support for a period of 4 hours or more. **If intubated, give surfactant within the first 48 hrs if in respiratory distress**	**Reintubation Criteria:** **Standard of Care**
Extubation Criteria:	**Attempt extubation within 24 hours of fulfilling all of the following criteria:** • $PaCO_2$ < 65 torr with a pH > 7.20 (arterial or capillary samples) • An indicated SpO2 ≥ 88% with an FiO2 ≤ 50% • Mean airway pressure (MAP) < 10 cm H_2O, vent rate ≤ 20 bpm, amplitude < 2X MAP if on HFV • Absence of clinically significant PDA • Hemodynamically stable	**Attempt extubation within 24 hours of fulfilling all of the following criteria** • $PaCO_2$ < 50 torr and pH > 7.30 (arterial or capillary samples) • FiO2 ≤ 35 with SpO2 > 88% • Mean airway pressure (MAP) < 8 cm H_2O, vent. rate ≤ 20 bpm, amplitude < 2X MAP on HFV • Absence of clinically significant PDA • Hemodynamically stable
Repeated Surfactant Doses:	Subsequent doses may be given at the manufacturer's recommended dose up to a total of 4 doses.	
Intubation:	Intubation may be performed at any time for the occurrence of repetitive apnea requiring bag and mask ventilation, clinical shock, sepsis, and/or the need for surgery.	
CPAP D/C:	In room air for at least 1 hour	
CPAP Resumption:	At any time	
Duration of Intervention:	14 Days	14 Days

5.3 Delivery of Interventions

5.3.1 CPAP/PEEP in the DR

CPAP and positive pressure ventilation (PPV) in the delivery room for Treatment infants will be administered via a T-piece resuscitator a neonatal ventilator, or an equivalent device that is currently used by the site for the delivery of CPAP.

5.3.2 Use of Nasal SIMV

For uniformity nasal SIMV may be used in place of CPAP ***only following extubation*** for both Treatment and Control infants.

5.3.3 Use of Caffeine

Caffeine may be administered 2 hours prior to planned extubation, and for any clinically significant apnea.

5.3.4 Surfactant Type

All centers are asked to follow current unit practice in determining the type of surfactant utilized and manufacturers' recommendations for re-dosing intervals.

At least one dose of surfactant **must** be administered to any infant intubated within 48 hours of birth, with evidence of respiratory distress, who has not previously received surfactant.

5.3.5 Postnatal Steroids

Postnatal steroids for the purpose of preventing or treating BPD/CLD will be prohibited for any infant in this trial in the first 21 days of life. Hydrocortisone for hypotension may be used as noted below.

If postnatal steroid use is considered after 21 days of life for any infant for the prevention/treatment of established lung disease the following guidelines should be followed:

1. The AAP statement and recommendations regarding Post-natal steroids should be adhered to.
2. The lowest dose of dexamethasone considered effective should be used and if ineffective after 24 – 48 hours they should be stopped.
3. Consider using hydrocortisone as a first therapy at a dose of 1 -2 mg/kg/day before using dexamethasone.
4. For hypotension, hydrocortisone in a dose of 1 mg/kg/dose should be given after fluid administration and standard doses of ionotropes/pressors have failed to correct the low blood pressure.

5.3.6 Head Ultrasound

If a Head ultrasound is done between days 4 and 21 the results will be recorded for this study. If one is not done for standard of care, the study requires that at least one HUS be completed during this window.

5.4 Protocol Violations

The occurrence of any one of the following criteria will determine whether an individual infant will be considered a protocol violation:

1. Intubation of an Early Extubation and CPAP infant in the DR for the exclusive purpose of giving surfactant, in the absence of bradycardia (HR< 100 bpm) and/or poor color or an SpO2< 85-90% in an infant with adequate spontaneous respirations or receiving adequate ventilation
2. Failure to continue CPAP on admission to the NICU for an Early Extubation and CPAP infant requiring `supplemental oxygen
3. Intubation and surfactant administration of an Early Extubation and CPAP infant without meeting stated protocol criteria.
4. Failure to extubate an Early Extubation and CPAP infant who fulfills all the extubation criteria.
5. Extubation of a Prophylactic/Early Surfactant and Ventilation infant who does not meet any of the extubation criteria.

All protocol violations will be reviewed by the center PI who will discuss each protocol violation with the involved clinicians and provide a written summary including steps taken to avoid future violations. The Protocol Violation/Deviation Form (SUPP06) should be completed each time a violation/deviation is encountered.

5.5 Adverse Events

Serious and unanticipated adverse events may be anticipated in this vulnerable population. Data on the following potential adverse events that may be related to the study maneuver will be recorded and evaluated as part of continuous safety monitoring during the trial by RTI:

1. Air leak on admission to the NICU, or during the initial 14 days of life
2. The need for chest compressions, and/or epinephrine in the delivery room or NICU
3. The occurrence of severe IVH (Grades III-IV, Papile)
4. Pulmonary hemorrhage
5. Nasal breakdown requiring discontinuation of nasal prongs
6. Death

These outcomes will be evaluated on a monthly basis by RTI using sequential analysis boundaries, and if the incidence of any of these outcomes differs among the treatment arms of the study this information will be provided to the DSMC for immediate evaluation and consideration of termination of the study or treatment arm. The SUPPO8 (Medwatch Form) should be completed in the event of a serious adverse event. It should be faxed to RTI (919) 485-7762 and Rosemary Higgins (301) 496-3790 within 24 hours or the next working day.

Chapter 6

Screening Log

6.1 Instructions for completing the Screening Log (SUPP01)

Each center will implement an effective and efficient screening procedure to identify all potential study subjects. A Screening Log (SUPP01) is provided to facilitate the tracking of infants with gestational age 27 weeks or less for whom a decision has been made to provide full resuscitation as necessary. The following information is used to identify each infant and is placed on the screening log.

Center Number
Each study center has been assigned a Network center number.

Site
Centers with more than one participating hospital also have a site code (A, B, C or 1, 2, 3).

THE FOLLOWING INFORMATION WILL BE FILLED OUT WHEN THE MOTHER IS FIRST SCREENED:

Mother's Last Name
The last name of the mother who is being screened should be written on this log. This confidential information is recorded for the convenience of the center and must not be submitted to the DCC.

Mother's Hospital Number
The hospital number of the mother should be recorded. This confidential information is recorded for the convenience of the center and must not be submitted to the DCC.

Gestational Age
Record the actual gestational age in weeks and days when the mother is identified.

Last Date Eligible
Record the date this mother will reach 27 6/7 completed weeks. This will be the date when her infant would no longer be eligible for enrollment in this study. This will be used as a guide to track a mother who may be at risk for premature delivery but who may not deliver within the window of the study.

Consent
Record 'Y' or 'N' if consent has been obtained. If consent is obtained this pregnancy/infant birth will be followed to determine eligibility.

THE FOLLOWING INFORMATION WILL BE FILLED OUT ON THOSE PATIENTS WHO HAVE GIVEN CONSENT WHEN THE INFANT IS BORN WITHIN THE ELIGIBLE WINDOW:

Date of Birth

Enrolled in Study
Record 'Y' or 'N' if infant was enrolled in this study. This will ensure that all potential infant outcomes were identified (including but not limited to: enrolled in the study, gestational age at birth >28 weeks, died in delivery room).

Network Number

Record the Network number of any infant enrolled in the study.

Chapter 7

Eligibility Form

7.1 Instructions for completing the Eligibility Form (SUPP02)

Heading- Infant's Identification
The following information is included in the heading section of all patient specific data forms: Center, Site, Network Number, Birth Number and Mother's Initials **(optional).**

7.1.1 Form Section A: Eligibility Criteria

If any criteria are not met, the infant is ineligible.

1. Inborn infant with a gestational age of 24 weeks 0 days to 27 6/7th completed weeks by best obstetrical estimate?
Code yes if the infant was 27 completed weeks or less by best obstetrical estimate or by appropriate clinical examination.

2. Infants who will receive full resuscitation as necessary?
Code yes if the infant will require full resuscitation as necessary

3. Infant who does not have know major congenital malformations?
Code yes if the infant does not have known major congenital malformations.

If any of the above questions are answered No the infant is NOT eligible.

7.1.2 Form Section B: Exclusion Criteria

1. The infant was born during a time when the research apparatus/study personnel are not available?
Code yes if there was no apparatus/study personnel available.
If Yes, indicate the reason:
1= Equipment not available
2= Personnel not available

7.2 Form Section C: Consent

Sample consent forms for this study are included in Appendices D and E.
Consent status:

Answer this question with one of the following codes, according to the following definitions:

0 = Not Eligible
Code '0' if one or more of the eligibility criteria questions are answered "No". If the infant is ineligible, regardless of whether consent was granted or not, this code should be used.

1 = Consent Granted
Code '1' if parenteral/guardian consent is obtained.

2 = Parent Unavailable
Code '2' if the parent or legal guardian is unavailable throughout the eligibility period

3 = Parent Refused Consent
Code '3' if a parent or legal guardian refuses consent.

4 = Consent Not Requested
Code '4' if consent for this study was not requested. Language or social problems as well as enrollment in conflicting trials should be recorded here.

5 = Physician Refused Consent
Code '5' if the infant was eligible for the study, but the attending physician refused to consider the baby for enrollment.

If the consent status is 3, 4, or 5, indicate the reason why consent was refused or not requested.

If the patient is eligible and consent is granted, but the patient is not randomized, indicate the reason why the eligible infant was not randomized into the study although consent from both parent/guardian and physician was obtained.

7.3 Form Section D: Randomization

An infant is eligible for randomization if all eligibility criteria are answered Yes in Section A. The infant is considered randomized at the time the randomization number is given.

1. **Was infant randomized into the study?** Record "Yes" if the infant was randomized into the study.
   If No, indicate the reason the infant was not randomized.
   If Yes,
   a. Date of Randomization- Enter the date on which the randomization envelope was opened to enroll the infant into the study. All dates for this study are recorded using the MM/DD/YYYY format.
   b. Time of Randomization- Enter the local time at which the envelope was opened to randomize the infant.
   c. Randomization Number-Enter the randomization Number. This number is recorded on the SUPP02 during the randomization. The randomization numbers are four digit numbers with a different set of numbers, stratified by gestational age, for each group. There will be a group with gestational age from 24 - 25 6/7 weeks and a group with gestational age 26 to 27 6/7 weeks. The groups for each Center will be as follows:

   24 - 25 6/7 weeks = 3001 - 3160
   26 - 27 6/7 weeks = 4001 – 4160

   d. Treatment Assignment:
   Enter 1= Early Extubation and CPAP or 2= Early Surfactant and Ventilation

   e. Oximeter Color Code
   Enter 1= Blue or 2=Orange

   All times for this study are recorded using the 24-hour clock format (00:00 to 23:59).

Chapter 8

Delivery Form

8.1 Instructions for completing the Delivery Form (SUPP03)

8.2 Form Section A: Delivery Room Information

1. Date and time of Delivery

a. Date:

Record the date on which child was born (day begins at 00:00, ends at 23:59).

b. Time:

Use a 24-hour clock with midnight coded as 00:00.

2. Was CPAP initiated in the DR? An application of CPAP will be considered the fitting of a mask over the infant's airway without intermittent positive pressure breaths or the placement of nasal prongs.

Record 'Y' if CPAP was initiated in the DR

a. If Yes, time of CPAP initiation

Use the 24-hour clock with midnight coded as 00:00

b. Device: Record Device.

1= Neopuff
2= Ventilator
3=Anesthesia Bag
4= Bubble
9 =Other

If Device is 5, specify the type.

3. Was positive pressure ventilation (PPV) initiated in the DR? PPV is defined as the administration of intermittent positive pressure breaths using either a mask or endotracheal tube.

4. Was positive end-expiratory pressure (PEEP) used in the DR?

Record 'Y' if PEEP was used in the DR

a. Maximum PEEP:

Record the maximum PEEP level as cm/H_20

5. Was intubation attempted in the DR?

a. **If Yes, was the intubation successful?**

Code Yes if the intubation was successful.

6. Indication for intubation

Record the indication for intubation;

1= Surfactant administration

2= Resuscitation
3 = Other (specify)
4 = As required by randomization assignment
Code 4 will be used to indicate that the infant was intubated because of the protocol assignment of Early Surfactant.

If for (2) Resuscitation
a. Low HR? Record Yes if the infant was resuscitated because of low HR.
b. Poor color? Record Yes if the infant was resuscitated because of poor color.
c. Apnea? Record Yes if the infant was resuscitated because of apnea.
d. Other? Record Yes if the infant was resuscitated for any other reason and specify the reason.
If for (3) Other, specify the indication for intubation.

7. Did the infant receive surfactant in the delivery room?
Record 'Y' if the infant received surfactant in the DR.
If Yes, Date and time of surfactant administration
a. Date: Record the date of surfactant administration using the mm/dd/yyyy format.
b. Time: Record the time of surfactant administration using the 24-hour clock with midnight coded as 00:00.

c. Type: Record the type of surfactant given
1= Infasurf
2= Curosurf
3= Survanta
4= Exosurf
5= Other, specify the type.

8. Was active resuscitation required? Record 'Y' if active resuscitation was required which would include bag and mask ventilation and/or intubation in the delivery room.
If Yes,
a. Chest compressions?
Record 'Y' for external pressure over central chest to contract heart.
If Yes,
1. Duration: Record the duration of chest compressions in minutes.
b. Epinephrine?
Record 'Y' if Epinephrine was provided to the infant at the time of birth irrespective of route (intratracheal or intravenous)
1. Number of doses: Record the number of doses the infant received.

9. Status following resuscitation:
Record 'the status of the infant at delivery.
1= Admitted to the NICU for further care
2= Infant died

Chapter 9

Admission to NICU Form

9.1 Instructions for completing the Admission to NICU Form (SUPP04)

The purpose of this form is to determine if the study interventions are applied as per the protocol

9.2 Section A. NICU Admission

1. Date and time of admission to the NICU:

a. Date: Record the date the infant was admitted to the NICU. Day begins at 00:00, ends at 23.59

b. Time: Record the time the infant was admitted to the NICU using the 24-hour clock with midnight coded as 00:00.

2. Respiratory support on admission to the NICU:

Record the respiratory support as:

1= HVF
2= CV
3= Nasal SIMV
4= CPAP
5= NC
6= Hood
7= No Support

3. SaO_2

Record the infant's SaO_2 on admission to the NICU.

4. FIO_2

Record the infant's FiO_2 on admission to the NICU.

5. Was a blood gas done after admission to the NICU?

If Yes, Record the first blood gas obtained following the NICU admission:

a. Date: Record the date the infant was admitted to the NICU. Day begins at 00:00, ends at 23.59

b. Time: Record the time the infant was admitted to the NICU using the 24-hour clock with midnight coded as 00:00

c. Source: Record the source of the first blood gas

1= Arterial
2=Venous
3= Capillary

Record the results of the first blood gas.

d. pH:
e. $pC0_2$:
f. pO_2:
g. FiO_2:

6. Date and time the study oximeter was placed on this infant.
Record the date and time:

a. Date: Record the date the infant was admitted to the NICU. Day begins at 00:00, ends at 23.59
b. Time: Record the time the infant was admitted to the NICU using the 24-hour clock with midnight coded as 00:00
c. Serial Number: Record the serial number that is pre-labeled on the oximeter.

9.3 Section B. NICU Procedures

1. Was the infant intubated for the first time after admission to the NICU within the first 14 days?

If Yes, Record the date and time:

a. Date: Record the date the infant was admitted to the NICU. Day begins at 00:00, ends at 23.59
b. Time: Record the time the infant was admitted to the NICU using the 24-hour clock with midnight coded as 00:00

c. Indication for intubation:

1. Surfactant?
2. FIO_2 > .50 to maintain $Sa0_2$ ≥88%?
3. $PaC0_2$ >65 on single blood gas?
4. Apnea requiring bag and mask ventilation?
5. If No to all above, state reason:

Record reason:
1= Hemodynamic instability
2= Clinical shock/sepsis
3= Other reason, If other, specify other reason.

2. Was a blood gas done within 30 minutes prior to intubation?

Note: Complete this question only if question B.1 = YES

If Yes, Record the date and time:

a. Date: Record the date the infant was admitted to the NICU. Day begins at 00:00, ends at 23.59
b. Time: Record the time the infant was admitted to the NICU using the 24-hour clock with midnight coded as 00:00
c. Source: Record the source of the first blood gas
1= Arterial
2=Venous
3= Capillary

Record the results of the first blood gas.
d. pH:
e. $pC0_2$:
f. pO_2:
g. FiO_2:

3. Was Surfactant given in the NICU?

If Yes, Record the following for each dose: <u>If more than 4 doses given see form SUPP04a</u>

a. Date: Record the date the infant received the first dose of surfactant in the NICU and for the first 14 days. Day begins at 00:00, ends at 23:59

b. Time: Record the time the infant received the first dose of surfactant in the NICU using using the 24-hour clock with midnight coded as 00:00

c. Type: Record the type:
   1= Infasurf
   2= Curosurf
   3= Survanta
   4= Exosurf
   5 = Other, If other, specify type.

<u>Note: If more than 4 doses were given, record each additional dose on form Supp04a..</u>

Chapter 10

Safety Monitoring Form
SUPP05 SUPP05A SUPP05B

10.1 Introduction

The SUPP05 form will collect respiratory data for Study Days 1-14 to monitor progress of the infant. The SUPP05A will monitor the incidence of intubation/extubations for each Study Day 1-14.

10.2 Instructions for completing the Safety Monitoring Form (SUPP05)

The purpose of this form is to record daily respiratory information **for each study day while infant is in the network hospital**. This form should be completed starting with DOL1 (study day 1) through DOL 14 (study day 14) and information recorded will be based on the calendar day and 24 hour clock.

1. Study Day: Enter the day this form is being completed.

2. Date: Enter the date that corresponds to the Study Day.

3. FiO2 Information: Record FiO2 and respiratory support closest to the Scheduled Time.

a. Scheduled Time
The scheduled time is given on the first column of the table. A scheduled time is assigned for a 24 hour period. The scheduled times are labeled as:

1. Scheduled Time: 02:00
2. Scheduled Time: 04:00
3. Scheduled Time: 06:00
4. Scheduled Time: 08:00
5. Scheduled Time: 10:00
6. Scheduled Time: 12:00
7. Scheduled Time: 14:00
8. Scheduled Time: 16:00
9. Scheduled Time: 18:00
10. Scheduled Time: 20:00
11. Scheduled Time: 22:00
12. Scheduled Time: 23:59

b. Time Measured
Record the actual time that the FiO2 was obtained based on a 24-hour clock. This time should be recorded adjacent to the closed Scheduled Time listed in column "a".

f. FiO_2
Record the FiO_2 at the scheduled time points. When a blood gas is obtained during a scheduled time, record the FiO2 corresponding to that blood gas. This will be the same FiO2 recorded in question 4 (f) and will supersede the blood gas obtained q2hrs.

h. Mode of Support
Record the respiratory support as:
1 = HFV
2 = CV
3 = Nasal SIMV
4 = CPAP
5 = NC
6 = Hood
7 = No Support
8 = Infant temporarily out of unit
9 = No Support all day and off Study oximeter

i. If Mode = 5 record Flow Rate
Record the flow rate for infants on nasal cannula

j. If Mode of Support =4 (CPAP), type used:
Record the type of CPAP
2= Ventilator
4= Bubble
6= Flow Driver
9 = Other

4. Blood Gas Information: Record results of blood gas analyses done at 3 daily time points closest to 08:00, 16:00, and 23:59 if available.

a. Scheduled Time
The scheduled time is given on the first column of the table. A scheduled time is assigned for a 24 hour period. The scheduled times are labeled as:

1. Scheduled Time: 08:00
2. Scheduled Time: 16:00
3. Scheduled Time: 23:59

b. Time Measured
For blood gas information record the actual time that the blood samples were collected based on a 24-hour clock. This time should be closest to 08:00, 16:00 or 23:59. If one blood gas qualifies as closest to two scheduled times (e.g. 23:59 and 8:00 the next day) enter the blood gas on the earlier of the selected times and enter ** : ** for the later one.

c. pH
Record the acid base status of the blood.
d. $C0_2$
e. PO_2:
f. FiO_2
Record the **FiO_2** corresponding to the blood gas at the scheduled time points. Record this FiO2 in question 3 "f" at the appropriate time measured.

g. Source:
Record the source of the blood gas
1= Arterial
2= Venous
3= Capillary

h. Mode of Support
Record the respiratory support as:
1 = HFV
2= CV
3 = Nasal SIMV
4 = CPAP
5 = NC
6 = Hood
7 = No Support
8 = Infant temporarily out of unit
9 = No Support all day and off Study oximeter

i. If Mode = 5 record Flow Rate
Record the flow rate for infants on nasal cannula

j. If Mode of Support =4 (CPAP), type used:
Record the type of CPAP
2= Ventilator
4= Bubble
6= Flow Driver
9 = Other

5. Oximeter Alarm Check.
The alarm checks should be recorded every 6 hours. Each center can use a 6 hours schedule that best fits their NICU's routine. The purpose of the oximeter alarm checks is to verify that alarms are being used and will be a measure of compliance of the protocol (i.e. to verify that the alarm limits are in place). The time points (q6h) can vary at each center but attempts should be made to use a 6 hour schedule. That is why the times are left open to fit each centers routine. Regardless whether the alarms are locked or not, we want to document that caregivers are noting alarm limits. We hope that this will increase awareness of the need for the limits to remain in place. And if changes are needed to the alarm limits, they should be made according to the study guideline

6. Was the infant intubated or extubated on this day?
If Yes, Complete the SUPP05A

10.3 Intubated/Extubated Information on the SUPP05A Form (For NICU ONLY)

This form should be completed if Question 6 on the SUPP05 is coded **"Yes".** If more than one intubation/extubation occurs complete a new report for each event. Record the intubation/extubation history if needed for each Study Day 1- 14. If the infant did not have an intubation/extubation on a study day, do not complete SUPP05A.

Report Number
Consecutively number each event as reported on the SUPP05a form.

1. Study Day
Record the study day (1 – 14) in which the intubation/extubation occurred in MM/DD/YYYY format

2. Date
Record the date in which the intubation/extubation occurred.

3 Was the infant intubated on this day?
Record Yes if the infant was intubated on this day.
If Yes,
a. Record the time of intubation:
b. Record the following information prior to intubation:

1. Were blood gases obtained within 6 hours prior to the event?
Code 'Yes' if the blood gas that, in the opinion of the investigator, is most associated with the event was obtained within 6 hours prior to the event. Record 'No' if there is no blood gas measurement associated with this event or was obtained >6 hours prior to the event.

Example: If an infant is stable and then requires emergent intubation and a blood gas was not obtained, code 'No'.

If Yes, record:
a. pH
b. PCO_2

2. FiO_2
3. Saturation
4. Apnea? Record Yes if the infant had Apnea on this day.
5. Sepsis/R/O Sepsis? Record Yes if the infant had Sepsis/R./O Sepsis on this day.
6. Hemodynamic instability? Record Yes if the infant had hemodynamic instability on this day.
7. Clinically significant PDA? Record Yes if the infant had clinically significant PDA on this day.
8. Other (specify). Record Yes if the infant had other conditions this day. Specify these.

4. Was the infant extubated on this day?
Record Yes if the infant was extubated on this day.

If Yes,
a. Record the time of intubation:

b. Type of extubation:
1= Planned
2= Accidental

c. Record the following prior to extubation

1. Were blood gases obtained within 6 hours prior to the event?
Code 'Yes' if the blood gas that, in the opinion of the investigator, is most associated with the event was obtained within 6 hours prior to the event. Record 'No' if there is no blood gas measurement associated with this event or was obtained >6 hours prior to the event.

Example: If an infant is stable and then requires emergent intubation and a blood gas was not obtained, code 'No'.

If Yes, record:
a. pH
b. PCO_2

2. FiO_2
3. Saturation

10.4 Instructions for completing the Replacement Oximeter Form (SUPP05B)

The purpose of this form is to record each time a study oximeter is replaced on an infant from study initiation to 36 weeks or status (whichever comes first).

a. Episode Number
Consecutively record each oximeter replacement as indicated by the preprinted episode number

b. Date Oximeter Replaced
Record the date the replacement oximeter was first utilized for this infant in MM/DD/YYYY format

c. Time Oximeter Replaced
Record the time the replacement oximeter was first utilized for this infant based on a 24-hour clock

d. Replacement Oximeter Serial Number
Record the six digit serial number of the replacement oximeter used.

e. Replacement Oximeter Color Code
Record the color code assigned to the replacement oximeter.
1= Blue
2= Orange

Note: Color codes are assigned by RTI when study oximeters are sent to participating Centers. Please contact RTI study coordinator at 919-485-7750, zaterka@rti.org to verify color code assignments if in question.

Chapter 11

Protocol Deviation Form

11. 1 Introduction

The purpose of the protocol deviation form is to facilitate the accurate documentation of the facts and circumstances surrounding a deviation from or violation of the protocol. This form should be completed for all randomized patients whenever a protocol deviation is encountered by study personnel. ***This form will be keyed at the sites.***

All protocol violations will be reviewed by the center PI who will discuss each protocol violation with the involved clinicians and provide a written summary including steps taken to avoid future violations.

11.2 Instructions for completing the Protocol Violation Report (SUPP06)

1. Date of Protocol Deviation:
Record the date the deviation was first encountered using the mm/dd/yyyy format.

2. Type of Protocol Deviation:
Record the type of protocol deviation:
1= Infant intubated without meeting study criteria
2= CPAP not initiated if required by the protocol
3= Surfactant not given in the first hour
4= Mechanical ventilation initiated for other than study criteria
5= NSIMV initiated in infant not previously intubated
6= Extubation (exclude unplanned extubation) for other than study criteria
7= Failure to extubate CPAP infant if all criteria are met
8= Infant received incorrect treatment assignment
If protocol deviation =8, indicate the treatment arm.
1= Ventilator strategy
2= Oximetry strategy
3= Both
9= Oximeter not started within 2 hours.
11= Infant randomized to incorrect gestational age group
12= Postnatal steroids given for BPD/CLD within 21 days of life
99= Other: Specify type of protocol deviation

3. Circumstances of the protocol deviation/violation:
Briefly describe the circumstances that led to the protocol deviation/violation. In particular, if there were medical reasons for deviating from/violating the protocol, describe them.

4. Additional comments:
Record any additional comments or information here such as steps taken to prevent recurrence of the deviation/violation.

5. Name of the person reporting the deviation/violation:
The name of the individual making the report should be recorded here.

6. Date Protocol Deviation Form is completed:
Record the date this form was completed.

Chapter 12

Reintubation Form

12.1 Introduction

The purpose of this form is to document all reintubations after day 14 for the duration of hospital stay.

12.1.1 Instructions for completing the Reintubation Form (SUPP07)

Complete this form for every reintubation and subsequent extubation after 14 days for the duration of hospital stay until status.

a. Event
Enter event code as:
1= Reintubation
2= Extubation

b. Date of event:
Enter the date of the event using the mm/dd/yyyy format.

c. Reasons for reintubation:
1 = Apnea / hypoventilation
2 = Increased respiratory effort
3 = Sepsis/Possible sepsis
4 = Atelectasis
5 = Elective procedures
6 = Upper airway abnormality
7= Self/Unplanned
8 = Other reasons

Record the code(s) corresponding to the reason(s) for the reintubation as recorded from the chart. There may be a maximum of three reasons recorded.

If code =8 other reasons, specify reason for reintubation if it is not listed.

d. Record FiO_2 and PCO_2 if available:
Record the FiO_2 and PCO_2, if within 6 hours prior to the event.

Chapter 13

Serious Adverse Experience

13.1 Introduction

Serious and unanticipated adverse events may be anticipated in this vulnerable population. **Data on the following potential adverse events that may be related to the study maneuver will be recorded and evaluated as part of continuous safety monitoring during the trial by RTI:**

13.2 Adverse Event Form (SUPP08)

Complete this for any randomized infant who experienced one or more of the following adverse events during the initial 14 days of life Record a consecutive Report Number in the header for each form submitted. This form should be completed and keyed at the sites as soon as possible.

1. Air leak

a. Pnemothorax
Record 'Y' if pneumothorax is documented in the infant's chart. Pneumothorax is a collection of air in the pleural space where a lucency is identified in the pleural space with displacement of the lung away from the chest wall. Do not include a pneumothorax resulting from a thoracotomy during surgery (e.g. PDA ligation). Otherwise code 'N'

b. Pulmonary Interstitial Emphysema (PIE)
Record 'Y' if pulmonary interstitial emphysema (PIE) is documented in a radiographic report in the infant's chart. PIE is a radiographic and pathologic diagnosis made when air ruptures from alveoli or small airways into the perivascular tissues of the lung. This diagnosis will only be documented if from the radiographic reports. Do not include PIE documented in patient notes unless there is radiographic documentation to support this diagnosis. Otherwise code 'N'

c. Pneumopericardium
Record 'Y' if pneumopericardium is documented in the infant's chart. This documentation may be found in a radiographic report, echocardiogram report or patient progress notes. Pneumopericardium is an extrapulmonary collection of air in which the air completely surrounds the heart, including its inferior border. Otherwise code 'N'.

If coding 'Y' to question 1.a, b or c above, code most proximate mode of ventilatory support for each occurrence as follows:

1 = HFV
2= CV

3 = Nasal SIMV
4 = CPAP
5= NC
6= Hood
7= No Support
8 = Infant temporarily out of unit
9= No Support all day and off Study oximeter

Record 'Date of Onset" and 'Attribution to SUPPORT study' for each occurrence.

2. The need for chest compressions, and/or epinephrine in the delivery room
3. The occurrence of severe IVH (Grades 3-4, Papile)[i]
4. Pulmonary Hemorrhage
5. Nasal breakdown requiring discontinuation of nasal prongs
6. Death
7. Other (specify) Specify if there were other adverse events.

13.3 Definition of a Serious Adverse Experience

1. An adverse experience is any undesirable experience associated with the use of a medical product in a patient.
2. Associated means that there is a reasonable possibility that the experience may have been caused by the drug.
3. Serious adverse experience means any experience that suggests a significant hazard, contraindication, side effect or precaution.
4. With respect to human clinical experience, a serious adverse drug experience includes any experience that is fatal or life threatening, is permanently disabling, requires inpatient hospitalization, or is a congenital anomaly, cancer, or overdose.

Death
Submit a report if the patient's death is suspected as being a direct outcome of the adverse event.

Life Threatening
Submit a report if the patient was at substantial risk of dying at the time of the adverse event or it is suspected that the use or continued use of the product would result in the patient's death
.
Examples are: pacemaker failure; gastrointestinal hemorrhage; bone marrow suppression; infusion pump failure which permits uncontrolled free flow, resulting in excessive drug dosing.

Inpatient Hospitalization (initial or prolonged)
Submit a report if admission to the hospital or prolongation of a hospital stay results because of an adverse event. Examples are: anaphylaxis, pseudomembranous colitis, or bleeding causing or prolonging hospitalization.

Disability
Submit a report if the adverse event resulted in a significant, persistent, or permanent change, impairment, damage or disruption in the patient's body function/structure, physical activities or

quality of life. Examples are: cerebrovascular accident due to drug-induced hypercoagulability, toxicity, peripheral neuropathy.

Requires Intervention to Prevent Permanent Impairment or Damage
Submit a report if you suspect that the use of a medical product may result in a condition which required medical or surgical intervention to preclude permanent impairment or damage to a patient. Examples are: acetaminophen overdose-induced hepatotoxicity requiring treatment with acetylcysteine to prevent permanent damage, burns from radiation equipment requiring drug therapy, breakage of a screw requiring replacement of hardware to prevent malunion of a fractured long bone.

Adverse experiences will be reviewed by the Data Safety and Monitoring Committee.

13.4 Completing the MedWatch Form (SUPPO8A)

In the event of a patient death or unexpected serious adverse event not documented in the case report form, the PI must be notified right away. The attending physician should write a detailed description of the clinical events to include all the elements of the FDA 3500A (MedWatch) form (see Appendix **A**), the patient's date of birth, Network number, and whether the treatment was stopped. The description should be faxed to Dr. Rosemary Higgins at NICHD (301 496-3790) with a copy sent to Kris Zaterka-Baxter at the DCC (919 485-7762).

Chapter 14

Outcome Status Form

14.1 Introduction

The purpose of this form is to document the final outcome status of the infant.

14.1.1 Instructions for completing the Outcome Status Form (SUPP09)

This form is to be completed when the infant is discharged to home, transferred, if hospitalized at 120 days, death or withdrawn (which ever comes first).

14.1.2 Section A - Infant Outcome

1. **Status of infant at time of completion of form:**

   - **Discharged to home**
     Record '1' if infant was discharged to home without returning in 7 days.

   - **Still in hospital at 120 days**
     Record '2' if infant is still in the hospital at 120 days.

   - **Transferred to another hospital**
     Record '3' if infant was transferred to another hospital without returning in 7 days.

   - **Transferred to chronic care facility**
     Record '4' if infant was transferred to a chronic care facility without returning in 7 days.

   - **Death**
     Record '5' if the infant died.

   - **Withdrawn form study**
     Record '6' if the infant was withdrawn from study by a parent, legal guardian or physician; Use the F5 key to comment on circumstances of withdrawal if known (i.e., parent or physician withdrawal)

2. **Date of status:**
   Give date at status.

14.1.3 Section B - Neurologic

1. Did the infant have a head ultrasound between 4 - 21 days of age?
Code Yes if an ultrasound was performed between 4 - 21 days. Code No otherwise. If a cranial ultrasound is not done for standard of care, the study requires that at least one HUS be completed during this window.

If Yes,
a. Date of ultrasound:
Record the date of the head ultrasound obtained using the mm/dd/yyyy format. **Note**: If more than one head ultrasound is done between 4 - 21 days of age, record the date of the most severe.

If Yes,
b. Time of ultrasound:
Enter the time of the head ultrasound obtained using the 24 hour clock format (00:00-23:59).

c. Infarct?
Code Yes if an infarct was diagnosed by the local sonographer. Code No otherwise.

d. IVH?
Code Yes if evidence of intraventricular hemorrhage was observed on the head ultrasound. Code No otherwise.

If Yes,
1) IVH Grade:
Enter the severity of the intraventricular hemorrhage observed on the head ultrasound using the Papile scale:

Grade I: Code 1 if the echodensity/hemorrhage is confined to the germinal matrix/subependymal area.

Grade II: Code 2 if there is an echodensity/hemorrhage in the lateral ventricle(s) without distention.

Grade III: Code 3 if there is an echodensity/hemorrhage in the lateral ventricle(s) with distention.

Grade IV: Code 4 if there is an echodense lesion in the parenchyma.

e. PVL?
Code Yes if periventricular leukomalacia (increased echogenicity or cysts in periventricular region) was observed on the head ultrasound. Code No otherwise.

14.1.4 Section C – Ophthalmology

1. **Was an exam performed for Retinopathy of Prematurity (ROP)?**
   Review the medical record to determine if an examination was performed for ROP.
   If Yes, complete the **SUPP10 Form** (ROP Outcomes And Tracking Summary).
   If NO, and the infant survived, complete the **SUPP10** (ROP) form based on subsequent exams (including back-transfer hospital and/or outpatient visits)

14.1.5 Section D – Postnatal Steroid Use

1. Did the infant receive postnatal steroids after the first 21 days of life?
If Yes, record the information on number of courses, start date, stop date, drug administered and total dose administered during the course in mg/kg. If No, the boxes are left blank.
Note: Only steroids given IV or PO are included for the purposes of this study. Inhaled steroids **are not** included.

a. Course:
A course is defined as all of the doses given in a period between an initial, usually high dose, and subsequent tapers. It may include a period when drug is given every other day. For the purposes of this study, a course is defined as ended when 72 hours passes without a steroid dose. If 72.5 hours passes and the infant receives another series of doses of the same or a different steroid, this is considered to be a second course.

b-c. Start and Stop Date:
The first and last doses given in a single course. RTI will use these dates to define the duration of exposure in days.

d. Drug:
Record the steroid administered using the following codes:
1= Dexamethasone
2= Betamethasone
3= Hydrocortisone
4= Prednisone
5= Other (Specify the other drug that was given)

e. Total Dose:
Calculate the total dose given in the course expressed as mg/kg. For example, the baby receives a course of dexamethasone beginning at 0.2 mg/kg for 2 days, and subsequent doses given as 0.1 mg/kg given for 2 days, 0.05 mg/kg for 2 days, 0.05 every other day for 2 doses, and then discontinue. The total dose administered to this patient is 0.2+0.2+0.1+0.1+0.05+0.05+0.05+0.05. The total dose administered is 0.8 mg/kg.

If the dose is not expressed in mg/kg in the medical record, the researcher calculates the mg/kg dose using: 1) the weight used in calculating the dose if documented, 2) the weight on the day the order was written to calculate the mg/kg.

Chapter 15

ROP Outcomes and Tracking Summary

15.1 Introduction

The purpose of this form is to track and document the acute ROP outcome of each eye. Tracking the course of ROP should begin with the first examination and will generally be much easier if the coordinator attends the examinations and asks the ophthalmologist in person about the categories to be recorded.

Data may be entered in the database from the form after each examination, or may be entered when the infant reaches "acute/final" status. However, monitoring of the examinations and progress will be much more complete and helpful if these are entered after each examination.

15.1.1 Instructions for completing the ROP Outcomes and tracking Summary (SUPP10)

Complete this form for all enrollees in SUPPORT who survive to have their first eye examination. This normally is scheduled at 31 weeks postmenstrual age (but not earlier than 4 weeks after birth).

Record the data for each eye examination until each eye has reached "acute/final" status (see definition below in 15.2). This will sometimes include examinations following discharge home or transfer to another hospital.

1. Date of Exam

If a confirming examination is conducted, each should be separately recorded.

2. Location of Exam

Code 1= inpatient for the primary hospital where the infant has been cared for, including other Units in that same hospital (step down units, pediatric intensive care, surgical care units, etc.)

Code 2=Outpatient for examinations in the outpatient ophthalmology department, private ophthalmologist's office or other outpatient visits. Include infants at a chronic care facility transported to the physician's office for an examination.

Code 3= Transfer Hospital when infants have been back transferred to a referring hospital or regional hospital.

Note: Outpatient and back transfer hospitals can be a common source of infants missing examinations and "slipping through the cracks". Be particularly attentive to ensuring timely repeat examinations in these cases and ensure that the family is aware of the importance and critical timing of the examinations.

3. **Lowest zone:** Record the lowest zone that contains vessels that end before crossing out of that zone. This may be zone I (the most immature), zone II (intermediate) or zone III (most mature). The ophthalmologist normally records this on the eye examination form. The most common for SUPPORT infants will be zone II at the early examinations. There may be vessels recorded in:
   - zone I and II (you record zone I)
   - zone I only (you record zone I)
   - zone II only (you record zone II)
   - zone III only (you record zone III)

   Note that by convention, disease is never to be recorded in zones II and III in the same eye. If the two nasal clock-hours are not fully vascularized, by convention, no vessels in that eye are to be recorded in zone III. If they are fully vascularized, the all the rest of that eye's vessels are in zone III.

4. **Highest stage in lowest zone** (not to be used if eye has had surgery)
   Look first at the lowest zone that has vessels ending in it (see previous answer). Then look to see if there is ROP in any of the clock hours of that zone. Choose the highest stage of ROP in that zone to record.

   Examples:
   If the eye has vessels ending in just zone I, but no ROP, the highest stage is zero.

   If the eye has vessels ending in zone I and zone II and the ROP in zone I is stage 2 while the ROP in zone II is stage 3, the highest stage in the lowest zone (I) is stage 2.

   If the eye has vessels ending in zone I, but there is no ROP in zone I, but there is stage 2 and stage 3 ROP in zone II, the answer would be 0=no ROP in the lowest zone.

5. **Highest stage in any zone** (not to be used if eye has had surgery)
   Look at the stage of ROP around the 12 clock-hours of the recorded examination. Choose the highest stage to record. In rank order going from lowest to highest the order is 0, 1, 2, 3, 4a, 4b, 5. The other categories are for less common cases.
   - Code 4 = stage 4a or 4b is a partial retinal detachment
   - Code 5 = stage 5 which is a total retinal detachment
   - Code 6 = Post laser/cyro (do not use stages)
   - Code 9 = Old scars, but no active ROP

6. **"Plus disease"**
   This is recorded by the ophthalmologist as present or not. Sometimes they provide comments like 'borderline plus' or 'possible early plus disease' or 'mild dilation, but not plus disease'. In these cases, do not record 'plus disease' as present. If the ophthalmologist records plus disease by quadrants, two or more quadrants are required to meet criteria for plus disease (i.e. only one quadrant of dilated/tortuous vessels is not sufficient.).

7. Threshold (New Type 1 threshold per ETROP)

The ophthalmologist who diagnoses threshold ROP needing surgery will normally state this prominently on the examination form. The criteria for the new threshold are any of the following four findings:

If in zone I: stage 3 ROP, even without plus disease
plus disease with any stage ROP

If in zone II: plus disease with stage 2 ROP
plus disease with stage 3 ROP

There may be times when disease is worse than this, but it should still be recorded as threshold.

There will be some times when the judgment of the retinal surgeon and neonatologist will be not to administer treatment (laser or cryo), even when there is new threshold. Normally infants are then followed extremely closely (every few days repeat examinations).

8. Surgery

For each examination date, record if surgery is performed on that day. (mostly will be no). If surgery was previously performed, but not on the day of that examination, record 0

9. Post-surgical Retinal Detachment after surgery

This at first looks like a repeat of the question asking for stage of ROP, but it is not since it is intended to be used only after surgery has occurred.

10. Final Acute Status Lost to Follow-up at 55 weeks PMA
Complete this question **only** for the final eye exam entered.

Record 'N' if the last examination meets criteria for final acute status reached (see section 15.2 below).

Record 'Y' if the final 'acute' ROP status is permanently missing because the infant is lost-to-follow up. For example, the last exam is not yet mature, or not yet in zone III for the second time in a row, or the baby still has ROP, but had not reached criteria for surgery. All attempts must have been made to capture this data from the follow up exams, and it is coded 'Y' as missing only when there was no final exam done (parents did not bring infant in).

By the time an infant has reached 55 weeks PMA, the eye disease will have reached final status, whether we know about it from an examination or not. That is why we make this determination at this time. If it is later learned that examinations actually were done, the results can be entered on the form with a late correction/edit.

Therefore, if you know the infant is less than 55 weeks PMA and has not had an exam that meets the final/acute criteria, you are still trying to get the family to bring

the baby in for exams because it is clinically important and also will give you a primary study outcome. If it is now past 55 weeks, you may give up trying to get them to come in because it's too late to identify disease that could be treated, and the time for the clinical outcome for the study is also past. Late outcomes will be collected at the 18-22 month follow up examination.

Potential merit of later exams: Most likely, they will reassure the infant that the eyes have healed. They may detect an important need for glasses at 6-9 months after birth. If the outcome is retinal detachments, the parents will learn the baby is not going to see and needs to be referred for early intervention. In either event, late exams that show retinal detachments will confirm that once upon a time, the baby did have bad ROP. Late exams that show good outcomes will NOT tell us if they once had ROP that has now regressed (healed).

Note: even in these circumstances where we have given up, the infant will still be tracked down for the 18-22 month follow up visit. At that time they are asked if any eye surgery was done after discharge / status. If yes, what surgery. If it was for ROP, then that will become a final status revision. Also, even if no surgery was done, but the child has experienced vision loss *from ROP*, this would also be a final outcome.

Note that some infants have vision loss that is not from ROP. This is usually "cortical vision loss" and is from brain injury.

11. Final ROP Status determined at 18 Moth Follow Up
Complete this question **only** for the final eye exam entered.

Answer this question as 'N' if the final acute status was already determined before 55 weeks PMA. That is, "no, we did not determine the final outcome based on the 18-22 month exam."

Also, answer this question as 'N' if the final status was not determined by 55 weeks PMA, AND it was not determined at the 18-22 month visit either. This would happen if there were no 18-22 month examination. It would also happen if there were an 18-22 month examination, but the parents report no eye surgery and no other eye exams so we don't know what happened to the ROP.

You can record 'Y' for the final ROP status obtained during the 18-22 month follow up visit only if the parents are now reporting to you eye surgery for ROP that you had not learned about before, or they are telling you about eye exams that you have not learned about before (or else you would have recorded it before). If this is the case, reports from the exam(s) and/or surgery should be obtained to determine what has happened. These data will likely require ophthalmology input to determine if the primary ROP outcome was reached. Examples: A. ROP can be assumed (imputed) to have reached surgical criteria if the infant's subsequent surgery is vitrectomy for retinal detachment, or is an exam under anesthesia with a diagnosis of ROP stage 4A, 4B or stage 5 ROP, or retinal fold crossing the macula. B. ROP may not have met laser/CRYO criteria if the surgery was for strabismus (crossed eye), plugged tear duct, or only examination under anesthesia, for example to rule out glaucoma.

15.2 Acute/final Status

An eye is 'acute/final" when it reaches one of the following points in time:
These can be a good outcome (favorable) as the ROP heals (regresses), or it can be the primary outcome variable event (unfavorable).

Favorable

- Vessel growth if mature to the ora serrata in all clock hours
- Vessels in zone III for two sequential eye examinations (i.e. two examinations in a row)

Unfavorable

- type I threshold ROP
- Laser (or cryo or both) surgery for acute ROP
- retinal detachment stage 5 retinal detachment stage 4b

Other

- Infant dies.

Chapter 16

Respiratory Support after 14 Days

16.1 Introduction

The purpose of this form is to document any respiratory support the infant receives after day 14.

16.1.1 Instructions for completing the Respiratory Support Form after 14 Days (SUPP11)

This form is to be completed daily from study day 15 through 36 weeks or status, whichever comes first.

Record the following information four times for each day. **Note**: the scheduled time points for each day are collected down each column

- **Date**
  Record the date corresponding to the Study day
- **Scheduled Time:**
  Record a - d for each study day for the scheduled time points 06:00, 12:00, 18:00, 23:59.
- **Highest Level of Support**
  Record the highest level of support the infant is in on at the scheduled time points during this **STUDY** day.
  Enter: 1= HFV, 2=CV, 3= Nasal SIMV, 4= CPAP, 5= NC, 6= Hood,
  7= No Support, 8= Infant temporarily out of unit 9= No Support all day and off the study oximeter*.

  * Code 9 should be recorded in the 0600 time period for each day the infant is in no support and is not on the study oximeter. Oxygen (b), flow rate (c), and oximeter alarm check (d) are not required for this time point. No further data are required for the following time points on this day.

- **Oxygen -Yes/No**
  Record "Yes" if the infant was on oxygen at the scheduled time point during the day. Disregard any temporary increases in FiO_2 for desaturation episodes, apnea, bradycardia or procedures where the infant returns to his/her previous FiO_2 in a reasonable amount of time (≤ 30 minutes). Record "No" if the infant is not in oxygen on this day.
- **Flow rate (Nasal Cannula only)**
  Record the highest flow rate the infant was on at the scheduled time-during the study day. Disregard any temporary increases in flow for desaturation episodes, apnea, bradycardia or procedures where the infant returns to his/her previous flow rate in a reasonable amount of time (≤ 30 minutes)***Flow rate should be recorded **only** if the

infant was on a nasal cannula that day. For purposes of recording, Vapotherm is considered a cannula.

- **Oximeter Alarm Check**
  Record the time the oximeter alarm check was done.
  The purpose of the oximeter alarm checks is to verify that alarms are being used and will be a measure of compliance of the protocol (i.e. to verify that the alarm limits are in place). The time points (q6h) can vary at each center but attempts should be made to use a 6 hour schedule. That is why the times are left open to fit each centers routine. Regardless whether the alarms are locked or not, we want to document that caregivers are noting alarm limits. We hope that this will increase awareness of the need for the limits to remain in place. And if changes are needed to the alarm limits, they should be made according to the study guideline

Chapter 17

OXIMETER SETUP

17.1 Oximeter Setup – Masimo Radical

Review the following EACH TIME the oximeter is placed on a baby.

17.1.1 Power

If possible, units should remain plugged in between uses. Where this is not possible the oximeter should be plugged in as soon as possible after randomization.

17.1.2 Initial Settings – [Radical Manual pp. 30-42]

Date – Check to see that the date and time are correct. This must be done prior to gathering data. **Changing the date or time after data collection has started will erase the memory!**

Sensitivity – Set to Normal Mode
Averaging Time – Set to 16 seconds
Alarm Limits – Sat: Suggested between 85 and 95.
Audible Delay – 10 seconds
Trend Period – [43-45] - 10 Seconds **Note: Changing this setting during a recording will erase all data !!**

17.1.3 Help – If you can not find these settings using your oximeter manual, or if you have any problems with the Masimo masked oximeters used in the SUPPORT study, please contact:

1. The local Masimo Clinical Specialist who did the inservicing for your center
   Please identify yourself as one of the SUPPORT centers, with questions about a masked oximeter.

   and/or

2. Masimo Technical Support at 800-326-4890, option 2. tech@Masimo.com
   Please identify yourself as one of the SUPPORT centers, with questions about a masked oximeter. The techs are aware of SUPPORT and the masked oximeters.

   and/or

3. Dr Maribeth Sayre, Director of Medical Affairs for Masimo, and the Masimo liaison for the SUPPORT study. Her contact information is: msayre@Masimo.com
   cell phone 925-337-3856

If a masked oximeter is malfunctioning, it must be sent back to Masimo headquarters. First, a RMA # (Return Material Authorization number) is needed. A copy of the form **is**

contained in Appendix E. . Please identify the facility as one of the SUPPORT centers, and the product as a masked Radical handheld or docking station.

If there are questions relating to alarm parameters, they should be referred to Wade Rich.

PLEASE COPY DR. MARIBETH SAYRE ON ALL EMAILS RELATED TO THE MASKED OXIMETERS.

17.2 Downloading Data

17.2.1 Software

The software used to download the data is called TExtract. If you have not gotten a copy, it is available by email from wrich@ucsd.edu or it can be downloaded to your Network computer by RTI.

Using TExtract
A powerpoint presentation showing how to use TExtract is included in the manual as Appendix D.

17.2.2 Cable

Data may be downloaded from the oximeter to a laptop using either a serial cable or a USB-to-Serial cable. A picture of a USB-Serial cable is included in the power-point presentation that was sent out to all the sites.

17.2.3 Preparing Masimo for Download

- Turn Oximeter on.
- Output should be Binary
- Select button
- Use arrow key to highlight "Output".
- Select button.
- Enter the Serial Menu by selecting the button.
- Use arrow key to select "Binary".
- Select ☑ button.
- Select ☒ button twice.

When to Download
Downloads should be done every 2 weeks, or earlier if a child reaches a study milestone (e.g. Off oxygen for 72 hrs, death, discharge, or 36 weeks PCA)

17.2.4 After the download:

Be sure to clear the memory of the Masimo after you have downloaded the data. Otherwise you will send RTI data which they already have along with the new data the next time you download. Clearing the memory is done as follows:

From the main screen when the Masimo is first turned on:
Select the → button.
Select the button.

Select the  button twice.
Select the 🗑 icon.
Select the ☑ icon and the data will be dumped.

17.2.5 Uploading Data to Network Computer

Data can be transferred from the laptop to the network computer by way of a floppy disk or a USB Memory Stick. The USB device is preferable because it will hold many studies instead of just one.

To upload this data to your Network computer the USB stick must be put into the USB port on the computer. This is often in the back. A USB extension cable will help make this easier, as one end can just be placed on the desk for easy reach.

The SUPPORT data entry software program from RTI will take you through the process of uploading. The information regarding how to label the files is included in the TExtract Power point appendix D to this manual.

17.2.6 Masimo Technical Issues

It is recommended that the Radical Handheld be docked to the docking station and attached to an AC power source when it is not in use to ensure that the battery remains fully charged. All batteries lose capacity with age. When battery run time is significantly reduced, it is advisable to completely discharge and fully recharge the battery pack. Masimo does not give a recommended TIME FRAME for performing a discharge cycle since every environment is different.

17.2.7 How to Deep-Discharge the Radical Battery

The discharge cycle will take approximately 16 hours to complete for the handheld battery. The Docking Station battery will take approximately 30 hours to complete. A message will appear in the service screen when the discharge cycle is complete. The batteries will be fully charged after completion of the cycle.

Note: *In order for the discharge cycle to be properly completed, the Handheld must be docked to a Docking Station and supplied with AC power throughout the cycle.*

Warning: WHEN DEEP-DISCHARGING THE HANDHELD OR DOCKING STATION BATTERY, MAKE SURE THAT THE DEVICE HAS BEEN REMOVED FROM SERVICE UNTIL FULL BATTERY CAPABILITY CAN BE RESTORED.

1. Press the three page button to access the main menu screen
2. Highlight the Service menu and press the single page button
3. Enter password 2 – 3 – 1
4. Press single page button
5. Confirm by pressing the checkmark
6. Wait until message of "Discharge Cycle is Complete"

17.2.8 Defective Equipment

If you need to return defective Masimo equipment, please contact Technical Support at Masimo 1-800-326-4890 for a Return Merchandise Authorization #.
You will need the device serial # when you call.

APPENDIX A

STUDY FORMS

SUPP01	**Screening Log**
SUPP02	**Eligibility Form**
SUPP03	**Delivery Form**
SUPP04	**NICU Admission Form**
Supp04a	**NICU Admission Form (Surfactant Doses)**
SUPP05	**Safety Monitoring Form**
SUPP06	**Protocol Deviation Form**
SUPP07	**Reintubation Form**
SUPP08	**Adverse Event Form**
SUPP08A	**MedWatch Form**
SUPP09	**Outcome Status Form**
SUPP10	**ROP Outcomes and Tracking Summary**
SUPP11	**Respiratory Support After 14 Days**

APPENDIX B

SAMPLE CONSENT FORM

University of California, San Diego
Consent to Act as a Research Subject

The Surfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants

The SUPPORT Trial of the NICHD Neonatal Research Network

Neil Finer, MD, his associates, and the National Institutes for Child Health and Human Development (NICHD) Neonatal Research Network are conducting a research study to find out more about treatment with CPAP (positive pressure applied with a face mask to help keep the lungs inflated) and learn the appropriate levels of oxygen saturation (oxygen levels in the blood) in premature babies. You are being asked to allow your child to be in the study because there is a possibility he/she will be born between 16 and 12 weeks early (24-28 weeks gestational age).

The purposes of this trial are the following:
1) To compare infants who receive delivery room CPAP and who have strict guidelines for having a breathing tube placed with infants who have the tube placed and surfactant (a liquid which helps babies with immature lungs breath easier by helping keep their lungs from collapsing) given in the delivery room.
2) To compare low range (85-89%) oxygen saturation levels with high range (91-95%) levels to determine if a lower range results in decreased ROP (Retinopathy of Prematurity, an eye disease that may result in impairment of vision or even blindness, which may be caused by excessive levels of oxygen.)

Duration of the Study: We expect to include about 1300 babies in the study from all the NICHD Neonatal Research Network hospitals over a two year period.

The use of CPAP and Intubation/Surfactant are both treatments currently used in the delivery room at UCSD. The decision as to which to use is currently made by the physician attending the delivery.

The oxygen level currently used in the NICU at UCSD is between 85% and 95%. Both treatment groups (85-89% and 91-95%) fall within that range. The study will attempt to keep babies in one of these two smaller ranges.

If you agree to allow your child to be in this study, the following will happen to your child:
Prior to delivery, and after your permission, your baby will be randomized (chosen by chance like the flip of a coin) to one of two lung treatment strategies. The treatments are as follows:
1) CPAP in the delivery room immediately after birth and continuing in the NICU, or
2) The placement of a tube in his/her trachea (windpipe) in the delivery room followed by surfactant administration and ventilation (breathing for the baby using a machine).

In addition to being randomly assigned to one of the two groups described above, your baby will be randomized to a High reading or Low reading oximeter (a monitor that displays how much oxygen is in the blood). The oximeters (oxygen monitors) used in this trial are FDA approved oximeters which have been modified for research purposes. This modification makes the monitors show a value which is either slightly higher or slightly lower than the true oxygen level when values are between 85 and 95%. Outside those ranges, the oximeter works the same as the standard of care device.

Which group your baby is randomized to will not be known to the nurse taking care of your baby, or his/her physician. Only the study coordinator will know which group your baby is in. Within the range of oxygen which we normally keep babies in, your baby will either be on the high end of normal or the low end of normal. He/she will remain on this device until he/she reaches 36 weeks adjusted age. (e. g. 24 wks gestation plus 12 weeks of age = 36 weeks adjusted age). Other care will be conducted as normal during his/her participation in the study. Your baby will be followed in our Infant Follow-up clinic at 6 and 12 months as standard of care for small babies. At 18-22 months corrected age your baby will receive, at no charge to you, a complete exam of their muscles, nerves, and mental and coordinated movement skills.

Participation in this study may involve some added risks or discomforts. Because all of the treatments proposed in this study are standard of care, there is no predictable increase in risk for your baby. Infants randomized to the CPAP group may, at some point in their care, require intubation and assisted ventilation (methods to help them breathe). If the attending physician deems this necessary, participation in the study will not affect this decision. Some unknown risks may be learned during the study. If these occur, you will be informed by the study personnel. The only other risk of this study is the risk to confidentiality. Every effort will be made to keep your child's medical record confidential. There will be no name or other patient identification in any study report that may be published after the study is completed. Measures taken to protect you and your baby's identity are described in the confidentiality section of this document.

There may be benefits to your child directly, including a possible decrease in chronic lung disease (need for extra oxygen near discharge) and/or a decrease in the need for eye surgery as a result of exposure to oxygen. Because we do not know in advance the actual strategies chosen for your child, or which of the treatment strategies is the most effective, it is also possible that your baby will receive no direct benefit. The knowledge learned from this study may help us treat babies in the future. However, as noted above, each of the 4 possible combinations of treatments is considered by some units to represent their desired approach.

If your child is injured as a direct result of participation in this research, the University of California will provide any medical care your child needs to treat those injuries. The University will not provide any other form of compensation to you if your child is injured. You may call the UCSD Human Research Protections Program office at (858) 455-5050 for more information about this, or to inquire about your rights as a research subject, or to report research-related problems.

_____ has explained this study to you and answered your questions. If you have other questions or research-related problems, you may reach Wade Rich, the Study Coordinator, or Renee Bridge, the Research Nurse, at 619-543-6560. You may contact the principal investigator Dr. Neil Finer at 619-543-3794

As an alternative to participation in this study you may decide to have your baby's doctor decide which treatment your baby will receive. If you decide not to include your child in this study, none of his/her medical information will be included in the study data. Participation in research is entirely voluntary. You may refuse to participate or withdraw at any time without jeopardy to the medical care your child will receive at this institution of other loss of benefits to which your child is entitled. If you withdraw your child from the study, the attending physician will decide whether to maintain current treatment or change it, based on your child's needs at the time of the decision. Data collection for research purposes will stop at that time.

Clinical information will be collected from your baby's chart by study personnel at UCSD. Information will be labeled with a code number. Coded information will be sent to the NICHD Neonatal Network's Data Collection Center at Research Triangle Institute (RTI) in Research Triangle Park, North Carolina. The study log linking the code number with your baby's identity will be kept under lock and key at UCSD. Information directly identifying your baby will not leave UCSD. Research records will be kept confidential to the extent provided by law.

You may withdraw your child from the study for any reason. In addition, the study doctors may decide to withdraw your child if they feel it is in his/her best interest to do so.

You have received a copy of this consent document to keep and the Experimental Subject's Bill of Rights

You agree to have your child participate.

_____

Parent's or legal guardian's signature DATE

_____

Relationship of legal guardian to subject DATE

_____

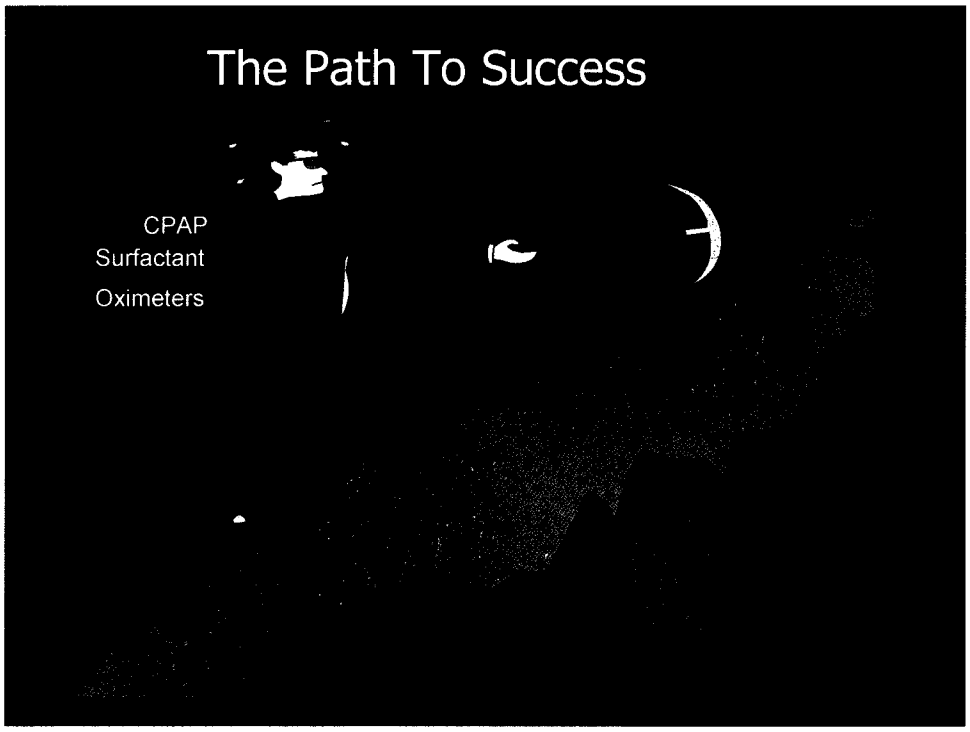
Signature of person explaining and getting consent DATE

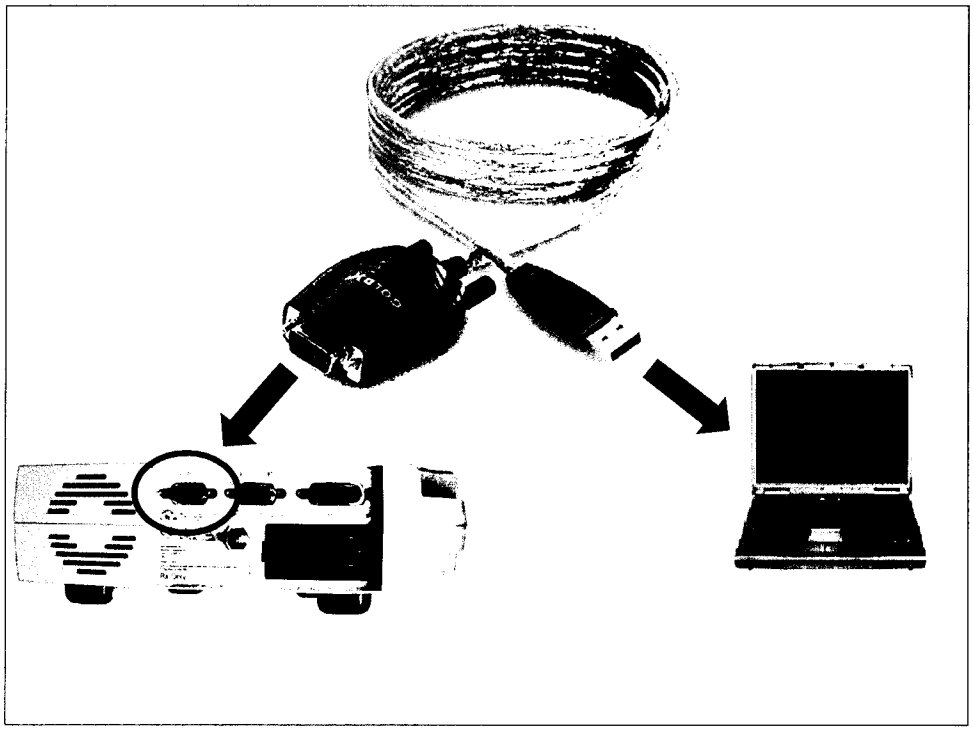
APPENDIX C

PHYSIOLOGIC DEFINITION OF BRONCHOPULMONARY DYSPLASIA (Refer to Stand Alone Protocol, Manual of Operations and Forms)

APPENDIX D

SUPPORT DOWN LOAD





Turn Oximeter on.

Select button.

Use arrow key to highlight "Output".

Select button.

Enter the Serial Menu by selecting the button.

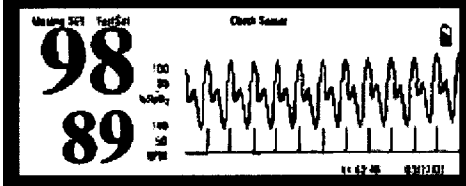
Use arrow key to select "Binary".

Select button.

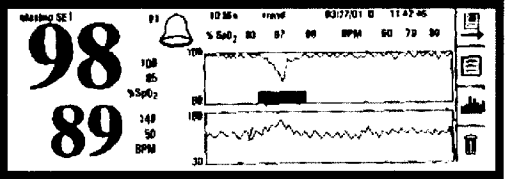
Select button twice.

Quick Reference on Masimo Extraction Utility
Masimo Unit Setup:

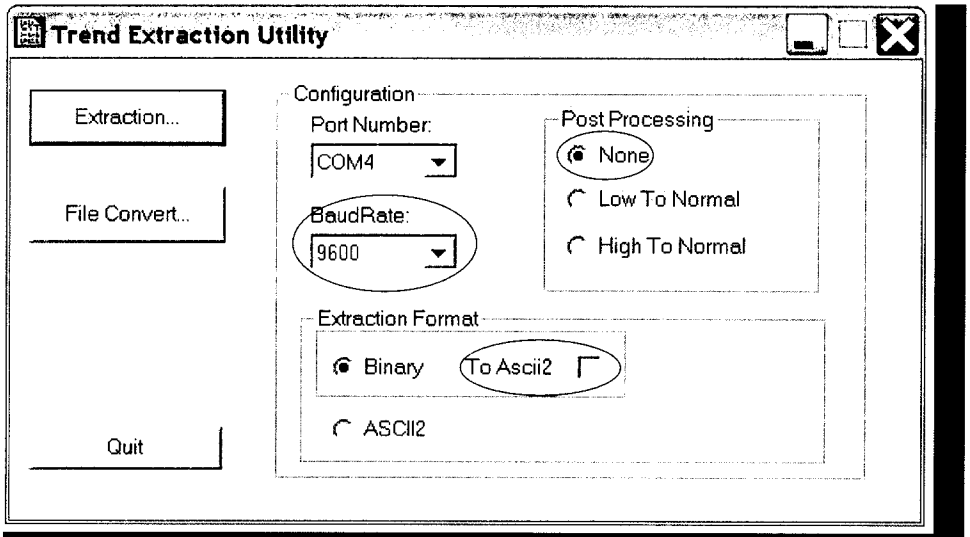
Make sure the Radical is in run mode and not in mode.



YES

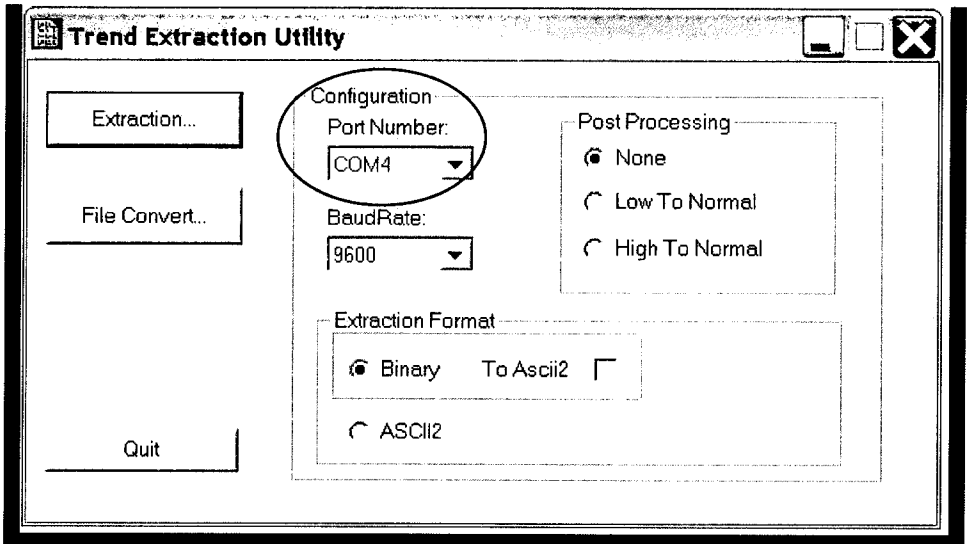


No

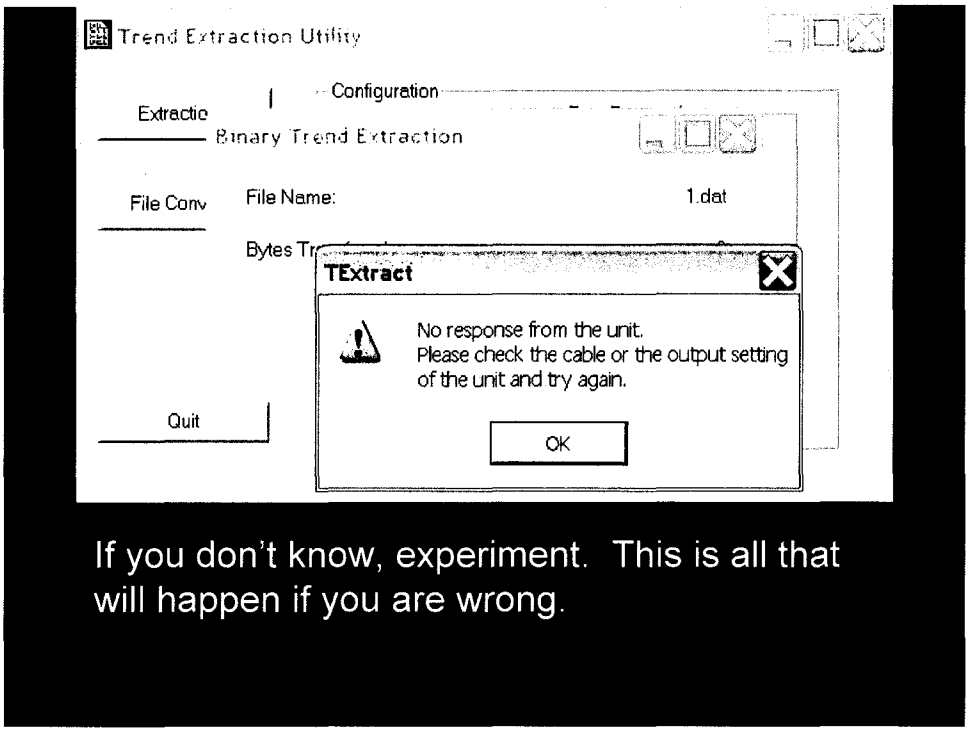


Execute the *TExtract.exe* utility

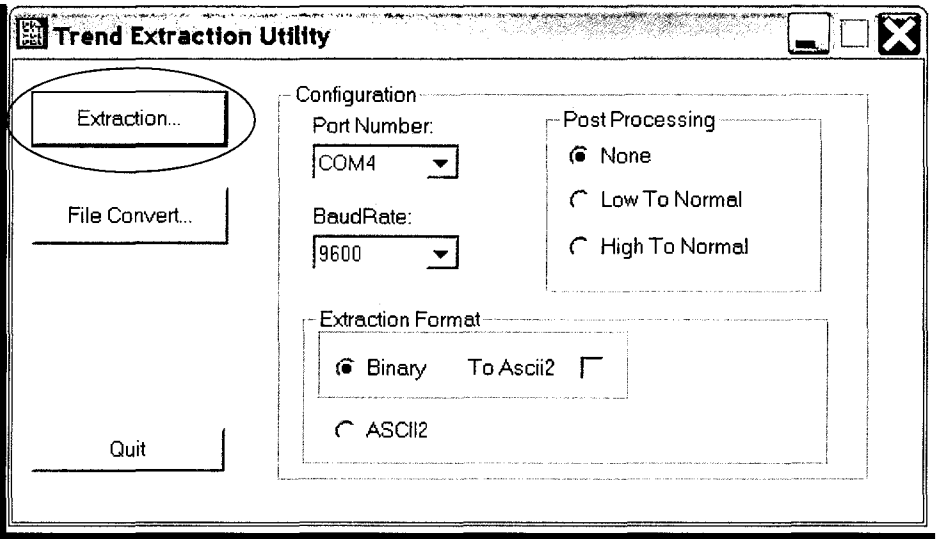
9600 Baud, No Post Processing, No Ascii2



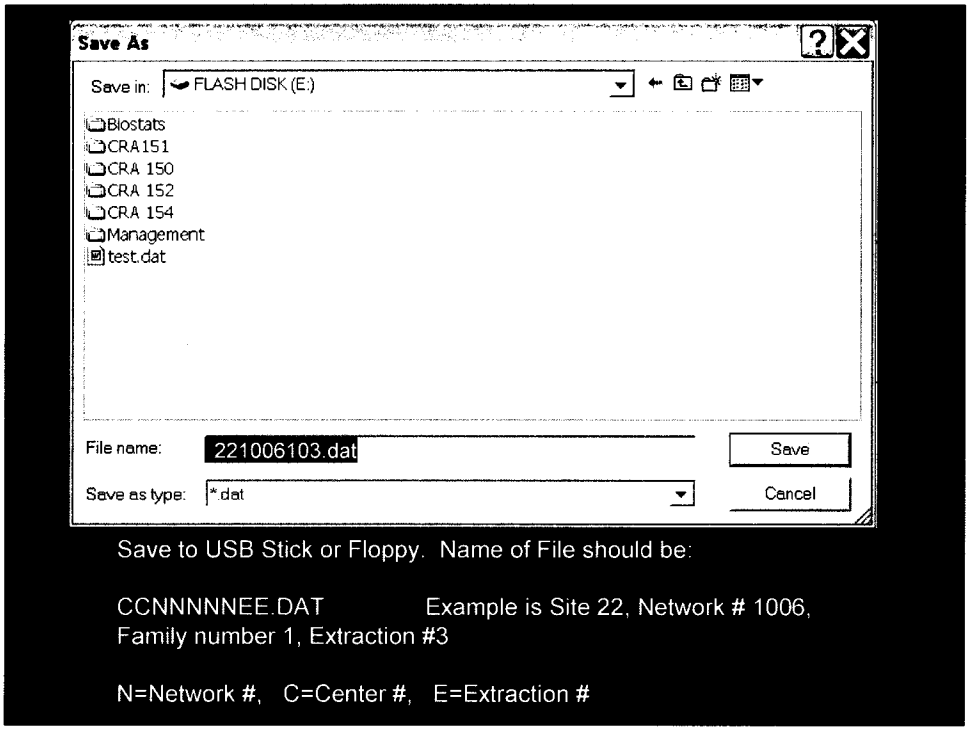
In the "*Configuration*" panel, select the COM port that is currently connected to the Radical unit.



If you don't know, experiment. This is all that will happen if you are wrong.



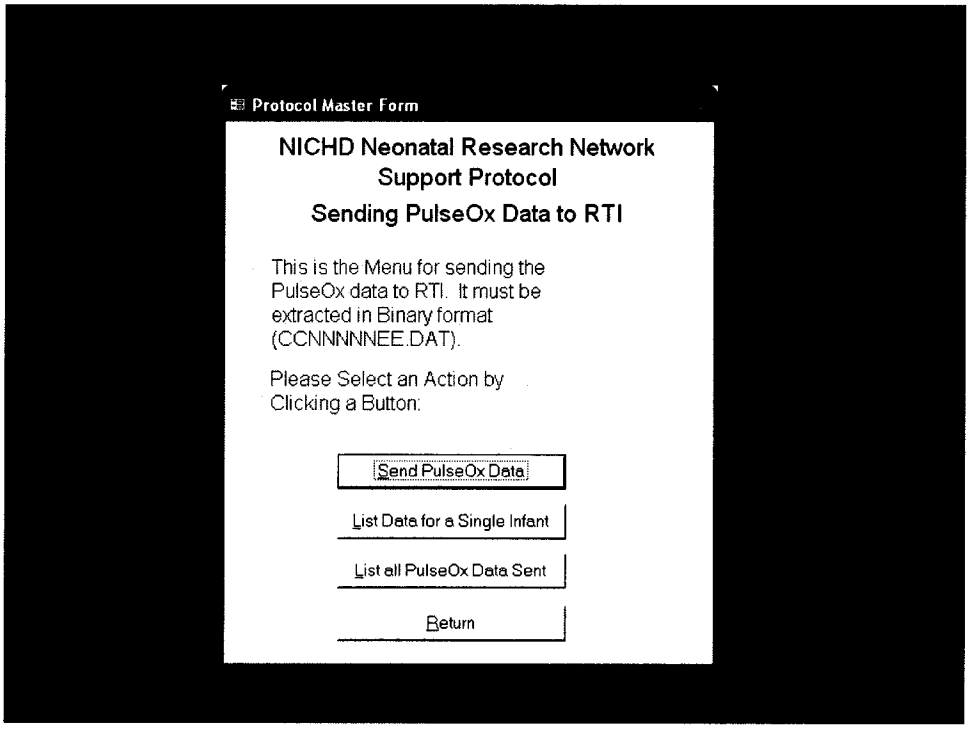
Hit Extraction.

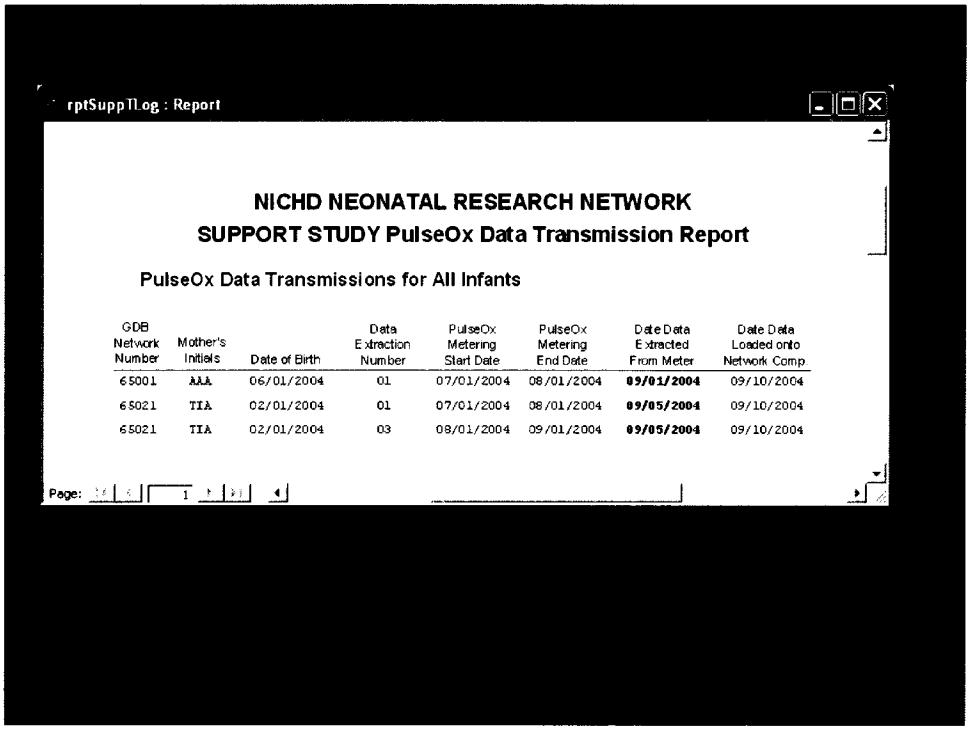


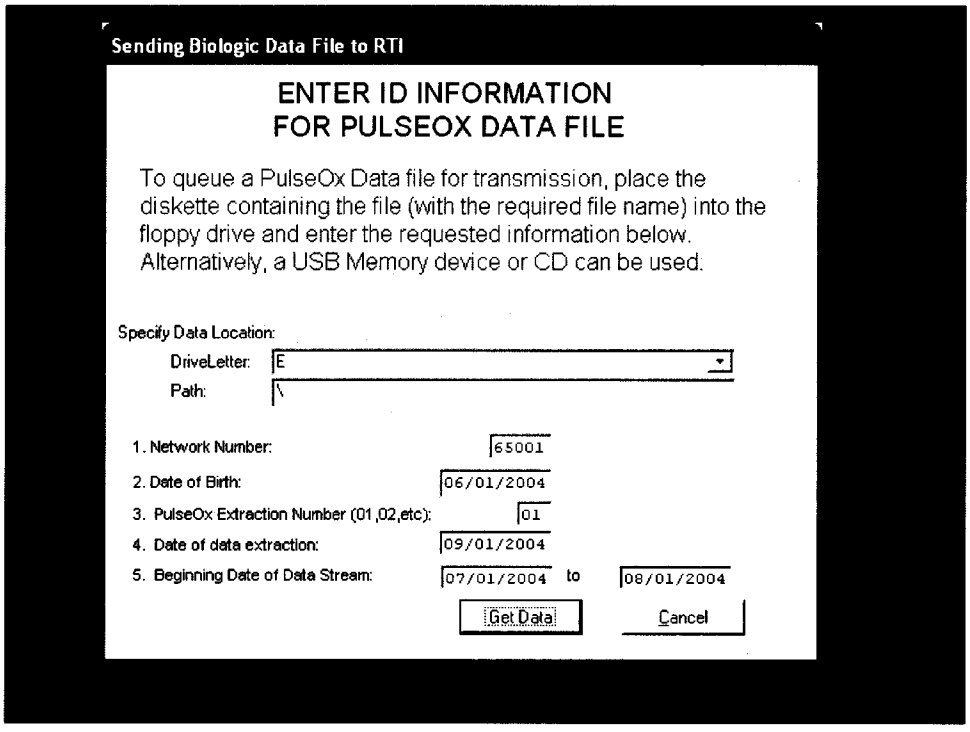
Save to USB Stick or Floppy. Name of File should be:

CCNNNNNEE.DAT Example is Site 22, Network # 1006, Family number 1, Extraction #3

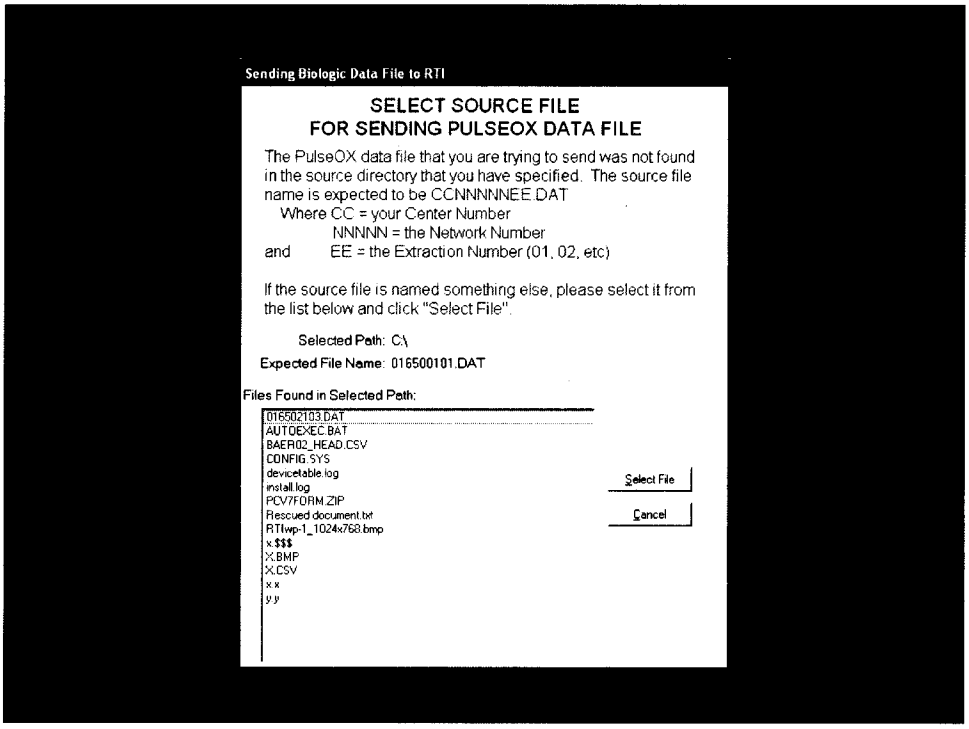
N=Network #, C=Center #, E=Extraction #

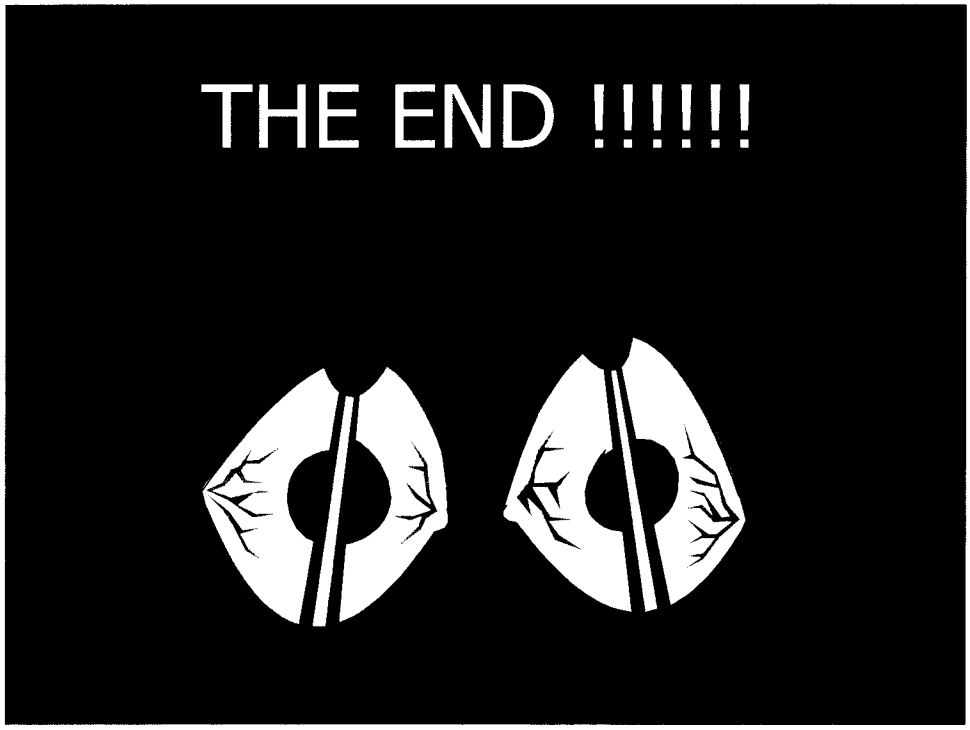



rptSuppTl.og : Report
NICHD NEONATAL RESEARCH NETWORK
SUPPORT STUDY PulseOx Data Transmission Report
PulseOx Data Transmissions for All Infants
GDB Network Number
Mother's Initials
Date of Birth
Data Extraction Number
PulseOx Metering Start Date
PulseOx Metering End Date
Date Data Extracted From Meter
Date Data Loaded onto Network Comp
65001 AAA 06/01/2004 01 07/01/2004 08/01/2004 09/01/2004 09/10/2004
65021 TIA 02/01/2004 01 07/01/2004 08/01/2004 09/05/2004 09/10/2004
65021 TIA 02/01/2004 03 08/01/2004 09/01/2004 09/05/2004 09/10/2004
Page:


Sending Biologic Data File to RTI
ENTER ID INFORMATION
FOR PULSEOX DATA FILE
To queue a PulseOx Data file for transmission, place the diskette containing the file (with the required file name) into the floppy drive and enter the requested information below. Alternatively, a USB Memory device or CD can be used.
Specify Data Location:
DriveLetter: E
Path: \
1. Network Number: 65001
2. Date of Birth: 06/01/2004
3. PulseOx Extraction Number (01,02,etc): 01
4. Date of data extraction: 09/01/2004
5. Beginning Date of Data Stream: 07/01/2004 to 08/01/2004
Get Data
Cancel


DISKETTE REQUIRED
Please plug the USB Memory Device into the computers' USB Port!
OK
Cancel


Sending Biologic Data File to RTI
SELECT SOURCE FILE
FOR SENDING PULSEOX DATA FILE
The PulseOX data file that you are trying to send was not found in the source directory that you have specified. The source file name is expected to be CCNNNNNEE.DAT
Where CC = your Center Number
NNNNN = the Network Number
and EE = the Extraction Number (01, 02, etc)
If the source file is named something else, please select it from the list below and click "Select File".
Selected Path: C:\
Expected File Name: 016500101.DAT
Files Found in Selected Path:
016502103.DAT
AUTOEXEC.BAT
BAER02_HEAD.CSV
CONFIG.SYS
devicetable.log
install.log
PCV7FORM.ZIP
Rescued document.txt
RTIwp-1_1024x768.bmp
x.$$$
X.BMP
X.CSV
x.x
y.y
Select File
Cancel


THE END !!!!!!

APPENDIX E

RETURN MATERIAL AUTHORIZATION FORM (RMA)

SHIP TO:

MASIMO®

40 Parker
Irvine, CA 92618 USA
Tel: 1 800 326-4890
Fax: 949-297-7499
Email tech@masimo.com

RETURNED MATERIAL AUTHORIZATION

xxxx

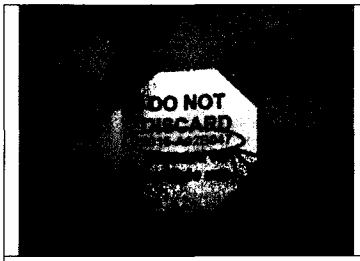
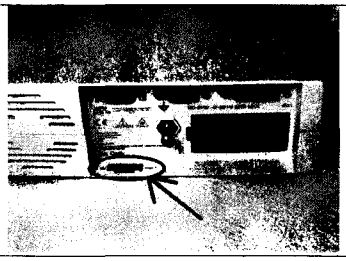
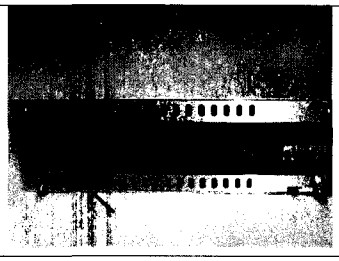
PLEASE ENSURE ALL RETURNED PRODUCTS ARE BIO HAZARD CLEANED

1. Complete this form.
2. Return this form with the product by affixing to the outside of the container with a clear shipper.

THANK YOU!

FACILITY NAME				
RETURN SHIP TO ADDRESS				
PHONE NUMBER				
FAX NUMBER				
EMAIL ADDRESS				
PO NUMBER				
CONTACT NAME				
DEPARTMENT				
PRODUCT				
SERIAL/LOT #				
DISCREPANCY				
PRODUCT				
SERIAL/LOT #				
DISCREPANCY				

How to locate the Serial or Lot number

			
Sensors & Cables (On DO NOT DISCARD label on cable)	**Radical™ Handheld (On rear of unit)**	**Radical™ Docking Station (On rear of unit)**	**Rad-9™ (On rear of unit)**

APPENDIX F

Management of Oxygen Concentrations and Oxygen Saturations in the Infant <28 weeks Gestational Age

OBJECTIVE: To avoid hyperoxia and high/low swings in oxygen saturations in the infant<28 wk GA while receiving supplemental oxygen.

1. Initiate the protocol with the admission of each infant with GA less than 28 weeks at birth.
2. No infant will be subject at any time to repeated swings in the amount of O2 being delivered in response to the saturation readings outside the acceptable range.

STATEMENTS OF PRACTICE:

a. Oxygen is a drug with potentially toxic side effects. Too much can be as damaging as too little. There is no evidence that <28 week infants need saturations in the 95-100% range (while receiving supplemental oxygen) and these levels are potentially dangerous. Alternating episodes of hypoxia and hyperoxia can cause significant alterations in the vascular tone of <28 week infants.

b. Saturation alarms:
   1. Assess the validity of the alarm:
   - Is the pulse wave appropriate?
   - Is there artifact interference?
   - Has the saturation been down low enough for long enough to warrant an increase in FiO2?
     (see Desaturation Management Guidelines)

c. Alarm settings: The alarms should be set at 84% and 96%. Note that Masimo alarms go off at the set value. Thus, these alarm settings are equivalent to alarms commonly set at 85% and 95% on other pulse oximeters. *The alarms should not be disabled at any time while receiving supplemental oxygen*

d. Weaning FiO2 and oxygen saturation levels:
   Wean by 2-5% if the saturation is high (>95%).
   - Weaning should be done as fast as necessary to avoid extended periods of hyperoxia. (But not faster than 2-5% at a time)

- Avoid weaning in increments >5% at a time; this could result in hypoxia, which would then lead to increasing the FiO2 again.

e. Increasing the FiO2 and saturation levels:
Increase the FiO2 by 2-5% if the saturation is low (<85%).

- When an increase is needed in the FiO2, the person making the change should stay with the infant until the infant has reached a stable saturation level.
- MD/NNP must be notified for any sustained need for an increase in FiO2 greater than 10% from the previously stable FiO2.

f. During and after procedures:
- FiO2 should not be routinely increased prior to a procedure. Individual infants may require modest increases (5-10%) if they tolerate handling poorly. Respond appropriately to the needs of the infant based on the saturations as well as the length and type of procedure.
- Monitor the infant after suctioning the ETT until the baby returns to their previously stable baseline.
- Consider that other settings (rate, PIP, PEEP) may need to be changed for a prolonged procedure.

g. Spontaneous oxygen desaturations:
- Assess both the infant and the ventilator and/or oxygen delivery systems.

h. Apnea:
- Choose the appropriate response based on assessment of the infant; increase respiratory rate, increase the approved parameters, tactile stimulation, or in severe cases manual ventilation.
- If the baby does not return to the previously stable baseline (same FiO2) within 10 minutes, the MD/NNP should be notified.

SUMMARY:

1. Set oxygen saturation monitor alarm limits at 84 and 96%.

2. Allow baby to fluctuate within the desired saturation parameters, making small movements up and down on FiO2 as needed.
3. Based on assessment, wean actively by 2-5% for saturations on the high side of parameters.
4. Never increase the FiO2 without first assessing the baby.
5. If the need for increased FiO2 is sustained, the MD/NNP should be notified.
6. Document saturation levels and oxygen requirements clearly (as per unit policy).
7. When altering the oxygen being delivered stay with the infant until the saturations have stabilized within an acceptable range.

I certify that I have read the above practice plan and agree to follow the objectives and statements of practice when caring for infants in the NICU.

_____

Printed Name (optional)

_____

Signature (optional)

_____

Date

APPENDIX G

SUPPORT
SATURATION RANGE
GOAL 85-95%
IF BABY IS OUT OF RANGE

SaO_2 is	Wait	Adjust FiO_2 by
80-85 or 95-99	1 min.	2%
70-80 or 100	1 min.	2-5%
<70	30 sec.	5%

NICU Network

The SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants
NICU Admission and Procedures Form

SUPP04 version 1.1
January 4, 2005
Revised November 1, 2006
Revised October 15, 2007

Center: ___ Site: ___ Network No. ____ Birth No. ___ Mother's Initials: ___

A. NICU ADMISSION

1. Date and time of NICU admission:

a. Date: __/__/__ (Month Day Year) b. Time: __:__ (Hour Min)

2. Respiratory Support on admission to the NICU: ___

1= HVF	2= CV	3= Nasal SIMV	4=CPAP	5= NC	6= Hood	7= No Support

3. SaO_2 ___

4. FiO_2 ___

5. Was a blood gas done after admission to the NICU? Y N

If yes, record the first blood gas after admission.

a. Date: __/__/__ (Month Day Year) b. Time: __:__ (Hour Min)

c. Source: ___

1= Arterial	2= Venous	3= Capillary

d. pH ___

e. pCO_2 ___

f. pO_2 ___

g. FiO_2 ___

6. Date and time the study oximeter was placed on this infant.

a. Date: __/__/__ (Month Day Year) b. Time: __:__ (Hour Min)

c. Serial number: ____

B. NICU PROCEDURES

1. Was the infant intubated for the first time within the first 14 days after admission to the NICU? Y N

If Yes,

a. Date: __/__/__ (Month Day Year) b. Time: __:__ (Hour Min)

c. Indication for intubation:

1. Surfactant? Y N
2. FiO_2 > .50 to maintain SaO_2 ≥88%? Y N
3. pCO_2 >65 on single blood gas? Y N
4. Apnea requiring bag and mask ventilation? Y N
5. If No to all above, state reason: ___

1= Hemodynamic instability	2 = Clinical shock/sepsis	3 = Other

If Other (3), specify_____

2. Was a blood gas done within 30 minutes prior to intubation? Y N
Complete this question only if Q.B.1 = YES

If Yes,

a. Date: __/__/__ (Month Day Year) b. Time: __:__ (Hour Min)

c. Source: ___

1= Arterial	2= Venous	3= Capillary

d. pH ___

e. pCO2 ___

f. pO2 ___

g. FiO2 ___

3. Was Surfactant given in the NICU? Y N

If Yes, record the following for each dose: If more than 4 doses given see FORM SUPP04a

a) Dose#	b) Date: (Month Day Year)	c) Time: (Hour Min)	d) Type:*
1	__/__/__	__:__	___
2	__/__/__	__:__	___
3	__/__/__	__:__	___
4	__/__/__	__:__	___

*1= Infasurf	2= Curosurf	3= Survanta	4= Exosurf	5= Other (Specify)

If Other (5), specify_____

Initials of person completing this form: ___

NICU Admission and Procedures Form (Surfactant Doses)

Center: ___ Site: ___ Network No. ____ Birth No. ___ Mother's Initials: ___

This form is to be completed if more that 4 surfactant doses are given between the first dose in the NICU and day 14 of study.

B. NICU PROCEDURES

Record additional surfactant doses below.

a) Dose#	b) Date:	c) Time:	d) Type:*
5	__/__/____ Month Day Year	__:__ Hour Min	___ (if code 5, specify _____)
6	__/__/____ Month Day Year	__:__ Hour Min	___ (if code 5, specify _____)
7	__/__/____ Month Day Year	__:__ Hour Min	___ (if code 5, specify _____)
8	__/__/____ Month Day Year	__:__ Hour Min	___ (if code 5, specify _____)
9	__/__/____ Month Day Year	__:__ Hour Min	___ (if code 5, specify _____)
10	__/__/____ Month Day Year	__:__ Hour Min	___ (if code 5, specify _____)
11	__/__/____ Month Day Year	__:__ Hour Min	___ (if code 5, specify _____)
12	__/__/____ Month Day Year	__:__ Hour Min	___ (if code 5, specify _____)
13	__/__/____ Month Day Year	__:__ Hour Min	___ (if code 5, specify _____)
14	__/__/____ Month Day Year	__:__ Hour Min	___ (if code 5, specify _____)
15	__/__/____ Month Day Year	__:__ Hour Min	___ (if code 5, specify _____)

*1= Infasurf 2= Curosurf 3= Survanta 4= Exosurf 5= Other (Specify)

Initials of person completing this form: ___

NICU Network

The SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants
SAFETY MONITORING FORM

SUPP05 version 4.0
October 3, 2005
Revised March 7, 2006,
Revised November 1, 2006
Revised October 15, 2007

Center: ___ Site No: ___ Network No: _____ Birth No: ___ Mother's Initials: ____

Complete a form each day through DOL 14 **1. Study Day:** ___ **2. Date:** ___/___/_____.

3. FiO2: Record FiO2 and respiratory support closest to the Scheduled Time.

(a) Scheduled Time	(b) Time Measured (hour : min)	(f) FiO_2	(h)** Mode of Support	(i) If Mode =5 record flow rate	***(j) If Mode =4 (CPAP) Type used
1. 02 : 00	___:___	__.___	___	__.___	___
2. 04 : 00	___:___	__.___	___	__.___	___
3. 06 : 00	___:___	__.___	___	__.___	___
4. 08 : 00	___:___	__.___	___	__.___	___
5. 10 : 00	___:___	__.___	___	__.___	___
6. 12 : 00	___:___	__.___	___	__.___	___
7. 14 : 00	___:___	__.___	___	__.___	___
8. 16 : 00	___:___	__.___	___	__.___	___
9. 18 : 00	___:___	__.___	___	__.___	___
10. 20 : 00	___:___	__.___	___	__.___	___
11. 22 : 00	___:___	__.___	___	__.___	___
12. 23 : 59	___:___	__.___	___	__.___	___

5. Oximeter Alarm Checks Q6hr/day

a. ___:___
b. ___:___
c. ___:___
d. ___:___

6. Was the Infant intubated or extubated on this day? Y N

If Yes, complete the SUPP05A

Initials of person completing this form: ___

4. Blood Gas Information: Record blood gas results closest to the Scheduled Time, if available.

(a) Scheduled Time	(b) Time Measured (hour : min)	(c) pH	(d) CO2	(e) PO2	(f) FiO_2	(g)* Source	(h)** Mode of Support	(i) If Mode =5 record flow rate	***(j) If Mode =4 (CPAP) Type used
1. 08 : 00	___:___	__.___	___	___	__.___	___	___	__.___	___
2. 16 : 00	___:___	__.___	___	___	__.___	___	___	__.___	___
3. 23 : 59	___:___	__.___	___	___	__.___	___	___	__.___	___

* Source	1= Arterial	2= Venous	3= Capillary

**Mode	1= HFV	2= CV	3= Nasal SIMV	4= CPAP	5= NC	6=Hood	7= No Support	8= Infant temporarily out of unit	9=No Support all day and off Study oximeter

***CPAP Type	2= Ventilator	4= Bubble	6 = Flow Driver	9= Other

NICU Network

The SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants
Adverse Event Form

SUPP08 version 3.0
March 10, 2005
Revised November 1, 2006
Revised October 15, 2007

Center: ___ Site No: ___ Network No: _____ Birth No: ___ Mother's Initials: ____ Report No. ___

Complete this form for any randomized infant who experienced one or more of the following adverse events during the initial 14 days of life.
This form will be keyed at the sites.

ADVERSE EVENT			DATE Of ONSET (mm/dd/yyyy)	ATTRIBUTABLE TO SUPPORT STUDY 0 = No 1 = Not likely 2 = Possibly 3 = Probably	COMMENTS
1. Air leak	(Code Y/N)	(If yes, Mode)*	If yes, record each date of onset		
a. Pneumothorax	Y N	___	__/__/____	___	
b. PIE	Y N	___	__/__/____	___	
c. Pneumopericardium	Y N	___	__/__/____	___	
2. Need for chest compressions and/or epinephrine in the delivery room			__/__/____	___	
3. The occurrence of severe IVH (grades III-IV)			__/__/____	___	
4. Pulmonary Hemorrhage			__/__/____	___	
5. Nasal breakdown requiring discontinuation of nasal prongs			__/__/____	___	
6. Death			Date of Death __/__/____	___	
7. Other (Specify) _____ _____ _____ ___			__/__/____	___	

*Code most proximate mode of ventilatory support for each occurrence.

1= HFV 2= CV 3= Nasal SIMV 4= CPAP 5= NC 6=Hood 7= No Support 8= Infant temporarily out of unit 9= No Support all day and not on study oximeter

Initials of Person Completing this Form: ___

NICU Network

The SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants
OUTCOME STATUS FORM

SUPP09 version 1.4
January 4, 2005
Revised October 26, 2005
Revised November 1, 2006
Revised January11, 2007
Revised October 15, 2007

Center: __ __ Site: __ Network No. __ __ __ __ Birth No. __ Mother's Initials: __ __ __

Complete this form when the infant is discharged to home, transferred, if hospitalized at 120 days, ~~or~~ death or withdrawn (whichever comes first).

A. INFANT OUTCOME

1. Status: _____

1 = Discharged home alive	4 = Transferred to a chronic care facility.
2 = Still in hospital at 120 Days	5 = Death
3 = Transferred to another hospital	6 = Withdrawn from study

2. Date of Status: __ __/__ __/__ __ __ __ (Month / Day / Year)

B. NEUROLOGIC

1. Did infant have a head ultrasound between 4 - 21 days of age? Y N

If YES,

a. Date: __ __/__ __/__ __ __ __ (Month / Day / Year) b. Time: __ __ : __ __ (Hour / Min)

c. Infarct? Y N

d. IVH? Y N

If YES,

1) IVH Grade: ___

1 = I 2 = II 3 = III 4 = IV

e. PVL? Y N

C. OPHTHALMOLOGY

1. Was an exam performed for ROP? Y N

If YES, Complete the SUPP10 Form

If No, and the infant survived, complete the SUPP10 (ROP) form based on subsequent exams (including back-transfer hospital and/or outpatient visits)

D. POSTNATAL STERIOD USE

1. Did the infant receive postnatal steroids after the first 21 days of life? Y N

If YES,

(a) Course	(b) Start Date (Month/ Day/ Year)	(c) Stop Date (Month/ Day/ Year)	(d) *Drug	(e) Total Dose (mg/kg)
1	__ __/__ __/__ __ __ __	__ __/__ __/__ __ __ __	___	__ __ . __ __
2	__ __/__ __/__ __ __ __	__ __/__ __/__ __ __ __	___	__ __ . __ __
3	__ __/__ __/__ __ __ __	__ __/__ __/__ __ __ __	___	__ __ . __ __
4	__ __/__ __/__ __ __ __	__ __/__ __/__ __ __ __	___	__ __ . __ __
5	__ __/__ __/__ __ __ __	__ __/__ __/__ __ __ __	___	__ __ . __ __

*Drug Codes	
1= Dexamethasone	4= Prednisone
2= Betamethasone	5= Other (Specify)_____
3= Hydrocortisone	

Initials of person completing this form: __ __ __

NICU Network

The SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants

SUPP10 Rel 2.0
March 10, 2005
Revised October 15, 2007

ROP OUTCOMES AND TRACKING SUMMARY

Center: ___ Site: ___ Network No. _____ Birth No. ___ Mother's Initials: _____

Record the data for each eye examination (in or outpatient) until both eyes are acute/final. Indicate when examinations switch from the NICU to a back-transfer hospital, or to outpatient

	Examination Results										Examination Results										STATUS***			
	Left Eye										Right Eye													
Date of Exam	Location of Exam	Lowest* Zone of any Vessels	Highest+ Stage in lowest Zone	Highest+ Stage In any Zone	"Plus Disease"		Threshold (New Type 1)		Surgery^	Post-surgical Retinal** Detachment	Lowest* Zone of any Vessels	Highest+ Stage in lowest zone	Highest+ Stage In any Zone	"Plus Disease"		Threshold (New Type 1)		Surgery^	Post-surgical Retinal** Detachment	Final Acute Status Lost to Follow-up at 55 weeks PMA		Final ROP Status determined at 18M Follow Up	
1.__/__/__	___	___	___	___	Y	N	Y	N	___	___	___	___	___	Y	N	Y	N	___	___	Y	N	Y	N
2.__/__/__	___	___	___	___	Y	N	Y	N	___	___	___	___	___	Y	N	Y	N	___	___	Y	N	Y	N
3.__/__/__	___	___	___	___	Y	N	Y	N	___	___	___	___	___	Y	N	Y	N	___	___	Y	N	Y	N
4.__/__/__	___	___	___	___	Y	N	Y	N	___	___	___	___	___	Y	N	Y	N	___	___	Y	N	Y	N
5.__/__/__	___	___	___	___	Y	N	Y	N	___	___	___	___	___	Y	N	Y	N	___	___	Y	N	Y	N
6.__/__/__	___	___	___	___	Y	N	Y	N	___	___	___	___	___	Y	N	Y	N	___	___	Y	N	Y	N
7.__/__/__	___	___	___	___	Y	N	Y	N	___	___	___	___	___	Y	N	Y	N	___	___	Y	N	Y	N
8.__/__/__	___	___	___	___	Y	N	Y	N	___	___	___	___	___	Y	N	Y	N	___	___	Y	N	Y	N
9.__/__/__	___	___	___	___	Y	N	Y	N	___	___	___	___	___	Y	N	Y	N	___	___	Y	N	Y	N
10.__/__/__	___	___	___	___	Y	N	Y	N	___	___	___	___	___	Y	N	Y	N	___	___	Y	N	Y	N

LOCATION:	1= Inpatient	2 = Outpatient	3= Transfer Hospital

*ZONE:	1= I	2 = II	3= III	4 = Mature	5= Status post laser/cryo	9=Unable to determine

+ STAGE:	0= No ROP	1= Stage 1	2=Stage 2	3= Stage 3	4= Stage 4a or 4b	5= Stage 5	6= Post laser/cryo (do not use stages)	9 = Old scars, but no active ROP

^ SURGERY:	0= No surgery this day	1= Laser	2= Cryotherapy	3= Both laser/cryo	4=Scleral buckle	5= Vitrectomy	6= Other

**RETINAL DETACHMENT:	0= None	3= Partial, not involving macula (stage 4a)	4 = Partial, does involve macula (stage 4b)	5 = Complete	9=View obscured, can't tell

*** *only answer these questions for the last eye exam entered*

Complete this form daily from study day 15 through 36 weeks or status, whichever comes first.

Date of 36 weeks __ __ / __ __ / __ __ __ __

Study Day	15 __ __/__ __/__ __ __ __ Month Day Year	16 __ __/__ __/__ __ __ __ Month Day Year	17 __ __/__ __/__ __ __ __ Month Day Year	18 __ __/__ __/__ __ __ __ Month Day Year	19 __ __/__ __/__ __ __ __ Month Day Year	20 __ __/__ __/__ __ __ __ Month Day Year
1. Scheduled Time: 06:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
2. Scheduled Time: 12:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
3. Scheduled Time: 18:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
4. Scheduled Time: 23:59	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __

****Mode** 1= HFV 2= CV 3= Nasal SIMV 4= CPAP 5= NC 6=Hood 7= No Support 8= Infant temporarily out of unit 9= No Support all day and not on study oximeter

Complete this form daily from study day 15 through 36 weeks or status, whichever comes first.

Date of 36 weeks __ __ / __ __ / __ __ __ __

Study Day	21	22	23	24	25	26
	__ __ / __ __ / __ __ __ __ Month Day Year	__ __ / __ __ / __ __ __ __ Month Day Year	__ __ / __ __ / __ __ __ __ Month Day Year	__ __ / __ __ / __ __ __ __ Month Day Year	__ __ / __ __ / __ __ __ __ Month Day Year	__ __ / __ __ / __ __ __ __ Month Day Year
1. Scheduled Time: 06:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
2. Scheduled Time: 12:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
3. Scheduled Time: 18:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
4. Scheduled Time: 23:59	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __

****Mode** 1= HFV 2= CV 3= Nasal SIMV 4= CPAP 5= NC 6=Hood 7= No Support 8= Infant temporarily out of unit 9= No Support all day and not on study oximeter

Complete this form daily from study day 15 through 36 weeks or status, whichever comes first.

Date of 36 weeks __ __ / __ __ / __ __ __ __

Study Day	27 __ __/__ __/__ __ __ __ Month Day Year	28 __ __/__ __/__ __ __ __ Month Day Year	29 __ __/__ __/__ __ __ __ Month Day Year	30 __ __/__ __/__ __ __ __ Month Day Year	31 __ __/__ __/__ __ __ __ Month Day Year	32 __ __/__ __/__ __ __ __ Month Day Year
1. Scheduled Time: 06:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
2. Scheduled Time: 12:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
3. Scheduled Time: 18:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
4. Scheduled Time: 23:59	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __

****Mode** 1= HFV 2= CV 3= Nasal SIMV 4= CPAP 5= NC 6=Hood 7= No Support 8= Infant temporarily out of unit 9= No Support all day and not on study oximeter

Complete this form daily from study day 15 through 36 weeks or status, whichever comes first.

Date of 36 weeks __ __ / __ __ / __ __ __ __

Study Day	33 __ __/__ __/__ __ __ __ Month Day Year	34 __ __/__ __/__ __ __ __ Month Day Year	35 __ __/__ __/__ __ __ __ Month Day Year	36 __ __/__ __/__ __ __ __ Month Day Year	37 __ __/__ __/__ __ __ __ Month Day Year	38 __ __/__ __/__ __ __ __ Month Day Year
1. Scheduled Time: 06:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
2. Scheduled Time: 12:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
3. Scheduled Time: 18:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
4. Scheduled Time: 23:59	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __

****Mode** 1= HFV 2= CV 3= Nasal SIMV 4= CPAP 5= NC 6=Hood 7= No Support 8= Infant temporarily out of unit 9= No Support all day and not on study oximeter

Complete this form daily from study day 15 through 36 weeks or status, whichever comes first.

Date of 36 weeks __ __ / __ __ / __ __ __ __

Study Day	39 __ __/__ __/__ __ __ __ Month Day Year	40 __ __/__ __/__ __ __ __ Month Day Year	41 __ __/__ __/__ __ __ __ Month Day Year	42 __ __/__ __/__ __ __ __ Month Day Year	43 __ __/__ __/__ __ __ __ Month Day Year	44 __ __/__ __/__ __ __ __ Month Day Year
1. Scheduled Time: 06:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
2. Scheduled Time: 12:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
3. Scheduled Time: 18:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
4. Scheduled Time: 23:59	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __

****Mode** 1= HFV 2= CV 3= Nasal SIMV 4= CPAP 5= NC 6=Hood 7= No Support 8= Infant temporarily out of unit 9= No Support all day and not on study oximeter

Complete this form daily from study day 15 through 36 weeks or status, whichever comes first.

Date of 36 weeks ___/___/____

Study Day	45 __ __/__ __/__ __ __ __ Month Day Year	46 __ __/__ __/__ __ __ __ Month Day Year	47 __ __/__ __/__ __ __ __ Month Day Year	48 __ __/__ __/__ __ __ __ Month Day Year	49 __ __/__ __/__ __ __ __ Month Day Year	50 __ __/__ __/__ __ __ __ Month Day Year
1. Scheduled Time: 06:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)						
(b) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
2. Scheduled Time: 12:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)						
(b) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
3. Scheduled Time: 18:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)						
(b) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
4. Scheduled Time: 23:59	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)						
(b) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __

****Mode** 1= HFV 2= CV 3= Nasal SIMV 4= CPAP 5= NC 6=Hood 7= No Support 8= Infant temporarily out of unit 9= No Support all day and not on study oximeter

Complete this form daily from study day 15 through 36 weeks or status, whichever comes first.

Date of 36 weeks __ __ / __ __ / __ __ __ __

Study Day	51 __ __/__ __/__ __ __ __ Month Day Year	52 __ __/__ __/__ __ __ __ Month Day Year	53 __ __/__ __/__ __ __ __ Month Day Year	54 __ __/__ __/__ __ __ __ Month Day Year	55 __ __/__ __/__ __ __ __ Month Day Year	56 __ __/__ __/__ __ __ __ Month Day Year
1. Scheduled Time: 06:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
2. Scheduled Time: 12:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
3. Scheduled Time: 18:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
4. Scheduled Time: 23:59	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __

****Mode** 1= HFV 2= CV 3= Nasal SIMV 4= CPAP 5= NC 6=Hood 7= No Support 8= Infant temporarily out of unit 9= No Support all day and not on study oximeter

Complete this form daily from study day 15 through 36 weeks or status, whichever comes first.

Date of 36 weeks __ __ / __ __ / __ __ __ __

Study Day	57 __ __/__ __/__ __ __ __ Month Day Year	58 __ __/__ __/__ __ __ __ Month Day Year	59 __ __/__ __/__ __ __ __ Month Day Year	60 __ __/__ __/__ __ __ __ Month Day Year	61 __ __/__ __/__ __ __ __ Month Day Year	62 __ __/__ __/__ __ __ __ Month Day Year
1. Scheduled Time: 06:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
2. Scheduled Time: 12:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
3. Scheduled Time: 18:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
4. Scheduled Time: 23:59	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.	__ __ . __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __

****Mode** 1= HFV 2= CV 3= Nasal SIMV 4= CPAP 5= NC 6=Hood 7= No Support 8= Infant temporarily out of unit 9= No Support all day and not on study oximeter

Complete this form daily from study day 15 through 36 weeks or status, whichever comes first.

Date of 36 weeks __ __ / __ __ / __ __ __ __

Study Day	63	64	65	66	67	68
	__ __ / __ __ / __ __ __ __ Month Day Year	__ __ / __ __ / __ __ __ __ Month Day Year	__ __ / __ __ / __ __ __ __ Month Day Year	__ __ / __ __ / __ __ __ __ Month Day Year	__ __ / __ __ / __ __ __ __ Month Day Year	__ __ / __ __ / __ __ __ __ Month Day Year
1. Scheduled Time: 06:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
2. Scheduled Time: 12:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
3. Scheduled Time: 18:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
4. Scheduled Time: 23:59	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __

****Mode** 1= HFV 2= CV 3= Nasal SIMV 4= CPAP 5= NC 6=Hood 7= No Support 8= Infant temporarily out of unit 9= No Support all day and not on study oximeter

Complete this form daily from study day 15 through 36 weeks or status, whichever comes first.

Date of 36 weeks __ __ / __ __ / __ __ __ __

Study Day	69 __ __/__ __/__ __ __ __ Month Day Year	70 __ __/__ __/__ __ __ __ Month Day Year	71 __ __/__ __/__ __ __ __ Month Day Year	72 __ __/__ __/__ __ __ __ Month Day Year	73 __ __/__ __/__ __ __ __ Month Day Year	74 __ __/__ __/__ __ __ __ Month Day Year
1. Scheduled Time: 06:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
2. Scheduled Time: 12:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
3. Scheduled Time: 18:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
4. Scheduled Time: 23:59	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __

****Mode** 1= HFV 2= CV 3= Nasal SIMV 4= CPAP 5= NC 6=Hood 7= No Support 8= Infant temporarily out of unit 9= No Support all day and not on study oximeter

Complete this form daily from study day 15 through 36 weeks or status, whichever comes first.

Date of 36 weeks __ __ / __ __ / __ __ __ __

Study Day	75 __ __/__ __/__ __ __ __ Month Day Year	76 __ __/__ __/__ __ __ __ Month Day Year	77 __ __/__ __/__ __ __ __ Month Day Year	78 __ __/__ __/__ __ __ __ Month Day Year	79 __ __/__ __/__ __ __ __ Month Day Year	80 __ __/__ __/__ __ __ __ Month Day Year
1. Scheduled Time: 06:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
2. Scheduled Time: 12:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
3. Scheduled Time: 18:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
4. Scheduled Time: 23:59	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)	__	__	__	__	__	__
(b) Oxygen	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO	YES / NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __

****Mode** 1= HFV 2= CV 3= Nasal SIMV 4= CPAP 5= NC 6=Hood 7= No Support 8= Infant temporarily out of unit 9= No Support all day and not on study oximeter

Complete this form daily from study day 15 through 36 weeks or status, whichever comes first.

Date of 36 weeks ___ / ___ / ____

Study Day	81 ___/___/____ Month Day Year	82 ___/___/____ Month Day Year	83 ___/___/____ Month Day Year	84 ___/___/____ Month Day Year	85 ___/___/____ Month Day Year	86 ___/___/____ Month Day Year
1. Scheduled Time: 06:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)						
(b) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
2. Scheduled Time: 12:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)						
(b) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
3. Scheduled Time: 18:00	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)						
(b) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
4. Scheduled Time: 23:59	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)	__ __ : __ __ (time measured)
(a) Highest Level of Support (Mode)						
(b) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(c) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(d) Oximeter Alarm Check	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __

****Mode** 1= HFV 2= CV 3= Nasal SIMV 4= CPAP 5= NC 6=Hood 7= No Support 8= Infant temporarily out of unit 9= No Support all day and not on study oximeter

From: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT
Date: Saturday, October 27, 2007 11:15:23 AM

Hi
I am wondering if we can bring up your site specific issue with NEC and saturations on the next coordinator call (nov - third thursday).? We have brought up site specific issues along the way and have found it helpful as the trial moves along. Let us know

Thanks
Rose

Sent from my BlackBerry Wireless Handheld

From:	Ellen Hale
To:	Higgins, Rosemary (NIH/NICHD) [E]; kzaterka@rti.org
Subject:	SUPPORT IRB renewal (Spanish)
Date:	Thursday, October 25, 2007 1:22:56 PM
Attachments:	1158-2004Modificationr11.2007.pdf

Please find attached our new approved Spanish consent and HIPAA.
Ellen

Institutional Review Board
1256 Briarcliff Road, 307-N
Atlanta, GA 30306

Phone (404) 712-0720
Fax (404) 727-1358
http://www.emory.edu/IRB

REQUEST FOR MODIFICATION

Modification #: _11_____

Section I: Investigator Information

IRB Number 1158-2004	Title The Surfactant Positive Pressure and Pulse Oxim	ry Trial in Extremely Low Birth Weight Infants
Principal Investigator Susie Buchter, MD	Interoffice Address (Include Departm	nt, Bldg, Room, & mail stop number PO Box 26015 80 Jesse Hill, Jr. Dr. Atlanta, GA 30030
Contact Name Ellen Hale, RN		
Phone 404-616-4218	Fax 404-524-3953	Email ehale@em ry.edu

Section II: Type of Modification Select All that apply

☐	Amendment	(Attach a Narrative and Supporting documentation) Amendment # _____ Date of Amendment _____
☐	New Procedures	Describe how the change affects the risk/benefit: (Atta h a description of the procedures)
☐	Change in Study Personnel	☐ add ☐ delete ☐ change Include role of personnel, address, pho e, fax, email for additions – REMEMBER, all persons on a study must have current C TI certification.
☐	Change of Site	☐ add ☐ delete ☐ modify (Attach a narrative that ists the resulting sites)
☐	Change in Enrollment	(Attach narrative justifying the change) increase #_____ decrease #_____ resulth total _____ to be enrolled
☒ ☐	Consent Change New Consent	Version Date: 10/04/2007 8/14/2007 RD Highlighted changes and A clean copy must be attached Date: _____ Targeted Population: _____
☐	Advertisement	Select All that apply and attach copies of ad or announ ement ☐ Newspaper Ad – Name of Paper _____ ☐ Radio Announcement – Station _____ ☐ Internet Posting - Web-site _____ ☐ Post on Clinical Trials Web site (www.emoryhealth are.org/clinicaltrials) ☐ Television Announcement – Station _____ ☐ Flyer – Distributed where _____ ☐ Information Brochure - Distributed how _____ ☐ Other - Describe:_____ Has this ad been approved by the sponsor? ☐ Yes ☐ No ☐ N/A
☐	Clinical Investigator's Brochure	Select one: ☐ Addendum ☐ Updated ☐ N v Date: Date: Date: Should consent be changed based upon this revision? ☐ Yes ☐ No
☐	Funding	☐ Add Agency Name: ☐ Delete Agency Name:
☐	Site	List all sites this amendment applies to:
☐	Other	(e.g., Annual Report, Package Insert, General Corresp idence) Describe and attach a narrative.

☒ Supporting documentation is attached. (e.g., Narrative, highlighted consent, form 1572, etc.) MANDATORY

PI Signature Susie Buchter, MD / Ellen Haller Date 10/13/07

Faculty Advisor (if PI is student) _____ Date _____

NARRATIVE: Please, find attached the Spanish translation of the informed consent and HIPAA authorization that was translated from the English version and was approved by the IRB on October 5, 2007. (The changes to the Spanish version are the same as the ones that were approved for the English version.) We currently do not have an approved Spanish version of these documents and request approval as soon as possible so that we may not miss approaching any families for this very important study.
Thank you for your continued support.

Section III. IRB USE ONLY

*** Protocol expiration is not changed by the approval of this modification***

✓ The Modification has been approved.

___ The Correspondence has been acknowledged.

✓ Consent(s) and/or HIPAA Authorization dated 4 Oct 07 has been approved.

___ Subjects currently enrolled must sign the new consent.

IRB Committee Member

Approval Date: 18 Oct 07 14 AUG 07 RD Approval Type: ___ Full ✓ Expedited

Section below for Research Studies Performed at the Atlanta VA

Section IV. RESEARCH & DEVELOPMENT COMMITTEE USE ONLY

___ Modification has been approved by the R&D Committee

R&D Committee Chair

Approval Date

Universidad Emory – Escuela de Medicina
Consentimiento para ser Sujeto de Investigación

Título: El Surfactante Presión Positiva de Vía Aerea y Ensayo de Pulso Oximetry en Infantes de Bajo Peso Extremo al Nacer

Investigador Principal: Susie Buchter, M.D.,I.P.
Barbara J. Stoll, M.D., Co-I.P.

Nombre del Patrocinador: Instituto Nacional de la Salud de Niño/a y Desarrollo Humano (NICHD) (en Inglés)

Introducción/Propósito:

A usted se le ha preguntado si voluntariamente permitiría que su bebé participe en un estudio de investigación. Hay la posibilidad de que su bebé nazca de 16 a 12 semanas antes (24-28 semanas de edad gestacional). Los bebés que nacen con esta anticipación, generalmente tienen dificultad en respirar. Los pulmones no están suficientemente maduros para trabajar bien y permitir la respiración independientemente. La mayoría de los bebés que nacen con esta anticipación necesitan ayuda para respirar y/o oxígeno adicional. Si necesitaría, esta ayuda empieza el momento del nacimiento en la sala de partos.

Este estudio examinará el uso de CPAP en la sala de partos. CPAP es una presión positiva aplicada con una máscara en la cara para ayudar a mantener los pulmones inflados. Este estudio también examinará los niveles de saturación de oxígeno (niveles de oxígeno en la sangre) en bebés prematuros.

Es sabido que los problemas de respiración de los bebés pueden mejorar al poner un líquido en sus pulmones (surfactante). Este líquido se pone en los pulmones colocando un tubo en la traquea (entubación). Luego, la respiración es mantenida con una máquina para respirar y/o oxígeno extra.

Sin embargo, cuando los bebés tienen este apoyo por mucho tiempo, esto empieza a hacerr daño a sus pulmones. Esto puede ser causa de que el bebé sea dependiente de este apoyo extra por largo tiempo. Estudios realizados en Europa han sugerido que el uso temprano de CPAP puede reducir la necesidad de entubación en bebés muy prematuros.

No hay una forma establecida para el uso de CPAP/Final positivo de la presión expiratoria para resuscitación en la sala de partos para infantes prematuros diminutos. Esta presión es dada usando una máscara puesta sobre la cara del bebé. La presión puede también ser dada usando unas puntas colocadas en la nariz del bebé. La presión se produce usando máquinas de respiración comunes. Hay también dispositivos especiales que son designados para transmitir tal presión.

Estudios han sugerido que el uso temprano de CPAP y tratar de no usar una máquina de respiración puede tener mejores resultados para los bebés. Estos bebés podrían tener también una disminución en la necesidad de la terapia con surfactante. Estos bebés podrían también tener una disminución en la necesidad de oxígeno adicional. El tratamiento corriente comunmente usado es la administración de surfactante. Surfactante es producido por el pulmón normal. Surfactante es carente en los infantes muy prematuros. El uso de surfactante ha sido asociado con la disminución de muertes y problemas respiratorios. Ambos, el uso de CPAP y

de surfactante pueden ser buenos. No ha habido un estudio para comparar el uso de CPAP con el tratamiento con surfactante que empiece luego del nacimiento y continue en la unidad de cuidados intensivos (NICU) .

Retinopatia de la Prematurez (ROP) es un problema comun en los ojos de los infantes prematuros diminutos. Los vasos sanguineos que nutren los ojos del infante prematuro no estan desarrollados totalmente. Vasos pequeños en la retina (parte del ojo) pueden tener períodos de aumento o crecimiento rápido y agresivo. Con el tiempo la ROP puede mejorar o empeorar. Usualmente la ROP sanará sin ningún problema. Si la ROP es peor que lo usual, hay la posibilidad de que los vasos sanguineos crezcan fuera de control. Si esto pasa, una cirugía puede ser necesaria para prevenir cicatrices dentro del ojo. Estas cicatrices pueden causar una pérdida de visión severa.

Recibir extra oxígeno por largo tiempo, puede tambien dañar los ojos del bebé. Otro estudio ha indicado que menos cirugías de los ojos fueron necesarias usando bajos limites de oxígeno.

Hay dos propósitos para este estudio. Primero, nosotros compararemos dos tipos de cuidado diferences en la sala de partos. Compararemos infantes que reciben CPAP en la sala de partos y los que tienen un tubo para respirar y que se les administra surfactante. Segundo, nosotros compararemos una escala baja (85-89%) nivel de saturación de oxígeno, con una escala alta (91-95%). Queremos saber si un bajo nivel de oxígeno en los bebés puede prevenir este problema grave en los ojos.

Este estudio se lleva a cabo en los Hospitales Grady Memorial Hospital y Crawford W. Long. Otros quince centros médicos en los Estados Unidos son también parte de este estudio. El Instituto Nacional de la Salud del Niño y Desarrollo Humano (NICHD) patrocina esta investigación. Su bebé será elegible para participar en este estudio solamente sin nace entre las semanas 24 y 27. Este estudio durará al rededor de dos años y se inscribirán aproximadamente 1.300 infantes a nivel nacional. Más o menos 100 bebés serán estudiados en Emory.

Procedimientos:

Si usted está de acuerdo con este estudio y autoriza la participación de su bebé, debe hacer lo siguiente: Antes del parto su bebé será asignado a uno de los dos tratamientos. Esto será al azar (como lanzar una moneda). En el primer grupo de tratamiento, su bebé podría recibir CPAP en la sala de partos para ayudarle con la respiración. Si su bebé es parte del segundo grupo de tratamiento, un tubo será puesto en la traquea del bebé para ayudarle a respirar. Después de que el tubo es instalado, una dosis de surfactante será administrada a través del tubo. Los dos grupos de tratamientos son criterios comunes del cuidado de los bebés prematuros en la sala de partos.

Al mismo tiempo que su bebé es asignado a un grupo de tratamiento, él o ella será asignado al azar (como lanzar una moneda) a un grupo de monitoreo de oxígeno alto o bajo. Su bebé será tratado usando un nivel de saturación del oxígeno ya sea bajo (85-89%) o alto (91-95%). Nosotros empezaremos el monitoreo de saturación del oxígeno a las 2 horas de edad. Los dos niveles de oxígeno usados en este estudio son en los mismos niveles que usamos en nuestras unidades de cuidados intensivos (NICU) actualmente. En este estudio nosotros trataremos de mantener a su bebé en uno de estos dos niveles. Cada uno de estos 4 grupos posibles de tratamiento es considerado cuidado establecido en las unidades de cuidado intensivo (NICU) en Emory. El estudio se llevará a cabo durante el tiempo completo que su bebé esté con oxígeno, mientras él o ella está en la unidad de cuidados intensivos (NICU).

Un exámen de los ojos final será realizado a los 3 meses de edad corregida (3 meses después de la fecha asignada para el nacimiento del bebé). Si su bebé ha sido dado de alta del hospital antes de esta fecha, una cita para el control de los ojos como paciente externo será programada. Esta cita para el control de los ojos es parte del cuidado regular. Como parte del estudio nosotros recogeremos información del exámen de los ojos. Podremos necesitar una copia del examen de los ojos de su bebé, si se lo hace despues de haberle dado el alta.

Como parte de este estudio nosotros controlaremos el crecimiento de su bebé. La enfermera encargada de la investigación medirá el largo del bebé y el diametro de su cabeza. Nosotros obtendremos la información del peso del bebé de los registro médicos. Obtendremos información acerca de la alimentación que el bebé recibe, de su registro médico. Esta información será recogida durante ocho diferentes veces empezando el día de nacimiento del bebé y finalizando el día que el bebé es dado de alta para ir a casa con usted. Queremos saber si la tasa de crecimiento de los bebés en este estudio es diferente o similar.

Queremos saber si su bebé tiene problemas respiratorios después de lo que fue dado de alta para ir a casa. También queremos saber si su bebé necesita cuidado extra para ayudarle a respirar. Como parte de este estudio nosotros seguiremos muy de cerca la evolución de su bebé obteniendo información de usted el momento que sea dado de alta y luego cuando él/ella esté en casa. Nosotros le llamaremos a usted por teléfono para recibir información, cuando el bebé tenga 6, 12, y 18 meses de edad. Cada llamada telefónica durará alrededor de 15 minutos de su tiempo. Un miembro del grupo de investigadores le hará preguntas acerca de la salud de las diferentes personas con las que su bebé tiene contacto . Usted será preguntado acerca de la respiración de su bebé. Se le preguntará acerca de las visitas que su bebé podria hacer al doctor, a la clínica, al departamento de emergencia o al hospital. Nosotros le daremos un folleto para ayudarle a coleccionar la información que nosotros necesitaremos acerca de su bebé.

Su bebé sera controlado por este estudio hasta que él o ella sea dado de alta del hospital. Como parte del cuidado establecido la Clínica Emory del Progreso Desarrollado (DCP en Inglés) seguirá la evolución de su bebé. A los 18 meses de edad, él o ella será examinado en la Clínica DPC como parte de un programa de seguimiento. En la visita de los 18 meses a usted se le solicitará que permita a su bebé ser parte de estudio de seguimiento. Se le solicitará a usted que firme un consentimiento separado. Esta información será compartida con el Estudio de seguimiento de todos los bebes prematuros diminutos NICHD. En ese momento nosotros controlaremos el crecimiento de su bebé. Nosotros también realizaremos exámenes físico, neurológico y de desarrollo.

Riesgos:

Los tratamientos de los cuales se han hablado en este estudio son de cuidado estandar. Sin embargo, entubación, administración de surfactante y CPAP tienen su riesgo. Riesgos por la entubación pueden incluir: inadecuada instalación del tubo y daño en la traquea por el tubo. Riesgos por el sufactante pueden ser: desigual distribución del liquido y sangrado en los pulmones. Otro riesgo podria ser efecto retardado del uso del surfactante mientras CPAP es usado. Riesgos del CPAP podrian ser daño de la nariz y demasiada inflación de los pulmones. No hay aumento previsible en riesgo sobre el cuidado estandar de su bebe. Algunos riesgos no conocidos podrían ser aprendidos durante el estudio. Si esto pasa, el grupo de investigadores le harán saber

Beneficios:

Si cualquier tratamiento de grupo es encontrado como un medio para trartar de mejor manera a los bebés, su bebé podría ser beneficiado por el estudio. Pero tomar parte en este estudio puede no bebeficiar a su bebé. Los doctors pueden aprender nuevas cosas que pueden ayudar a los bebés en el futuro.

Alternativas:

Usted puede escoger que su bebé no sea parte de este estudio y su bebé continuará recibiendo un cuidado establecido de salud. El cuidado básico establecido en Grady y Crawford Long es evaluar la respiración del bebé al nacer. La mayoría de los bebés muy prematuros son entubados y reciben surfactane. Pocos recibirán CPAP en la sala de partos o más tarde en la unidad de cuidados intensivos. Las escalas de oxígeno usadas en este estudio, son las mismas escalas que se usan en nuestra Unidad de Cuidados Intensivos.

Confidencialidad:

Otras personas además de los que están realizando el estudio, pueden revisar tanto los registros médicos como los registros del estudio. Agencias que hacen las reglas y políticas acerca de cómo la investigación está hecha tienen derecho de revisar los registros. También las agencias que pagan por el estudio. Todos aquellos con derecho de revisar los registros de estudio de su bebé son: Administración de Alimientos y Medicinas, la Oficina para la Protección de Investigación Humana, el Instituto Nacional de la Salud del Niño y Desarrollo Humano, la Junta de Revisión Institucional de la Universidad Emory, el Comité Grady que controla las Equivocaciones en la Investigación. Los registros pueden ser abiertos por la orden de un juzgado. Nosotros guardaremos los registros de su bebé en privado en todo lo permitido por la ley. Nosotros haremos esto aún si la revisión es por personas u organizaciones externas. Nosotros usaremos un número de estudio en lugar del nombre de su bebé en los registros del estudio donde nosotros podamos. El nombre de su bebé y otros datos que puedan señalar que se trata de él o ella no aparecerán cuando nosotros presentemos este estudio o publiquemos los resultados.

Si usted es o ha sido un paciente de los hospitales de Emory, usted debe tener registros médicos en los hospitales de Emory. Si usted no es y nunca ha sido un paciente de los hospitales de Emory, no se creará ningún registro médico solo por su participación en este estudio de investigación.

Los resultados de los exámenes de este estudio y procedimientos que se han llevado a cabo, analizado y/o leído en o para los hospitales de Emory, y que pueden ser usados con propósitos del cuidado de la salud serán puestos en los registros médicos que usted tienen con los hospitales de Emory. Además una copia del formulario de consentimiento y el formulario de autorización HIPPA que usted firmó, serán puestos con todos sus registros médicos que usted tenga en los hospitles de Emory. Las personas que tienen acceso a sus registros médicos, tendrán acceso a todos los resultados y documentos puestos en los registros, y los resultados y documentos pueden ser utilizados por los hospitales de Emory como ayuda para proveerle a usted de cuidado médico. Cualquier resultado y documento que son guardados como parte de su registro médico no son cubiertos por ciertas leyes federales y estatales y regulaciones que pueden impedir la revelación de los datos de investigación. Sin embargo, la confidencialidad de los resultados y otros documentos en el registro médico será dictada por leyes tales como HIPPA que involucra registros médicos.

La Universidad Emory no tiene ningún control sobre los resultados de exámenes y procedimientos llevados a cabo y/o analizados o leídos en instalaciones que no son de los Hospitales de Emory. Estos resultados NO son rutinariamente incluídos en los registros médicos de los hospitales de Emory, y no estarán disponibles necesariamente para los proveedores de salud de Emory. La Universidad Emory tampoco tiene control sobre otro registro médico que usted pueda tener con otros proveedores del cuidado de la salud y no enviará ningún resultado de examene o procedimientos de este estudio a esos proveedores. Es su decisión dejar saber a estos proveedores de salud de su participacion es este ensayo clinico.

Algunos exámenes y procedimientos que pueden ser llevados a cabo durante este estudio por los hospitales de Emory u otros hospitales y personas NO PODRAN SER EXAMINADOS NI LEIDOS PARA NINGUN PROPOSITO DE TRATAMIENTO O DIAGNOSTICO DEL CUIDADO DE SALUD. ESTOS EXAMENES Y PROCEDIMIENTOS SOLO SERAN EXAMINADOS CON PROPOSITOS DE LA INVESTIGACION Y LOS RESULTADOS NO SERAN REVISADOS PARA HACER DECISIONES ACERCA DE SU SALUD PERSONAL O TRATAMIENTO. Tipos específicos de exámenes o procedimientos, si hay alguno, que es parte de esta categoría son listados debajo:
NINGUNO

Costos y Compensación:

No habrá ningún costo para usted o su bebé por participar en este estudio. No se le pagará a usted por estar en este estudio. Si su bebé es lesionado como resultado de esta investigación, habrá cuidado médico disponible. Sin embargo la Universidad Emory (incluyendo el Hospital Crawford Long) y el Sistema de Salud de Grady no han reservado fondos para pagarle por este cuidado o compensarle si ocurre este percance. Si usted cree que su bebé ha sido lesionado por esta investigación, usted debería contactar a la Dra. Susie Buchter, la investigadora a cargo del estudio, al número de teléfono: 404-778-1450.

Persona a quien contactar:

Llame a la Dra. Susie Buchter al número de teléfono (404) 778-1450 si tiene preguntas acerca de este estudio o si siente que su bebé ha sido perjudicado por estar en éste estudio. Si usted tiene alguna pregunta o preocupación acerca de sus derechos como participante en el estudio, llame a Colleen Dilorio, Ph.D., Presidenta de la Junta Institucional de Revisión de la Universidad Emory al número de teléfono (404) 712-0720. Si su bebé es un paciente del Hospital Grady, usted puede llamar al Dr. Curtis Lewis, Vice Presidente Superior de los Asuntos Médicos, al número de teléfono (404) 616-4261.

Nuevos Encuentros:

Nosotros nos podemos enterar de nuevas cosas durante el estudio que usted puede necesitar saber. Nosotros nos podemos enterar también de cosas que podrían hacer que usted quiera dejar de participar en el estudio. Si eso pasa, le notificaremos cualquier información nueva.

Participación Voluntaria y Abstinencia:

La participacion en este estudio es voluntaria. Usted tienen el derecho de rechazar la participación de su bebe en este estudio. Si usted decide dejar que su bebé participe en el estudio y cambia de manera de pensar, usted tiene el derecho de retirarse en cualquier momento Esta decisión no afectará de ninguna manera el cuidado médico presente y futuro de su bebé. Esta decisión no afectará ningún otro beneficio que se le haya dado.

A pesar que su bebé será tratado de acuerdo a un plan específico (protocolo), circunstancias individuales pueden surgir. En tales casos, la salud de su bebé siempre será considerada más importante que seguir el estudio estrictamente. Cambios serán discutidos antes de ser realizados cuando sea possible.

Nosotros le daremos una copia de este formulario de consentimiento para que lo guarde.

Si usted está dispuesto a ofrecer la participación de su bebé en esta investigación, por favor firme debajo.

_____
Nombre del Sujeto

_____	_____	_____
Representante Legal del Sujeto	***Fecha***	***Hora***
_____	_____	_____
Persona que Obtiene el Consentimiento	***Fecha***	***Hora***

IRB#: 1158-2004

Consent Form Approval Period

FROM: 10-18-07 **TO:** 9-24-08

AUTHORIZATION: RD

Universidad Emory – Escuela de Medicina

Sujeto de Investigación, Autorización HIPAA para el Uso o Revelación de Información Médica que lo identifique a usted para un Estudio de Investigación

Nombre del Estudio: **El Surfactante Presión Positiva de Vía Aerea y Ensayo de Pulso Oximetry en Infantes de Bajo Peso Extremo al Nacer**

Número del Estudio: 1158-2004

Nombre del Investigador Principal: Susie Buchter, MD, Investigador Principal

Barbara J. Stoll, MD, Co-Investigator Principal

Nombre del Sujeto:_____

La privacidad de su información médica es importante para nosotros. Para proteger su información médica que lo identifica a usted, nosotros seguiremos todos los requerimientos que aplica el Decreto de Responsabilidad y Portabilidad del Seguro Médico ("HIPAA" siglas en Inglés). Este formulario le hará saber a usted como usaremos cualquier información médica que le identifique a usted y que usted nos proporcione para este estudio.

Por favor lea este formulario con cuidado y si está de acuerdo con lo que dice, firme al final.

Estudio de Investigación: Este studio lo lleva a cabo el Instituto Nacional de la Salud de Niño y el Desarrollo Humano (NICHD en Inglés). El propósito de este estudio es comparar infantes que reciben CPAP en la sala de partos y quienes tienen pautas estrictas por tener instalado un tubo para poder respirar, con infantes que tienen instalado el tubo y se les administra surfactante en la sala de partos. Este studio también comparará el bajo alcance de los niveles de saturación del oxigeno con un alto alcance para determinar si el resultado del alcance bajo resulta en la disminución de los limites de la enfermedad de los ojos y/o la necesidad de una cirugia de los ojos.

Personas que Usarán o Revelarán su Información Médica y Propósitos de éste Uso o Revelación:

La siguientes personas y grupos usarán y revelarán su información médica en relación con este estudio. En este formulario, todas estas personas y grupos son llamados los "Usuarios de Información ":

El Investigador Principal, su personal de investigadores, y personas y organizaciones que él o ella usa como ayuda para llevar a cabo este estudio de investigación usarán y revelarán su información médica para hacer este trabajo. .

El Instituto Nacional de la Salud del Niño y Desarrollo Humano es el patrocinador de esta investigación. El Patrocinador, y todas las otras persona y organizaciones que el patrocinador contrata como ayuda para dirigir y supervisar el Estudio de Investigación pueden usar o revelar su información médica para estar seguros de que la investigación ha sido hecha correctamente y para recoger y analizar los resultados de la investigación.

Hay un número de personas y unidades de la Universidad, agencias del gobierno, y otros individuos y organizaciones que pueden usar y revelar su información médica para estar seguros de que el Estudio de Investigación se esta llevando a cabo en una forma correcta y segura, y para controlar y regular la investigación o asuntos de salud pública. Entre estas personas y organizaciones se incluyen las siguientes: La Junta de Revisión Institucional de la Universida Emory; El Comité Grady que controla las Equivocaciones en la Investigación (ROC en Inglés); La Oficina de Ensayos Clínicos de la Universida Emory; la Oficina de Adaptabilidad de la Investigación de la Universidad Emory; El Instituto de Investigación Triangular (RTI en Inglés); controladores y críticos de la investigación; juntas que controlan la segurida de los datos; cualquier agencia de gobierno que regule la investigación, incluyendo la Ofinica de Protección de Investigación con Humanos; el Instituo Nacional de la Salud del Niño y Desarrollo Humano; y el Departamento de Pediatría de la Universida de Rochester.

Al firmar este document usted está de acuerdo en permitir a cualquiera de estos Usuarios de Información el uso o revelación de su información médica que lo identifica, para llevar a cabo este Estudio de Investigación, o para controlar o regular la investigación. Además nosotros acataremos toda ley que require que nosotros revelemos su información médica, tales leyes como las que requieren que nosotros reportemos abuso de menores, o de ancianos. También nosotros acataremos solicitudes legales u ordenes que requieren que nosotros revelemos su información médica tales como citaciones u ordenes de un juzgado. Finalmente nosotros podemos compartir su información médica con una autoridad de salud pública que la ley autorise para recoger o recibir tal información con el propósito de controlar o prevenir enfermedades, lesiones, o incapacidad y/o conducir vigilancias, investigaciones o intervensiones de salud pública

Descripción de la Información Médica que lo identifica y que será usada o revelada.

La Información: Los usuarios pueden usar o revelar la siguiente información médica acerca de usted: registro médico, resultados de examenes de laboratorio, reportes radiológicos, examenes de los ojos, respuestas a las preguntas de la encuesta, y resultados del estudio.

Revocando su Autorización:

Usted no tiene que firmar esta autorización. Además, si usted firma esta autorización, luego usted puede cambiar su manera de pensar en cualquier momento y revocar (retractarse) de esta Autorización. Si usted quiere revocar esta autorización usted debe escribir a :

Dra. Susie Buchter
P.O. Box 26015, 80 Jesse Hill, Jr. Drive
Atlanta, GA 30303.

Si usted revoca su Autorización, los investigadores no recogerán más información médica suya, pero ellos puede usar o reveler información identificable que usted ya les haya dado a ellos para notificar a cualquiera de los otros usuarios que usted ha revocado su autorizacion; para mantener la integridad y confiabilidad del Estudio de Investigación y para cumplir con cualquier ley que es requisito obedecer.

Otros Puntos que Usted Debería Saber:

HIPAA aplica solo a personas y organizaciones que son proveedores del servicio médico, los que pagan por los servicios médicos o para intercambio de información de los servicios médicos. HIPAA puede no aplicar a todos los Usuarios de Información. Si HIPAA no aplica a un Usuario de Información, entonces ese usuario no tiene que seguir los requerimientos de HIPAA cuando usa o revela su información médica.

Usted no tiene que firmar este formulario de autorización, pero si usted no firma, usted puede no participar en el Estudio de Investigación o recibir tratamiento relacionado a la investigación. Pero usted puede todavía recibir tratamiento no- relacionado a la investigación.

Nosotros pondremos una copia de su informe de consentimiento firmado para el Estudio de Investigación y el formulario de su Autorización HIPPA firmada en todo registro médico que usted pueda tener con los Hospitales de Emory. Los resultados de procedimientos médicos y de laboratorio recibidos de los hospitales de Emory podrían ser puestos en los registros médicos que usted tiene con los Hospitales de Emory.

Si el estudio de investigación incluye tratamiento médico, entonces para mantener la integridad del estudio de Investigación, usted generalmente no tendrá acceso a su información médica personal relacionada con el estudio de investigación hasta que se complete el estudio. Cuando se complete el estudio, entonces, si usted solicita, usted puede tener acceso a alguna de su información médica personal relacionada con la investigación que completa una parte de la información médica y /o otros registros que su proveedor de cuidado de su salud usa para hacer decisiones acerca de usted. Si el acceso a esta información es necesaria antes de finalizar el Estudio de Investigación para su tratamiento, entonces esta información será facilitada a su médico.

Si la información que lo identifica es quitada de su información médica, entonces la información que queda no será sujeto de esta autorización, ni será cubierta por HIPPA, y esta puede ser usada o revelada a otras personas u organizaciones y/o para otros propósitos.

Fecha de Expiración: Esta autorización expirará al finalizar el período de investigación y todos los períodos relacionados con el mantenimiento de registros.

Como participante en el estudio, si usted tiene alguna pregunta relacionada con el estudio, usted puede llama a la Dra. Susie Buchter, Investigadora Principal del Estudio al número de teléfono (404) 778-1450. Si usted tiene alguna pregunta referente a sus derechos como sujeto del estudio, usted puede llamar a la Dra. Colleen DiIorio, Presidenta de la Junta de Revisión Institucional de la Universidad Emory, al número de teléfono (404) 712-0720.

Una copia de este formulario de autorización le será dada a usted.

_____

Firma del Sujeto de Estudio O Representante Legal Autorizado del Sujeto

Fecha _____ Hora_____

IRB#: 1158-2004

Consent Form Approval Period

FROM: 10-18-07 TO: 9-24-08

AUTHORIZATION: RD

_____

Nombre Impreso del Sujeto de Estudio O Representante Legal Autorizado del Sujeto

Si es el Representante, Cuál es la Relación con el Sujeto del Estudio:

_____

_____

Firma de la Persona que Obtiene la Autorización

Fecha _____ Hora _____

IRB#: 1158-2004

Consent Form Approval Period

FROM: 10-18-07 TO: 9-24-08

AUTHORIZATION: RD

Version Date(s): 11/22/2005; revised 8/14/2007

From: Ellen Hale
To: Higgins, Rosemary (NIH/NICHD) [E]; kzaterka@rti.org
Subject: SUPPORT IRB renewal (English)
Date: Thursday, October 25, 2007 1:21:34 PM
Attachments: 1158-2004RenewalApproval07.pdf

Please find attached our IRB renewal for SUPPORT with English consent.
Ellen

EMORY UNIVERSITY | Institutional Review Board

Susie Buchter
SOM: Pediatrics
2015 Uppergate Drive
Atlanta, GA 30322

RE: **NOTIFICATION OF RENEWAL APPROVAL**
PI: Susie Buchter
IRB ID: **1158-2004**

TITLE: The Surfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants

DATE: October 05, 2007

Renewal Review Type: Full

The continuing approval request referenced above was reviewed and APPROVED by the IRB. This approval is valid from **09/25/2007 until 09/24/2008.** Thereafter, continued approval is contingent upon the submission of a renewal form that must be reviewed and approved by the IRB prior to the expiration date of this study.

A partial waiver of authorization has been granted by the Emory University IRB for the purpose of determining eligibility or recruiting subjects for this protocol. This waiver was reviewed and approved under the review procedure note above. The approval is granted based on this board's determination that all criteria for waiver of authorization have been met. As subjects are enrolled, you are required to obtain authorization. The PHI that may be used or disclosed for this use is limited to: Hospital records, Laboratory results, Pathology results, Radiology results.

Any serious adverse events or issues resulting from this study should be reported immediately to the IRB and to any sponsoring agency (if any). Amendments to protocols and/or revisions to informed consent forms/process must have approval of the IRB before being implemented.

All inquiries and correspondence concerning this protocol must include the IRB number and the name of the Principal Investigator.

If you have any questions or concerns, please contact the IRB office at 404-712-0720 or at email address irb@emory.edu . Our web address is http://www.emory.edu/IRB . Thank you.

Sincerely,

Ann M. Haight, MD
Vice Chair
Institutional Review Board

cc: Ellen Hale R.N.
Barbara J. Stoll MD

This approval is valid from 10/5/2007 until 10/4/2008.

PAGE 2 of RENEWAL APPROVAL

IRB ID: **1158-2004** DATE: October 05, 2007

TITLE: The Surfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants

The above referenced protocol renewal was approved including the information below. Please review this information for accuracy. If there are any discrepancies, please notify your IRB coordinator immediately.

Informed Consents Associated with this protocol:

Version Date	Description
8 /14/2007	HIPAA Authorization
10/4 /2007	Main Consent: Surfactant Positive Airway

Personnel		**Human Subjects Education Certification Information**
Hale, Ellen	Protocol Contact	CITI - MED Refresher Course (30-Jun-2006)
Blackwelder, Ann M	Study Nurse	CITI - MED Refresher (24-Aug-2006)
Buchter, Susie	Main Investigator	CITI - MED Refresher (23-Oct-2006)
Piazza, Anthony J	Co-Investigator	CITI - MED 1, 2, 3, 4, 5, 6, 7, 9, 10, 11, 12, 14 (19-Dec-2006)
Stoll, Barbara J.	Co-Investigator	CITI - MED Refresher Course (29-Jun-2006)
Tidwell, Freda Michelle	Study Nurse	CITI - MED 1, 2, 3, 7, 8, 10, 12, 14, 17 (20-feb-2006)

Number of Approved Emory Subjects 100 **(This number indicates the number of subjects you can consent.)**

Sites

Crawford Long Hospital

Grady Memorial Hospital

Funding Agencies

NICHD - National Institute of Child Health and Human

Emory University School of Medicine
Consent to be a Research Subject

Title: The Surfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants

Principal Investigator: Susie Buchter, M.D., P.I.
Barbara J. Stoll, M.D., Co-P.I.

Sponsor's Name: National Institute of Child Health and Human Development (NICHD)

Introduction/Purpose:

You are being asked to volunteer your baby for a research study. There is a possibility that your baby will be born between 16 and 12 weeks early (24-28 weeks gestational age). Babies born this early usually have difficulty breathing. Their lungs are not mature enough to work well so that the babies can breathe on their own. Most all babies born at this early age will need assistance breathing and or extra oxygen. If needed, this support begins at birth in the delivery room.

This study will look at the use of CPAP in the delivery room. CPAP is positive pressure applied with a facemask to help keep the lungs inflated. This study will also look at the levels of oxygen saturation (oxygen levels in the blood) in premature babies.

It is known that the breathing problems of babies can be improved by putting a liquid in the lungs (surfactant). This liquid is put into the lungs by placing a tube in the windpipe (intubation). Afterwards, breathing is supported with a breathing machine and or extra oxygen.

However, when babies get this support for a long time, their lungs can become injured. This may cause the baby to be dependent upon the extra support for a long time. Studies from Europe have suggested that early CPAP can reduce the need for intubation in very premature infants.

There is no standard way to use CPAP/Positive End Expiratory Pressure for resuscitation in the delivery room for tiny premature infants. This pressure is given using a mask placed on the baby's face. The pressure may also be given using prongs placed in the infant's nostrils. The pressure is produced using current breathing machines. There are also special devices that are designed to deliver such pressures.

Studies have suggested that the use of early CPAP and trying not to use a breathing machine may have a better outcome for babies. These babies may also have a decreased need for surfactant therapy. These babies may also have a decreased need for additional oxygen. The current commonly used treatment is surfactant administration. Surfactant is produced by the normal lung. It is lacking in very preterm infants. Its use has been connected with a decrease in death and respiratory problems. Both the uses of CPAP and surfactant may be good. There has not been a study to compare the use of CPAP with surfactant treatment begins after delivery and continues in the NICU.

Retinopathy of Prematurity (ROP) is a common eye problem in tiny premature infants. Blood vessels that nourish the preterm infant's eyes are not fully developed. Small vessels in the retina (part of the eye) may have periods of increased or rapid and wild growth. Over time ROP can get

better or get worse. Usually ROP will heal without any problems. If the ROP is worse than usual, there is a chance that the blood vessels will grow out of control. If this happens, surgery may be needed to prevent scars inside the eye. These scars can cause severe vision loss.

Getting extra oxygen for a long time can also damage the baby's eyes. Another study has shown that less eye surgery was needed in special nurseries using lower oxygen limits.

There are two purposes of this study. First of all, we will compare two different types of care in the delivery room. We will compare infants who receive delivery room CPAP and those who have a breathing tube and surfactant given. Secondly, we will compare low range (85-89%) oxygen saturation levels with a high range (91-95%). We want to know if a lower oxygen level in babies can prevent this bad eye problem.

This study is being performed at Grady Memorial Hospital and Crawford W. Long Hospital. Fifteen other medical centers in the U.S. are also part of this study. The National Institute of Child Health and Human Development (NICHD) sponsors this research. Your baby will only be eligible for this study if you deliver between 24 and 27 weeks. The study will last about two years and will enroll about 1300 infants nationally. About 100 babies will be studied at Emory.

Procedures:

If you agree to this study and give consent for your baby, the following will happen. Prior to delivery, your baby will be assigned to one of two treatments. Assignment will be random (like flipping a coin). In the first treatment group, your baby would be placed on CPAP in the delivery room to help with their breathing. If your baby is in the second treatment group, a tube will be placed in his/her trachea (windpipe) to help with their breathing. After the tube is placed, a dose of Surfactant will be given in the tube. Both of these treatment groups are current standards of care for preterm babies in the delivery room.

At the same time that your baby is assigned to the above treatment group, he/she will also be randomly (like flipping a coin) assigned to a high or low oxygen monitoring group. Your baby will be treated using either a lower (85-89%) or higher (91-95%) oxygen saturation range. We will start this monitoring of oxygen saturation by 2 hours of age. Both of the ranges for oxygen used in this study are within the range that we currently use in our NICU. In this study we will try to maintain your baby within one of these 2 ranges. Each of these 4 possible treatment groups is considered the standard of care in the NICU at Emory. The study will take place during the entire time your baby is on oxygen while he/she is in the NICU.

A final eye exam will be done at 3 months corrected age (3 months after your due date for this baby). If your baby has been discharged from the hospital prior to this, an outpatient eye appointment will be scheduled. This eye appointment is part of standard of care. As part of the study, we will collect information about the eye exam. We may need to request a copy of your baby's eye exam if it is done after discharge.

As part of this study we will follow your baby's growth. A research nurse will measure your baby's length and the measurement around their head. We will collect your baby's weight from their chart. We will collect information about feedings your baby receives from the baby's chart. This information will be collected up to eight different times beginning on the day your baby is born and ending the day your baby is discharged to go home with you. We want to know if babies in this study grow at different rates or the same rate.

We want to know if your baby has breathing problems after they go home. We also want to know if your baby needs extra care to help them with their breathing. As part of this study we will follow your baby and collect information from you at discharge and after the baby goes home. We will call you by phone to get information when your baby is about 6, 12, and 18 months old. Each phone call will take about 15 minutes of your time. A member of the research team will ask you questions about the health of different people your baby comes in contact with. You will be asked questions about your baby's breathing. You will be asked questions about any visits your baby might have to the doctor, clinic, emergency room and hospital admissions. We will give you a brochure to help you record the information we will need about your baby.

Your baby will be followed for this study until he/she is discharged from the hospital. As part of standard of care the Emory Developmental Progress Clinic (DCP) will follow your baby. At 18 months of age, he/she will be seen in the DPC as part of our routine follow-up program. At the 18 month visit you will be asked to allow your baby to be part of a follow up study. You will be asked to sign a separate consent. Information will be shared with the NICHD Follow-up Study of very tiny premature babies. At that time we will look at your baby's growth. We will also perform physical and neurological testing and developmental testing.

Risks:

The treatments talked about in this study are all standard of care. However, intubation, administration of surfactant and CPAP are not without risk. Risks of intubation may include improper placement of tube and windpipe damage from the tube. Risks of surfactant could be unequal distribution of the liquid and bleeding into the lungs. Another risk could be delayed surfactant use while CPAP is being used. Risks of CPAP could be damage to the nose and overinflation of the lungs. There is no predictable increase in risks above standard of care for your baby. Some unknown risks may be learned during the study. If this happens, the research team will let you know.

Benefits:

If either treatment group is found to be a better way to treat babies, your baby may benefit from the study. But taking part in this study may not benefit your baby. Doctors may learn new things that may help babies in the future.

Alternatives:

You may choose not to have your baby take part in this study and your baby will continue to get the standard of care. The current standard of care at Grady and Crawford Long is to assess the baby's breathing at birth. The majority of babies born at this early date will be intubated and given surfactant. A few will receive CPAP in the delivery room or later in the intensive care nursery. Both of the ranges for oxygen used in this study are within the range that we currently use in our NICU.

Confidentiality:

People other than those doing the study may look at both medical charts and study records. Agencies that make rules and policy about how research is done have the right to review these records. So do agencies that pay for the study. Those with the right to look at your baby's study records include the Food and Drug Administration, the Office for Human Research Protections, National Institute of Child Health and Human Development, the Emory University Institutional Review Board, and Grady's Research Oversight Committee. Records can also be opened by court order. We will keep your baby's records private to the extent allowed by law. We will do this

even if outside review occurs. We will use a study number rather than your baby's name on study records where we can. Your baby's name and other facts that might point to him/her will not appear when we present this study or publish its results.

If you are or have been a patient at an Emory Healthcare facility, then you will have an Emory Healthcare medical record. If you are not and have never been a patient at an Emory Healthcare facility then no Emory Healthcare medical record will be created for you just because you are participating in a research study.

Results from study tests and procedures that are performed, analyzed and/or read at or for Emory Healthcare facilities that can be used for healthcare purposes will be placed in any medical record that you have with Emory Healthcare facilities. In addition, a copy of the informed consent form and HIPAA authorization form that you sign will be placed in any Emory Healthcare medical record you may have. Persons who have access to your medical record will be able to have access to all results and documents that are placed there, and the results/documents may be used by Emory Healthcare facilities to help provide you with medical care. Any results and documents that are kept as part of your medical record are not covered by certain state and federal laws and regulations that may prevent the disclosure of, research data. However, the confidentiality of the results and other documents in the medical record will be governed by laws such as HIPAA that concern medical records.

Emory University does not have any control over results from tests and procedures performed and/or analyzed or read at non-Emory Healthcare facilities. These results are NOT routinely included in medical records at Emory Healthcare facilities, and they will not necessarily be available to Emory Healthcare providers. Emory University also does not have control over any other medical records that you may have with other healthcare providers and will not send any test or procedure results from the study to these providers. It is up to you to let these healthcare providers know that you are participating in a clinical trial.

Some tests and procedures that may be performed during this study by Emory Healthcare or other facilities or persons MAY NOT BE LOOKED AT OR READ FOR ANY HEALTHCARE TREATMENT OR DIAGNOSTIC PURPOSES. THESE TESTS AND PROCEDURES WILL ONLY BE LOOKED AT FOR RESEARCH PURPOSES AND THE RESULTS WILL NOT BE REVIEWED TO MAKE DECISIONS ABOUT YOUR PERSONAL HEALTH OR TREATMENT. The specific types of tests or procedures, if any, that fall within this category are listed below: NONE

Costs and Compensation:

There will be no cost to you or your baby for being in this study. You will not be paid for being in this study. If your baby is injured as a result of this research, medical care will be available. However, Emory University (including Crawford Long Hospital) and the Grady Health System have not set aside funds to pay for this care or to compensate you if a mishap occurs. If you believe your baby has been injured by this research, you should contact Dr. Susie Buchter, the investigator in charge at 404-778-1450.

Contact Persons:

Call Dr. Susie Buchter at (404) 778-1450 if you have questions about this study or if you feel your baby has been harmed from being in this study. If you have any questions or concerns about your rights as a participant in this research study, contact Colleen Dilorio, Ph.D., Chairman, Emory University Institutional Review Board, at (404) 712-0720. If your baby is a patient at Grady

Hospital you may contact Dr. Curtis Lewis, Senior Vice President for Medical Affairs, at (404) 616-4261.

New Findings:

We may learn new things during the study that you may need to know. We can also learn about things that might make you want to stop participating in the study. If so, you will be notified about any new information.

Voluntary Participation and Withdrawal:

Participation in the study is voluntary. You have the right to refuse to let your baby be in this study. If you decide to let your baby be in this study and change your mind, you have the right to drop out at any time. This decision will not affect in any way your baby's current or future medical care. This decision will not affect any other benefits to which you are otherwise given.

Although your infant will be treated according to a specific plan (protocol), individual circumstances may arise. In such cases, your infant's health will always be considered more important than strictly following the study. Changes will be discussed before they are made whenever possible.

We will give you a copy of this consent form to keep.

If you're willing to volunteer your baby for this research, please sign below.

_____
Subject's name

_____	_____	_____
Subject's legally authorized representative	***Date***	***Time***
_____	_____	_____
Person Obtaining Consent	***Date***	***Time***

IRB#: 1158-2004
Consent Form Approval Period
FROM: 9/25/07 TO: 9/24/09
AUTHORIZATION: YLM

Emory University School of Medicine

Research Subject HIPAA **Authorization** to Use or Disclose Health Information that Identifies You for a Research Study

Name of Study: **The Surfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants** Study Number: 1158-2004

Name of Principal Investigator: Susie Buchter, MD, Principal Investigator

Barbara J. Stoll, MD, Co-Principal Investigator

Subject Name:_____

The privacy of your health information is important to us. In protecting your health information that identifies you, we will follow all requirements of the Health Insurance Portability and Accountability Act ("HIPAA" for short) that apply. This form will let you know how we will use any health information that you give us for this study that identifies you.

Please read this form carefully and if you agree with it, sign it at the end.

Research Study: This study is being conducted by the National Institute of Child Health and Human Development (NICHD). The purpose of this study is to compare infants who receive delivery room CPAP and who have strict guidelines for having a breathing tube placed with infants who have the tube placed and surfactant given in the delivery room. This study will also compare low range oxygen saturation levels with a high range to determine if a lower range results in decreased threshold eye disease and/or need for eye surgery.

People That Will Use or Disclose Your Health Information that Identifies You and Purpose of Use/Disclosure:

The following people and groups will use and disclose your health information in connection with the study. In this form, all of these people and groups are called the "Information Users":

The principal investigator, his/her research staff and people and organizations that he uses to help him conduct the Research Study will use and disclose your health information to do this work.

The National Institute of Child Health and Human Development is the sponsor of this Research. The sponsor and all other people and organizations that the sponsor retain to help it conduct and oversee the Research Study may use and disclose your health information to make sure that the research is being done correctly and to collect and analyze the results of the research.

There are a number of University persons/units, government agencies and other individuals and organizations that may use and disclose your health information to make sure that the Research Study is being conducted correctly and safely, and to monitor and regulate the research or public health issues. These people and organizations include the following: the Emory University Institutional Review Board; Grady Research Oversight

Committee (ROC); the Emory University Clinical Trials Office; the Emory University Office of Research Compliance; Research Triangle Institute (RTI); research monitors and reviewers; data safety monitoring boards; any government agencies who regulate the research including the Office of Human Subjects Research Protections; National Institute of Child Health and Human Development; and Department of Pediatrics University of Rochester.

By signing this document you agree to allow any of these Information Users to use or disclose your health information that identifies you in order to conduct the Research Study, or to monitor or regulate research. In addition, we will comply with any laws that require us to disclose your health information, such as laws that require us to report child abuse or elder abuse. We also will comply with legal requests, or orders that that require us to disclose your health information, such as subpoenas or court orders. Finally, we may share your health information with a public health authority that the law authorizes to collect or receive such information for the purpose of preventing or controlling disease, injury or disability and/or conducting public health surveillance, investigations or interventions.

Description of Health Information that Identifies You that Will be Used or Disclosed

The Information Users may use or disclose the following health information about you: medical record; laboratory results; radiology reports; eye examinations; answers to survey questions; and study results.

Revoking your Authorization:
You do not have to sign this Authorization. In addition, if you sign this Authorization, later, you may change your mind at any time and revoke (take back) this Authorization. If you want to revoke this Authorization you must write to:

Dr. Susie Buchter
P.O. Box 26015, 80 Jesse Hill, Jr. Drive
Atlanta, GA 30303.

If you revoke your Authorization, the Researchers will not collect any more health information that identifies you, but they may use or disclose identifiable information that you already gave them in order to notify any of the other Information Users that you have taken back your authorization; to maintain the integrity or reliability of the Research Study; and to comply with any law that they are required to obey.

Other Items You Should Know:

HIPAA only applies to people or organizations that are health care providers, health care payers or healthcare clearinghouses. HIPAA may not apply to all Information Users. If HIPAA doesn't apply to an Information User, then that User doesn't have to follow HIPAA requirements when it uses or discloses your health information..

You do not have to sign this authorization form, but if you do not, you may not participate in the Research Study or receive research-related treatment. You may still receive non-research related treatment.

We will put a copy of your signed informed consent form for the Research Study and your signed HIPAA Authorization form into any medical record that you may have with

Emory Healthcare facilities. Laboratory and medical procedure results received from Emory Healthcare facilities may also be placed in any medical record that you have with Emory Healthcare facilities.

If the Research Study involves medical treatment, then, in order to maintain the integrity of the research study, you generally will not have access to your personal health information related to this Research Study until the study is complete. When the study is complete, then, at your request, you may generally have access to any of your personal health information related to the research that makes up a part of the medical information and/or other records that your health care providers use to make decisions about you. If access to this information is needed before the end of the Research Study for your treatment, then the information may be provided to your physician.

If your identifying information is removed from your health information, then the information that remains will not be subject to this authorization or covered by HIPAA, and it may be used or disclosed to other persons or organizations, and/or for other purposes.

Expiration Date: This authorization will expire at the end of the research period and all related record-keeping periods.

As a study participant, if you any questions regarding the study, you may call Dr. Susie Buchter the study's Principal Investigator at (404) 778-1450. If you have any questions regarding your rights as a study subject, you may call Dr. Colleen DiIorio, Chair of the Emory University Institutional Review Board at (404) 712-0720.

A copy of this authorization form will be given to you.

_____

Signature of Study Subject OR Subject's Legal Authorized Representative –

Date _____---Time_____

_____

Printed Name of Study Subject OR Subject's Legally Authorized Representative

If Representative, Relationship to Study Subject: _____

_____

Signature of Person Obtaining Authorization

_____ _____

Date ----------Time

IRB#: 1158-2004
Consent Form Approval Period
FROM: 9/25/07 TO: 9/24/08
AUTHORIZATION: [signature]

Version Date(s): 11/22/2005; revised 8/14/2007

From: Zaterka-Baxter, Kristin
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Das, Abhik
Subject: FW: NICHD NRN DSMC Support Trial Review 12/11/07
Date: Thursday, October 25, 2007 9:53:51 AM

Hi,
Please see below; I will forward all contact info closer to the meeting. Should I forward this email below to Drs. Laptook and Tyson?
Thanks,
Kris

From: Zaterka-Baxter, Kristin
Sent: Monday, September 17, 2007 3:27 PM
To: Zaterka-Baxter, Kristin; 'Gordon Avery'; 'rjb6j@hscmail.mcc.virginia.edu'; 'cgleason@u.washington.edu'; [SCRN] Willinger, Marian; 'tclemons@emmes.com'; 'mikeross@ucla.edu'; 'kant@unc.edu'; 'merran.thomson@ic.ac.uk'; 'mcallen@jhmi.edu'; 'GailD@nih.gov'
Cc: Das, Abhik; Gantz, Marie; Poole, W. Kenneth; Auman, Jeanette O.; 'bprice@obgyn.humc.edu'; 'milhil@u.washington.edu'; 'meganhb@u.washington.edu'
Subject: NICHD NRN DSMC Support Trial Review 12/11/07

Hi all,
We have scheduled the next NICHD NRN DSMC conference call for Tuesday December 11, 2007 from 3:00 pm to 6:00 pm (EST). This call will be to:

1. Review the Support Trial Interim analysis at 50% infant status (3:00 – 5:00 pm EST)
2. Review a new NRN Study titled *"Evaluation of Systemic Hypothermia Initiated After 6 Hours of Age in Infants = 36 Weeks Gestation with Hypoxic-Ischemic Encephalopathy: A Bayesian Evaluation"* (5:00 – 6:00 pm EST)

The meeting agenda and **new** study materials will be distributed mid November and the Support Trial safety report will be distributed one week prior to the conference call.

Thanks and please let me know if you have any questions at all.
Kris

Kris Zaterka-Baxter, RN, CCRP
RTI International
4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From: Susan Hintz
To: Ira Adams-Chapman
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: support mri secondary
Date: Tuesday, October 23, 2007 1:14:33 AM

Thanks so much for working so diligently on this Ira! This is great!

Susan

> Hi Susan and Rose,
> Hope that all is well. I am actively working on getting our site on board with the MRI secondary for the SUPPORT trial. I will need to work with the billing people about reimbursement for the study. Is there a budgeted amount for the technical cost to perform the study as well as the local professional fee to interpret the study? If so, how much is it. We are submitting the IRB and everyone is on board to try to use the hugger device. Will keep you posted.
>
> Ira Adams-Chapman, MD
> Director, Developmental Progress Clinic
> Assistant Professor of Pediatrics
> Emory University School of Medicine
> Department of Pediatrics/Division of Neonatology
>
> 404-778-1450 (O)
>
> ira_adams-chapman@oz.ped.emory.edu

From: Zaterka-Baxter, Kristin
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Support tech memo
Date: Thursday, October 18, 2007 2:35:49 PM

Sure can, Dale wanted to take a closer look at the SUPP10 ROP revisions
so I'm waiting for her to get back to me before I post it.
Thanks,
Kris
-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, October 18, 2007 2:32 PM
To: Zaterka-Baxter, Kristin
Subject: Support tech memo

Kris
Can you change the site PI at brown to abbot (he is also the support
study) and the site PI to beena Sood at Wayne?
Otherwise looks great, thanks
Rose

Sent from my BlackBerry Wireless Handheld

From:	Zaterka-Baxter, Kristin
To:	Cunningham, Meg
Cc:	Higgins, Rosemary (NIH/NICHD) [E]
Subject:	FW: Support Revisions
Date:	Saturday, October 13, 2007 3:29:33 PM

I have copies just in case - thanks

Kris

From: Zaterka-Baxter, Kristin
Sent: Saturday, October 13, 2007 3:23 PM
To: 'nfiner@ucsd.edu'; 'Wade Rich (wrich@ucsd.edu)'; 'nancy newman'
Cc: Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik; Gantz, Marie; Auman, Jeanette O.; Cunningham, Meg
Subject: Support Revisions

Hi all,
Please find attached final revisions to the SUPPORT study manual and forms SUPP04, 04a (new), 05, 08, 09, 10, and 11. These changes have been approved by Dr. Finer and most have been reviewed by the subcommittee but not all (ie. SUPP10 ROP form and manual changes). If there is time, we can discuss these changes during the Support subcommittee or I can send them out via email after the meeting next week. In case you would like to review these during the meeting, I will bring copies of all materials. Please note I have also included a version of the MOP with only those sections that have been revised (SuppotManualRevisionsOnly[uc]20071015.doc)
Thanks,
Kris

From: Cunningham, Meg
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: SUPPORT materials
Date: Thursday, October 11, 2007 6:35:26 PM

Rose-

Let me know if you want me to copy.

From: Gantz, Marie
Sent: Thursday, October 11, 2007 6:35 PM
To: 'Higgins, Rosemary (NIH/NICHD) [E]'; nfiner@ucsd.edu; Wade Rich
Cc: Cunningham, Meg
Subject: RE: SUPPORT materials

Attached is the pulse oximeter data update for SUPPORT.

Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-6255

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, October 10, 2007 4:13 PM
To: Gantz, Marie; nfiner@ucsd.edu; Wade Rich
Cc: Cunningham, Meg
Subject: RE: SUPPORT materials

Thanks
Just forward them over and we can get them copied.

Rose

From: Gantz, Marie [mailto:mgantz@rti.org]
Sent: Wednesday, October 10, 2007 4:11 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; nfiner@ucsd.edu; Wade Rich
Cc: Cunningham, Meg
Subject: RE: SUPPORT materials

I am working on the handouts right now. The enrollment, AE and protocol deviation reports will be sent to Neil this afternoon. The pulse oximeter reports will be sent either today or tomorrow.

Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-6255

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, October 10, 2007 4:09 PM
To: nfiner@ucsd.edu; Wade Rich; Gantz, Marie
Cc: Cunningham, Meg
Subject: SUPPORT materials

Hi,
Do we have any handouts for the SUPPORT Subcommittee meeting?
Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Neil Finer
To:	Edmund Hey
Cc:	Lisa Askie; Higgins, Rosemary (NIH/NICHD) [E]
Subject:	RE: BOOST-II UK
Date:	Monday, October 08, 2007 12:39:58 PM

Hi Edmund
Congratulations on initiating the trial.
The funding for SUPPORT was available in September 2004 via NIH.
The first enrolled infant was in February 2005. At present we have enrolled over 800 infants.
Hope this helps
Neil

Neil N. Finer, M.D.
Professor of Pediatrics
Director, Division of Neonatal-Perinatal Medicine
UC San Diego School of Medicine
UC San Diego Medical Center, Hillcrest
402 Dickinson St., MPF 1-140
San Diego, CA 92103-8774
Telephone: 619.543-3759
Facsimile: 619.543.3812

From: Edmund Hey [mailto:shey@easynet.co.uk]
Sent: Monday, October 08, 2007 4:10 AM
To: Neil Finer
Cc: Lisa Askie
Subject: BOOST-II UK
Importance: High

Neil,

I thought you would like to know that the UK arm of the BOOST/NeOProM collaboration finally got off the ground when the first two babies were recruited last week. Recruitment should pick up quickly now that the NPEU in Oxford have finally managed to get through all the regulatory paperwork involved with at least the first four of the 36 planned recruitig centres (a full 22 months after they were first told funding had been approved).

There is a critically important meeting at the MRC on Wednesday to review why this has all taken so long and to reassure those who hold the money strings in the UK how the other trials are progressing. If you could send me just a one line response saying [a] when funding for SUPPORT came through [b] when recruitment started and [c] how many babies have now been recruited I would be extremely grateful.

Edmund

From: Wade Rich
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE:
Date: Friday, October 05, 2007 1:23:33 PM

Within the next 2 weeks.
W

-----Original Message-----
From: "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov>
To: "Wade Rich" <wrich@ucsd.edu>
Sent: 10/5/2007 12:12 PM
Subject: RE:

Wade

When would you like these??
Thanks

Rose

From: Wade Rich [mailto:wrich@ucsd.edu]
Sent: Thursday, October 04, 2007 8:47 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW:

Rose,

I only have 1 of each left. Can we get some for Maynard?

wade

From: Maynard Rasmussen, MD [mailto:Maynard.Rasmussen@sharp.com]
Sent: Thursday, October 04, 2007 4:08 PM
To: Wade Rich
Cc: Neil Finer
Subject:

Hey Wade,

We need to obtain Support Oximeters for Sharp. Are they available?

Thanks,

Maynard

From:	Neil Finer
To:	niki.stratis@rwh.org.au
Cc:	Wade Rich; Tina Leone; Higgins, Rosemary (NIH/NICHD) [E]
Subject:	FW: Neonatal Resuscitation Research Workshop
Date:	Thursday, October 04, 2007 6:26:47 PM

Hello Niki
For the Professor:- I forgot an important topic – Consent for research – especially resuscitation Research. Wade Rich can present the results of his Antenatal Consent trial or at least report on its progress with NRN permission – This is very relevant to resuscitation research.
Thanks
Neil Finer

From: Neil Finer
Sent: Wednesday, October 03, 2007 8:25 PM
To: niki.stratis@rwh.org.au
Cc: Tina Leone; Wade Rich; Jon.E.Tyson@uth.tmc.edu; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Neonatal Resuscitation Research Workshop

Hello Niki
Tell the Professor that we would be delighted to participate.
We could discuss the following –
The development of standards of care for Neonatal Resuscitation,
The development of new technologies to facilitate Resuscitation
Future studies required regarding the amount of oxygen for resuscitation the VLBW and to evaluate important longer term outcomes
I can review the status of the SUPPORT Trial for the Neonatal Network pending Steering Committee approval

I would suggest that Jon Tyson of Texas be invited
Regards
Neil Finer

From: niki.stratis@rwh.org.au [mailto:niki.stratis@rwh.org.au]
Sent: Tuesday, October 02, 2007 7:51 PM
To: 'Alan Jobe'; 'Arjan te Pas'; 'Augustus Sola'; 'Ben Stenson'; 'Charles Rohr'; 'Colm O'Donnell'; 'Edgardo Szyld'; 'Fiona Wood'; 'Frank Pohlandt'; 'Graeme Polglase'; 'Hany Aly'; 'Jacqui Coalson'; 'Jane Pillow'; 'Jeff Perlman'; 'Jennifer Dawson'; 'Lars Bjorklund'; 'Lou Halamek'; 'Luc Brion'; 'Mark Tracy'; 'Masanori Tamaura'; 'Max Vento'; 'Megan Wallace'; 'Merran Thomson'; 'Myra Wyckoff'; 'N E Vain'; 'Nalini Singhal'; Neil Finer; 'Ola Saugstad'; 'Omar Kamlin'; 'Richard Bland'; 'Ruth Guinsburg'; 'Sam Richardson'; 'Sandri'; 'Stuart Hooper'; 'Susan Niermeyer'; Tina Leone; Wade Rich; 'Wally Carlo'; 'Wolfgang Linder'
Subject: Neonatal Resuscitation Research Workshop

Dear All

Professor Colin Morley from The Royal Women's Hospital would like to invite you to attend the neonatal resuscitation workshop to be held after the SPR on the 7th and 8th May 2008 in Honolulu.

Please find attached the letter of invitation.

Yours sincerely

Niki Stratis
Assistant to Professor/Director of Neonatal Medicine

Niki Stratis
Assistant to Professor/Director of Neonatal Medicine
Neonatal Services
The Royal Women's Hospital
132 Grattan Street
CARLTON VIC 3053
AUSTRALIA
Phone: + 613 9344 2524
Fax: + 613 9347 2731
E-mail: niki.stratis@rwh.org.au

From: Susan Hintz
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: extended follow up for SUPPORT neuroimaging patients
Date: Wednesday, September 26, 2007 6:41:00 PM

Hi Rose

I note that Krisa's secondary analysis proposal had formal comments from the subcommittee. Should I expect formal comments on the SUPPORT extended follow-up proposal before the Steering Committee? I sent the BIG version of the proposal to Neil and Seetha too.

Let me know

me

--

Susan R. Hintz, M.D., M.S. Epi
Associate Professor of Pediatrics
Division of Neonatal and Developmental Medicine
Stanford University School of Medicine
750 Welch Road, Suite 315
Palo Alto, CA 94304
ph: 650-723-5711
fax: 650-725-8351

From: Richard, Leslie D
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT OUTCOMES
Date: Monday, September 24, 2007 6:29:34 AM

Thank you for noticing!

Leslie Richard, RN
Indiana University
NIH Follow Up Coordinator
office (317)278-0737
pager (317)312-1827
fax (317)278-0126

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, September 21, 2007 11:12 AM
To: Poindexter, Brenda B; Wilson, Leslie Dawn; Dusick, Anna M.; Richard, Leslie D
Cc: adas@rti.org; mgantz@rti.org
Subject: SUPPORT OUTCOMES

HI,
CONGRATULATIONS for having no missing ROP, BPD, or FU outcomes for SUPPORT on this month's data analysis. Keep up the good work!!!
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Zaterka-Baxter, Kristin
To:	mcw3@cwru.edu; Pablo.Sanchez@UTSouthwestern.edu; sshankar@med.wayne.edu; [SCRN] Stoll, Barbara; kurt.schibler@cchmc.org; bpoindex@iupui.edu; richard.ehrenkranz@yale.edu; alaptook@WIHRI.org; vanmeurs@stanford.edu; wcarlo@peds.uab.edu; Kathleen.A.Kennedy@uth.tmc.edu; goldb008@mc.duke.edu; IFrantz@tufts-nemc.org; edward-bell@uiowa.edu; Roger.Faix@hsc.utah.edu; kwatterberg@salud.unm.edu; nxs5@cwru.edu; Nancy.Miller@UTSouthwestern.edu; melissa.leps@utsouthwestern.edu; ae5357@wayne.edu; crosman@med.wayne.edu; ellen_hale@oz.ped.emory.edu; grisbyca@email.uc.edu; ldw@iupui.edu; monica.konstantino@yale.edu; ahensman@wihri.org; mbball@leland.stanford.edu; mcollins@peds.uab.edu; Georgia.E.McDavid@uth.tmc.edu; auten002@mc.duke.edu; bmackinnon@tufts-nemc.org; karen-johnson@uiowa.edu; karen.osborne@hsc.utah.edu; CBackstrom@salud.unm.edu; Linda Reubens
Cc:	Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik; Phelps, Dale; nfiner@ucsd.edu; Wade Rich; Gantz, Marie; Wrage, Lisa Ann; Auman, Jeanette O.; Pickett, James
Subject:	Support and Inositol Single Dose Pk Study Enrollment
Date:	Tuesday, September 11, 2007 4:50:03 PM

Hi all,

Per Dr. Higgins, this email is to clarify that an infant **can** be enrolled in both the Support study and the IND Inositol Single Dose Pk study at the same time.

Thanks and please let me know if you have any questions.
Kris

Kris Zaterka-Baxter
RTI International
4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From: Monica Konstantino
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: support patient
Date: Wednesday, September 05, 2007 4:28:13 PM

Higgins, Rosemary (NIH/NICHD) [E] wrote:

>All deaths should be reported on the medwatch - sorry about the baby
>Rose
>
>-----Original Message-----
>From: Monica Konstantino [mailto:monica.konstantino@yale.edu]
>Sent: Wednesday, September 05, 2007 3:34 PM
>To: Higgins, Rosemary (NIH/NICHD) [E]
>Subject: support patient
>
>Hi Rose, our last support patient died on DOL 19 from respiratory
>failure with sepsis, Rich knows about it. We were not sure if we needed
>to do a MedWatch on the baby, what is your opinion? thanks.
>Monica
>
>
>
thanks, all done.

From:	Walsh, Michele
To:	Higgins, Rosemary (NIH/NICHD) [E]; mcw3@case.edu; nxs5@cwru.edu; drficmd@aol.com; Bonnie Siner
Subject:	RE: SUPPORT OUTCOMES
Date:	Thursday, August 30, 2007 3:15:14 PM

Yahoo! Great work everyone!

Michele Walsh
phone: 216-844-3759

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, August 30, 2007 12:30 PM
To: mcw3@case.edu; nxs5@cwru.edu; Personal Email; Bonnie Siner
Cc: Marie Gantz; Das, Abhik
Subject: SUPPORT OUTCOMES
Importance: High

CONGRATULATIONS – there are no missing SUPPORT OUTCOMES for you site as of last week – thanks you very, very much and keep up the excellent recruitment!!!!
Thanks again
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
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Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Utah call notes
Date: Tuesday, August 28, 2007 10:42:25 AM

I'll send out the notes and ask for any additions/comments.

Stephanie Wilson Archer
Neonatal Research Network
National Institute of Child Health and Human Development
6100 Executive Boulevard, Room 4B03 (MSC 7510)
Bethesda, MD 20892
Tel: 301-496-0430
Fax: 301-496-3790
archerst@mail.nih.gov

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Tuesday, August 28, 2007 10:42 AM
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: Re: Utah call notes

I don't know -ask karen

Sent from my BlackBerry Wireless Handheld

----- Original Message -----
From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Tue Aug 28 10:39:13 2007
Subject: Utah call notes

You marked an "Eddie" from Utah. I don't have anyone by that name at Utah on the address book. What's his last name?

Stephanie Wilson Archer

Neonatal Research Network <http://www.nichd.nih.gov/research/supported/nrn.cfm>

National Institute of Child Health and Human Development

6100 Executive Boulevard, Room 4B03 (MSC 7510)

Bethesda, MD 20892

Tel: 301-496-0430

Fax: 301-496-3790

archerst@mail.nih.gov

From: Webb, Robin E.
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: SUPPORT CALL WITH UTAH
Date: Tuesday, August 21, 2007 1:35:30 PM

Hi Rose,

What is your availability for 8/23 and 8/24? I used what I had from other calls for the rest of the days. Is that ok or has it changed a lot since then?

Thanks,
Robin

From: Webb, Robin E.
Sent: Monday, August 20, 2007 10:26 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik; nfiner@ucsd.edu; Archer, Stephanie (NIH/NICHD) [E]; 'Roger Faix'; Bradley.Yoder@hsc.utah.edu; Zaterka-Baxter, Kristin; karen.osborne@hsc.utah.edu
Cc: fmartinez@ucsd.edu; Webb, Robin E.
Subject: FW: SUPPORT CALL WITH UTAH

We need to schedule a call to discuss strategies to optimize SUPPORT recruitment. Please let me know your availability for the days below, indicating time zone if other than ET.

Thanks,
Robin

Thurs 8/23
Fri 8/24

Mon 8/27
Tues 8/28
Wed 8/29
Thurs 8/30
Fri 8/31

Tues 9/4
Wed 9/5
Thurs 9/6

From: Wally Carlo, M.D.
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT
Date: Saturday, August 18, 2007 12:32:22 AM

Rose:

Sorry that I did not respond. I was out of the office during this week and I am getting back to the emails. I am always available to help.

wally

Wally Carlo, M.D.
Edwin M. Dixon Professor of Pediatrics
University of Alabama at Birmingham
Director, Division of Neonatology
Director, Newborn Nurseries
619 South 20th Street
525 New Hillman Building
Birmingham, AL 35233-7335
Phone: 205 934 4680
FAX: 205 934 3100
Cell: 205 266 4004

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, August 02, 2007 11:29 AM
To: wacarlo@uab.edu
Subject: SUPPORT
Importance: High

Wally – Are your reachable by email?? I want to send out an email to folks telling them to contact you or I for SUPPORT questions.

Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
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301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Neil Finer
To:	Maynard Rasmussen, MD; Higgins, Rosemary (NIH/NICHD) [E]; Wade Rich
Cc:	Kathy Arnell
Subject:	RE: SUPPORT APPROVAL FOR SHARP
Date:	Thursday, August 16, 2007 6:06:19 PM

Maynard
This is great
Last months enrollments were somewhat down, so you can help make a significant difference.
Let me know what Wade and I can do to assist you.
Be well
Neil

From: Maynard Rasmussen, MD [mailto:Maynard.Rasmussen@sharp.com]
Sent: Thursday, August 16, 2007 2:51 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; Wade Rich
Cc: Neil Finer; Kathy Arnell
Subject: RE: SUPPORT APPROVAL FOR SHARP

Hi All,
I was just informed by the IRB that we are approved.
I will fax you a copy of the officially stamped document as soon as I receive it.
Thanks,
Maynard.

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, August 15, 2007 7:06 AM
To: Wade Rich
Cc: Neil Finer; Maynard Rasmussen, MD
Subject: SUPPORT APPROVAL FOR SHARP

Hi
Do you have an IRB approval for SUPPORT at Sharp? If so, send us a copy.

Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
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Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Auman, Jeanette O.
To: Zaterka-Baxter, Kristin; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Support Study ROP Exam Tracking
Date: Thursday, August 16, 2007 2:44:36 PM

I'm asking Scott if he has any memory of why those outcomes columns were added to the table. He initially programmed the table with Dales' specs.

From: Zaterka-Baxter, Kristin
Sent: Thursday, August 16, 2007 2:42 PM
To: 'Higgins, Rosemary (NIH/NICHD) [E]'
Cc: Auman, Jeanette O.
Subject: FW: Support Study ROP Exam Tracking

This might explain some of it;
Thanks,
Kris

From: Zaterka-Baxter, Kristin
Sent: Thursday, May 18, 2006 10:48 AM
To: 'Phelps, Dale'
Subject: FW: Support Study ROP Exam Tracking

Hi,
Attached is a template (below the email) of what Scott sent to all the sites requesting the missing ROP final exam data. We sent it to the coordinators first to allow time to send in any data they may have. This report will be added to the monthly report next month. Rose is aware and is fine with this process. Please let me know if this is alright with you as well.

Thanks,
Kris

From: Schaefer, Scott E.
Sent: Thursday, May 11, 2006 5:23 PM
To:
Cc: Zaterka-Baxter, Kristin
Subject: Support Study ROP Exam Tracking

Attached you will find a Word Doc that explains the new tracking of ROP exams that I have just implemented. ROP status is a primary outcome of the Support Study so entering the eye exams until final status is reached in both eyes is very important.

Included in the document is the list of cases that you have reached final eye exam status for and those that are still pending.

Scott *8-)

P.S. I will be out of the office tomorrow (Friday May 12th)

From: Zaterka-Baxter, Kristin
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Auman, Jeanette O.
Subject: FW: Support Study ROP Exam Tracking
Date: Thursday, August 16, 2007 2:42:15 PM
Attachments: Template ROP_EXAM_TRACKING_22.doc

This might explain some of it;
Thanks,
Kris

From: Zaterka-Baxter, Kristin
Sent: Thursday, May 18, 2006 10:48 AM
To: 'Phelps, Dale'
Subject: FW: Support Study ROP Exam Tracking

Hi,
Attached is a template (below the email) of what Scott sent to all the sites requesting the missing ROP final exam data. We sent it to the coordinators first to allow time to send in any data they may have. This report will be added to the monthly report next month. Rose is aware and is fine with this process. Please let me know if this is alright with you as well.

Thanks,
Kris

From: Schaefer, Scott E.
Sent: Thursday, May 11, 2006 5:23 PM
To:
Cc: Zaterka-Baxter, Kristin
Subject: Support Study ROP Exam Tracking

Attached you will find a Word Doc that explains the new tracking of ROP exams that I have just implemented. ROP status is a primary outcome of the Support Study so entering the eye exams until final status is reached in both eyes is very important.

Included in the document is the list of cases that you have reached final eye exam status for and those that are still pending.

Scott *8-)

P.S. I will be out of the office tomorrow (Friday May 12th)

NICHD
NEONATAL RESEARCH NETWORK
SUPPORT TRIAL ROP EXAM TRACKING

From: Scott E. Schaefer
Date: 05/10/2006
Subj.: New tracking of ROP exams for final status reached in both eyes.

INTRODUCTION:

As all of you are aware, one of the Support Trial's primary outcomes is ROP status of the infant's eyes. The SUPP10 form is provided to allow you to record the results of each eye exam until a favorable or unfavorable outcome is reached for both eyes. This new tracking system has been created to alert you of the subject's that have not reached final status and still require additional eye exams to be recorded.

At the end of this message, you will find a list of all subjects that are requiring additional SUPP10 forms. These are listed by Network Number. After this preliminary listing, these messages will be included in the *Missing Forms Report* that Jenny Auman generates.

METHODS USED:

The tracking is for all subjects that were randomized into the Support Trial. Subjects that are known to have died early are automatically excused from the tracking, though you are allowed to enter SUPP10 forms for them if they were in fact examined. ROP exams are normally expected at 31 weeks PMA or after 4 weeks of life. Any subject that died up to 4 weeks after this time point has been reached is automatically excused.

Question C1 on the SUPP09 form states, "Was an exam performed for ROP?" If this is 'N' (No), the infant is also excused from ROP tracking.

For infants with SUPP10 forms, each eye is tracked across forms until final status is reached for both eyes. The rules for the favorable and unfavorable outcomes are listed in the MOP Section 15.2. If the Threshold (New Type 1) question is 'Y' (Yes), the outcome is unfavorable. How I have interpreted the other outcomes as they relate to the SUPP10 form's codes is listed below (**codes not listed do not contribute to final status**):

Zone Codes:

Code Value	Code Description	Outcome Status
3	Zone III	Favorable if two exams in a row.
4	Mature	Favorable
5	Status Post laser/cryo	Unfavorable

Stage Codes:

Code Value	Code Description	Outcome Status
4	Stage 4a or 4b	Unfavorable
5	Stage 5	Unfavorable
6	Post laser/cryo	Unfavorable

Surgery Codes:

Code Value	Code Description	Outcome Status
1	Laser	Unfavorable
2	Cryotherapy	Unfavorable
3	Both laser/cryo	Unfavorable
4	Scleral Buckle	Unfavorable
5	Vitrectomy	Unfavorable
6	Other	Unfavorable

Retinal Detachment Codes:

Code Value	Code Description	Outcome Status
3	Partial, not involving macula (stage 4a)	Unfavorable
4	Partial, does involve macula (stage 4b)	Unfavorable
5	Complete	Unfavorable

MESSAGE TYPES:

A grace period of 50 weeks PMA is used before the listing of the non-final subjects. This hopefully will allow most subjects to first reach final status. These messages will be reported in the *Missing Forms Report* generated by Jenny Auman.

Error Message	Occurrence
No SUPP10 forms have been entered though 50 weeks PMA has been reached and the infant did not die early.	No SUPP09 or SUPP10 forms have been keyed.
No SUPP10 records have been entered even though SUPP09 Question C1 indicates that an exam for ROP was performed.	SUPP09 Question C1 (Was an exam performed for ROP?) is 'Y' (Yes), but no SUPP10 forms exist.
SUPP10 records have been entered even though SUPP09 Question C1 indicates that no exam for ROP was performed.	SUPP10 forms exist, but SUPP09 Question C1 incorrectly indicates otherwise.
50 weeks PMA has been reached and final ROP exam status has not been reported on the SUPP10 for either eye.	SUPP10 forms exist but final status has not been reached.
50 weeks PMA has been reached and final	Same as previous.

Error Message	Occurrence
ROP exam status has not been reported on the SUPP10 for the left eye.	
50 weeks PMA has been reached and final ROP exam status has not been reported on the SUPP10 for the right eye.	Same as previous.

EXCUSING SUBJECTS:

Understanding that some of the subjects will die before final status is reached, or the parents may refuse any more contact, a mechanism is built into the ROP tracking program to allow non-final subjects to be excused from the reporting. Since the ROP status is so important to the Support Study, excused cases will be entered here at RTI once they have been approved. Please inform Scott Schaefer of any cases that need to be excused and why.

All efforts should be taken to record every eye exam possible for non-final subjects, even for the excused cases.

LIST OF YOUR CENTER'S PENDING CASES:

LIST OF YOUR CENTER'S COMPLETED CASES:

From:	Neil Finer
To:	Higgins, Rosemary (NIH/NICHD) [E]
Cc:	Wade Rich
Subject:	RE: SUPPORT APPROVAL FOR SHARP
Date:	Wednesday, August 15, 2007 1:14:04 PM

Hi Rose
We keep asking – I am uncertain what is happening there – I will continue to press this issue.
Neil

Neil N. Finer, M.D.
Professor of Pediatrics
Director, Division of Neonatal-Perinatal Medicine
UC San Diego School of Medicine
UC San Diego Medical Center, Hillcrest
402 Dickinson St., MPF 1-140
San Diego, CA 92103-8774
Telephone: 619.543-3759
Facsimile: 619.543.3812

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, August 15, 2007 7:06 AM
To: Wade Rich
Cc: Neil Finer; Maynard Rasmussen, MD
Subject: SUPPORT APPROVAL FOR SHARP

Hi
Do you have an IRB approval for SUPPORT at Sharp? If so, send us a copy.

Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Zaterka-Baxter, Kristin
To:	Higgins, Rosemary (NIH/NICHD) [E]; Kathleen Bridges
Cc:	Barbara Alexander; Cathy Grisby; Estelle Fischer; Jody Shively; Lenora Jackson; Das, Abhik; kurt.schibler@cchmc.org
Subject:	RE: SUPPORT issue
Date:	Tuesday, August 07, 2007 11:29:32 AM

Hi all,
320 randomization envelops were initially sent to Cincinnati; if you can tell me how they were divided up between your sites, that would be very helpful. In addition, to determine the randomization cards missing; we'll need a list of randomization card numbers from each site so we can then compare those lists to the randomizations used to determine which cards to regenerate for Good Sam(unless you already have a list of cards sent to each site, then we can work from that list).
Thanks much
Kris

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, August 07, 2007 11:14 AM
To: Kathleen Bridges; Zaterka-Baxter, Kristin
Cc: Barbara Alexander; Cathy Grisby; Estelle Fischer; Jody Shively; Lenora Jackson; Das, Abhik; kurt.schibler@cchmc.org
Subject: RE: SUPPORT issue

Kate
You may use envelopes from UH as needed for the time being and RTI will generate more envelopes for you - they will be in touch with you. We don't want to lose any potential deliveries for "Lack of randomization card."

Thanks
Rose

-----Original Message-----
From: Kathleen Bridges [mailto:Kathleen.Bridges@cchmc.org]
Sent: Tuesday, August 07, 2007 11:07 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; kzaterka@rti.org
Cc: Barbara Alexander; Cathy Grisby; Estelle Fischer; Jody Shively; Lenora Jackson
Subject: SUPPORT issue

Hi,
We have a situation here in Cincinnati at one of our sites (C) with which we need some assistance. The entire NICU at Good Sam has temporarily moved to another floor while some renovations are performed. Amidst the chaos, our oximeters and randomization envelopes for the SUPPORT Trial have been misplaced. We have been reassured that they are "somewhere", we're just not sure where yet. we're actively looking. but in the meantime, we have one woman consented (and more potentials to talk to.) we will bring over some oximeters from site A, but we're not sure what to do re: randomization envelopes. your thoughts?

thanks,
kate bridges

From: Kathleen Bridges
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT issue
Date: Tuesday, August 07, 2007 11:22:22 AM

---

great. thanks again for your prompt reply! i'll let Kris know as soon as we find our original envelopes and maybe we won't have to have new ones generated.
thanks,
kate

>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> 08/07/07 11:13 AM >>>
Kate
You may use envelopes from UH as needed for the time being and RTI will generate more envelopes for you - they will be in touch with you. We don't want to lose any potential deliveries for "Lack of randomization card."

Thanks
Rose

-----Original Message-----
From: Kathleen Bridges [mailto:Kathleen.Bridges@cchmc.org]
Sent: Tuesday, August 07, 2007 11:07 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; kzaterka@rti.org
Cc: Barbara Alexander; Cathy Grisby; Estelle Fischer; Jody Shively; Lenora Jackson
Subject: SUPPORT issue

Hi,
We have a situation here in Cincinnati at one of our sites (C) with which we need some assistance. The entire NICU at Good Sam has temporarily moved to another floor while some renovations are performed. Amidst the chaos, our oximeters and randomization envelopes for the SUPPORT Trial have been misplaced. We have been reassured that they are "somewhere", we're just not sure where yet. we're actively looking. but in the meantime, we have one woman consented (and more potentials to talk to.) we will bring over some oximeters from site A, but we're not sure what to do re: randomization envelopes. your thoughts?

thanks,
kate bridges

From: Nancy Miller
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Melissa Leps; Pablo Sanchez
Subject: Re: SUPPORT DATA
Date: Tuesday, July 31, 2007 8:00:04 PM

Rose,
I can't tell you much about the ROP outcomes because Janet will be out until 8/5/07. I've told Janet about those kids and follow up is going to talk to the parents since they are seeing them in clinic. I know no exams have been done since I checked last. I'll let you know as soon as I hear anything.
As far as the BPD message...that baby reached 36 weeks and I completed the PHY01 The snapshot for 36 weeks on the NG07 isn't completed because the baby is still here. We don't key these in until discharge (same for the NG03).
Thanks,
Nancy

Nancy A. Miller, R.N.
Department of Pediatrics
Division of Neonatal-Perinatal Medicine
UT Southwestern Medical Center at Dallas
5323 Harry Hines Blvd. E3-502
Dallas, Texas 75390-9063
214-648-3780
pager 972-206-9151

From: Neil Finer
To: Edmund Hey
Cc: Wade Rich; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Defining end points for SUPPORT and BOOST (again)
Date: Monday, July 30, 2007 6:08:44 PM

Hi Edmund
Good to hear that you will soon be starting.
I agree with Wades response – Unless we know the actual level of CPAP, which we do not, we do not categorize an infant receiving HiFlow NC as receiving CPAP
We do data during the first 14 days whether within any 2 hour window whether an infant was on SIMV. After 14 days we have similar data but only 4 times/day.
We will have the total of whatever type of SUPPORT. I would like to see NSIMV identified separately, but I doubt that everyone will have this data. As a default, I would categorize an infant on NSIMV as receiving at least CPAP. In the individual meta analyses it would be great to add more information about NSIMV
Look forward to hearing when you start enrolling
Regards
Neil Finer
From: Edmund Hey [mailto:shey@easynet.co.uk]
Sent: Sunday, July 29, 2007 12:30 AM
To: Neil Finer
Cc: Wade Rich
Subject: Defining end points for SUPPORT and BOOST (again)

Neil,

We are *finally* moving nearer to getting the first UK baby recruited into BOOST and a little rivalry is building up to see which units make it first. It has all been a painfully slow process. I will let you know when D-Day arrives !

One of the important secondary end points for your trial, and for all the BOOST trials, is the total number of days the baby is ventilated and the number of days the baby is offered nasal CPAP. Am I right in believing that you are also collecting duration of time on nSIMV too ? I do not think the other trials are collecting this separately. Would you be happy to see this merged with the time spent on nasal CPAP when Lisa Askie finally comes round to merging the various data sets ? Several trials are collecting data as to how old the baby is when last ventilated (and when last offered CPAP support) as well.to the total number of days of support. Is that data you would be able to provide for any meta-analysis to which we all eventually sign up ?

We are still finalising the outcome data collection forms for the UK trial, and I am being asked whether babies offered oxygen (or, for that matter, air) through a high-flow nasal cannula should be classed as having nasal CPAP. Humidified gas is increasingly being given in this way using devises such as the Vapotherm 2000i in the UK and, even though the flow rate can be varied quite widely these devices, many units seem to routinely start babies on flow rate of 8 l/min which must generate quite substantial positive pressure to the upper airway. I have been unable to find any papers defining exactly how much pressure such an arrangement delivers (it will obviously vary with the exact positioning of the cannula) but the papers by Sreenan (*Pediatrics* 2001;107:1081-3) and Shoemaker (*J Perinatol* 2007;27:85-91) suggest that it must be substantial. Have the units recruiting into SUPPORT come to any sort of consensus as to when it is right to classify a baby having high-low support from a cannula should be classified as having nCPAP ? Even if this is not possibly retrospectively for SUPPORT do you have any advice on what we should do in the UK BOOST trial given that we have not even started collecting data yet ? My instinct was to say, somewhat arbitrarily, that when flow through a nasal cannula was 3 l/min or more the baby should be classified as having the equivalent of nasal CPAP. There must be a flow rate at which the only advantage of using a Vapotherm is that the supplemental oxygen it delivers to the baby is warm and fully humidified rather than cold and dry !

I really would be grateful for your thoughts on this, as we need to finalise the UK trial's discharge data collection form within the next couple of weeks if possible.

Edmund

From:	Zaterka-Baxter, Kristin
To:	mcw3@cwru.edu; Pablo.Sanchez@UTSouthwestern.edu; sshankar@med.wayne.edu; [SCRN] Stoll, Barbara; kurt.schibler@cchmc.org; bpoindex@iupui.edu; richard.ehrenkranz@yale.edu; alaptook@WIHRI.org; vanmeurs@stanford.edu; wcarlo@peds.uab.edu; Kathleen.A.Kennedy@uth.tmc.edu; goldb008@mc.duke.edu; IFrantz@tufts-nemc.org; edward-bell@uiowa.edu; Roger.Faix@hsc.utah.edu; kwatterberg@salud.unm.edu; nfiner@ucsd.edu; Sood, Beena; Bradley Yoder; nxs5@cwru.edu; Nancy.Miller@UTSouthwestern.edu; melissa.leps@utsouthwestern.edu; ae5357@wayne.edu; crosman@med.wayne.edu; ellen_hale@oz.ped.emory.edu; grisbyca@email.uc.edu; ldw@iupui.edu; monica.konstantino@yale.edu; ahensman@wihri.org; mbball@leland.stanford.edu; mcollins@peds.uab.edu; Georgia.E.McDavid@uth.tmc.edu; auten002@mc.duke.edu; bmackinnon@tufts-nemc.org; karen-johnson@uiowa.edu; karen.osborne@hsc.utah.edu; CBackstrom@salud.unm.edu; Elizabeth Billian
Cc:	Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik; Gantz, Marie; Auman, Jeanette O.; Price, Jeffrey M.
Subject:	NRN Center Specific Support Study Oximeter Reports
Date:	Monday, July 30, 2007 12:15:14 PM

Hi,

Please note the center specific Support study oximeter reports through June 2007 have been posted on the NRN website (https://neonatal.rti.org) under the Private Gateway/Administration/Site Reports link. This oximeter data was processed as of 07/12/07 to capture more of the June downloads. Please note if your site specific data is not currently listed, it will be added to this report when sufficient oximeter downloads have been completed. Please contact Marie Gantz (mgantz@rti.org) for any questions you may have regarding this report.

Thanks,

Kris

Kris Zaterka-Baxter
RTI International
4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From:	Neil Finer
To:	Higgins, Rosemary (NIH/NICHD) [E]
Subject:	RE: SUPPORT compliance data
Date:	Wednesday, July 25, 2007 11:14:40 AM

Thanks Rose

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, July 25, 2007 8:11 AM
To: Neil Finer; Lisa Askie
Cc: Das, Abhik
Subject: RE: SUPPORT compliance data

HI,
I need to check with our DSMC and Dr. Alexander.

I will get back to you

Thanks
Rose

From: Neil Finer [mailto:nfiner@ucsd.edu]
Sent: Wednesday, July 25, 2007 9:41 AM
To: Lisa Askie
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT compliance data

Hi Lisa
I will discus with Rose and see what information we are able to share with you.
Neil

From: Lisa Askie [mailto:laskie@ctc.usyd.edu.au]
Sent: Tuesday, July 24, 2007 11:37 PM
To: Neil Finer
Cc: Wade Rich
Subject: SUPPORT compliance data

Neil,
We are in the process of assessing our oxygen saturation compliance data in BOOST II Australia. As part of this process, we have looked again at the compliance data from SUPPORT that you kindly shared with us last year. One of your DSMC's recommendations was that compliance be assessed again after another 100-150 babies were recruited. Have you done this again for SUPPORT, and if so are you able to share the results with us (confidentially)? Once discussed with our Trial Management Committee I anticipate we will be able to share the BOOST compliance results with the rest of the NeOProM group.

Regards,
Lisa

<><><><><><><><><><><><><><><><><><><>
Lisa Askie PhD MPH

Research Fellow, School of Public Health
Manager, Australian Clinical Trials Registry

NHMRC Clinical Trials Centre
University of Sydney, Australia

Tel: +61 (0)2 9562 5000
Fax: +61 (0)2 9565 1863
Mobile: +61 (0)4 2333 0089
Email: laskie@ctc.usyd.edu.au
<><><><><><><><><><><><><><><><><><><><><><>

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: ROP natural outcomes
Date: Monday, July 23, 2007 5:07:25 PM

Hi Rose
Thanks
I will look at it when it comes
Be well
Neil

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, July 23, 2007 1:49 PM
To: Neil Finer
Subject: ROP natural outcomes

Neil
Kathleen Kennedy would like to pursue a secondary to SUPPORT looking at the ROP data to develop a natural outcomes study. She will send us a protocol for subcommittee review. She is planning on working with Dale and Helen Hintner from UT Houston.

I hope thing are going OK with you and your family.
Take care
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Webb, Robin E.
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Support call
Date: Monday, July 23, 2007 2:21:32 PM

Hi Rose,

Is Mickey Caplan still on the Probiotics subcommittee? I do have Ed Bell on the list, I'm not sure why he missed some of the emails.

Thanks,
Robin

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, July 20, 2007 11:24 AM
To: Webb, Robin E.
Cc: Das, Abhik; Cunningham, Meg
Subject: Support call

Robin
Can you set up a SUPPORT call to discuss air leak definition?

Probiotics also needs a call to discuss the Ang secondary proposal.

Also, ED Bell has been left off of some of the emails for probiotics - do you have him on the list?
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

From:	Webb, Robin E.
To:	Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik; kurt.schibler@cchmc.org; alaptook@WIHRI.org; mcw3@cwru.edu; wcarlo@peds.uab.edu; Roger.Faix@hsc.utah.edu; nfiner@ucsd.edu; Bradley.Yoder@hsc.utah.edu; Gantz, Marie; nxs5@cwru.edu; wrich@ucsd.edu; Zaterka-Baxter, Kristin
Cc:	msumner@peds.uab.edu; fmartinez@ucsd.edu; Webb, Robin E.
Subject:	SUPPORT Call
Date:	Monday, July 23, 2007 2:17:07 PM

We need to set up a SUPPORT call to discuss air leak definition. Please let me know your availability for the days below, indicating time zone if other than ET.

Thanks,

Robin Webb
RTI, International
6110 Executive Blvd, Suite 902
Rockville, MD 20852

Mon 8/13
Tues 8/14
Wed 8/15
Thurs 8/16
Fri 8/17

Mon 8/20
Tues 8/21
Wed 8/22
Thurs 8/23
Fri 8/24

From:	Zaterka-Baxter, Kristin
To:	Walsh, Michele
Cc:	Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik
Subject:	FW: BPD adjusted forms and MOP
Date:	Monday, July 16, 2007 3:30:35 PM
Attachments:	MOP adjusted for altitude.doc PHY BPD Form 1_altitude.doc PHY BPD Form 2_altitude.doc

Hi all,
Please see the attached documents from Dr. Yoder regarding modifications for altitude adjustments with respect to the physiologic challenge and definition of BPD. Rose asked that I send these documents to your first for review.
Thanks,
Kris

From: Karen Osborne RN [mailto:Karen.Osborne@hsc.utah.edu]
Sent: Thursday, July 12, 2007 3:20 PM
To: Zaterka-Baxter, Kristin
Cc: Bradley Yoder
Subject: BPD adjusted forms and MOP

Hi Kris,

I have attached the forms and MOP pages for the BPD study that Brad adjusted for our altitude. The MOP pages will probably need to be formatted to your requirements. In fact, I just opened the attachment and it looks really weird, not at all how I formatted it! Maybe when you save it to file it will revert to what is should be like.
Let me know if you have questions!

Karen Osborne RN BSN CCRC
Project Manager
Neonatal Research Network
University of Utah
Dept of Pediatrics, Division of Neonatology
PO Box 581289
Salt Lake City, UT 84158
Phone # (801)213-3298
Pager # (801) 3393525
Fax # (801) 587-3618

PHYSIOLOGIC DEFINITION OF BPD
Manual of Operation – Altitude Corrected

2.1 Purpose

The Physiologic Definition of BPD protocol will be utilized for the Generic Database and any study within the NICHD Neonatal Research Network which has a primary or secondary outcome of bronchopulmonary dysplasia. This protocol will allow the definition of BPD to become standardized across network sites.

For centers located at significant altitude (Utah and New Mexico) a correction factor of 1.2 is used to adjust FiO2 values to an equivalent alveolar p02 at sea level (decrease in BP ~ 1mm Hg per every 40 feet elevation).

Table 1. Correction factors for elevation

Altitude	Correction factor	$FiO2_{eff}$ ~ 0.21 at sea level
1000 ft	1.04	0.22
2000 ft	1.07	0.22-0.23
3000 ft	1.11	0.23
4000 ft	1.16	0.24
5000 ft	1.21	0.25
6000 ft	1.26	0.26-0.27
7000 ft	1.32	0.28
8000 ft	1.39	0.29
9000 ft	1.46	0.31
10000 ft	1.54	0.32

Thus the FiO2 partial pressure of oxygen in the air at sea level increases by ~0.01 for every increase in elevation of 1000 feet.

Effective FiO2 ($FiO2_{eff}$) is determined for nasal cannula flow based on the infants weight, nasal cannula flow rate and the FiO2 provided as shown in Appendix A.

2.2 Eligibility Criteria

2.2.1 Inclusion Criteria

1. Infant with birthweight 401-1500 grams who are alive at 36+1 week corrected age
2. Supplemental oxygen as follows:
   - A. Infants receiving oxygen by hood at rest$_{\Delta}$:
     1. $FiO2_{eff}$** by hood <36% with majority* of saturations ≥ 90% in prior 24 hours.
   - B. Infants receiving oxygen by nasal cannula at rest$_{\Delta}$:
     1. $FiO2_{eff}$ ** by nasal cannula <36% and majority* of saturations ≥ 90% in prior 24 hours.
   - C. Infants receiving room air by nasal cannula at ANY liter per minute flow.

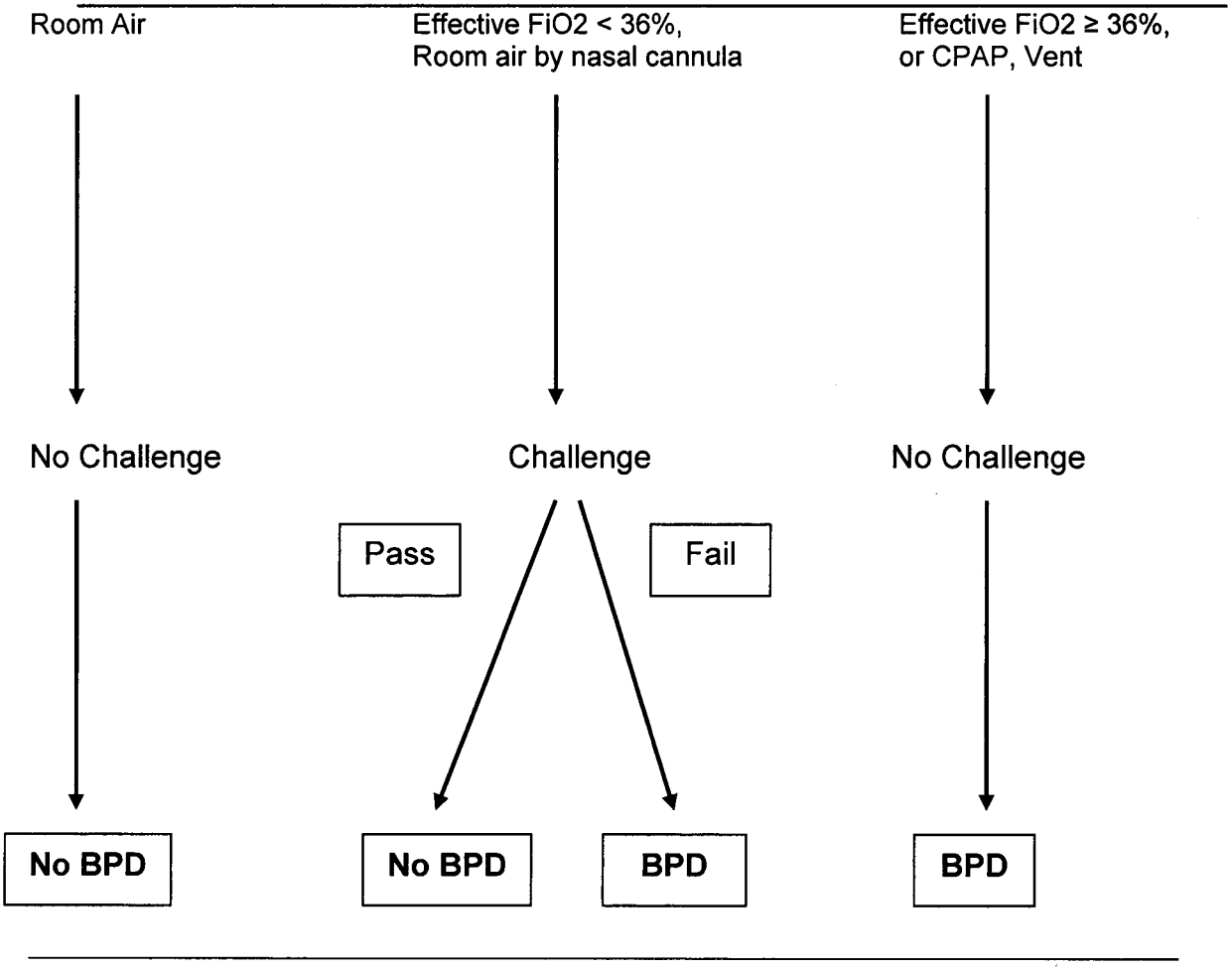
2.2.2 Exclusion Criteria

1. Need for mechanical ventilation or continuous positive airway pressure (CPAP).
2. Oxygen by hood >36%.
3. $FiO2_{eff}$ ** by nasal cannula >36%

.

*Majority defined as >90% of saturation reading during the 24 hour time period
***EFFECTIVE* oxygen applies to infants receiving oxygen via nasal cannula only.
EFFECTIVE oxygen is determined from tables in Appendix A.
ΔSupplemental oxygen requirement is determined at rest. Disregard any temporary increases in O2 requirement (for desaturation episodes, apnea, bradycardia or procedures where infant returns to baseline in a reasonable amount of time [< 2 hours]). Do not include supplemental oxygen given only with feeds.

Flow Diagram of Support and Need for Oxygen Reduction Challenge



CHAPTER 3

METHODS FOR PHYSIOLOGIC EVALUATION OF BPD

3.1.1 Objective

To conduct a physiologic monitored reduction of oxygen in eligible infants at 36 +1 weeks corrected age who are receiving oxygen to establish the definition of bronchopulmonary dysplasia. Infants are screened at exactly 36 weeks of age and if eligible receive the challenge as close as possible to 36 weeks but no later than 37 weeks PMA.
If needed at your institution, permission from parent(s) and/or attending of record will be secured prior to the evaluation.

3.1.2 Preparation for Evaluation

1. All infants should be studied in the supine position.
2. Feedings and medications should be given 30 minutes before the evaluation.
3. Bolus feedings should not be given during the evaluation.
4. Infants on continuous feeding may continue feeds during the evaluation.

3.2 Instructions for Completion of the Baseline Form (PHY01)

This form is to be completed for all infants with birthweight 401-1500 grams who survived >12 hours and who have reached 36 weeks corrected gestational age who are receiving any respiratory support. Respiratory support is defined as the need for support with ventilation or CPAP, oxygen by hood or nasal cannula or room air by nasal cannula. This form serves to determine the eligibility for the Physiologic Definition Challenge.

The PHY01 form will be expected if on the NG07, Section 'A', Snapshot @36 weeks, question 1 - 4 or 7 or 8 are answered 'Yes" or question 6 FiO2 > .21%.

A. Date for Physiologic Evaluation

1. Date of 36 week corrected age.

Record the date using mm/dd/yyyy format.

2. Patient available for Physiologic Evaluation

Record 'Y' if infant is available for the physiologic evaluation and continue to Section B.

a. Record 'N' if infant is not available for the evaluation and record the reason using the codes:
1= discharge, 3= transferred, 9=Other

b. If code 3 (transferred) and FiO2 > .21 at transfer, call the receiving hospital and answer question c.

c. Is the patient in room air at 36 wks?
Record 'Y' if infant is in room air at 36 weeks? Otherwise record 'N' or 'UK' if unknown.

B. Eligibility Criteria for Physiologic Evaluation

1. **Birthweight 401-1500 gm and now 36(+1) week corrected age.**
   Record 'Y' if infant's birthweight 401-1500 grams and is now at 36(+1) week corrected age.
2. **Attending physician gives permission.**
   Record Y/NA if attending physician gives permission **if** required at your institution OR if permission by the attending physician is not required at your institution.
   Record 'N' if attending physician refuses permission for the infant to have a physiologic evaluation.
3. **Parent gives permission.**
   Record 'Y/NA' if parent(s) give permission **if** required at your institution OR if permission by the parent(s) is not required at your institution.
   Record 'N' if the parent refuses permission for the infant to have a physiologic evaluation.
4. **Is patient receiving ventilator or nasal CPAP?**
   Record 'Y' if infant is receiving support with ventilator (nSIMV, conventional or high frequency) or with CPAP. Otherwise record 'N'.
5. **Effective oxygen <36% AND majority of saturations ≥ 90%.**
   Record 'Y' if infant is receiving oxygen support <36% by hood or nasal cannula and majority of saturations are ≥ 90%. Otherwise record 'N'.
6. **Room air by nasal cannula.**
   Record 'Y' if infant is receiving liter flow at any rate with oxygen support 21%. Otherwise record 'N'.
   If all of 1-3 AND either 5, 6 or 7 are answered YES or NA, patient is eligible for Physiologic Evaluation.

7. **If patient eligible and evaluation not done, code reason.**
   Code reason/circumstances why evaluation was not done.
   Eligible and Evaluation Not Done Reason codes:
   These codes are used if patient was eligible at 36 weeks but condition changed before challenge was done at 36 + 1 week,
   1= Increased FiO2
   effective FiO2 now exceeds evaluation criteria
   2= Increased respiratory support (CPAP or ventilator)
   infant placed on CPAP or ventilator
   3= Instability (Including Surgery/Sepsis)
   infant unstable or underwent surgery or new onset infection
   6= Weaned to room air on/before day of evaluation
   9= Other- explain on lines provided on PHY01

CHAPTER 4

PHYSIOLOGIC EVALUATION FORM (PHY02)

This form will be used for all infants who are eligible and have an oxygen reduction challenge. Eligibility for the Physiologic Evaluation will be determined from PHY01, Section B, questions 1-3 and 5-7. If **all** of questions **1-3** and **either** question **5, 6, or 7** are answered YES or N/A, the patient is eligible for the Physiologic Evaluation. The data center will then expect the PHY02 forms.

The infant should be positioned and the pulse oximeter in position with good signal prior to collecting baseline data. Baseline data is collected in infant's current oxygen. Do not record any data in the 5 minutes after placing the pulse oximeter.

4.1 A. Baseline Measurements:

(Time 0 occurs 5 minutes after you have placed the pulse ox.)

1. Record the date the evaluation will be performed in mm/dd/yyyy format
   a. Record the infant's baseline FiO2 and b. lpm flow if receiving oxygen by nasal cannula.
   c. Record the time of baseline measurements
   d. Record the saturations
2. Record the type of oximeter used during the oxygen challenge.
   Use the codes listed for the type of oximeter used during the challenge. Code 1 = Nellcor, 2= Ohmeda, 3= Hewlett Packard, 4=Space Labs, 5 = Masimo, 6=Other
3. Will the first oxygen wean place the patient in room air?
   If yes, PHY02Reduc not needed. Complete PHY02RA.

4.1.1 B. SAFETY DATA:

Premature infants have physiologic alterations of respiratory control that may result in ongoing apnea and bradycardia that resolve without intervention. Therefore, each infant will undergo baseline assessment and assessment during the 1 hour after the physiologic evaluation.
Document the frequency of apnea, bradycardia and desaturation and each infant will serve as his/her control.

Safety data will be recorded by reviewing the infant's hospital record inthe 1 hour prior to the evaluation AND during the 1 hour after theoxygen reduction challenge. Record 'Y' or 'N' for the following questions:

1. CONTROL DATA IN THE 1 HOUR BEFORE Physiologic Evaluation

a. Did the infant have saturations <88% lasting for >5 minutes?
b. Did the infant have FiO2 increased 5%?
c. Did the infant require initiation of ventilator?
d. Did the infant have an apnea which lasted >20 seconds?
e. Did the infant have a bradycardia (HR <80 for >10 seconds)?
f. Did the infant have a severe bradycardia (HR <70 for >20 seconds)?

2. DURING AND 1 HOUR AFTER Physiologic Evaluation

a. Did the infant have saturations <88% lasting for >5 minutes?
b. Did the infant have FiO2 increased 5%?
c. Did the infant require initiation of ventilator?
d. Did the infant have an apnea which lasted >20 seconds?
e. Did the infant have a bradycardia (HR <80 for >10 seconds)?
f. Did the infant have a severe bradycardia (HR <70 for >20 seconds)?

METHODS FOR PHYSIOLOGIC EVALUATION OF BPD

Determine Eligibility for Physiologic Evaluation as noted previously

1. If eligible for evaluation, based on the altitude and current weight determine the $FiO2_{eff}$ that will be equivlanet to 0.21 at sea level.
   a. Use Tables to determine $FiO2_{eff}$
   b. Remember at 5000 ft $FiO2_{eff}$ = 0.25 equates to 0.21 at sea level
   c. Record the Blender FiO2 at 0.5 lpm producing $FiO2_{eff}$ = 0.25 or
   d. Record the low flow rate at 100% O2 producing $FiO2_{eff}$ = 0.25

4.2 C. Oxygen Reduction Phase:

Perform Oxygen Reduction testing.

a. **CONTINUE** to reduce fiO2/flow every 5 minutes if SAT remains ≥ 90%

b. **STOP REDUCTION** if SAT < 90% for 5 continuous minutes OR SAT < 80% for 15 seconds with good signal fidelity – infant has failed

The infant is to be weaned as follows:

1. For infants receiving oxygen by hood:

- decrease FiO2 by 2% every 5 minutes

2. For infants receiving oxygen by nasal cannula:

-wean flow in increments of 0.5 lpm every 5 minutes until a flow of 0.5 lpm is reached. (Option to stop at 0.5 lpm and continue with Method A or B)
-continue with method A or method B:

-Method A- using oxygen blender: with flow at 0.5 lpm, wean blender FiO2 by 10% every 5 minutes to predetermined $FiO2_{eff}$ as calculated above

-**Method B**- Using ultra-low flow with 100% oxygen wean flow to 250 ml/min. Thereafter wean flow by 50 ml/min every 5 minutes to predetermined flow for $FiO2_{eff}$ as determined above.

-**For both methods** attempt to wean Blender FiO2 or ultra-low flow at least one step further than calculated, or to room air as tolerated.

If able to wean off NC flow, gently remove cannula from nares (but do not remove NC completely from face)

3. **For infants receiving room air by nasal cannula:**
   -If flow > 2 lpm: Wean flow in increments of 1.0 lpm every 5 minutes until a flow of 2 lpm is reached.
   -If flow 0.5-2.0 lpm: wean flow in increments of 0.5 lpm every 5 minutes until a flow of 0.5 lpm is reached. Then turn off flow.
   -If flow is 0.01-0.49 lpm: turn off flow, gently remove cannula from nares.

Data collection for the oxygen reduction phase will include:

1. Reduction step#

Record each step sequentially starting with #1.

a. FiO2

Record the FiO2 at each reduction step.

b. lpm

Record the lpm flow if infant is receiving oxygen by nasal cannula

c. Record the time during each reduction step

d. Record the saturation data each minute during the reduction step.

Continue with reduction steps until the infant is in room air.

4.3 D. Room Air Phase

The infant will be monitored in room air ($FiO2_{eff}$ at altitude < 0.21) for 30 minutes If saturations remain ≥ 90% the infant will be considered to have passed the oxygen reduction challenge. The infant should then be placed back in his/her baseline oxygen or kept in room air per the attending MD/NNP.

The infant may qualify for a RAPID PASS if all saturations ≥ 96% in room air for 15 consecutive minutes.

If the infant has saturations <90% for 5 continuous minutes or <80% for 15 seconds, the infant should be immediately placed back in his/her baseline oxygen. The infant will be considered to have NOT passed the challenge.

4.4 E. OUTCOME OF CHALLENGE

1. Patient Passed?
   Record 'Y' if the patient passed the challenge.

CHAPTER 5

CERTIFICATION

It is important that all personnel who will perform the oxygen reduction challenge to determine the Physiologic Definition of BPD are familiar with the background, patient population and procedures to complete the evaluation and challenge. All personnel are required to read the manual of operations and become familiar with the data forms. They must complete the certification exam and have the first challenge they perform reviewed by a certified examiner.

5.1 Certification Exam:

Each individual who desires to become certified to perform the Physiologic Evaluation should complete the certification exam to assure their familiarity which the methods and evaluation procedures.

APPENDIX B
CERTIFICATION EXAM
(Duplicate as many as needed for your site before completion)
Name _____ Center _____
1. Consult the Table in the Methods section and indicate whether the following infants should undergo physiologic evaluation for BPD.
A. An infant on a mechanical ventilator Y N
B. Infant at 33 weeks gestation Y N
C. Infant in room air Y N
0. 2.0 kg infant in 2 liters nasal cannula with 100% oxygen, saturation 90-96% Y N
E. 1.8 kg infant in 0.5 liters nasal cannula, 60% oxygen, saturation 90 - 96% V N
F. 1.8 kg infant in 0.20 liters nasal cannula, 100% oxygen, saturation >96% V N
G. 3.1 kg infant in 0.10 liters nasal cannula, and 100% oxygen, saturation >96% V N
H. 3.6 kg infant in 0.5 liters nasal cannula, 40% oxygen, saturation >96% Y N
2. Determine the final classification (BPD/no BPD) of the following scenarios:
A. infant has all saturations >96% for 15 minutes in room air BPD No BPD
B. Infant has saturation < 90% for 6 minutes BPD No BPD
C. Infant has saturation > 90% for 30 minutes BPD No BPD
D. Infant has most saturation > 90%, but has one minute period of saturation of 85% that resolves on its own, and returns to > 90% BPD No BPD
3. During the physiologic evaluation, the infant has an apnea. What should the researcher do:
a. Observe the infant without intervention.
b. Institute the usual routines used in that institution for an apneic infant that generally include increasing levels of support after a brief period of observation to allow the infant to arouse on his/her own.

CALCULATING FiO2 FROM CONVERSION TABLES for INFANTS on NASAL CANNULA

1. Tables 1 & 2 are based on data derived from equations (3) and (4) in the paper by Benaron and Benitz, "Maximizing the stability of oxygen delivered by nasal cannula", Arch Pediatr Adoles Med 1994; 148: 294-300

2. These tables include the following assumptions:
   - There is constant nasal flow over the inspiratory cycle
   - The upper airway does not act as a reservoir
   - Inspiration time = 0.3 seconds
   - Tidal Volume = 5 ml/kg
   - That either inspiration is entirely nasal or that cannula flow is sufficiently low to allow complete exhalation via the cannula on each inspiration

2. **Examples:**

What is the effective FiO2 in a 2500 gm infant on 40% oxygen at 0.5 lpm?
ANSWER:
   a. Use Table 1
   b. Locate intersection of 2500 gm and 40% in Table 1
   c. The intersection occurs in the 'pink' shaded area of the Table indication an $FiO2_{eff}$ <0.26, thus the infants' $FiO2_{eff}$ corrected to sea level is ≤ 0.21 and the infant is NOT eligible for physiologic evaluation (does not have BPD)

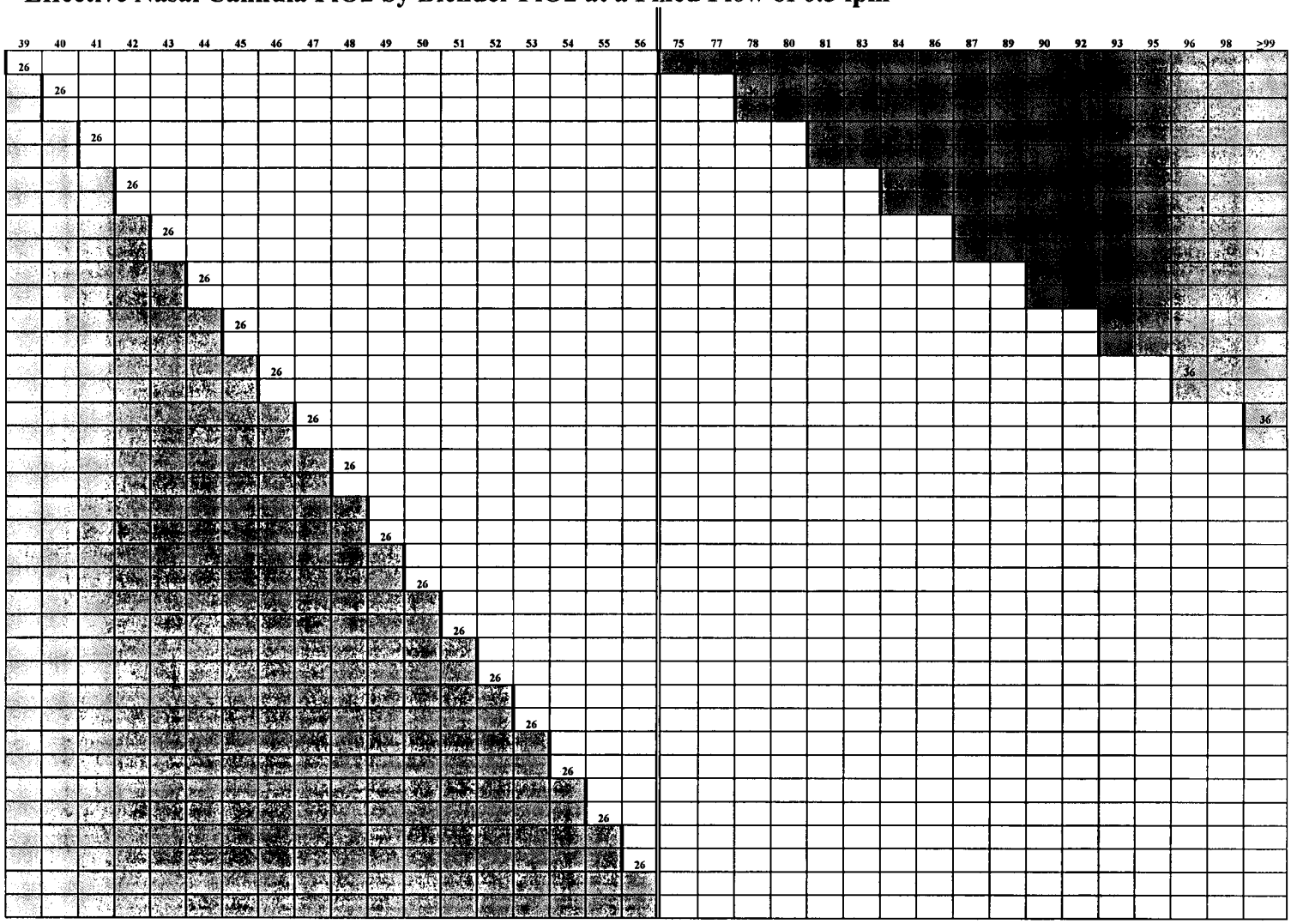
What is the effective FO2 in a 1900 gm infant on 90% oxygen at 0.5lpm?
ANSWER:
   a. Use Table 1
   b. Locate intersection of 1900 gm and 90% in Table 1
   c. The intersection occurs in the 'blue shaded area of the Table indicating an $FiO2_{eff}$ >0.36, thus the infants' $FiO2_{eff}$ corrected to sea level is ≥ 0.30 and the infant is NOT eligible for physiologic evaluation (has BPD)

What is the effective FiO2 in a 2.0 kg infant on 100% cannula at a flow of 0.15 lpm?
ANSWER:
   a. Use Table 2
   b. 0.15 lpm = 150 ml/min
   c. The $FiO2_{eff}$ is 0.27 which is . 0.25 but < 0.36 thus the infant is eligible for physiologic evaluation

   NOTE: Altitude correction to 5000 feet would result in and effective FiO2 = 0.27/1.21 = 0.223 or 0.22

   For this infant (2.0 kg) and $FiO2_{eff}$ = 0.21 (corrected for altitiude) the goal is to wean flow to a minimum of 100 ml/min and then one step further if possible.

Effective Nasal Cannula FiO2 by Blender FiO2 at a Fixed Flow of 0.5 lpm



Effective FiO2 by Nasal Cannula Flow with Blender FiO2 at 100%

Wt / *Flow**	1500	1750	2000	2250	2500	2750	3000	3250	3500	3750	4000
50	0.24	0.24	0.23	0.23	0.23	0.23	0.23	0.23	0.22	0.22	0.22
100	0.26	0.26	0.25	0.25	0.24	0.24	0.23	0.23	0.23	0.23	0.23
150	0.29	0.28	0.27	0.27	0.26	0.26	0.25	0.25	0.24	0.24	0.24
200	0.32	0.31	0.29	0.28	0.27	0.27	0.27	0.26	0.26	0.25	0.25
250	0.34	0.33	0.31	0.30	0.29	0.28	0.27	0.27	0.27	0.26	0.26
0.5 lpm	0.47	0.44	0.41	0.39	0.37	0.36	0.34	0.33	0.32	0.32	0.31

* flow in ml/min except as indicated

At 5,000 ft: - babies in the PINK range have an effective FiO2 ≤ 0.21 at sea level
- babies in the BLUE range have an effective FiO2 > 0.35, thus "Physiologic BPD"
- babies in the WHITE range meet criteria for O2 Reduction Test

Center: __ __ Site: ___ Network No: __ __ __ __ Birth No: ___ Mother's Initials: __ __ __

Complete PHY01 for all GDB infants 401 - 1500 grams birthweight or study infants who are alive at 36 weeks gestation and on ANY respiratory support to determine eligibility for RA challenge. [See Manual]

A. DATE FOR PHYSIOLOGIC EVALUATION:

1. Date of 36 Week Corrected Age: __ __/__ __/__ __ __ __ (Month / Day / Year)
2. Patient available for Physiologic Evaluation? Y N

If Yes, Continue to Section B.

a. If No, record reason: ___

1= Discharged	3= Transferred	9= other

b. If Code =3, and if FiO2 > 21% (> 25% at altitude) at transfer, call receiving hospital and answer c.

c. Is the patient in room air (< 26% at altitude) at 36 weeks? Y N UK

B. ELIGIBILITY FOR PHYSIOLOGIC EVALUATION:

Complete For All Infants in Hospital At 36 Weeks Corrected age receiving respiratory support more than room air.

1. Birthweight 401-1500 gms and now at 36 + 1 weeks corrected age Y N
2. Attending physician gives permission Y/NA N
3. Parent gives permission Y/NA N
4. Is patient receiving ventilator, nasal CPAP, or HFNC > 2 lpm? Y N
   If Yes, STOP. Pt is not eligible for challenge.
5. Effective oxygen < 27% (<33% at altitude) AND majority saturation ≥ 90% Y N
6. Effective oxygen (27-30% (33-36% at altitude) AND majority saturation ≥ 96% Y N
7. Room air (<26% at altitude) by nasal cannula Y N

If all of 1 - 3 AND either 5, 6, or 7 are answered YES or NA, patient is eligible for Physiologic Evaluation.

8. If patient was eligible and evaluation not done, code reason: ___

Initials of Person Completing this form: __ __ __

Eligible and Evaluation Not Done Reason codes:

1= Increased FiO2
2= Increased respiratory support (cpap or vent)
3= Instability (including Surgery/Sepsis)
6= Weaned to room air on/before day of evaluation
9= Other- explain

NICU Network	PHYSIOLOGIC DEFINITION OF BRONCHOPULMONARY DYSPLASIA OXYGEN REDUCTION DATA FORM BASELINE DATA *(Altitude Corrected Form)*	PHY02BASE Rel 2.0 September 8, 2005
Center: __ __ Site: ___ Network No. __ __ __ __	Mother's Initials: __ __ __ Birth No: ___	Page 1 of ___

Complete this form on all infants eligible for oxygen reduction.

Instructions:

- **Position infant supine and place pulse oximeter.**
- **Allow 5 minute recovery period after placing pulse oximeter and prior to baseline data collection.**
- **Baseline data collection is done in infant's current oxygen.**
- **Based on current weight determine the Nasal Cannula Flow & FiO2 which will produce an $FiO2_{eff}$ < 0.26; record that data here: FiO2:____ Flow rate: ____lpm**

A. BASELINE MEASUREMENTS

1. **Date:** __ __ / __ __ / __ __ __ __
   Month Day Year

Baseline Data:	a. FiO2: __ . __ __		b. Lpm: __ . __ __			
	0 min	1 min	2 min	3 min	4 min	5 min
c. Time	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
d. Saturation	___	___	___	___	___	___

2. **Type of Oximeter used in Challenge:** ___

1= Nellcor	2= Ohmeda	3= Hewlett Packard
4= Space labs	5= Masimo	6= Other

3. **Will the first wean place the patient in room air (< 26% altitude)?** Y N
   If yes, PHY02Reduc not needed. Complete PHY02RA.

B. SAFETY DATA:

1. CONTROL DATA IN THE 1 HOUR BEFORE physiologic evaluation

a. Did the infant have saturations <88% lasting for > 5 minutes? Y N

b. Did the infant have FiO_2 increased > 5%? Y N

c. Did the infant require initiation of ventilator? Y N

d. Did the infant have an apnea which lasted >20 seconds? Y N

e. Did the infant have a bradycardia (HR <80 for >10 sec)? Y N

f. Did the infant have a severe bradycardia (HR <70 for > 20 sec)? Y N

2. DURING AND 1 HOUR AFTER physiologic evaluation

a. Did the infant have saturations <88% lasting for > 5 minutes? Y N

b. Did the infant have FiO_2 increased > 5%? Y N

c. Did the infant require initiation of ventilator? Y N

d. Did the infant have an apnea which lasted >20 seconds? Y N

e. Did the infant have a bradycardia (HR <80 for >10 sec)? Y N

f. Did the infant have a severe bradycardia (HR <70 for > 20 sec)? Y N

Use as many copies of this form as needed to complete the reduction

C. OXYGEN REDUCTION PHASE:

1. Reduction Step # __ __: a. FiO2__ . __ __ b. Lpm: __ . __ __ __

	Minutes					
	0	1	2	3	4	5
c. Time	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
d. Saturation	__ __ __	__ __ __	__ __ __	__ __ __	__ __ __	__ __ __

2. Reduction Step # __ __: a. FiO2__ . __ __ b. Lpm: __ . __ __ __

	Minutes					
	0	1	2	3	4	5
c. Time	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
d. Saturation	__ __ __	__ __ __	__ __ __	__ __ __	__ __ __	__ __ __

3. Reduction Step # __ __: a. FiO2__ . __ __ b. Lpm: __ . __ __ __

	Minutes					
	0	1	2	3	4	5
c. Time	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
d. Saturation	__ __ __	__ __ __	__ __ __	__ __ __	__ __ __	__ __ __

4. Reduction Step # __ __: a. FiO2__ . __ __ b. Lpm: __ . __ __ __

	Minutes					
	0	1	2	3	4	5
c. Time	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
d. Saturation	__ __ __	__ __ __	__ __ __	__ __ __	__ __ __	__ __ __

5. Reduction Step # __ __: a. FiO2__ . __ __ b. Lpm: __ . __ __ __

	Minutes					
	0	1	2	3	4	5
c. Time	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
d. Saturation	__ __ __	__ __ __	__ __ __	__ __ __	__ __ __	__ __ __

CONTINUE TO NEXT IF SATURATION ≥90% X 5 MINUTES

STOP REDUCTION IF SATURATION <90% X 5 continuous MINUTES or <80% FOR 15 SECONDS

WEANING INSTRUCTIONS

Oxygen by hood:
Decrease FiO_2 by 2% every 5 minutes if saturation ≥ 90% until FiO2 < 0.26

Oxygen by nasal cannuale ≥26%:
Wean flow in increments of 0.5 lpm every 5 minutes until flow = 0.5 lpm

Method A- Weaning by FiO2
Determine $_{Eff}FiO2$:
$_{Eff}FiO2$ = 0.25 at 0.5 lpm & FiO_2= ___

With flow at 0.5 lpm wean FiO_2 by 10% every 5 minutes to predetermined FiO_2 above.

Method B- Weaning by flow
Determine $_{Eff}FiO2$:
$_{Eff}FiO2$ = 0.25 at 100% & flow = ___

With FiO_2 at 100% wean flow to 250 ml/min. Thereafter wean flow by 50 ml/min every 5 minutes to predetermined flow for FiO2 above.

For both methods and room air by nasal cannula- Turn off flow. Gently remove cannula from nares. Continue with room air if SAT ≥90%.

Room air by nasal cannula:
1. If flow ≥ 2lpm, see manual
2. If flow < 2 lpm, wean flow by 0.5 lpm every 5 minutes to 0.5 lpm.

NICU Network

PHYSIOLOGIC DEFINITION OF BRONCHOPULMONARY DYSPLASIA
OXYGEN REDUCTION DATA FORM
ROOM AIR PHASE

PHY02RA Rel 2.0
September 8, 2005

Center: __ __ Site: ___ Network No. __ __ __ __ Birth No: ___ Mother's Initials: __ __ __

D. **BEGIN ROOM AIR:**

	Minutes					
	1	2	3	4	5	6
1. Time	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
2. Saturation	___	___	___	___	___	___

Fail Criteria: Saturation <90% for 5 continuous minutes
or <80% for 15 seconds.

Rapid Pass Criteria:
Saturation ≥ 96% for 15 consecutive minutes.

	Minutes								
	7	8	9	10	11	12	13	14	15 RAPID PASS
1. Time	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
2. Saturation	___	___	___	___	___	___	___	___	___

	16	17	18	19	20	21	22	23	24
1. Time	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
2. Saturation	___	___	___	___	___	___	___	___	___

	25	26	27	28	29	30 END TEST
1. Time	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
2. Saturation	___	___	___	___	___	___

E. **OUTCOME OF CHALLENGE:**

1. Patient Passed? Y N

Blender FiO2 at end of challenge: __.____

Cannula flow rate at end of challenge: __.____ lpm

Infant weight at time of challenge: _____ gms

Initials of person completing this form ___

From: Abbot Laptook
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: for SUPPORT call
Date: Monday, July 16, 2007 11:20:23 AM

Rose
just to clarify, there isn't a conference call; this is for the subcommittee meeting in Washington. Correct? AL

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, July 16, 2007 11:07 AM
To: mcw3@case.edu; wacarlo@uab.edu; Neil Finer; Bradley.yoder@hsc.utah.edu; Roger Faix; Abbot Laptook; kurt.schibler@cchmc.org; Nancy Newman; Wade Rich; Das, Abhik; Poole Kenneth (E-mail); Gantz, Marie
Cc: Cunningham, Meg; Archer, Stephanie (NIH/NICHD) [E]; Zaterka-Baxter, Kristin; Susan Hintz
Subject: FW: for SUPPORT call

For the SUPPORT Subcommittee

Rose

-----Original Message-----
From: Susan Hintz [mailto:srhintz@stanford.edu]
Sent: Monday, July 16, 2007 11:01 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: neil finer
Subject: for SUPPORT call

Hi Rose and Neil,

Attached are materials for Neuroimaging secondary part of SUPPORT subcommittee meeting. It looks like a lot but I will be brief and to the point. I think I already sent you guys the blurb from MRIsafety.com and the Shellock paper, but here they are again.

Thanks. Let me know if any questions -

Susan

--
Susan R. Hintz, M.D., M.S. Epi
Associate Professor of Pediatrics
Division of Neonatal and Developmental Medicine Stanford University
School of Medicine 750 Welch Road, Suite 315 Palo Alto, CA 94304
ph: 650-723-5711
fax: 650-725-8351

From: Wade Rich
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: for SUPPORT call
Date: Monday, July 16, 2007 11:11:40 AM

Hi Rose,
Can you forward Neil and I the info for the subcomitte call?
Tx.
wade

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, July 16, 2007 8:07 AM
To: mcw3@case.edu; wacarlo@uab.edu; Neil Finer; Bradley.yoder@hsc.utah.edu; Roger Faix; alaptook@WIHRI.org; kurt.schibler@cchmc.org; Nancy Newman; Wade Rich; Das, Abhik; Poole Kenneth (E-mail); Gantz, Marie
Cc: Cunningham, Meg; Archer, Stephanie (NIH/NICHD) [E]; Zaterka-Baxter, Kristin; Susan Hintz
Subject: FW: for SUPPORT call

For the SUPPORT Subcommittee

Rose

-----Original Message-----
From: Susan Hintz [mailto:srhintz@stanford.edu]
Sent: Monday, July 16, 2007 11:01 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: neil finer
Subject: for SUPPORT call

Hi Rose and Neil,

Attached are materials for Neuroimaging secondary part of SUPPORT subcommittee meeting. It looks like a lot but I will be brief and to the point. I think I already sent you guys the blurb from MRIsafety.com and the Shellock paper, but here they are again.

Thanks. Let me know if any questions -

Susan

--
Susan R. Hintz, M.D., M.S. Epi
Associate Professor of Pediatrics
Division of Neonatal and Developmental Medicine Stanford University School of Medicine 750 Welch Road, Suite 315 Palo Alto, CA 94304
ph: 650-723-5711
fax: 650-725-8351

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: ROP
Date: Friday, July 13, 2007 10:57:10 PM

That would be great
Neil

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, July 13, 2007 9:21 AM
To: Neil Finer
Subject: ROP

Neil
Shall we have Dale join the SUPPORT subcommittee on thursday next week
for the ROP outcomes?
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]; Spong, Catherine (NIH/NICHD) [E]; Raju, Tonse (NIH/NICHD) [E]
Subject: RE: congress testimony
Date: Friday, July 13, 2007 2:05:11 PM

For Congressional testimony, should we provide documents in laymen's terms?

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Friday, July 13, 2007 10:34 AM
To: Spong, Catherine (NIH/NICHD) [E]; Raju, Tonse (NIH/NICHD) [E]
Cc: Archer, Stephanie (NIH/NICHD) [E]
Subject: congress testimony

Hi,
Here is a summary of one paper (benefits of breast milk in ELBW infants at 18 m. FU) and the inositol and SUPPORT Trials for the document for congress. Let me know if you want a different format or other items included.

Thanks
Rose

From: Raju, Tonse (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT TRIAL
Date: Wednesday, July 11, 2007 6:12:39 PM

Thanks. I read the PDF. So, when do you give surfactant to the two Early CPAP with Permissive ventilation groups? Do infants in all four groups receive surfactant at comparable time periods?

Tonse N. K. Raju, MD

Program Scientist/Medical Officer

Pregnancy and Perinatology Branch/CDBPM

NICHD/NIH, 6100 Executive Blvd

Bethesda, MD 20892-MS7510

phone: 301-402-1872

Fax: 301-496-3790

e-mail. rajut@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wednesday, July 11, 2007 2:03 PM
To: Raju, Tonse (NIH/NICHD) [E]
Subject: RE: SUPPORT TRIAL

1) no intubation/no surfactant/but DR CPAP
2) routine intubation and surfactant and mechanical ventilation

The link is https://neonatal.rti.org/pdf/StudySummary/summ_SUPPORT.pdf

Rose

From: Raju, Tonse (NIH/NICHD) [E]
Sent: Wednesday, July 11, 2007 1:36 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT TRIAL

Hi,

I wanted to know which of the following two are in the SUPPORT trial?

3) intubation/surfactant/extubation followed by CPAP
4) no intubation/no surfactant/but DR CPAP

5) routine intubation and surfactant and mechanical ventilation
6) no surfactant in the DR, just CPAP/

Thanks

Tonse N. K. Raju, MD

Medical Officer/Program Scientist
Pregnancy and Perinatology Branch

National Institute of Child Health and Human Development

National Institutes of Health

6100 Executive Blvd, Room 4B03

***Bethesda, MD, 20892.**

Phone: 301-402-1872; Fax: 301-496-3790

***(for courier services, use Rockville, MD 20852)**

From: Raju, Tonse (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT TRIAL
Date: Wednesday, July 11, 2007 3:51:33 PM

Thanks very mich, Rose. I will tell you tomorrow why I asked.

Sent from my BlackBerry Wireless Handheld

----- Original Message -----
From: Higgins, Rosemary (NIH/NICHD) [E]
To: Raju, Tonse (NIH/NICHD) [E]
Sent: Wed Jul 11 14:30:23 2007
Subject: RE: SUPPORT TRIAL

It is on the PDF
24 0/7 weeks to 27 6/7 weeks.

Rose

-----Original Message-----
From: Raju, Tonse (NIH/NICHD) [E]
Sent: Wednesday, July 11, 2007 2:20 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT TRIAL

Thanks. Do you have all between 20 and 27 weeks?

Sent from my BlackBerry Wireless Handheld

----- Original Message -----
From: Higgins, Rosemary (NIH/NICHD) [E]
To: Raju, Tonse (NIH/NICHD) [E]
Sent: Wed Jul 11 14:02:34 2007
Subject: RE: SUPPORT TRIAL

1) no intubation/no surfactant/but DR CPAP
2) routine intubation and surfactant and mechanical ventilation

The link is https://neonatal.rti.org/pdf/StudySummary/summ_SUPPORT.pdf

Rose

From: Raju, Tonse (NIH/NICHD) [E]
Sent: Wednesday, July 11, 2007 1:36 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT TRIAL

Hi,

I wanted to know which of the following two are in the SUPPORT trial?

3) intubation/surfactant/extubation followed by CPAP

4) no intubation/no surfactant/but DR CPAP
5) routine intubation and surfactant and mechanical ventilation
6) no surfactant in the DR, just CPAP/

Thanks

Tonse N. K. Raju, MD
Medical Officer/Program Scientist
Pregnancy and Perinatology Branch
National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd, Room 4B03
*Bethesda, MD, 20892.
Phone: 301-402-1872; Fax: 301-496-3790
*(for courier services, use Rockville, MD 20852)

From:	Neil Finer
To:	Abbot Laptook; Walsh, Michele; Roger Faix; Zaterka-Baxter, Kristin; wcarlo@peds.uab.edu; mcw3@cwru.edu; Bradley Yoder; kurt.schibler@cchmc.org; Nancy Newman; Wade Rich
Cc:	Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik; Gantz, Marie; Auman, Jeanette O.
Subject:	RE: Support study definition of air leak
Date:	Wednesday, June 27, 2007 12:09:13 PM

Hi Kris
Here is a Proposed Agenda for Steering Committee Meeting July 07

1. Review Enrollments to date
2. Discuss Eye follow-up and the need for intermediate eye outcome – ie 1 year
3. Issues from Coordinators Call
   Discuss definition of Airleak for SUPPORT trial
   Clarification of Steroid Dose issue from Coordinators Call

4. Review status of Secondaries-
   MRI – Susan Hintz
   Breathing Outcomes – Tim Stevens
   Nutrition – Christine Navarette
   Antenatal consent –Wade Rich

5. Discuss Prospective Meta Analysis
6. Other Issues

Please let me know if anyone would like to add additional items.
Regards
Neil Finer

From: Zaterka-Baxter, Kristin
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT Pulse Oximeter
Date: Friday, June 22, 2007 8:59:06 AM

Yup - will do.
Thanks,
Kris

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, June 22, 2007 3:29 AM
To: Zaterka-Baxter, Kristin
Subject: Fw: SUPPORT Pulse Oximeter

Can you help???

Sent from my BlackBerry Wireless Handheld

----- Original Message -----
From: Nancy Miller <Nancy.Miller@UTSouthwestern.edu>
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thu Jun 21 18:01:40 2007
Subject: Re: SUPPORT Pulse Oximeter

Rose,
Sorry to get hold of you so late but I just consented another Mom. I need a blue and orange pulse ox.
Thanks,
Nancy

P.S. I won't be able to answer any e-mails because I have to leave the office as soon as I send this. My address is on the Network website.

Nancy A. Miller, R.N.
Department of Pediatrics
Division of Neonatal-Perinatal Medicine
UT Southwestern Medical Center at Dallas
5323 Harry Hines Blvd. E3-502
Dallas, Texas 75390-9063
214-648-3780
pager 972-206-9151

From: Nancy Miller
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT Pulse Oximeter
Date: Thursday, June 21, 2007 6:01:52 PM

Rose,
Sorry to get hold of you so late but I just consented another Mom. I need a blue and orange pulse ox.
Thanks,
Nancy

P.S. I won't be able to answer any e-mails because I have to leave the office as soon as I send this. My address is on the Network website.

Nancy A. Miller, R.N.
Department of Pediatrics
Division of Neonatal-Perinatal Medicine
UT Southwestern Medical Center at Dallas
5323 Harry Hines Blvd. E3-502
Dallas, Texas 75390-9063
214-648-3780
pager 972-206-9151

From: Fernando Martinez
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Neil Finer; Wade Rich
Subject: Letter to Dr. Maynard Rasmussen
Date: Tuesday, June 19, 2007 11:26:27 AM
Attachments: Maynard Rasmussen - Sharp Mary Birch Hospital for Women.pdf

---

Dear Dr. Higgins,

Please find attached a copy of a letter Dr. Finer wrote to Dr. Maynard Rasmussen regarding the SUPPORT trial.

Regards,
Fernando Martinez

Assistant to Dr. Neil Finer
UC San Diego School of Medicine
UC San Diego Medical Center, Hillcrest
Division of Neonatology
402 Dickinson St., MPF 1-140
San Diego, CA 92103-8774
Telephone: 619-543-3759
Facsimile: 619-543-3812

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NEIL N. FINER, M.D.
PROFESSOR OF PEDIATRICS
DIRECTOR, DIVISION OF NEONATOLOGY
DEPARTMENT OF PEDIATRICS

200 WEST ARBOR DRIVE, MC 8774
SAN DIEGO, CA 92103-8774
TEL: (619) 543-3759
FAX: (619) 543-3812

June 5, 2007

Maynard Rasmussen, M.D.
Sharp Mary Birch Hospital for Women
Division of Neonatology
3003 Health Center Drive
San Diego, CA 92123

Dear Maynard,

The NICHD has granted the UCSD Site funding for 30 new infants to be enrolled in the SUPPORT trial over the next year. It is our desire to continue to partner with Sharp Mary Birch to enroll these subjects as we have done previously. We have received approval from Rose Higgins at the NICHD to include Sharp Mary Birch for this trial. Funding is at the level of $2000.00 per subject. If the subjects are enrolled in the MRI study, there is an additional allowance of $1314.00 for fully completed infants.

We appreciate the opportunity to work with you on this project in the past, and hope that Sharp Mary Birch will continue to partner with us for this exciting project.

Sincerely,

Neil Finer, MD
Professor of Pediatrics
Director, Division of Neonatology
UCSD Medical Center

cc: Rose Higgins, M.D.

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Orange oximeters to Duke
Date: Monday, June 11, 2007 4:52:44 PM

This sounds very good.
Thanks Rose
Neil

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, June 11, 2007 1:31 PM
To: Neil Finer
Subject: Fw: Orange oximeters to Duke

FYI,
Also we have 673 enrolled in the trial as of last week.
Kris is in the process of scheduling a DSMC meeting in the fall.

We have also sent the teleconference minutes from the SUPPORT recruitment calls on to NHLBI and kris will forward to the DSMC.

Thanks for your continued commitment. My best to you and Ginny
Take care
Rose

Sent from my BlackBerry Wireless Handheld

----- Original Message -----
From: Higgins, Rosemary (NIH/NICHD) [E]
To: 'kzaterka@rti.org' <kzaterka@rti.org>;
'Georgia.E.McDavid@uth.tmc.edu' <Georgia.E.McDavid@uth.tmc.edu>
Cc: 'auten002@mc.duke.edu' <auten002@mc.duke.edu>
Sent: Mon Jun 11 16:17:45 2007
Subject: Re: Orange oximeters to Duke

Thanks to all of you!!
Rose

Sent from my BlackBerry Wireless Handheld

----- Original Message -----
From: Zaterka-Baxter, Kristin <kzaterka@rti.org>
To: Mcdavid, Georgia E <Georgia.E.McDavid@uth.tmc.edu>
Cc: Kathy J Auten <auten002@mc.duke.edu>; Higgins, Rosemary (NIH/NICHD) [E]
Sent: Mon Jun 11 16:17:10 2007
Subject: Orange oximeters to Duke

Hi Georgia,

Thanks so much for your help! Please send TWO ORANGE oximeters to Kathy Auten at Duke; address below.

Duke University Medical Center

Bell Bldg., Rm. 141
Bell Service Dr.
Durham 27710

Phone: 919-681-5859

Email; auten002@mc.duke.edu

Attn: Kathy Auten

Thanks again,

Kirs

From: Zaterka-Baxter, Kristin
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Growth Support Secondary
Date: Friday, June 08, 2007 5:43:55 PM

Hi Rose,
Are all sites required to participate in the Support Growth Secondary or is this optional?
Thanks,
Kris

From:	Zaterka-Baxter, Kristin
To:	Kathy J Auten
Cc:	Higgins, Rosemary (NIH/NICHD) [E]
Subject:	RE: MedWatch for SUPPORT subject death
Date:	Thursday, June 07, 2007 5:34:15 PM

Thanks Kathy,

Kris

From: Kathy J Auten [mailto:auten002@mc.duke.edu]
Sent: Thursday, June 07, 2007 5:28 PM
To: Zaterka-Baxter, Kristin
Subject: MedWatch for SUPPORT subject death

Kris,
This is the SAE report for a death in the SUPPORT Study. It was determined to be unrelated to the study, and not unexpected in this population. I have reported it to our IRB.
Kathy

Kathy J. Auten, MSHS
Project Manager
NICHD Neonatal Research Network Trials
Duke University Medical Center
Box 3179
Bell Building, Room 141
Durham, NC 27710 USA
919-681-5859 tel
919-681-4868 fax
kathy.auten@duke.edu

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Wade Rich
Subject: RE: SUPPORT Recruitment
Date: Wednesday, June 06, 2007 8:02:32 PM

Hi Rose
I have asked Maynard and am waiting for his reply
I will let you know as soon as I hear.
Be well
Neil

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, June 06, 2007 4:27 PM
To: Neil Finer
Subject: SUPPORT Recruitment

Neil,
We are in the budget process and are looking at SUPPORT projections for the coming year by site. Did Maynard get IRB approval??
If I should call you, let me know

Thanks
I hope Ginny is OK

Rose

Sent from my BlackBerry Wireless Handheld

From:	Wally Carlo, M.D.
To:	Higgins, Rosemary (NIH/NICHD) [E]; Neil Finer; mcw3@case.edu; Bradley Yoder; Roger.Faix@hsc.utah.edu; Abbot Laptook; kurt.schibler@cchmc.org; Das, Abhik; Wade Rich; nancy newman; Gantz, Marie
Cc:	Archer, Stephanie (NIH/NICHD) [E]; Cunningham, Meg; Webb, Robin E.; Zaterka-Baxter, Kristin
Subject:	RE: CONFIDENTIAL SUPPORT META ANALYSIS variables
Date:	Tuesday, May 29, 2007 2:01:30 PM
Attachments:	NeOProM variable coding form - V4_30 April07 RTI comments.doc

Wally Carlo, M.D.
Edwin M. Dixon Professor of Pediatrics
University of Alabama at Birmingham
Director, Division of Neonatology
Director, Newborn Nurseries
619 South 20th Street
525 New Hillman Building
Birmingham, AL 35233-7335
Phone: 205 934 4680
FAX: 205 934 3100
Cell: 205 266 4004

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, May 09, 2007 3:08 PM
To: Neil Finer; Wally Carlo, M.D.; mcw3@case.edu; Bradley Yoder; Roger.Faix@hsc.utah.edu; Abbot Laptook; kurt.schibler@cchmc.org; Das, Abhik; Wade Rich; nancy newman; Gantz, Marie
Cc: Archer, Stephanie (NIH/NICHD) [E]; Cunningham, Meg; Webb, Robin E.; Zaterka-Baxter, Kristin
Subject: CONFIDENTIAL SUPPORT META ANALYSIS variables

Hi,
I have attached the proposal for the meta analysis - Lisa Aksie has asked for input on the variables to be collected for the prospective meta analysis. As you probably recall, the NRN steering committee agreed in principle to be part of the prospective metaanalysis following a presentation by Dr. Cole at the Steering Committee meeting in Jan. 2005.
The group is also interested in seeing data from the first 50 patients recruited into each trial. I had informed them that this is not normally done with NRN trials.

We also need to develop a potential timeline for data release for this collaboration which will need to be approved by the steering committee.

On a very positive note, the SUPPORT Trial is way ahead of any of the other ongoing trials with respect to enrollment!!

I will have Robin set up a call with the SUPPORT Subcommittee in the next month for discussion.

Thanks
Rose

<<NeOProM variable coding form - V4_30 April07 RTI comments.doc>>

NeOProM Neonatal Oxygenation Prospective Meta-analysis Collaboration

Please use the variable coding below when submitting your trial data

Enrolment characteristics

Variable name	Variable coding
patient ID	unique patient ID used within your trial (anonymised, no patient names, can be character or number format)
allocated treatment	1=lower SpO_2; 2=higher SpO_2
date of birth*	date of birth
time of birth#	time of birth
gestation at birth	in completed weeks using best estimate; or 99=unknown
date of randomisation*	date of randomisation
time of randomisation#	time of randomisation
date of intervention commencement*	date when study oximeter first attached to infant
time of intervention commencement#	time when study oximeter first attached to infant
inborn / outborn status^	1=inborn; 2=outborn; 9=unknown
antenatal corticosteroids We only know if steroids were given and, if so, if a complete course was given within 7 days prior to delivery	1=none; 2=incomplete (<24 hrs before birth); 3=complete (24hrs-7 days before birth); 4=last course completed more than 7 days before birth; 9=unknown
onset of labour We do not have this information	1=spontaneous; 2=induced; 3=pre-labour Caesarean Section; 9=unknown
mode of delivery	1=vaginal vertex delivery; 2=vaginal breech delivery; 3=Caesarean Section; 9=unknown
surfactant therapy	0=none; 1=yes, before randomisation only; 2=yes, after randomisation only; 3=yes, given both before and after randomisation; 9=unknown
primary cause of preterm birth We know if there was hypertension, diabetes or PROM from the NG02, but we do not specifically record whether those conditions were the primary cause of preterm birth	1=prelabour rupture of membranes (PROM); 2=preterm labour (without PROM); 3=pregnancy induced hypertension (± APH); 4=APH; 5=other maternal illness (such as essential hypertension, renal disease, diabetes, or infection); 6=poor fetal growth and/or fetal distress (mother well); 9=unknown

Infant outcomes at 36 weeks postmenstrual age

(record outcomes on date closest to 36 weeks 0 days postmenstrual age)

Variable name	Variable coding
infant weight 36 weeks We have this only if the infant was hospitalized at 36 weeks	weight at 36 wks postmenstrual age, in grams; 9999=unknown
nasal CPAP for ≥30mins on day 36 wks pma We have whether the infant was on CPAP (NG07) but not for how long	0=no; 1=yes; 9=unknown
ventilation via ETT for ≥30mins on day 36wks pma We have whether the infant was on vent (NG07) but not for how long (not sure what ETT is, though)	0=no; 1=yes; 9=unknown
maximum sustained (≥30mins) inspired oxygen on day 36 wks We have FiO2 (except if the infant is on NC), but not length of time	as percent (21-100), to nearest whole number; 999=unknown
nasal cannulae oxygen for ≥30mins on day 36 wks We have whether the infant was on NC (NG07) but not for how long	0=no; 1=yes; 9=unknown
nasal cannulae oxygen concentration on day 36 wks We do not have this information (we do have flow rate on SUPP11)	as percent (21-100), to nearest whole number; 999=unknown; if applicable
nasal cannulae flow rate on day 36 wks	as Litres/min, to 2 decimal places (e.g. 0.04L/min); if applicable

Infant outcomes at discharge from hospital

total days with endotracheal or tracheostomy tube This would be calculated based on intubations and extubations (SUPP05A and SUPP07)	days; 9999=unknown
total days of CPAP	days; 9999=unknown
date and when last received supplemental oxygen* We will not know this date if supplemental oxygen continues past 36 weeks (before that we can look at the SUPP11)	date when supplemental oxygen no longer required
gestational age when last received supplemental oxygen See above	if date when supplemental oxygen ceased unknown, please supply gestational age
date when trial intervention ceased* We do not record this date, but we can calculate it based on the last day the infant received supplemental oxygen	date when targeting the allocated oxygen saturation range ceases
gestational age when trial intervention ceased* See above	if date when trial intervention ceased unknown, please supply gestational age
patent ductus arteriosus£	0=no; 1=yes; 9=unknown
necrotising enterocolitis✠	0=no; 1=yes; 9=unknown
major cerebral abnormality *need highest grade of IVH as well?* We do not record all of these abnormalities (we do have porencephalic cysts, PVL, IVH)	0=nil; 1=ventriculomegaly; 2=intraparenchymal echodense lesion; 3=porencephalic cysts; 4=cystic periventricular leukomalacia; 5=cortical atrophy not resolved post-discharge; 6=others; 9=unknown

For further information, contact: **Lisa Askie** laskie@ctc.usyd.edu.au **Phone: +61 (0)2 9562 5000 Direct: +61 (0)2 9562 5040**

		postnatal steroids for lung disease	0=no; 1=yes; 9=unknown
birthweight	birthweight, in grams; 9999=unknown	highest stage of ROP before discharge❖ This would have to be based on the last eye exam before discharge	0=no ROP;1=Stage 1, 2=Stage 2, 3=Stage 3, 4=Stage 4, 5=Stage 5; 9=unknown
gender	0=female; 1=male; 9=unknown	ROP treatment with oxygen or surgery¥ I do not think we have any data on treatment with oxygen	0=no; 1=high levels supplemental oxygen; 2=retinal surgery; 3=supplemental oxygen and retinal surgery; 9=unknown
multiple birth	0=singleton; 1=multiple; 9=unknown	date at discharge home*	date of discharge
5 min Apgar score	whole number (0-10); 99=unknown	gestational age at discharge home*	if date when discharged home unknown, please supply gestational age
first pH or base excess	*for discussion*	discharge home on supplemental oxygen	0=no; 1=yes; 9=unknown
ethinicity	*for discussion*	date of death	date of death
respiratory support immediately prior to intervention commencement We have respiratory support upon admission to the NICU (SUPP04)	*for discussion*	primary cause of death We do not have COD if infant dies after initial discharge. Also, we do not record meningitis as a specific COD.	1=congenital abnormality; 2=pulmonary hypoplasia; 3= severe RDS; 4=chronic lung disease; 5=pneumonia; 6=grade 3/4 IVH; 7=meningitis; 8=septicaemia; 9=necrotising enterocolitis (NEC); 10=Sudden Infant Death Syndrome (SIDS); 11=other, 12=unknown

Infant outcomes at 18-24 months corrected age

The protocol refers to 18-24 months PMA. What we collect is 18-24 months as measured after full term is reached. It is unclear to me which definition they are referring to as "corrected age."

Variable name	Variable coding
date of neurodevelopmental assessment*	date Bayley 3 assessed done
Bayley 3 (BSID-3) cognitive score of <70	0=no; 1=yes; 9=not recorded
severe visual loss¶	0=no; 1=yes; 9=not recorded
cerebral palsy§	0=no; 1=yes; 9=not recorded
deafness¤	0=no; 1=yes; 9=not recorded
Re-admissions to hospital up to 18-24 months corrected age	0=no; 1=yes; 9=not recorded
date growth measures recorded*	date growth measures assessed
infant weight	weight at date of assessment, in grams; 9999=unknown
infant height	Height at date of assessment, in cm; 9999=unknown

Notes

- * dates should be in the format: dd/mm/yyyy or dd/mm/yy
- # times should be in 24 hour format: e.g. 23:56 for 11.56pm
- ^ infant born at a hospital with neonatal intensive care facilities (inborn) or at a hospital without neonatal intensive care facilities (outborn)
- ❖ using International Classification of Retinopathy of Prematurity definitions
- ¥ prescription of high range oxygen saturation targeting for a short period to arrest the progress of pre-threshold ROP
- £ diagnosed by ultrasound and requiring medical or surgical treatment Our PDA is not necessarily diagnosed by ultrasound (MOP specifies "clinical evidence")
- ❄ radiological diagnosis, clinical history plus either pneumatosis intestinalis, or portal vein gas, or a persistent dilated loop on serial X-rays Does this mesh with Bell's Staging Criteria?
- ¶ cannot fixate or is legally blind (<6/60) in both eyes
- § inability to walk at 18-24 months postmenstrual age with GMFCS level ≥2 or MACS level ≥2[1-3]
- ¤ requiring hearing aids in either air or too deaf to benefit from a hearing aid[4]

Please refer to the NeOProM protocol for more detailed definitions if required.

Please see next page for description of GFSC and MACS system classifications.

References

1. Eliasson AC, Krumlinde-Sundholm L, Rosblad B. Beckung E, Arner M, Ohrvall AM, Rosenbaum P. The Manual Ability Classification System (MACS) for children with cerebral palsy: scale development and evidence of validity and reliability. *Developmental Medicine & Child Neurology* 2006;**48**(7):549-54.
2. Wood E, Rosenbaum P. The gross motor function classification system for cerebral palsy: a study of reliability and stability over time. *Developmental Medicine & Child Neurology* 2000;**42**(5):292-6.
3. Palisano R, Rosenbaum P, Walter S, Russell D, Wood E, Galuppi B. Development and reliability of a system to classify gross motor function in children with cerebral palsy. *Developmental Medicine & Child Neurology* 1997;**39**(4):214-23.
4. Anon. Disability and Perinatal Care: report of two working groups. Oxford: NPEU & Oxford HA, 1995.

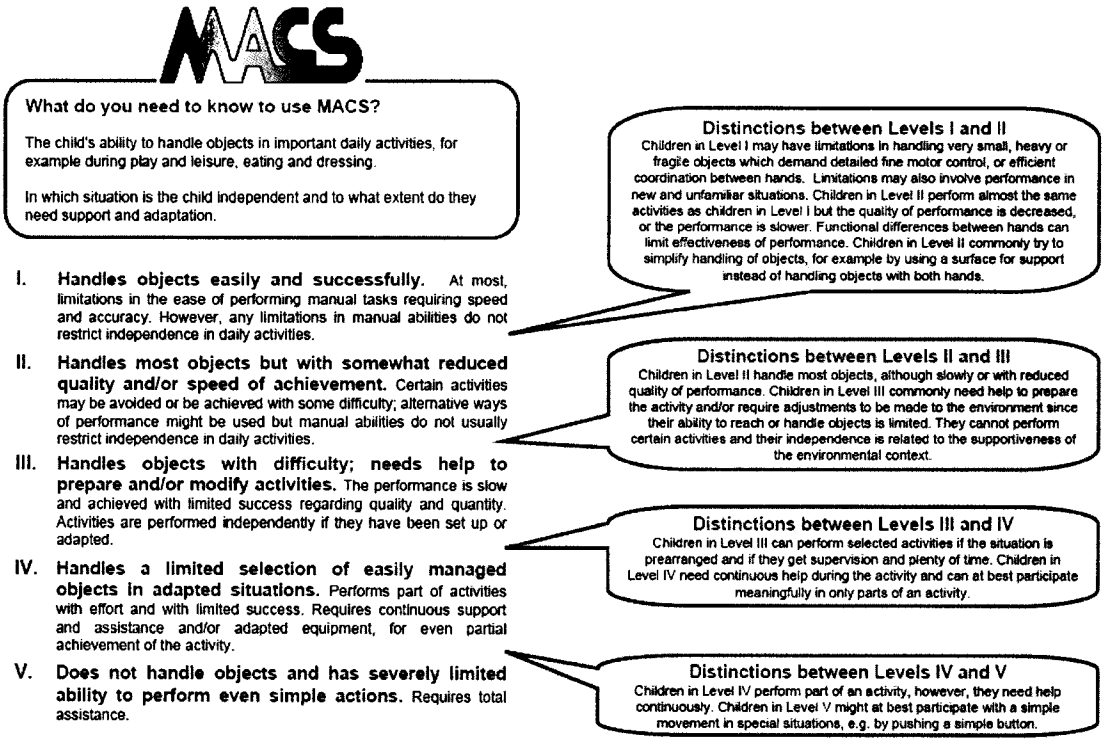
Gross Motor Function Classification System for Cerebral Palsy (GMFCS) [1-3]

Before 2nd Birthday

- **Level I** Infants move in and out of sitting and floor sit with both hands free to manipulate objects. Infants crawl on hands and knees, pull to stand and take steps holding on to furniture. Infants walk between 18 months and 2 years of age without the need for any assistive mobility device.
- **Level II** Infants maintain floor sitting but may need to use their hands for support to maintain balance. Infants creep on their stomach or crawl on hands and knees. Infants may pull to stand and take steps holding on to furniture.
- **Level III** Infants maintain floor sitting when the low back is supported. Infants roll and creep forward on their stomachs.
- **Level IV** Infants have head control but trunk support is required for floor sitting. Infants can roll to supine and may roll to prone.
- **Level V** Physical impairments limit voluntary control of movement. Infants are unable to maintain antigravity head and trunk postures in prone and sitting. Infants require adult assistance to roll.

Between 2nd and 4th Birthday

- **Level I** Children floor sit with both hands free to manipulate objects. Movements in and out of floor sitting and standing are performed without adult assistance. Children walk as the preferred method of mobility without the need for any assistive mobility device.
- **Level II** Children floor sit but may have difficulty with balance when both hands are free to manipulate objects. Movements in and out of sitting are performed without adult assistance. Children pull to stand on a stable surface. Children crawl on hands and knees with a reciprocal pattern, cruise holding onto furniture and walk using an assistive mobility device as preferred methods of mobility.
- **Level III** Children maintain floor sitting often by "W-sitting" (sitting between flexed and internally rotated hips and knees) and may require adult assistance to assume sitting. Children creep on their stomach or crawl on hands and knees (often without reciprocal leg movements) as their primary methods of selfmobility. Children may pull to stand on a stable surface and cruise short distances. Children may walk short distances indoors using an assistive mobility device and adult assistance for steering and turning.
- **Level IV** Children floor sit when placed, but are unable to maintain alignment and balance without use of their hands for support. Children frequently require adaptive equipment for sitting and standing. Selfmobility for short distances (within a room) is achieved through rolling, creeping on stomach, or crawling on hands and knees without reciprocal leg movement.
- **Level V** Physical impairments restrict voluntary control of movement and the ability to maintain antigravity head and trunk postures. All areas of motor function are limited. Functional limitations in sitting and standing are not fully compensated for through the use of adaptive equipment and assistive technology. At Level V, children have no means of independent mobility and are transported. Some children achieve self-mobility using a power wheelchair with extensive adaptations.



From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Wade Rich
Subject: RE: SUPPORT question
Date: Thursday, May 24, 2007 11:07:43 AM

Hi Rose
We are still waiting.
Neil

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, May 24, 2007 3:55 AM
To: Neil Finer
Cc: Wade Rich
Subject: SUPPORT question

Neil
Did Maynard get his IRB to re-activate SUPPORT, and if so - can you send us a copy of the approval?
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

From: Wally Carlo, M.D.
To: Higgins, Rosemary (NIH/NICHD) [E]; wacarlo@uab.edu
Cc: Webb, Robin E.
Subject: RE: SUPPORT CALL
Date: Monday, May 21, 2007 6:06:24 PM

Rose.

The 29th is open all times. On the 31st, i can do it if the call ends by 12:30.

Wally

-----Original Message-----
From: "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov>
To: "wacarlo@uab.edu" <wacarlo@uab.edu>
Cc: "Webb, Robin E." <rwebb@rti.org>
Sent: 5/21/2007 1:34 PM
Subject: SUPPORT CALL

Wally - are you available for a SUPPORT call during either of these
times?
Thanks

Rose

Tues 5/29 11-5

Thu 5/31 11-2

Rosemary D. Higgins, M.D.

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

NICHD, NIH

6100 Executive Blvd., Room 4B03B

MSC 7510

Bethesda, MD 20892

(For overnight delivery, use Rockville, MD 20852)

301-435-7909

301-496-3790 (FAX)

higginsr@mail.nih.gov

Blansfield, Earl (NIH/NICHD) [E]

From: Monica Collins <MCollins@peds.uab.edu>
Sent: Tuesday, May 15, 2007 3:10 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: As we ship Masimos all around the country...

Sure, that's not a problem. I'm just trying to make sure that sites know that they need to return the ones that they borrow.
Monica

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, May 15, 2007 2:09 PM
To: Monica Collins
Subject: RE: As we ship Masimos all around the country...

Yes, But can we wait a couple of days? Why ship twice- it is likely that someone else will ask for oximeters before the end of the week.

Thanks
Rose

From: Monica Collins [mailto:MCollins@peds.uab.edu]
Sent: Tuesday, May 15, 2007 3:08 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: As we ship Masimos all around the country...

I understand—if they are supposed to come back to Alabama, should they send them back to us if they are not using them?
Monica

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, May 15, 2007 2:05 PM
To: Monica Collins; Zaterka-Baxter, Kristin; Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: As we ship Masimos all around the country...

Utah sent us an email and definitely has 3 blues that they could spare (for the next request).

Thanks
Rose

From: Monica Collins [mailto:MCollins@peds.uab.edu]
Sent: Tuesday, May 15, 2007 3:03 PM
To: Zaterka-Baxter, Kristin; Archer, Stephanie (NIH/NICHD) [E]; Higgins, Rosemary (NIH/NICHD) [E]
Subject: As we ship Masimos all around the country...

Kris,
As we send these Masimos all around the country, I noticed that Utah has 3 blues that they can send to someone. I have attached a spreadsheet with our Masimo numbers—the highlighted ones are still out to othercenters. Because we have so many new coordinators, we think it is possible that sites don't know that they are supposed to send the borrowed ones back to the site that sent them to them—in a timely fashion. If they are in use, it is not a problem. We currently have 13 out and these may have been sent on to other sites without our knowledge.

We are concerned ours may be out somewhere that we don't know. Could you check? If sites are finished with ours, we would like to put them back in the repository to have available for other sites. Unless we are changing the procedure--
Thanks,
Monica

From: Wally Carlo, M.D.
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT MRI
Date: Tuesday, May 15, 2007 1:04:32 PM

Rose: THANKS. We are on a roll! wally

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, May 15, 2007 10:16 AM
To: Shirley Cosby
Cc: wacarlo@uab.edu; Poe, Grace (NIH/NICHD) [E]; Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: SUPPORT MRI

Hi Shirley,
You may enroll up to 150 infants into the SUPPORT MRI study at the UAB site.

Thanks
Rose

From: Shirley Cosby [mailto:SCosby@peds.uab.edu]
Sent: Tuesday, May 15, 2007 11:14 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT MRI

Good Morning!
I have what I hope is an easy request from you. I have recently sent the SUPPORT MRI renewal to our IRB. Our original submission indicated that we would enroll 50 patients (we had just divided the total number across the network sites) and now that we have just reached that number they are requesting that we submit an amendment in which an increase in the number of participant is requested in order to continue enrollment. I need to get some type of documentation from you saying that we may continue to enroll patients in this study so that I can complete this amendment paperwork.

Thanks,
Shirley

From: Wade Rich
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT
Date: Tuesday, May 15, 2007 11:50:31 AM

Turns out they were doing non-support babies. Thanks .
wade

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, May 15, 2007 7:14 AM
To: Wade Rich
Subject: RE: SUPPORT

It depends on the study – we need to see the protocol (or at the very least, an overview of the research)>
Thanks
Rose

From: Wade Rich [mailto:wrich@ucsd.edu]
Sent: Monday, May 14, 2007 11:26 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: SUPPORT

Rose,
I think this may be for another study. Can a unit download a SUPPORT oximeter and use the data for another study? Just wondering before I call Leslie back.
wade

From: Wilson, Leslie Dawn [mailto:ldw@iupui.edu]
Sent: Monday, May 14, 2007 8:22 AM
To: Wade Rich
Subject: SUPPORT

Hi. Me again- Couple o' questions.

First—I need to order the Masimo LNOP Neo-L <10 Kg SpO2 adhesive sensors. Our unit does not stock them and we are close to being out. Do you know with whom I would request these?

Second-Our neonatal unit is beginning to work on securing the capabilities of downloading the bedside data from the oximeters (although from a central monitor). I was wondering if you were doing that on your unit or if you knew of any site that might be. They were hoping to not have to start at the beginning of this process. Do you know where you obtained your TExtract.exe-as I know they would need this. Then, do you know the software you use so that once you have the data it sorts the data points (?)? You can tell I have a real handle on this process...

Thirdly—I had to purchase a new laptop as the old one crashed. Our IT downloaded the textract, and I downloaded the CD for the Belkin serial adapter but it will not extract. It will not do anything with the COM 4, with COM 3 the error comes up that is in the instructions-No response from the unit. Please check the cable or the output setting. I don't know if you have had this in the past—Tonight I am going to Best Buy to purchase another adapter as it has never really fit that well.

Thanks---leslie

Leslie Dawn Wilson, RN, BSN
Research Manager
Neonatal Network Coordinator
Riley Hospital RR 208
ldw@iupui.edu (e-mail)
699 West Dr
Indianapolis, IN 46202
317.274.8255 (phone)
317.274.8963 (fax)
317.312.1121 (pager)

From:	Archer, Stephanie (NIH/NICHD) [E]
To:	"Wade Rich"; "Johnson, Karen"; "ahensman@wihri.org"; "mbball@leland.stanford.edu"; "bmackinnon@tufts-nemc.org"; "crosman@med.wayne.edu"; "grisbyca@email.uc.edu"; "CBackstrom@salud.unm.edu"; "ellen_hale@oz.ped.emory.edu"; "Georgia.E.McDavid@uth.tmc.edu"; "jennifer.j.jensen@hsc.utah.edu"; "jrohr@salud.unm.edu"; "karena.strong@intermountainmail.org"; "auten002@mc.duke.edu"; "kimberlee.weaverlewis@intermountainmail.org"; "ldw@iupui.edu"; "linda_reubens@urmc.rochester.edu"; "mcollins@peds.uab.edu"; "monica.konstantino@yale.edu"; "Nancy.Miller@UTSouthwestern.edu"; "nxs5@cwru.edu"; "ae5357@wayne.edu"; "scosby@peds.uab.edu"
Cc:	Higgins, Rosemary (NIH/NICHD) [E]; "Melissa Leps (melissa.leps@utsouthwestern.edu)"
Subject:	RE: SUPPORT Pulse Oximeters (orange) needed
Date:	Monday, May 14, 2007 2:48:30 PM

Got the third one from Alabama. Thanks everyone for your responses!

From: Archer, Stephanie (NIH/NICHD) [E]
Sent: Monday, May 14, 2007 2:03 PM
To: 'Wade Rich'; Johnson, Karen; ahensman@wihri.org; mbball@leland.stanford.edu; bmackinnon@tufts-nemc.org; crosman@med.wayne.edu; grisbyca@email.uc.edu; CBackstrom@salud.unm.edu; ellen_hale@oz.ped.emory.edu; Georgia.E.McDavid@uth.tmc.edu; jennifer.j.jensen@hsc.utah.edu; jrohr@salud.unm.edu; karena.strong@intermountainmail.org; auten002@mc.duke.edu; kimberlee.weaverlewis@intermountainmail.org; ldw@iupui.edu; linda_reubens@urmc.rochester.edu; mcollins@peds.uab.edu; monica.konstantino@yale.edu; Nancy.Miller@UTSouthwestern.edu; nxs5@cwru.edu; ae5357@wayne.edu; scosby@peds.uab.edu
Cc: Higgins, Rosemary (NIH/NICHD) [E]; Melissa Leps (melissa.leps@utsouthwestern.edu)
Subject: RE: SUPPORT Pulse Oximeters (orange) needed

Nancy Newman at Case Western will send the 2 she has -- thanks, Nancy for your help!

We still need 1 more! Can anyone spare one?

Machines need to go to:

UT Southwestern
Attn: Nancy Miller, RN
5323 Harry Hines, office E3.404B
Dallas, TX 75390
214-648-3780

Stephanie

From: Archer, Stephanie (NIH/NICHD) [E] [mailto:archerst@mail.nih.gov]
Sent: Monday, May 14, 2007 11:34 AM
To: ahensman@wihri.org; mbball@leland.stanford.edu; bmackinnon@tufts-nemc.org; crosman@med.wayne.edu; grisbyca@email.uc.edu; CBackstrom@salud.unm.edu; ellen_hale@oz.ped.emory.edu; Georgia.E.McDavid@uth.tmc.edu; jennifer.j.jensen@hsc.utah.edu; jrohr@salud.unm.edu; Johnson, Karen; karena.strong@intermountainmail.org; auten002@mc.duke.edu; kimberlee.weaverlewis@intermountainmail.org; ldw@iupui.edu; linda_reubens@urmc.rochester.edu; mcollins@peds.uab.edu; monica.konstantino@yale.edu; Nancy.Miller@UTSouthwestern.edu; nxs5@cwru.edu; ae5357@wayne.edu; scosby@peds.uab.edu; wrich@ucsd.edu
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT Pulse Oximeters (orange) needed
Importance: High

UT Southwestern (Dallas) needs 3 orange pulse oximeters ASAP. Can anyone provide these?

Please contact Missy Leps (a new coordinator) at UT-Dallas: 214-648-3780.

Thanks!
Stephanie

Stephanie Wilson Archer
Neonatal Research Network
National Institute of Child Health and Human Development
6100 Executive Boulevard, Room 4B03 (MSC 7510)
Bethesda, MD 20892
Tel: 301-496-0430
Fax: 301-496-3790
archerst@mail.nih.gov

From:	Archer, Stephanie (NIH/NICHD) [E]
To:	"Monica Collins"
Cc:	"Melissa Leps (melissa.leps@utsouthwestern.edu)"; Higgins, Rosemary (NIH/NICHD) [E]
Subject:	RE: SUPPORT Pulse Oximeters (orange) needed
Date:	Monday, May 14, 2007 2:47:14 PM

Great. Thanks, Monica.

Stephanie Wilson Archer
Neonatal Research Network
National Institute of Child Health and Human Development
6100 Executive Boulevard, Room 4B03 (MSC 7510)
Bethesda, MD 20892
Tel: 301-496-0430
Fax: 301-496-3790
archerst@mail.nih.gov

From: Monica Collins [mailto:MCollins@peds.uab.edu]
Sent: Monday, May 14, 2007 2:44 PM
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: SUPPORT Pulse Oximeters (orange) needed

Stephanie,
I think we can spare one!
Monica Collins
UAB

From: Archer, Stephanie (NIH/NICHD) [E] [mailto:archerst@mail.nih.gov]
Sent: Mon 5/14/2007 1:03 PM
To: Wade Rich; Johnson, Karen; ahensman@wihri.org; mbball@leland.stanford.edu; bmackinnon@tufts-nemc.org; crosman@med.wayne.edu; grisbyca@email.uc.edu; CBackstrom@salud.unm.edu; ellen_hale@oz.ped.emory.edu; Georgia.E.McDavid@uth.tmc.edu; jennifer.j.jensen@hsc.utah.edu; jrohr@salud.unm.edu; karena.strong@intermountainmail.org; auten002@mc.duke.edu; kimberlee.weaverlewis@intermountainmail.org; ldw@iupui.edu; linda_reubens@urmc.rochester.edu; Monica Collins; monica.konstantino@yale.edu; Nancy.Miller@UTSouthwestern.edu; nxs5@cwru.edu; ae5357@wayne.edu; Shirley Cosby
Cc: Higgins, Rosemary (NIH/NICHD) [E]; melissa.leps@utsouthwestern.edu
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Sent: Monday, May 14, 2007 11:34 AM
To: ahensman@wihri.org; mbball@leland.stanford.edu; bmackinnon@tufts-nemc.org; crosman@med.wayne.edu; grisbyca@email.uc.edu; CBackstrom@salud.unm.edu; ellen_hale@oz.ped.emory.edu; Georgia.E.McDavid@uth.tmc.edu; jennifer.j.jensen@hsc.utah.edu; jrohr@salud.unm.edu; Johnson, Karen; karena.strong@intermountainmail.org; auten002@mc.duke.edu; kimberlee.weaverlewis@intermountainmail.org; ldw@iupui.edu; linda_reubens@urmc.rochester.edu; mcollins@peds.uab.edu; monica.konstantino@yale.edu; Nancy.Miller@UTSouthwestern.edu; nxs5@cwru.edu; ae5357@wayne.edu; scosby@peds.uab.edu; wrich@ucsd.edu
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archerst@mail.nih.gov

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: SUPPORT Pulse Oximeters (orange) needed
Date: Monday, May 14, 2007 2:42:48 PM

FYI

From: Monica Collins [mailto:MCollins@peds.uab.edu]
Sent: Monday, May 14, 2007 2:42 PM
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: SUPPORT Pulse Oximeters (orange) needed

We are using ours--sorry!
Monica

From: Archer, Stephanie (NIH/NICHD) [E] [mailto:archerst@mail.nih.gov]
Sent: Mon 5/14/2007 11:33 AM
To: ahensman@wihri.org; mbball@leland.stanford.edu; bmackinnon@tufts-nemc.org; crosman@med.wayne.edu; grisbyca@email.uc.edu; CBackstrom@salud.unm.edu; ellen_hale@oz.ped.emory.edu; Georgia.E.McDavid@uth.tmc.edu; jennifer.j.jensen@hsc.utah.edu; jrohr@salud.unm.edu; karen-johnson@uiowa.edu; karena.strong@intermountainmail.org; auten002@mc.duke.edu; kimberlee.weaverlewis@intermountainmail.org; ldw@iupui.edu; linda_reubens@urmc.rochester.edu; Monica Collins; monica.konstantino@yale.edu; Nancy.Miller@UTSouthwestern.edu; nxs5@cwru.edu; ae5357@wayne.edu; Shirley Cosby; wrich@ucsd.edu
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From:	Wade Rich
To:	Johnson, Karen; Archer, Stephanie (NIH/NICHD) [E]; ahensman@wihri.org; mbball@leland.stanford.edu; bmackinnon@tufts-nemc.org; crosman@med.wayne.edu; grisbyca@email.uc.edu; CBackstrom@salud.unm.edu; ellen_hale@oz.ped.emory.edu; Georgia.E.McDavid@uth.tmc.edu; jennifer.j.jensen@hsc.utah.edu; jrohr@salud.unm.edu; karena.strong@intermountainmail.org; auten002@mc.duke.edu; kimberlee.weaverlewis@intermountainmail.org; ldw@iupui.edu; linda_reubens@urmc.rochester.edu; mcollins@peds.uab.edu; monica.konstantino@yale.edu; Nancy.Miller@UTSouthwestern.edu; nxs5@cwru.edu; ae5357@wayne.edu; scosby@peds.uab.edu
Cc:	Higgins, Rosemary (NIH/NICHD) [E]
Subject:	RE: SUPPORT Pulse Oximeters (orange) needed
Date:	Monday, May 14, 2007 1:54:06 PM

Me too!
Wade
UCSD

From: Johnson, Karen [mailto:karen-johnson@uiowa.edu]
Sent: Monday, May 14, 2007 10:51 AM
To: Archer, Stephanie (NIH/NICHD) [E]; ahensman@wihri.org; mbball@leland.stanford.edu; bmackinnon@tufts-nemc.org; crosman@med.wayne.edu; grisbyca@email.uc.edu; CBackstrom@salud.unm.edu; ellen_hale@oz.ped.emory.edu; Georgia.E.McDavid@uth.tmc.edu; jennifer.j.jensen@hsc.utah.edu; jrohr@salud.unm.edu; karena.strong@intermountainmail.org; auten002@mc.duke.edu; kimberlee.weaverlewis@intermountainmail.org; ldw@iupui.edu; linda_reubens@urmc.rochester.edu; mcollins@peds.uab.edu; monica.konstantino@yale.edu; Nancy.Miller@UTSouthwestern.edu; nxs5@cwru.edu; ae5357@wayne.edu; scosby@peds.uab.edu; Wade Rich
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT Pulse Oximeters (orange) needed

Sorry, I just sent our extras to Case.
Karen

From: Archer, Stephanie (NIH/NICHD) [E] [mailto:archerst@mail.nih.gov]
Sent: Monday, May 14, 2007 11:34 AM
To: ahensman@wihri.org; mbball@leland.stanford.edu; bmackinnon@tufts-nemc.org; crosman@med.wayne.edu; grisbyca@email.uc.edu; CBackstrom@salud.unm.edu; ellen_hale@oz.ped.emory.edu; Georgia.E.McDavid@uth.tmc.edu; jennifer.j.jensen@hsc.utah.edu; jrohr@salud.unm.edu; Johnson, Karen; karena.strong@intermountainmail.org; auten002@mc.duke.edu; kimberlee.weaverlewis@intermountainmail.org; ldw@iupui.edu; linda_reubens@urmc.rochester.edu; mcollins@peds.uab.edu; monica.konstantino@yale.edu; Nancy.Miller@UTSouthwestern.edu; nxs5@cwru.edu; ae5357@wayne.edu; scosby@peds.uab.edu; wrich@ucsd.edu
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT Pulse Oximeters (orange) needed
Importance: High

UT Southwestern (Dallas) needs 3 orange pulse oximeters ASAP. Can anyone provide these?

Please contact Missy Leps (a new coordinator) at UT-Dallas: 214-648-3780.

Thanks!
Stephanie

Stephanie Wilson Archer
Neonatal Research Network
National Institute of Child Health and Human Development
6100 Executive Boulevard, Room 4B03 (MSC 7510)

Bethesda, MD 20892
Tel: 301-496-0430
Fax: 301-496-3790
archerst@mail.nih.gov

From:	CATHY A. GRISBY
To:	Archer, Stephanie (NIH/NICHD) [E]; ahensman@wihri.org; mbball@leland.stanford.edu; bmackinnon@tufts-nemc.org; crosman@med.wayne.edu; CBackstrom@salud.unm.edu; ellen_hale@oz.ped.emory.edu; Georgia.E.McDavid@uth.tmc.edu; jennifer.j.jensen@hsc.utah.edu; jrohr@salud.unm.edu; karen-johnson@uiowa.edu; karena.strong@intermountainmail.org; auten002@mc.duke.edu; kimberlee.weaverlewis@intermountainmail.org; ldw@iupui.edu; linda_reubens@urmc.rochester.edu; mcollins@peds.uab.edu; monica.konstantino@yale.edu; Nancy.Miller@UTSouthwestern.edu; nxs5@cwru.edu; ae5357@wayne.edu; scosby@peds.uab.edu; wrich@ucsd.edu
Cc:	Higgins, Rosemary (NIH/NICHD) [E]
Subject:	Re: SUPPORT Pulse Oximeters (orange) needed
Date:	Monday, May 14, 2007 1:43:42 PM
Importance:	High

We do not have extras here in Cincinnati.

---- Original message ----

Date: Mon, 14 May 2007 12:33:54 -0400
From: "Archer, Stephanie (NIH/NICHD) [E]" <archerst@mail.nih.gov>
Subject: SUPPORT Pulse Oximeters (orange) needed
To: <ahensman@wihri.org>, <mbball@leland.stanford.edu>, <bmackinnon@tufts-nemc.org>, <crosman@med.wayne.edu>, <grisbyca@email.uc.edu>, <CBackstrom@salud.unm.edu>, <ellen_hale@oz.ped.emory.edu>, <Georgia.E.McDavid@uth.tmc.edu>, <jennifer.j.jensen@hsc.utah.edu>, <jrohr@salud.unm.edu>, <karen-johnson@uiowa.edu>, <karena.strong@intermountainmail.org>, <auten002@mc.duke.edu>, <kimberlee.weaverlewis@intermountainmail.org>, <ldw@iupui.edu>, <linda_reubens@urmc.rochester.edu>, <mcollins@peds.uab.edu>, <monica.konstantino@yale.edu>, <Nancy.Miller@UTSouthwestern.edu>, <nxs5@cwru.edu>, <ae5357@wayne.edu>, <scosby@peds.uab.edu>, <wrich@ucsd.edu>
Cc: "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov>

UT Southwestern (Dallas) needs 3 orange pulse oximeters

ASAP. Can anyone provide these?

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214-648-3780.

Thanks!

Stephanie

Stephanie Wilson Archer

Neonatal Research Network

National Institute
of Child Health and Human
Development

6100 Executive
Boulevard, Room 4B03 (MSC 7510)

Bethesda, MD 20892

Tel: 301-496-0430

Fax: 301-496-3790

archerst@mail.nih.gov

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT Pulse Oximeters (orange) needed
Date: Monday, May 14, 2007 1:38:16 PM

Left msgs at UAB and Brown. Nancy Newman at Case is checking, but she just got a few back and thinks she may need them.

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Monday, May 14, 2007 1:21 PM
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: Re: SUPPORT Pulse Oximeters (orange) needed

Stephanie
Extras are available at UAB (alabama, Case western, and brown)- can you call one of these sites to see if they can send them?sorry - I was in the middle of the retirement ceremony

Rose

Sent from my BlackBerry Wireless Handheld

----- Original Message -----
From: Archer, Stephanie (NIH/NICHD) [E]
Subject: SUPPORT Pulse Oximeters (orange) needed

UT Southwestern (Dallas) needs 3 orange pulse oximeters ASAP. Can anyone provide these?

Please contact Missy Leps (a new coordinator) at UT-Dallas: 214-648-3780.

Thanks!

Stephanie

Stephanie Wilson Archer

Neonatal Research Network

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6100 Executive Boulevard, Room 4B03 (MSC 7510)

Bethesda, MD 20892

Tel: 301-496-0430

Fax: 301-496-3790

archerst@mail.nih.gov

From:	Kathy J Auten
To:	Archer, Stephanie (NIH/NICHD) [E]
Cc:	ae5357@wayne.edu; ahensman@wihri.org; bmackinnon@tufts-nemc.org; CBackstrom@salud.unm.edu; crosman@med.wayne.edu; ellen_hale@oz.ped.emory.edu; Georgia.E.McDavid@uth.tmc.edu; grisbyca@email.uc.edu; Higgins, Rosemary (NIH/NICHD) [E]; jennifer.j.jensen@hsc.utah.edu; jrohr@salud.unm.edu; karen-johnson@uiowa.edu; karena.strong@intermountainmail.org; kimberlee.weaverlewis@intermountainmail.org; ldw@iupui.edu; linda_reubens@urmc.rochester.edu; mbbali@leland.stanford.edu; mcollins@peds.uab.edu; monica.konstantino@yale.edu; Nancy.Miller@UTSouthwestern.edu; nxs5@cwru.edu; scosby@peds.uab.edu; wrich@ucsd.edu
Subject:	Re: SUPPORT Pulse Oximeters (orange) needed
Date:	Monday, May 14, 2007 12:55:22 PM

Sorry I can't help this time.
Kathy

Kathy J. Auten, MSHS
Project Manager
NICHD Neonatal Research Network Trials
Duke University Medical Center
Box 3179
Bell Building, Room 141
Durham, NC 27710 USA
919-681-5859 tel
919-681-4868 fax
kathy.auten@duke.edu

"Archer, Stephanie (NIH/NICHD) [E]" <archerst@mail.nih.gov> wrote on 05/14/2007 12:33:54 PM:

> UT Southwestern (Dallas) needs 3 orange pulse oximeters ASAP. Can
> anyone provide these?
>
> Please contact Missy Leps (a new coordinator) at UT-Dallas: 214-648-3780.
>
> Thanks!
> Stephanie
>
> _____
> Stephanie Wilson Archer
> Neonatal Research Network
> National Institute of Child Health and Human Development
> 6100 Executive Boulevard, Room 4B03 (MSC 7510)
> Bethesda, MD 20892
> Tel: 301-496-0430
> Fax: 301-496-3790
> archerst@mail.nih.gov
>

From:	Zaterka-Baxter, Kristin
To:	Higgins, Rosemary (NIH/NICHD) [E]
Cc:	Susan Hintz
Subject:	RE: SUPPORT EMBEDDED CONSENTS
Date:	Friday, May 11, 2007 11:12:51 AM

Sure thing.
Thanks,
Kris

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, May 11, 2007 11:09 AM
To: Zaterka-Baxter, Kristin
Cc: Susan Hintz
Subject: SUPPORT EMBEDDED CONSENTS

Kris
Can you send the Emory site a couple of the embedded consent forms for MRI and SUPPORT?
Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Webb, Robin E.
To:	Higgins, Rosemary (NIH/NICHD) [E]; Neil Finer; Wally Carlo, M.D.; mcw3@case.edu; Bradley Yoder; Roger.Faix@hsc.utah.edu; Abbot Laptook; kurt.schibler@cchmc.org; Das, Abhik; Wade Rich; nancy newman; Gantz, Marie
Cc:	Archer, Stephanie (NIH/NICHD) [E]; Cunningham, Meg; Zaterka-Baxter, Kristin
Subject:	RE: CONFIDENTIAL SUPPORT META ANALYSIS variables
Date:	Thursday, May 10, 2007 12:35:08 PM

Please let me know your availability for the days below, indicating time zone if other than ET.

Thanks,
Robin

Mon 5/21
Tues 5/22
Wed 5/23
Thurs 5/24
Fri 5/25

Tues 5/29
Wed 5/30
Thurs 5/31
Fri 6/1

Mon 6/4
Tues 6/5
Wed 6/6

From:	Zaterka-Baxter, Kristin
To:	Angelita Hensman; Abbot Laptook
Cc:	Pickett, James; Das, Abhik; Wade Rich; Higgins, Rosemary (NIH/NICHD) [E]; Brenda Vecchio
Subject:	RE: Support Monitoring Visit (Brown)
Date:	Friday, May 04, 2007 10:17:31 AM

Thanks Dr. Laptook and Angelita for responding so quickly; we will plan to visit your site on June 6th and 7th. Please let me know if for some reason your schedules change and we can work with the dates. We will be sending you an agenda and a list of cases to be reviewed by the end of next week.

Much appreciated,
Kris

Kris Zaterka-Baxter, RN, CCRP
RTI International
4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From: Angelita Hensman [mailto:AHensman@WIHRI.org]
Sent: Thursday, May 03, 2007 1:28 AM
To: Abbot Laptook; Zaterka-Baxter, Kristin
Cc: Das, Abhik; Pickett, James; Das, Abhik; Wade Rich; Pickett, James; higginsr@mail.nih.gov; Brenda Vecchio
Subject: RE: Support Monitoring Visit (Brown)

Hi Kris,

Any of the dates below should be ok.

Thanks
Angelita

From: Abbot Laptook
Sent: Wed 5/2/2007 8:31 PM
To: 'Zaterka-Baxter, Kristin'; Angelita Hensman
Cc: Das, Abhik; Pickett, James; Das, Abhik; Wade Rich; Pickett, James; higginsr@mail.nih.gov; Brenda Vecchio
Subject: RE: Support Monitoring Visit (Brown)

Kris
Those dates will work for me but Angelita is on vacation and will not be back until May 18. I am not sure how often she will check her e mail so I guess we need to wait for her to respond. AL

From: Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]
Sent: Wednesday, May 02, 2007 12:34 PM
To: Abbot Laptook; Angelita Hensman
Cc: Das, Abhik; Pickett, James; Das, Abhik; Wade Rich; Pickett, James; higginsr@mail.nih.gov
Subject: Support Monitoring Visit (Brown)

Hi Dr. Laptook and Angelita,

As we discussed during our last Steering Committee meeting in April, RTI recently began site monitoring visits for the Support Trial as directed by the DSMC. As one of the highest enrolling centers, we would like to visit your site next. We would like to try to schedule a two day visit between June 6th and 8th or the following Monday and Tuesday June 11th and 12th. This is a preliminary request for availability and we realize it's a tight time frame so please don't hesitate to give me alternative dates depending on your schedules. Once a date has been determined, we will send out a randomly generated list of approximately 10% of infants enrolled for case review.

Thanks and please let me know if you have any questions at all.
Kris

RTI International
4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From:	Angelita Hensman
To:	Abbot Laptook; Zaterka-Baxter, Kristin
Cc:	Das, Abhik; Pickett, James; Das, Abhik; Wade Rich; Pickett, James; Higgins, Rosemary (NIH/NICHD) [E]; Brenda Vecchio
Subject:	RE: Support Monitoring Visit (Brown)
Date:	Thursday, May 03, 2007 1:30:09 AM

Hi Kris,

Any of the dates below should be ok.

Thanks
Angelita

From: Abbot Laptook
Sent: Wed 5/2/2007 8:31 PM
To: 'Zaterka-Baxter, Kristin'; Angelita Hensman
Cc: Das, Abhik; Pickett, James; Das, Abhik; Wade Rich; Pickett, James; higginsr@mail.nih.gov; Brenda Vecchio
Subject: RE: Support Monitoring Visit (Brown)

Kris
Those dates will work for me but Angelita is on vacation and will not be back until May 18. I am not sure how often she will check her e mail so I guess we need to wait for her to respond. AL

From: Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]
Sent: Wednesday, May 02, 2007 12:34 PM
To: Abbot Laptook; Angelita Hensman
Cc: Das, Abhik; Pickett, James; Das, Abhik; Wade Rich; Pickett, James; higginsr@mail.nih.gov
Subject: Support Monitoring Visit (Brown)

Hi Dr. Laptook and Angelita,

As we discussed during our last Steering Committee meeting in April, RTI recently began site monitoring visits for the Support Trial as directed by the DSMC. As one of the highest enrolling centers, we would like to visit your site next. We would like to try to schedule a two day visit between June 6th and 8th or the following Monday and Tuesday June 11th and 12th. This is a preliminary request for availability and we realize it's a tight time frame so please don't hesitate to give me alternative dates depending on your schedules. Once a date has been determined, we will send out a randomly generated list of approximately 10% of infants enrolled for case review.

Thanks and please let me know if you have any questions at all.
Kris

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Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From: Wally Carlo, M.D.
To: Higgins, Rosemary (NIH/NICHD) [E]; mcw3@case.edu
Subject: RE: Additional masked oximeters for SUPPORT
Date: Tuesday, May 01, 2007 9:29:53 AM

Rose:

Sure. It is not a problem.

wally

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, May 01, 2007 7:39 AM
To: mcw3@case.edu; Wally Carlo, M.D.
Subject: FW: Additional masked oximeters for SUPPORT

Michele and Wally – Would your site have room for some more spare oximeters (10 to each site)? We would be providing funds in order to move the trial along and not miss any children.
Let me know.

Thanks
Rose

From: Maribeth Sayre [mailto:MSayre@masimo.com]
Sent: Monday, April 30, 2007 7:52 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Wade Rich; Neil Finer
Subject: Additional masked oximeters for SUPPORT

Hi Rosemary,

Masimo will be glad to sell additional masked oximeters to SUPPORT.
However, we have an unprecedented demand for oximeters, both masked and unmasked, at this time. Thus, the earliest shipping date for additional SUPPORT masked oximeters would be July 2007 or later.

Please let me know if you would like to place an order for additional masked oximeters. I will keep you informed about a potential shipping date, and will try to get them to you sooner.

Best regards,
Maribeth

From: Walsh, Michele
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Additional masked oximeters for SUPPORT
Date: Tuesday, May 01, 2007 9:12:34 AM

Space is a hugh issue for us as we start construction on the new NICU. Let me see what we can do. Is it really an issue with not enough equipment? BTW: I am going to Albequerque on the way back from ATS. Nancy and I will do their certification visit.
Michele

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, May 01, 2007 8:39 AM
To: mcw3@case.edu; Wally Carlo, M.D.
Subject: FW: Additional masked oximeters for SUPPORT

Michele and Wally – Would your site have room for some more spare oximeters (10 to each site)? We would be providing funds in order to move the trial along and not miss any children.
Let me know.

Thanks
Rose

From: Maribeth Sayre [mailto:MSayre@masimo.com]
Sent: Monday, April 30, 2007 7:52 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Wade Rich; Neil Finer
Subject: Additional masked oximeters for SUPPORT

Hi Rosemary,

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Please let me know if you would like to place an order for additional masked oximeters. I will keep you informed about a potential shipping date, and will try to get them to you sooner.

Best regards,
Maribeth

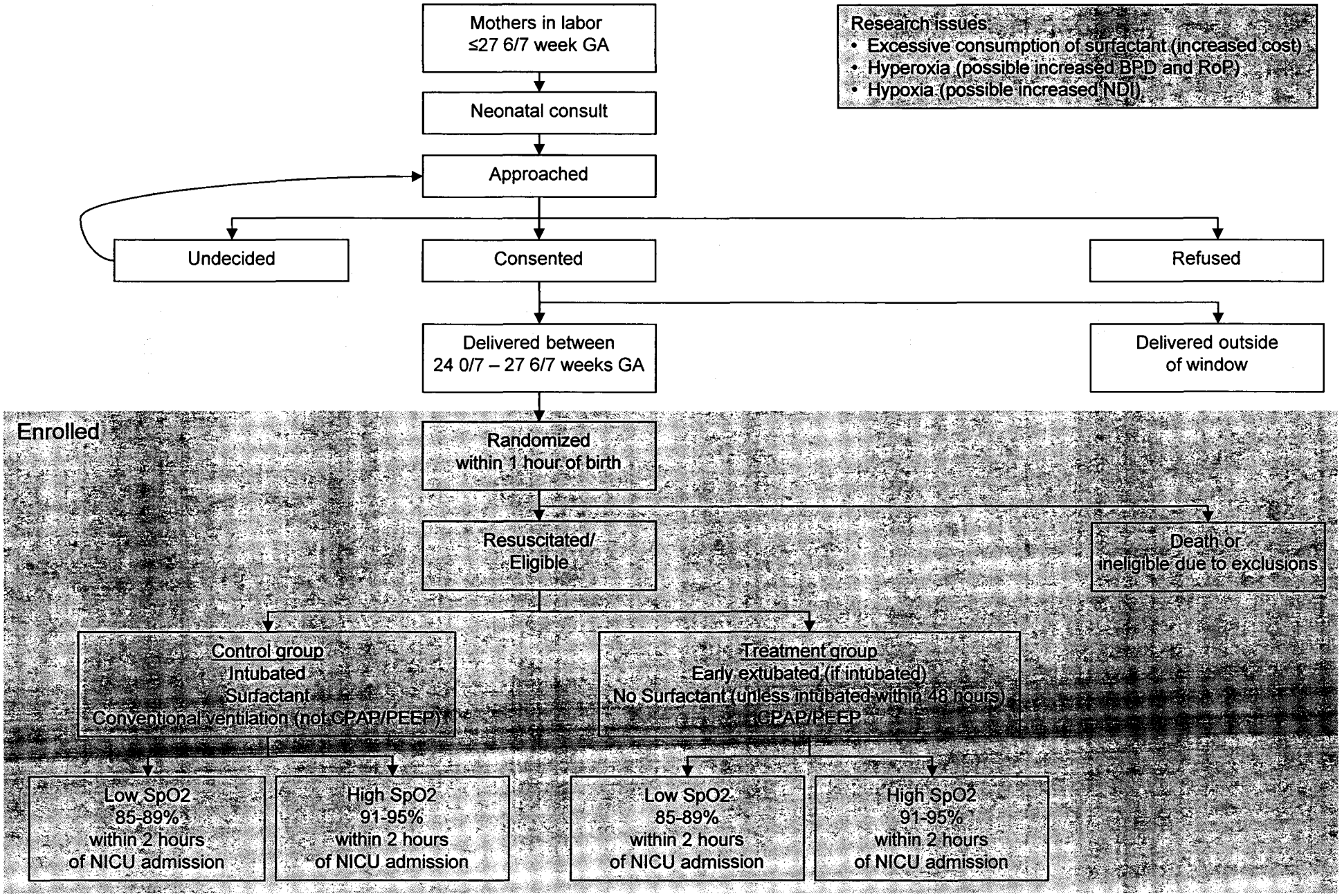
The enclosed information is STRICTLY CONFIDENTIAL and is intended for the use of the addressee only. University Hospitals and its affiliates disclaim any responsibility for unauthorized disclosure of this information to anyone other than the addressee.

Federal and Ohio law protect patient medical information, including psychiatric_disorders, (H.I.V) test results, A.I.Ds-related conditions, alcohol, and/or drug_dependence or abuse disclosed in this email. Federal regulation (42 CFR Part 2) and Ohio Revised Code section 5122.31 and 3701.243 prohibit disclosure of this information without the specific written consent of the person to whom it pertains, or as otherwise permitted by law.

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT flowchart
Date: Monday, April 30, 2007 11:42:05 AM
Attachments: SUPPORT Flowchart.ppt

FYI, I revised the flowchart I put together for SUPPORT. Here it is.

SUPPORT Flowchart



From: Gantz, Marie
To: Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik
Subject: RE: SUPPORT FU
Date: Monday, April 30, 2007 9:23:21 AM

Rose, I would be happy to provide that information.

Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-6255

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, April 30, 2007 9:17 AM
To: Das, Abhik; Gantz, Marie
Subject: SUPPORT FU

HI,
I know it is very late notice, BUT can I get the following for the SUPPORT FU meeting:
List of sites with FU seen, follow up pending, lost to FU, and complete for FU outcome (NDI or normal).
Also, can you project for sites through March 31, 2008 the number of children entering the FU windows?
Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	CATHY A. GRISBY
To:	Archer, Stephanie (NIH/NICHD) [E]; nfiner@ucsd.edu; adas@rti.org; Higgins, Rosemary (NIH/NICHD) [E]; kurt.schibler@cchmc.org; kzaterka@rti.org
Cc:	Barb; Estelle; Holly; Jody; Kate; Lenora Jackson
Subject:	Re: SUPPORT| Recruitment teleconference with U. Cincinnati
Date:	Thursday, April 26, 2007 3:10:20 PM

Hi Stephanie,

My additions/comments are in blue. I've cc'ed the rest of my group in case they have additions/clarifications.

Thanks,

Cathy

---- Original message ----

Date: Thu, 26 Apr 2007 10:40:39 -0400
From: "Archer, Stephanie \(NIH/NICHD\) [E]" <archerst@mail.nih.gov>
Subject: SUPPORT| Recruitment teleconference with U. Cincinnati
To: <nfiner@ucsd.edu>, <adas@rti.org>, "Higgins, Rosemary \(NIH/NICHD\) [E]" <higginsr@mail.nih.gov>, <kurt.schibler@cchmc.org>, <kzaterka@rti.org>, <grisbyca@email.uc.edu>

Attached are my notes from our teleconference early this week about SUPPORT recruitment issues. Please review these notes and send me any comments/corrections by May 1st.

Thanks!

Stephanie

Stephanie Wilson Archer

Neonatal Research Network

National Institute
of Child Health and Human
Development

6100 Executive
Boulevard, Room 4B03 (MSC 7510)

Bethesda, MD 20892

Tel: 301-496-0430

Fax: 301-496-3790

archerst@mail.nih.gov

>_____ >U Cinn, recruitment, telcon notes, 04-25-07.doc (63k bytes)

From:	Dusick, Anna M.
To:	Archer, Stephanie (NIH/NICHD) [E]; nfiner@ucsd.edu; adas@rti.org; Higgins, Rosemary (NIH/NICHD) [E]; richard.ehrenkranz@yale.edu; kzaterka@rti.org
Cc:	Poindexter, Brenda B
Subject:	RE: SUPPORT| Recruitment teleconference with Yale
Date:	Thursday, April 26, 2007 12:38:11 PM

I was not part of this call.

Anna M. Dusick, MD
Associate Professor of Clinical Pediatrics
Riley Hospital for Children
702 E. Barnhill Drive, Room 1601
Indianapolis, IN 46202

Phone: 317-274-4846
Fax: 317-278-0126

From: Archer, Stephanie (NIH/NICHD) [E] [mailto:archerst@mail.nih.gov]
Sent: Thursday, April 26, 2007 10:39 AM
To: nfiner@ucsd.edu; adas@rti.org; Higgins, Rosemary (NIH/NICHD) [E]; richard.ehrenkranz@yale.edu; kzaterka@rti.org; Dusick, Anna M.
Subject: SUPPORT| Recruitment teleconference with Yale

Attached are my notes from our teleconference early this week about SUPPORT recruitment issues.
Please review these notes and send me any comments/corrections by May 1st.

Thanks!
Stephanie

Stephanie Wilson Archer
Neonatal Research Network
National Institute of Child Health and Human Development
6100 Executive Boulevard, Room 4B03 (MSC 7510)
Bethesda, MD 20892
Tel: 301-496-0430
Fax: 301-496-3790
archerst@mail.nih.gov

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT| Excess surfactant
Date: Thursday, April 26, 2007 11:52:29 AM

Cost of surfactant replacement treatment for severe neonatal respiratory distress syndrome: a randomised controlled trial.

T R Tubman, H L Halliday, and C Normand
BMJ. 1990 October 13; 301(6756): 842–845.

Looks like they were using 700-2000g babies. It looks like they were factoring in the 75 extra days in the hospital in the cost for an estimated 43% increase in the survival rate. It does mention that the treatment group tended to be lower birth weight babies.

Abstract

OBJECTIVE--To estimate the cost of treating babies with severe respiratory distress syndrome with natural porcine surfactant. DESIGN--Retrospective controlled survey. SETTING--Regional neonatal intensive care unit, Belfast. PATIENTS--33 Preterm babies with severe respiratory distress syndrome who were enrolled in a European multicentre trial during 1985-7. 19 Babies were treated with surfactant and 14 served as controls. INTERVENTIONS--Treatment with natural porcine surfactant. MAIN OUTCOME MEASURE--Cost associated with surfactant replacement treatment per extra survivor in the treatment group and cost per quality adjusted life year for each extra survivor. RESULTS--Fifteen (79%) of the 19 treated babies and five (36%) of the 14 control babies survived. On average, the control babies required 20 days in hospital compared with 61 days for the treated babies (or 95 [corrected] days per extra survivor in the treatment group). The cost per extra survivor in the treatment group was pounds 13,720, with the cost per quality adjusted life year estimated at pounds 710. CONCLUSION--These costs compare favourably with those of established forms of treatment in adults. Thus surfactant replacement treatment for severe respiratory distress syndrome is fairly inexpensive and cost effective.

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thursday, April 26, 2007 11:40 AM
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: SUPPORT| Excess surfactant

The cost used to be $500/dose (some kids get up to 4-6 doses) in the late 1990's. Which 1991 article are you referring to? It may be that the babies were little (500-700 grams) and would not have survived without it.

Rose

From: Archer, Stephanie (NIH/NICHD) [E]
Sent: Thursday, April 26, 2007 11:30 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT| Excess surfactant

How much does it cost per dose? I saw one 1991 article that suggested the babies are hospitalized longer, but now how much the actual medicine costs (of course, the pharma companies don't publish that on their websites!).

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thursday, April 26, 2007 9:49 AM
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: SUPPORT| Excess surfactant

Cost!!

From: Archer, Stephanie (NIH/NICHD) [E]
Sent: Thursday, April 26, 2007 9:46 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT| Excess surfactant

The SUPPORT protocol mentions that CPAP may reduce "excessive consumption of surfactant." What are the dangers of excessive consumption? Hyperoxia?

From:	Neil Finer
To:	Archer, Stephanie (NIH/NICHD) [E]; Higgins, Rosemary (NIH/NICHD) [E]
Cc:	Neil Finer; "Abhik Das; Leslie Dawn Wilson; Brenda Poindexter
Subject:	RE: SUPPORT| Recruitment teleconference with Indiana U.
Date:	Thursday, April 26, 2007 11:21:00 AM

Thanks Stephanie
This looks fine to me
Neil

From: Archer, Stephanie (NIH/NICHD) [E] [mailto:archerst@mail.nih.gov]
Sent: Thursday, April 26, 2007 8:12 AM
To: Neil Finer
Subject: FW: SUPPORT| Recruitment teleconference with Indiana U.

Here is Indiana.

From: Archer, Stephanie (NIH/NICHD) [E]
Sent: Thursday, April 26, 2007 10:33 AM
To: 'Neil Finer (nfiner@ucsd.edu)'; 'Abhik Das (adas@rti.org)'; Higgins, Rosemary (NIH/NICHD) [E]; Leslie Dawn Wilson (ldw@iupui.edu); Brenda Poindexter (bpoindex@iupui.edu)
Subject: SUPPORT| Recruitment teleconference with Indiana U.

Attached are my notes from our teleconference early this week about SUPPORT recruitment issues. Please review these notes and send me any comments/corrections by May 1st.

Thanks!
Stephanie

Stephanie Wilson Archer
Neonatal Research Network
National Institute of Child Health and Human Development
6100 Executive Boulevard, Room 4B03 (MSC 7510)
Bethesda, MD 20892
Tel: 301-496-0430
Fax: 301-496-3790
archerst@mail.nih.gov

From:	Neil Finer
To:	Archer, Stephanie (NIH/NICHD) [E]; adas@rti.org; Higgins, Rosemary (NIH/NICHD) [E]; richard.ehrenkranz@yale.edu; kzaterka@rti.org; adusick@iupui.edu
Subject:	RE: SUPPORT| Recruitment teleconference with Yale
Date:	Thursday, April 26, 2007 11:10:56 AM

This looks accurate to me.
Neil

From: Archer, Stephanie (NIH/NICHD) [E] [mailto:archerst@mail.nih.gov]
Sent: Thursday, April 26, 2007 7:39 AM
To: Neil Finer; adas@rti.org; Higgins, Rosemary (NIH/NICHD) [E]; richard.ehrenkranz@yale.edu; kzaterka@rti.org; adusick@iupui.edu
Subject: SUPPORT| Recruitment teleconference with Yale

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Tel: 301-496-0430
Fax: 301-496-3790
archerst@mail.nih.gov

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: SUPPORT| Recruitment teleconference with Indiana U.
Date: Thursday, April 26, 2007 10:48:16 AM

FYI

From: Brenda Poindexter [mailto:bpoindex@iupui.edu]
Sent: Thursday, April 26, 2007 11:46 AM
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: Re: SUPPORT| Recruitment teleconference with Indiana U.

Stephanie,
There are several items that need corrected and clarified – Leslie and I will go over this and send make our corrections.

Brenda B. Poindexter, M.D., M.S.
Associate Professor of Clinical Pediatrics
Section of Neonatal-Perinatal Medicine
Indiana University School of Medicine
Riley Hospital for Children
(317) 274-4920

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Stephanie

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National Institute of Child Health and Human Development
6100 Executive Boulevard, Room 4B03 (MSC 7510)
Bethesda, MD 20892
Tel: 301-496-0430
Fax: 301-496-3790
archerst@mail.nih.gov

From: Neil Finer
To: Archer, Stephanie (NIH/NICHD) [E]; kwatterberg@salud.unm.edu; jrohr@salud.unm.edu; adas@rti.org; Higgins, Rosemary (NIH/NICHD) [E]; CBackstrom@salud.unm.edu
Subject: RE: SUPPORT| Recruitment teleconference with UNM
Date: Thursday, April 26, 2007 10:40:56 AM

This looks fine to me.
Neil Finer

From: Archer, Stephanie (NIH/NICHD) [E] [mailto:archerst@mail.nih.gov]
Sent: Thursday, April 26, 2007 7:33 AM
To: Neil Finer; kwatterberg@salud.unm.edu; jrohr@salud.unm.edu; adas@rti.org; Higgins, Rosemary (NIH/NICHD) [E]; CBackstrom@salud.unm.edu
Subject: SUPPORT| Recruitment teleconference with UNM

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Thanks!
Stephanie

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6100 Executive Boulevard, Room 4B03 (MSC 7510)
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Tel: 301-496-0430
Fax: 301-496-3790
archerst@mail.nih.gov

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT| permissive vs. conventional ventilation
Date: Thursday, April 26, 2007 8:59:52 AM

The test groups for SUPPORT are given permissive ventilation via Neopuff, but the protocol mentions that the control group is given only "conventional ventilation." Why the difference and will this affect how well you can compare the test groups to the control?

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT| Neopuff usage
Date: Thursday, April 26, 2007 8:58:10 AM

I'm continuing to read through the SUPPORT protocol. Do we know which sites are using Neopuff and which are using other CPAP equipment?

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Question | Oxygen saturation acronyms
Date: Monday, April 23, 2007 4:24:01 PM

So SpO2 is the same as SO2? For SUPPORT and the pulse oximeters, is it really SaO2 that we are measuring?

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Monday, April 23, 2007 4:22 PM
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: Re: Question | Oxygen saturation acronyms

It refers to oxygen saturation. We have two target groups: 91-95 and 85-89. The oximeter (machine that reads oxygen saturation) is set to read 88-92 for both groups when the child is in the correct range. The oximeters have custom software to do this. We are testing these two ranges to see if one is better than the other for short term (lung disease, eye issues, etc) and long term (follow up at 18-22 months) outcome.

Rose

Sent from my BlackBerry Wireless Handheld

----- Original Message -----
From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Mon Apr 23 16:17:07 2007
Subject: Question | Oxygen saturation acronyms

Hi Rose,

I'm reading through the SUPPORT protocol and looking up unfamiliar terms in Wikipedia. Can you tell me what SpO2 is?

I found:

SO2	Oxygen saturation
SaO2	Arterial oxygen saturation; SaO2 below 90% is termed hypoxemia
SpO2	
StO2	Tissue oxygen saturation
SvO2	Ventricular oxygen saturation; SvO2 below 60%, indicates that the body is in lack of oxygen, and ischemic diseases occur.

Just wondering what the "p" is.

Steph

From: Das, Abhik
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT site calls
Date: Tuesday, April 24, 2007 1:14:55 PM

Oops; I must have missed that one somehow; it is not in my Outlook calender.

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, April 24, 2007 1:13 PM
To: Das, Abhik
Subject: RE: SUPPORT site calls

I have Cincinnati for tomorrow at 11 am

From: Das, Abhik [mailto:adas@rti.org]
Sent: Tuesday, April 24, 2007 1:04 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT site calls

Are we going to talk to Cincinnati as well? Their % GDB randomized is also fairly low!

Thanks

Abhik

Abhik Das, Ph.D.
Senior Research Statistician
RTI International
6110 Executive Blvd., Suite 902
Rockville, MD 20852-3903
e-mail: adas@rti.org
Phone: 301-770-8214
Fax: 301-230-4646

From: Wade Rich
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Presentation
Date: Friday, April 20, 2007 2:30:35 PM
Attachments: PresentationSeaTac (4_2a).ppt

Yes

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, April 20, 2007 10:43 AM
To: Wade Rich
Subject: Presentation

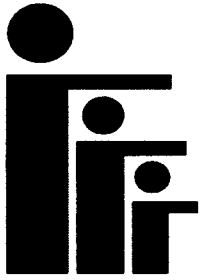
Can you send me your final presentation for the support antenatal
consent to circulate to the network?
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

2007 ACRP GLOBAL CONFERENCE & EXHIBITION
Tomorrow's Clinical Research Team: delivering on the promise for innovation for medicine
April 20-24, 2007 Seattle, Washington

Pre-screening and Antenatal Informed Consent for Neonatal Trials: *A Research Conundrum*

Wade Rich BSHS,RRT,CCRC, **Kathy Auten** MSHS, **Marie Gantz** PhD, **Ellen Hale** RN,BS, **Angelita Hensman** RNC, **Nancy Newman** RNC, **Nancy Peters** RN CCRP, **for the NICHD Neonatal Research Network**



RTI INTERNATIONAL

NICHD Neonatal Research Network

- 16 Academic Centers
- Centralized Data Management & Data Safety Monitoring Committee
- Sites average 500 NICU admissions per year, > 70% inborn
- Active maternal-fetal medicine service

NICHD Neonatal Research Network

- Cooperative research projects in neonates
- Primarily critically ill newborns
- Trials are historically funded based on capitation
- This does not always work.

Antenatal Consent Trial - NRN

- Secondary to the SUPPORT Trial
- Based on input from study coordinators regarding time/effort involved in enrollment
- Target is 50 infants who delivered in the window per center

Primary Goals

- Average number of attempts to present the study
- Average length of time it takes to obtain an answer regarding enrollment
- To determine the number of mothers that must be approached for consent to yield one enrolled subject

Primary Goals

- **To determine reasons for failure to enroll consented newborns**

- **To determine the amount of personnel time it takes to yield one enrolled subject**

Primary Goals

- To determine reasons for failure to obtain consent

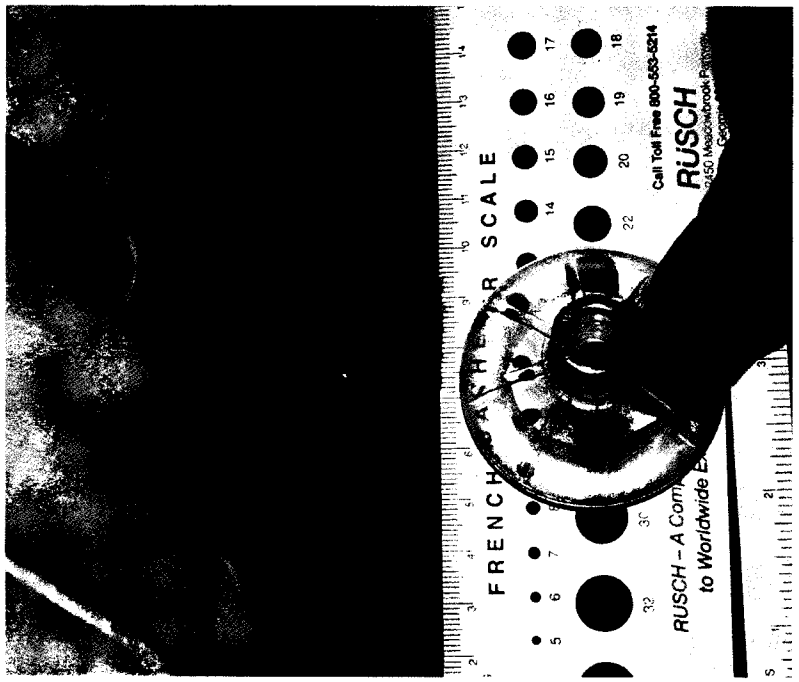
- To make recommendations regarding budgeting and antenatal recruitment practices for future neonatal studies

The Trials

- **DR CPAP – A small pilot trial**
- **SUPPORT – A large multi-center interventional trial**
- **Antenatal Consent – A secondary to SUPPORT**

The DR CPAP Trial – 2002
Finer, et al.

- <28 weeks Gestation (Best OB)
- Inborn
- N= 100



- Primary Question – Was CPAP in DR possible?

The DR CPAP Trial – 2002
Finer, et al.

- **DR CPAP was subcommittee members (committed)**
- **Individual site visits from study PI**
- **4 of 5 centers enrolled under waiver**

DR CPAP Trial Enrollment

- **5 centers enrolled 100 subjects in 6 months**

- **Using this model, 16 centers in the main SUPPORT trial would enroll 600 babies per year, and the trial would take about 2.5 years**

Pilot Enrollment Data

- 281 infants <28wks GA infants delivered
- 162/281 of these were screened → 120 eligible
- 104/120 consented & enrolled
- Enrollment rate = ***83%***

Pilot Enrollment Data

- **There were 281 infants of less than 28 weeks who delivered in the study hospitals during the period of the study.** Did not Deliver? Transferred?
- **Of whom 162 infants were screened by study personnel.** We assumed incentive would increase this.
- **Forty-two were determined to be ineligible by the study criteria.** Includes "out of window"
- **104 infants were consented of the 126 eligible patients, for an enrollment rate of *83%*." Were there 239 eligible ?**

The Main Trial - SUPPORT

- **Support trial was based on the DR CPAP model, using data from the pilot study as a benchmark**

- **Startup was not "shotgun"; covered over one year**

- **All centers required an informed consent (i.e. No Waivers)**

Why Centers Did Not Enroll Under Waiver

- **Studies which involve treatment in the delivery room have historically been either consented antenatally or have functioned under a *waiver of consent* as established in the Code of Federal Regulations**

45 CFR 46.116[d]

(d) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

(1) The research involves no more than minimal risk to the subjects;

(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;

(3) The research could not practicably be carried out without the waiver or alteration;

(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

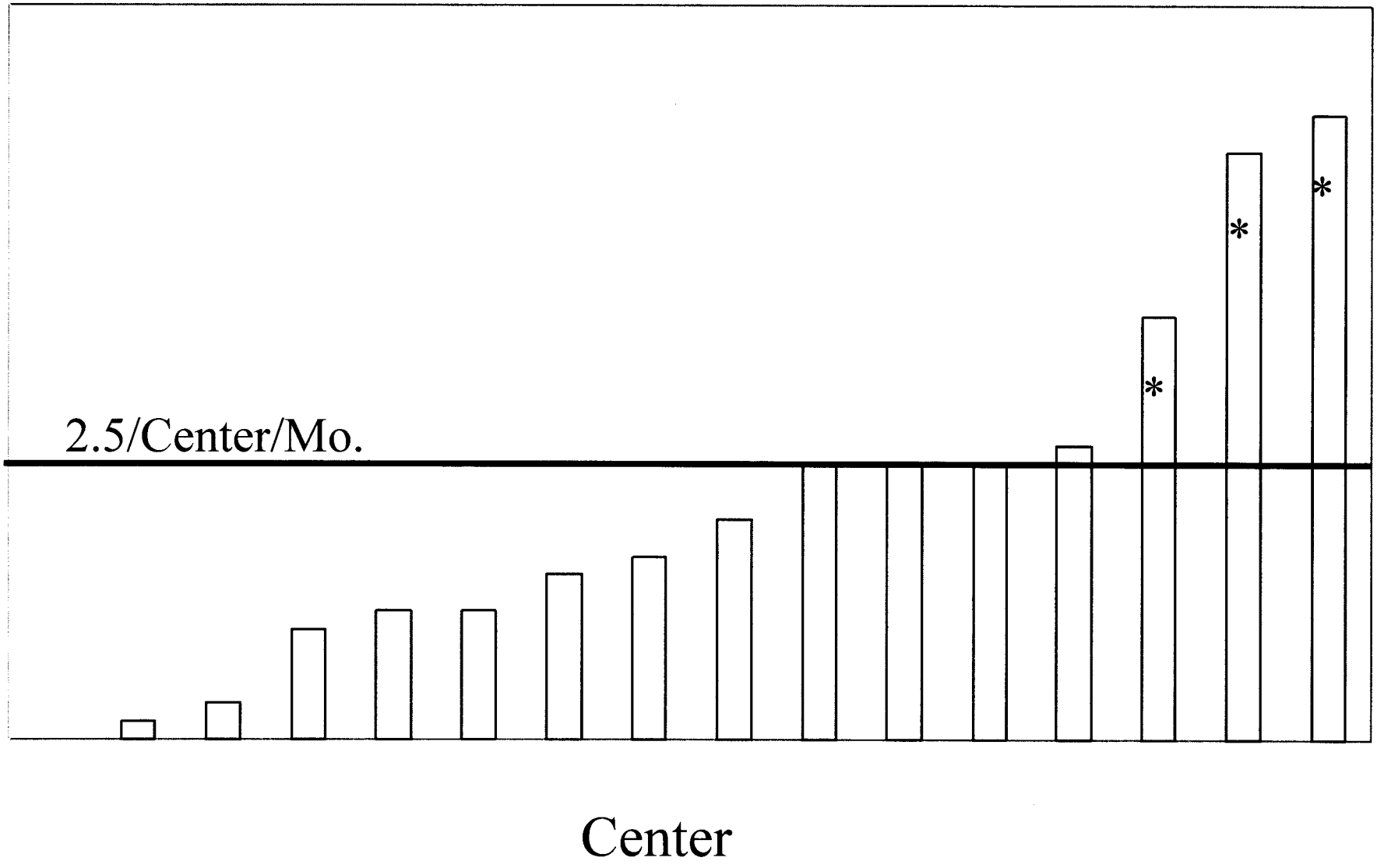
SUPPORT – The Primary Trial

- 24 – 27 6/7 GA - 4 week enrollment window
- Target enrollment = 1310
- Pool of Candidates (Delivered) = 1100/year
- Projected enrollment 33 to 50% of those eligible $\longrightarrow$ or ~ 36/month or 2+/center/month
- Estimated time to completion ~ 3 years

The 6 month Report Card

- Averaging 2 enrollments per center per month
- Centers reporting difficulty with complexity of trial
- Coordinators describing lengthy process for obtaining consent

Enrollment Distribution – 6 mos



Why We Can't Enroll

- **"Our IRB won't let us talk to moms in labor"**
- **"The consent requires multiple visits – ↑Time"**
- **"Moms are already overwhelmed by other studies"**
- **"We consent them, then they deliver out of the window"**

Antenatal Consent Secondary

- Started enrolling in October 2005 or later
- 1288 mothers have been pre-screened
- We have screening data from 18 centers

Multiple Births

- **15% of pregnancies yield multiple fetuses**
- **27% of infants are from a multiple pregnancy**

What is Antenatal Consent & Pre-Screening?

Pre-Screening

Identify women hospitalized for risk of premature delivery

Antenatal Consent

Present study & ask for consent

Screening

Is infant born in window ? No congenital anomalies?

Enrollment

Randomize & start study treatments

Phase 1 - Pre-Screening

- **Coordinators and PI need to have a relationship with the perinatal service**
- **Every mother carrying a 23 week infant is not a candidate for consent**
- **Mothers move !**

Communication – OB

- 60% of the time OB permission was obtained prior to approaching a mother for consent

- This increases the time needed to obtain a consent, but provides a framework for two-way communication when qualifying infants arrive on Labor deck

Neonatal Consult

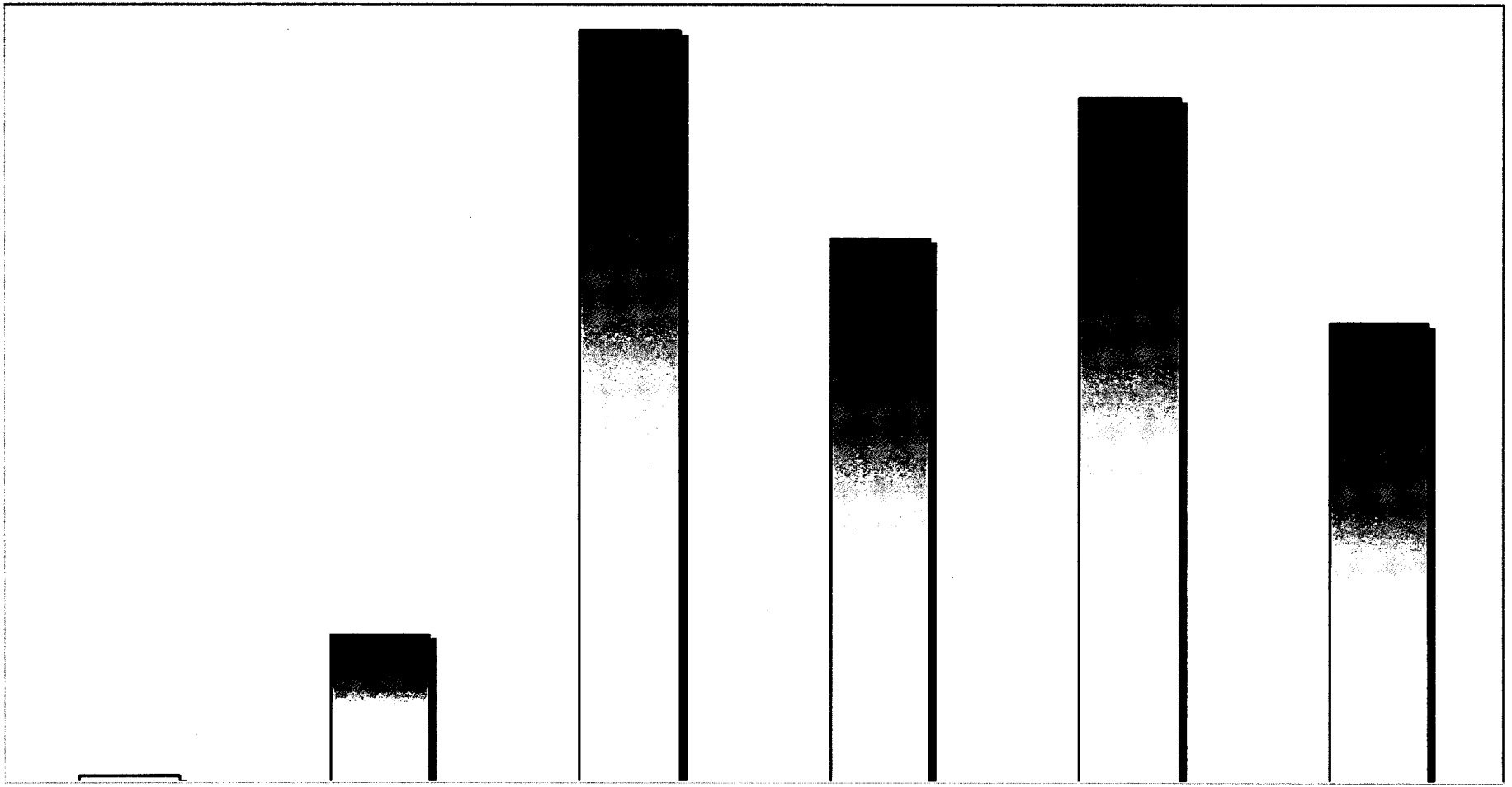
- A neonatal consult was done on 66% of the mothers approached for this trial
- A mother for whom a consult was provided was significantly more likely to consent to the trial than one who did not have a consult. ($p<.02$)
- Centers who do consults on 100% of infants in the trial were not significantly more successful obtaining consent

Neonatal Consult

- **In infants who had a consult, the SUPPORT trial was discussed about 1/3rd of the time**
- **Nearly 10% of infants were consented during the neonatal consult**
- **Consult becomes functional part of pre-screening process**

Phase 2 – Approaching for Consent

- When are mom's approached
- Understanding of site-specific regulations
- Determining why some mom's are not approached



Effect of GA Approached on Study

- 41% of enrollments in the 24-25 week GA stratum
- 59% of enrollments in the 26-27 week stratum
- About 40% of mothers are approached after 25 weeks
- We do not know how long mothers were in-house prior to being approached

Why Was Mother Not Approached ?

• Active Labor	13.3%
• Insufficient Time	15.5
• Week Night, Weekend, Holiday	8.9
• Neonatal Consult not Done	3.7
• Not notified/aware of admission	5.5
• Other	53.1 %

"Other" Reasons for Not Approaching Mother

- **Most Common –**
  - **Congenital Abnormalities**

- **Other common non-specified reasons:**
  - **Maternal illness which precluded consent**
  - **Language**

Number of Attempts

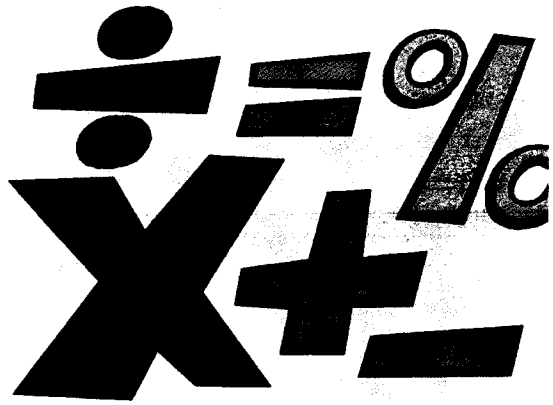
- 77 % of attempts to approach mom done by Coordinator/ Research RN
- 77% of mothers were approached 2 or less times
- Range was 1-11 attempts

Too Many Consents

- We were concerned that mothers who were in "Multi-Network" centers, those who were in Neonatal and Maternal NICHD networks, would overwhelm moms with consents

- Only 5% of screened subjects were specifically identified as being in another maternal study, and 8% in a neonatal study

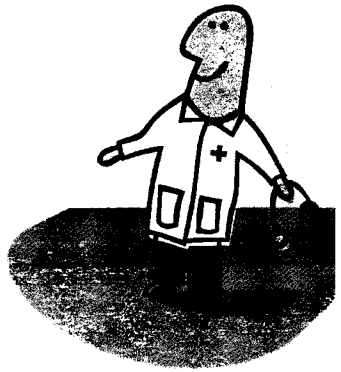
Consent Rate



- **Of the 1288 mothers pre-screened, 1017 have current data forms indicating status of consent**

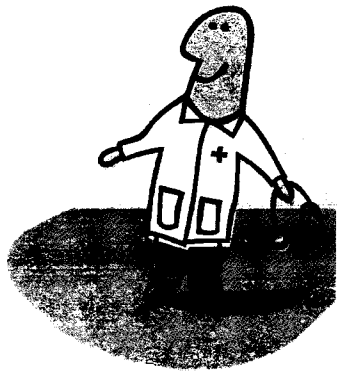
- **551 were consented , for a consent rate of 54.2 %**

What Affects Consent Rate?



- Is the rate of consent effected by gestational age at which we approach the mother ?
- Is it affected by who obtains the consent?
- Other factors?

What Affects Consent Rate?



- There is a significant relationship between doing a neonatal consult and obtaining consent (P< .02)

- Translation: You were more likely to get a consent if a consult was done

Phase 3 - Screening

- Post-Consent tracking – Moved, Transferred, D/C'd, Readmitted
- Delivery status - Does everyone know about delivery?
- Equipment status - enough for multiples?
- Tracking through window of eligibility

Delivery in the Study Window

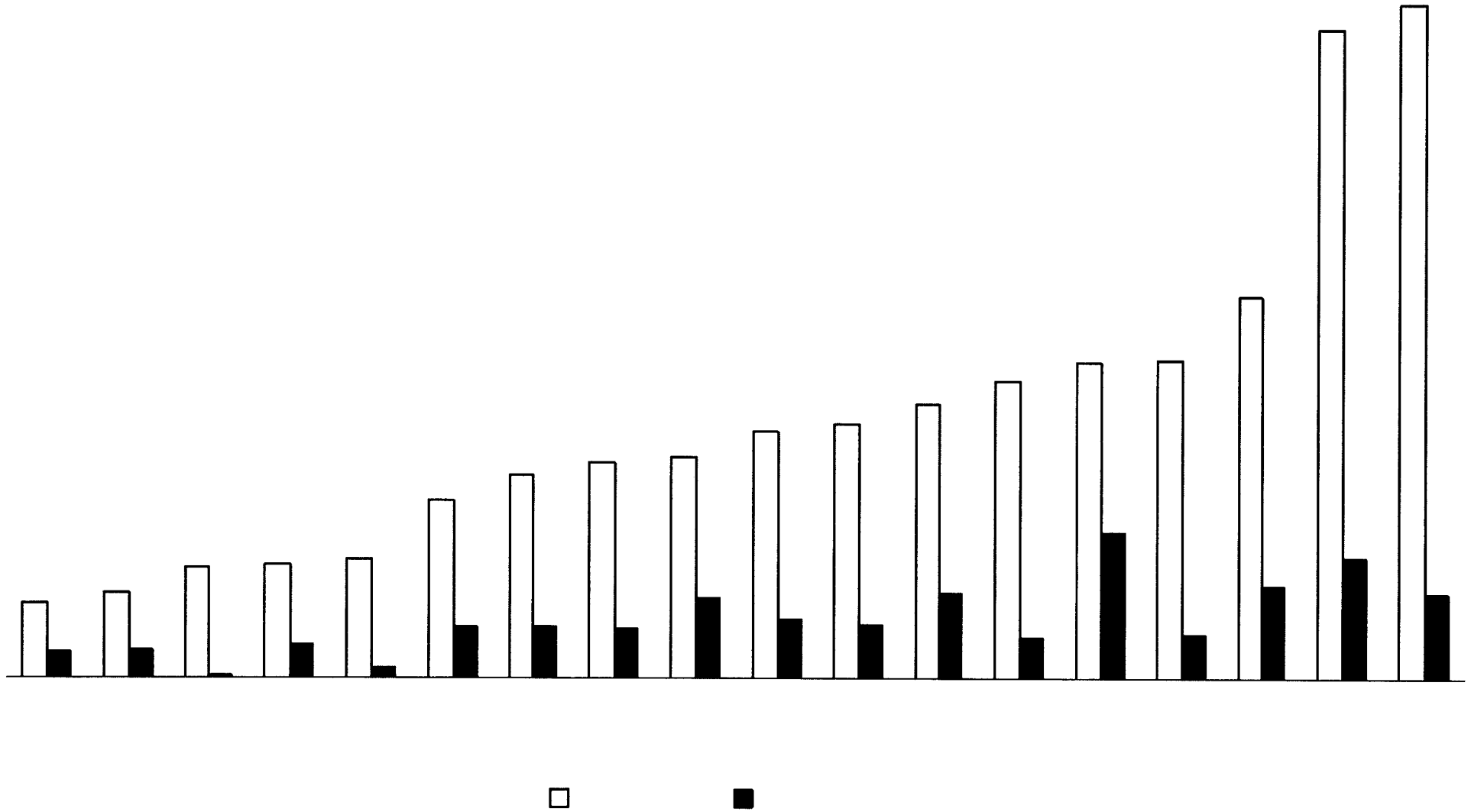
- **Only 51.5% of women who consented delivered an infant in the study window**
- **Range was 25 – 76%**
- **SUPPORT – An effective tocolytic !**

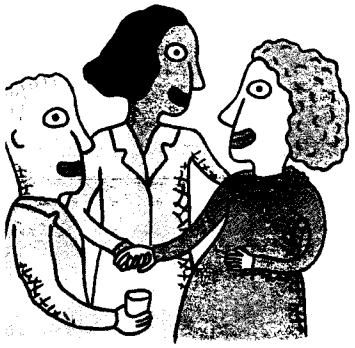
Not Delivered in the Window

- **38 % delivered out of the window in the study hospital**
- **9 % were transferred or discharged prior to delivery**
- **1 % died *in utero***

Phase 4 - Enrollment

- What was the rate of enrollment ?
- What factors effected that rate?
- Who were the most efficient enrollers ?

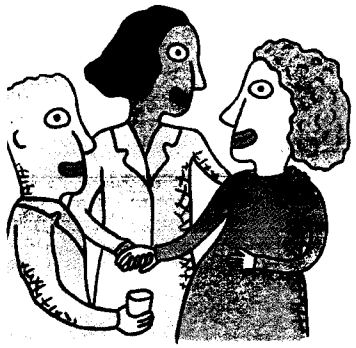




When Mothers Were Approached

Gestational Age at first contact (Weeks)

Weeks	#	%
22	2	0.2
23	58	5.7
24	295	29.0
25	214	21.0
26	268	26.4
27	180	17.7



When Mothers Were Approached

The average GA at which mothers were first approach was not significantly different for those who consented and those who did not .

Too Many Consents

- **Centers who have both types of Networks in place are now 4 of the top 5 enrollers**

- **These centers approach more women, get more consults, enrolled at a higher rate, and were more likely to use <30 minutes to obtain a consent**

The Current Numbers - Overview

- 1288 moms were screened
- 1017 were approached for consent
- 551 agreed to allow their infants to participate
- 289 infants and 254 moms enrolled in the trial
- 1288/254 = 5:1 screening to enrollment ratio

SUPPORT – Workload

Each enrolled subject required the following:

- **4 unsuccessful screenings (1-11 visits ea.) at 1.2 hour.**
- **1 successful screening (1-11visits ea.) at 1.2 hours for this subject**
- **6 hours screening/subject.**

The Bottom Line

- **In a trial with antenatal consent and a 4 week delivery window, we found that you must approach five women and spend about six hours just in the pre-enrollment process in order to enroll *one* infant in the trial .**

Limitations of the Study

- Data was collected by coordinators
- We are missing the overall denominator
- No information regarding comparing coordinators with physicians regarding consent rates
- Data collection is not yet complete

Implications

- **Studies requiring antenatal consent must budget more coordinator time for recruitment**

- **When establishing timelines for a trial, a screening to recruitment ratio of 5:1 is reasonable**

Where do we go from here?

- How does this estimate differ from the amount of time it takes to consent for studies at/after birth? Should studies requiring antenatal consent be budgeted differently than post-natal consent studies?

- Are there ways to shorten the amount of time spent doing antenatal consent?

Participating Centers

Case Western Univ.
Univ. of Texas-Dallas
Univ. of Miami
Emory University
Univ. of Cincinnati
Indiana Univ.
Brown Univ.
Wayne St. Univ.
Stanford University

Stanford University
Univ. of Alabama – Birmingham
Univ. of Texas – Houston
Duke Univ.
Yale Univ.
UCSD
Tufts Univ.
Univ. of Utah
Univ. of New Mexico
University of Iowa

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: THANKS!!!
Date: Friday, April 20, 2007 1:35:05 PM

Hi Rose
Thanks for your comments - The trial is moving ahead and I think that
the calls and visits are effective.
Neil
-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, April 20, 2007 9:06 AM
To: Neil Finer
Subject: THANKS!!!

Neil
Thank you for your commitment to the SUPPORT trial and for joining us.
I truly appreciate your dedication!!
With warmest regards and respect,
Rose

Sent from my BlackBerry Wireless Handheld

From:	Neil Finer
To:	Higgins, Rosemary (NIH/NICHD) [E]; Shankaran, Seetha; Adas@rti.org; Sood, Beena; Pappas, Athina; du2744@wayne.edu; Rosman, Carolyn; Bara, Rebecca; kathymw@wayne.edu; ksawaya@wayne.edu; lsumner@netzero.net; KATHLEEN F ABRAMCZYK
Cc:	Susan Hintz
Subject:	RE: HIC Correspondence for Protocol #025607MP4F
Date:	Tuesday, April 17, 2007 7:24:58 PM

Great news Seetha!!
Talk to you in the morning
Neil

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, April 17, 2007 2:02 PM
To: Shankaran, Seetha; Adas@rti.org; Sood, Beena; Pappas, Athina; du2744@wayne.edu; Rosman, Carolyn; Bara, Rebecca; kathymw@wayne.edu; ksawaya@wayne.edu; lsumner@netzero.net; KATHLEEN F ABRAMCZYK
Cc: Neil Finer; Susan Hintz
Subject: RE: HIC Correspondence for Protocol #025607MP4F

TERRIFIC!
Rose

-----Original Message-----
From: Shankaran, Seetha [mailto:sshankar@med.wayne.edu]
Sent: Tuesday, April 17, 2007 4:31 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; Adas@rti.org; Sood, Beena; Pappas, Athina; du2744@wayne.edu; Rosman, Carolyn; Bara, Rebecca; kathymw@wayne.edu; ksawaya@wayne.edu; lsumner@netzero.net; KATHLEEN F ABRAMCZYK
Cc: Neil; Susan Hintz
Subject: FW: HIC Correspondence for Protocol #025607MP4F

Hi all
Good news, finally, re MRI secondary for SUPPORT
Seetha

Seetha Shankaran, M.D.
Professor of Pediatrics
Wayne State University School of Medicine
Director, Neonatal-Perinatal Medicine
Children's Hospital of Michigan and
Hutzel Women's Hospital

Tel 313-745-1436
Fax 313-745-5867

Email sshankar@med.wayne.edu

received this in error, please (1) do not forward or use this information in any way, (2) delete or destroy this message and its attachments and (3) please contact me immediately.

-----Original Message-----
From: Amanda Reese [mailto:ad1137@wayne.edu]
Sent: Tuesday, April 17, 2007 10:38 AM
To: Shankaran, Seetha
Cc: Bara, Rebecca
Subject: HIC Correspondence for Protocol #025607MP4F

Attached please find correspondence from the Human Investigation Committee regarding your protocol. A signed hard copy with attachments (if applicable) will be sent via inter-office mail or U.S. Postal Service.

Amanda C. Reese
Research Compliance Administrator
Human Investigation Committee
Wayne State University
101 East Alexandrine
Detroit, MI 48201
phone: (313) 577-1628
fax: (313) 993-7122

From: Pablo Sanchez
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Nancy Miller
Subject: Re: FW: SUPPORT MRI
Date: Tuesday, April 17, 2007 4:28:20 PM

Rose--see below--pablo

>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> 4/16/07 11:57 AM >>>

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thursday, April 12, 2007 6:04 PM
To: Wally Carlo, M.D.; mcw3@case.edu; Brenda Poindexter; Abbot Laptook; vanmeurs@stanford.edu; Tyson, Jon E; Morris, Brenda H; Ronald N Goldberg
Cc: srhintz@stanford.edu
Subject: SUPPORT MRI

Please respond to the following questions by APRIL 18th.

1) How many patients have been enrolled to date in the SUPPORT Neuroimaging secondary at your site? 13

2) How many have completed 35-42 week neuroimaging studies (MRI and CUS) : 12

3) If you have enrolled patients that have not completed 35-42 week neuroimaging, please tell us:

a) How many died before reaching the 35-42 week window? NONE

b) How many have not yet reached the window?

c) How many have reached the window, but have not yet been imaged? 1

d) How many "missed"/were unsuccessful with a neuroimaging study? NONE

Please describe: _____

e) Other issues?

Please describe: _____NONE--all successfully enrolled_____

Thank you for your hard work and dedication on SUPPORT and the Neuroimaging Secondary!

Alabama

Case

Dallas

Indiana

Brown

Stanford

Houston

Duke

Iowa

Utah

Tufts

UCSD

Rosemary D. Higgins, M.D.

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

NICHD, NIH

6100 Executive Blvd., Room 4B03B

MSC 7510

Bethesda, MD 20892

(For overnight delivery, use Rockville, MD 20852)

301-435-7909

301-496-3790 (FAX)

higginsr@mail.nih.gov <mailto:higginsr@mail.nih.gov>

From: Wade Rich
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Agenda - April SC Meeting
Date: Tuesday, April 17, 2007 1:48:04 PM

Rose,
I need to update SUPPORT. Do we have an official report from last DSMC meeting?
wade

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, April 16, 2007 1:51 PM
To: Cunningham, Meg; ahensman@wihri.org; nxs5@cwru.edu; auten002@mc.duke.edu; ellen_hale@oz.ped.emory.edu; ldw@iupui.edu; Huitema, Carolyn Petrie; Zaterka-Baxter, Kristin; mbball@leland.stanford.edu; mcollins@peds.uab.edu; grisbyca@email.uc.edu; Nancy.Miller@UTSouthwestern.edu; Georgia.E.McDavid@uth.tmc.edu; ae5357@wayne.edu; du2744@wayne.edu; monica.konstantino@yale.edu; Karen.Osborne@hsc.utah.edu; BMackinnon@tufts-nemc.org; karen-johnson@uiowa.edu; Cbackstrom@salud.unm.edu; aaf2@cwru.edu; dstevenson@stanford.edu; cotte010@mc.duke.edu; Walid.Salhab@UTsouthwestern.edu; WOh@Lifespan.org; jlemons@iupui.edu; Poole, W. Kenneth; edward.donovan@chmcc.org; BENJA005@dcri.duke.edu; Carl_Dangio@urmc.rochester.edu; mblakely@utmem.edu; Brenda.H.Morris@uth.tmc.edu; dale_phelps@urmc.rochester.edu; Neil Finer; kurt.schibler@cchmc.org; bpoindex@iupui.edu; Das, Abhik; alaptook@WIHRI.org; mcw3@cwru.edu; goldb008@mc.duke.edu; [SCRN] Stoll, Barbara; vanmeurs@leland.stanford.edu; wcarlo@peds.uab.edu; jon.e.tyson@uth.tmc.edu; sshankar@med.wayne.edu; richard.ehrenkranz@yale.edu; Ifrantz@tufts-nemc.org; Roger.Faix@hsc.utah.edu; kwatterberg@salud.unm.edu; edward-bell@uiowa.edu; Pablo.Sanchez@UTSouthwestern.edu; mca113@northwestern.edu; bvohr@wihri.org; Crosman@med.wayne.edu; Kathleen.A.Kennedy@uth.tmc.edu; Michael Cotten
Cc: Brinkley, Margo F.; Auman, Jeanette O.; Schaefer, Scott E.; Pickett, James; Gantz, Marie; McDonald, Scott A.; Wade Rich; jeff-murray@uiowa.edu; francie.english@utmg.org; msumner@peds.uab.edu; diane.timmer@cchmc.org; gonza025@mc.duke.edu; Karen.Kirby@UTSouthwestern.edu; Ktownsen@med.wayne.edu; mary.j.brunner@UC.edu; lisa.joo@stanford.edu; [SCRN] Dunbar-Scott, Renee; Alice.J.Reardon@uth.tmc.edu; jrose@wihri.org; axt25@po.cwru.edu; debra.camputaro@yale.edu; mlg@cwru.edu; bvecchio@careNE.org; christina.hayden@duke.edu; cameyer@iupui.edu; mary-mcconnell@uiowa.edu; Monica Bocaner; fenglish@utmem.edu; carolyn.grier@uhhospitals.org; archerst@mail.nih.gov; Zaterka-Baxter, Kristin
Subject: RE: Agenda - April SC Meeting

Hi,
We are pleased to announce the appointment of an NICHD NRN Coordinator, Stephanie Archer, who started with us today. You will meet her at the upcoming meeting.

Also -

Here is the weather for the meeting days:
Wednesday

Mostly Cloudy
High: 55
Low: 41
Precip Chance: 14%

Thursday

Chance light rain showers

High: 60
Low: 41
Precip Chance: 27%

Friday

Partly cloudy
High: 61
Low: 46
Precip Chance: 9%

From: Cunningham, Meg [mailto:mcunningham@rti.org]
Sent: Monday, April 16, 2007 9:07 AM
To: Cunningham, Meg; ahensman@wihri.org; nxs5@cwru.edu; auten002@mc.duke.edu; ellen_hale@oz.ped.emory.edu; ldw@iupui.edu; Huitema, Carolyn Petrie; Zaterka-Baxter, Kristin; mbball@leland.stanford.edu; mcollins@peds.uab.edu; grisbyca@email.uc.edu; Nancy.Miller@UTSouthwestern.edu; Georgia.E.McDavid@uth.tmc.edu; ae5357@wayne.edu; du2744@wayne.edu; monica.konstantino@yale.edu; Karen.Osborne@hsc.utah.edu; BMackinnon@tufts-nemc.org; karen-johnson@uiowa.edu; Cbackstrom@salud.unm.edu; aaf2@cwru.edu; dstevenson@stanford.edu; cotte010@mc.duke.edu; Walid.Salhab@UTsouthwestern.edu; WOh@Lifespan.org; jlemons@iupui.edu; Poole, W. Kenneth; edward.donovan@chmcc.org; BENJA005@dcri.duke.edu; Carl_Dangio@urmc.rochester.edu; mblakely@utmem.edu; Brenda.H.Morris@uth.tmc.edu; dale_phelps@urmc.rochester.edu; nfiner@ucsd.edu; kurt.schibler@cchmc.org; bpoindex@iupui.edu; Das, Abhik; alaptook@WIHRI.org; mcw3@cwru.edu; goldb008@mc.duke.edu; [SCRN] Stoll, Barbara; Higgins, Rosemary (NIH/NICHD) [E]; vanmeurs@leland.stanford.edu; wcarlo@peds.uab.edu; jon.e.tyson@uth.tmc.edu; sshankar@med.wayne.edu; richard.ehrenkranz@yale.edu; Ifrantz@tufts-nemc.org; Roger.Faix@hsc.utah.edu; kwatterberg@salud.unm.edu; edward-bell@uiowa.edu; Pablo.Sanchez@UTSouthwestern.edu; mca113@northwestern.edu; bvohr@wihri.org; Crosman@med.wayne.edu; Kathleen.A.Kennedy@uth.tmc.edu
Cc: Brinkley, Margo F.; Auman, Jeanette O.; Schaefer, Scott E.; Pickett, James; Gantz, Marie; McDonald, Scott A.; wrich@ucsd.edu; jeff-murray@uiowa.edu; francie.english@utmg.org; msumner@peds.uab.edu; diane.timmer@cchmc.org; gonza025@mc.duke.edu; Karen.Kirby@UTSouthwestern.edu; Ktownsen@med.wayne.edu; mary.j.brunner@UC.edu; lisa.joo@stanford.edu; [SCRN] Dunbar-Scott, Renee; Alice.J.Reardon@uth.tmc.edu; jrose@wihri.org; axt25@po.cwru.edu; debra.camputaro@yale.edu; mlg@cwru.edu; bvecchio@careNE.org; christina.hayden@duke.edu; cameyer@iupui.edu; mary-mcconnell@uiowa.edu; Monica Bocaner; fenglish@utmem.edu; carolyn.grier@uhhospitals.org
Subject: Agenda - April SC Meeting

Dear All-

Attached you will find an updated agenda for April's Steering Committee Meeting. There was one minor change to the second day of the meeting. Please let me know if you have any questions or concerns. I look forward to seeing you all later this week.

Thanks,
Meg

Meg Cunningham
RTI International
701 13th Street, NW
Suite 750
Washington, D.C. 20005-3967

tel. 202-974-7837
www.rti.org

From: Shirley Cosby
To: Namasivayam Ambalavanan; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT MRI
Date: Monday, April 16, 2007 2:52:37 PM

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thursday, April 12, 2007 6:04 PM
To: Wally Carlo, M.D.; mcw3@case.edu; Brenda Poindexter; Abbot Laptook; vanmeurs@stanford.edu; Tyson, Jon E; Morris, Brenda H; Ronald N Goldberg
Cc: srhintz@stanford.edu
Subject: SUPPORT MRI

Please respond to the following questions by **APRIL 16th.**

1) How many patients have been enrolled to date in the **SUPPORT Neuroimaging secondary** at your site? We have enrolled 50

2) How many have completed 35-42 week neuroimaging studies (MRI and CUS) completed 37 all the way through

3) If you have enrolled patients that have **not** completed 35-42 week neuroimaging, please tell us:

a) How many died before reaching the 35-42 week window? 8 died but 5 of these had an early HUS prior to death

b) How many have not yet reached the window? 5

c) How many have reached the window, but have not yet been imaged? 1

d) How many "missed"/were unsuccessful with a neuroimaging study?

Please describe: one infant was uncooperative and mom requested that she be removed from MRI machine prior to completing the exam.

e) Other issues?

Please describe: _____

****Thank you** for your hard work and dedication on SUPPORT and the Neuroimaging Secondary!**

Alabama
Case
Dallas
Indiana
Brown
Stanford
Houston
Duke

Iowa
Utah
Tufts
UCSD

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Cunningham, Meg
To: Scott, Francilia (NIH/OD) [C]
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT Agenda
Date: Wednesday, April 11, 2007 12:32:30 PM
Attachments: SUPPORT-agenda.doc

Hi Francilia,

Attached is an agenda for the SUPPORT meeting on Thursday of the Steering Committee meeting. Could you make 12 copies of this? Thanks!

Meg

Meg Cunningham
RTI International
701 13th Street, NW
Suite 750
Washington, D.C. 20005-3967
tel. 202-974-7837
www.rti.org

SUPPORT – Agenda

1. Review Enrollments to date, and the need to potentially add additional centers
2. Review the reporting of serious adverse events
3. Review any site issues
4. Report from Secondary PIs, including Consent study.
5. Other business.

From: Neil Finer
To: Zaterka-Baxter, Kristin; Wade Rich
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: DSMC Minutes (Support Study review)
Date: Wednesday, April 11, 2007 11:53:55 AM

Hi Kris
Here is an Agenda for the SUPPORT Meeting at next weeks Steering Committee

1. Review Enrollments to date, and the need to potentially add additional centers
2. Review the reporting of serious adverse events
3. Review any site issues
4. Report from Secondary PIs, including Consent study.
5. Other business.

Regards
Neil Finer

c

From: Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]
Sent: Tuesday, April 10, 2007 11:35 AM
To: Neil Finer; Wade Rich
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: DSMC Minutes (Support Study review)

Hi Dr. Finer,

Please find attached minutes from the first planned DSMC review of Support Study interim analysis held in Rockville, MD on February 6, 2007. These minutes were sent to all centers as well, my apologies for not copying you on the first email.

Thanks, and please let me know if you have any questions.
Kris

Kris Zaterka-Baxter, RN, CCRP
RTI International
4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: ROP outcome for SUPPORT
Date: Tuesday, April 10, 2007 1:39:25 PM

Thanks Rose
Safe travels
Neil

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, April 10, 2007 10:02 AM
To: Neil Finer
Cc: Fernando Martinez
Subject: RE: ROP outcome for SUPPORT

Neil
Here is the CV.
See you tomorrow.

Rose

From: Neil Finer [mailto:nfiner@ucsd.edu]
Sent: Tuesday, April 10, 2007 12:46 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Fernando Martinez
Subject: RE: ROP outcome for SUPPORT

Rose
Can you send me your current CV for the meeting?
Many thanks and safe travels.
See you tomorrow.
Neil

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, April 10, 2007 9:27 AM
To: Neil Finer; Phelps, Dale
Cc: Karen Osborne RN; Roger.Faix@hsc.utah.edu; Bradley Yoder; Gantz, Marie; Das, Abhik
Subject: ROP outcome for SUPPORT

HI
For infants who have laser surgery for support and then go on to have a scleral buckle procedure, are both recorded, or does the infant reach status when the laser procedure is done??

Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B

MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Zaterka-Baxter, Kristin
To:	Nancy Newman; Nancy.Miller@UTSouthwestern.edu; grisbyca@email.uc.edu; ldw@iupui.edu; monica.konstantino@yale.edu; Angelita Hensman; mbball@leland.stanford.edu; mcollins@peds.uab.edu; Georgia E McDavid; Kathy J Auten; Mackinnon, Brenda; Johnson, Karen; Karen Osborne; Conra Lacy; mcw3@cwru.edu; Pablo.Sanchez@UTSouthwestern.edu; sshankar@med.wayne.edu; kurt.schibler@cchmc.org; bpoindex@iupui.edu; richard.ehrenkranz@yale.edu; Abbot Laptook; Krisa Van Meurs; wcarlo@peds.uab.edu; Walid.Salhab@UTSouthwestern.edu; jon.e.tyson@uth.tmc.edu; goldb008@mc.duke.edu; Frantz, Ivan; Bell, Edward; Roger Faix; Kristi Watterberg; KATHLEEN F ABRAMCZYK; crosman@med.wayne.edu; [SCRN] Stoll, Barbara; ellen_hale@oz.ped.emory.edu
Cc:	Das, Abhik; Higgins, Rosemary (NIH/NICHD) [E]; Auman, Jeanette O.; Pickett, James; Huitema, Carolyn Petrie; Cunningham, Meg; Price, Jeffrey M.; Newman, Jamie; Gantz, Marie
Subject:	RE: Support Secondary Post-Natal Growth Study Revisions
Date:	Monday, April 09, 2007 7:21:29 PM
Attachments:	GRO-01(revised)support secondary.doc

Please find attached the corrected technical memo; last sentence:

*"Please begin using this updated form version for all infants born on or **after** April 6, 2007 with IRB approval as necessary."*

Thanks,
Kris

RTI International
4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From: Zaterka-Baxter, Kristin
Sent: Monday, April 09, 2007 7:16 PM
To: 'Nancy Newman'; 'Nancy Miller (Nancy.Miller@UTSouthwestern.edu)'; 'Cathy Grisby (grisbyca@email.uc.edu)'; 'ldw@iupui.edu'; 'Monica Konstantino (monica.konstantino@yale.edu)'; 'Angelita Hensman'; 'mbball@leland.stanford.edu'; 'mcollins@peds.uab.edu'; 'Georgia E McDavid'; 'Kathy J Auten'; 'Mackinnon, Brenda'; 'Johnson, Karen'; 'Karen Osborne'; 'Conra Lacy'; 'M. D. Michele Walsh (mcw3@cwru.edu)'; 'Pablo.Sanchez@UTSouthwestern.edu'; 'M. D. Seetha Shankaran (sshankar@med.wayne.edu)'; 'Kurt Schibler MD (kurt.schibler@cchmc.org)'; 'bpoindex@iupui.edu'; 'richard.ehrenkranz@yale.edu'; 'Abbot Laptook'; 'Krisa Van Meurs'; 'wcarlo@peds.uab.edu'; ' (Walid.Salhab@UTSouthwestern.edu)'; 'jon.e.tyson@uth.tmc.edu'; 'M. D. Ronald Goldberg (goldb008@mc.duke.edu)'; 'Frantz, Ivan'; 'Bell, Edward'; 'Roger Faix'; 'Kristi Watterberg'; 'KATHLEEN F ABRAMCZYK'; 'crosman@med.wayne.edu'; [SCRN] Stoll, Barbara; 'ellen_hale@oz.ped.emory.edu'
Cc: Das, Abhik; 'Higgins, Rosemary (NIH/NICHD) [E]'; Auman, Jeanette O.; Pickett, James; Huitema, Carolyn Petrie; Cunningham, Meg; Price, Jeffrey M.; Newman, Jamie; Gantz, Marie
Subject: Support Secondary Post-Natal Growth Study Revisions

Hi all,
Please find attached the revisions to the Postnatal Growth Secondary Study to Support based on discussion during our last Steering Committee meeting in January 2007 and as voted upon shortly there after. Specifically please find attached both clean and highlighted copies of the following study documents as well as technical memo GRO-01):

Revised Study Manual (version 1.1; version date 04/06/07)
Revised Form GRO-01 (version 1.1; version date 04/06/07)

Thanks and please let me know if you have any questions. All updated study documents will be posted on the NRN website shortly (neonatal.rti.org)

Kris

RTI International
4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

RTI INTERNATIONAL | **Memorandum**

April 6, 2006

Post-natal Growth of Infants Enrolled in the NICHD Neonatal Network Oxygen Saturation (SUPPORT) Study **TECHNICAL MEMO # 1 (GRO1)**

TO: Network Coordinators
Network PIs

FROM: The Data Coordinating Center

SUBJECT: Anthropometric measurement time point clarification
Amino Acid unit of measurement

---

1. Currently, the protocol states weight, length and head circumference will be measured at birth, postnatal age 7, 14, 21, and 28 days, 32 weeks postmenstrual age, 36 weeks postmenstrual age and discharge. We are amending the measurement times points to the following (manual page 1-2, 1-3. 3-1, 3-2, 3-3):

   "..., postnatal age 7, 14, 21, and 28 days, 32 weeks postmenstrual age and 36 weeks postmenstrual age ~~and~~ or discharge whichever comes first."

---

2. The window of time for anthropometric measurement collection has been increased from +/- 1 day to +/- 4 days of each time point and this has been revised as follows (manual page 3-1):

   "This form will be completed on all enrolled infants on days 1, 7, 14, 21 and 28, and on postmenstrual age 32 and 36 weeks ~~and~~ or discharge whichever comes first (all measurement time points may be +/- 4 days with the exception of days 1). The clinical team(attending, fellow, or nurse) should assess ~~Plus/minus one day (±1) will entail assessing~~ the infant 24 hours before actual data collection day for severity of illness. Severe illness may ~~as per clinical team (attending, fellow, or nurse) that would~~ preclude anthropometric measurements. If the infant is too ill for measurements, re-assessments are to be made for the next 48 hours."

---

3. We have updated the Parenteral Nutrition Section A, question 2, bullet 2 to clarify amino acids may be recorded either in grams/kg/day or in grams/liter as follows (manual page 3-3):

- *"Amino acids: Record the number of grams/kg/day (AA Ordered) of amino acids as ordered by the physician for this bag of parenteral nutrition (record to the nearest tenth) **OR** record the concentration of amino acids in grams/liter (AA Concentration) in a given bag"*

Form GRO-01 has been revised accordingly (version 1.1; version date April 6, 2007)

Please note the updated GRO-01 form is available in the Data Entry system and all updated materials will be posted on the NRN web site shortly (neonatal@rti.org). Please begin using this updated form version for all infants born on or **after** April 6, 2007 with IRB approval as necessary.

Cc. Rosemary Higgins, MD

From:	Zaterka-Baxter, Kristin
To:	Nancy Newman; Nancy.Miller@UTSouthwestern.edu; grisbyca@email.uc.edu; ldw@iupui.edu; monica.konstantino@yale.edu; Angelita Hensman; mbball@leland.stanford.edu; mcollins@peds.uab.edu; Georgia E McDavid; Kathy J Auten; Mackinnon, Brenda; Johnson, Karen; Karen Osborne; Conra Lacy; mcw3@cwru.edu; Pablo.Sanchez@UTSouthwestern.edu; sshankar@med.wayne.edu; kurt.schibler@cchmc.org; bpoindex@iupui.edu; richard.ehrenkranz@yale.edu; Abbot Laptook; Krisa Van Meurs; wcarlo@peds.uab.edu; Walid.Salhab@UTSouthwestern.edu; jon.e.tyson@uth.tmc.edu; goldb008@mc.duke.edu; Frantz, Ivan; Bell, Edward; Roger Faix; Kristi Watterberg; KATHLEEN F ABRAMCZYK; crosman@med.wayne.edu; [SCRN] Stoll, Barbara; ellen_hale@oz.ped.emory.edu
Cc:	Das, Abhik; Higgins, Rosemary (NIH/NICHD) [E]; Auman, Jeanette O.; Pickett, James; Huitema, Carolyn Petrie; Cunningham, Meg; Price, Jeffrey M.; Newman, Jamie; Gantz, Marie
Subject:	Support Secondary Post-Natal Growth Study Revisions
Date:	Monday, April 09, 2007 7:15:46 PM
Attachments:	GRO1[support secondary].doc MOP Growth(version1 1uc)20070406.doc Growth MOP(version1.1cc)20070406.doc GRO-01Nutrition Data(uc)20070406.doc GRO-01Nutrition Data(cc)20070406.doc

---

Hi all,

Please find attached the revisions to the Postnatal Growth Secondary Study to Support based on discussion during our last Steering Committee meeting in January 2007 and as voted upon shortly there after. Specifically please find attached both clean and highlighted copies of the following study documents as well as technical memo GRO-01):

Revised Study Manual (version 1.1; version date 04/06/07)
Revised Form GRO-01 (version 1.1; version date 04/06/07)

Thanks and please let me know if you have any questions. All updated study documents will be posted on the NRN website shortly (neonatal.rti.org)

Kris

RTI International
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RTI INTERNATIONAL | **Memorandum**

April 6, 2006

Post-natal Growth of Infants Enrolled in the NICHD Neonatal Network Oxygen Saturation (SUPPORT) Study **TECHNICAL MEMO # 1 (GRO1)**

TO: Network Coordinators
Network PIs

FROM: The Data Coordinating Center

SUBJECT: Anthropometric measurement time point clarification
Amino Acid unit of measurement

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1. Currently, the protocol states weight, length and head circumference will be measured at birth, postnatal age 7, 14, 21, and 28 days, 32 weeks postmenstrual age, 36 weeks postmenstrual age and discharge. We are amending the measurement times points to the following (manual page 1-2, 1-3. 3-1, 3-2, 3-3):

   "..., postnatal age 7, 14, 21, and 28 days, 32 weeks postmenstrual age and 36 weeks postmenstrual age ~~and~~ or discharge whichever comes first."

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2. The window of time for anthropometric measurement collection has been increased from +/- 1 day to +/- 4 days of each time point and this has been revised as follows (manual page 3-1):

   "This form will be completed on all enrolled infants on days 1, 7, 14, 21 and 28, and on postmenstrual age 32 and 36 weeks ~~and~~ or discharge whichever comes first (all measurement time points may be +/- 4 days with the exception of days 1). The clinical team(attending, fellow, or nurse) should assess ~~Plus/minus one day (±1) will entail assessing~~ the infant 24 hours before actual data collection day for severity of illness. Severe illness may ~~as per clinical team (attending, fellow, or nurse) that would~~ preclude anthropometric measurements. If the infant is too ill for measurements, re-assessments are to be made for the next 48 hours."

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3. We have updated the Parenteral Nutrition Section A, question 2, bullet 2 to clarify amino acids may be recorded either in grams/kg/day or in grams/liter as follows (manual page 3-3):

- *"Amino acids: Record the number of grams/kg/day (AA Ordered) of amino acids as ordered by the physician for this bag of parenteral nutrition (record to the nearest tenth) **OR** record the concentration of amino acids in grams/liter (AA Concentration) in a given bag"*

Form GRO-01 has been revised accordingly (version 1.1; version date April 6, 2007)

Please note the updated GRO-01 form is available in the Data Entry system and all updated materials will be posted on the NRN web site shortly (neonatal@rti.org). Please begin using this form updated form version for all infants born on or before April 6, 2007 with IRB approval as necessary.

Cc. Rosemary Higgins, MD

Manual of Operations for the NICHD Neonatal Research Network

Post-natal Growth of Infants Enrolled in the NICHD Neonatal Network Oxygen Saturation (SUPPORT) Study

January 26, 2006
Revised April 6, 2007

Version 1.1; *This version supersedes version date 01/26/06.*

Table of Contents

Chapter 1

Objectives and Trial Design

1.0 Introduction

This manual provides detailed instructions for the secondary study of *Post-natal Growth of Infants Enrolled in the NICHD Neonatal Network Oxygen Saturation (SUPPORT) Study.* The manual is meant to serve as a reference guide for study staff including investigators, coordinators and data managers. The trial objectives and design are summarized briefly below. For further discussion of the study background and design, please refer to the protocol.

Post-natal growth restriction is a major problem in preterm infants. Perturbations in oxygenation are recognized to influence post-natal growth; hypoxic conditions can directly impair growth and hyperoxic conditions predispose infants to BPD, which in turn has been linked to poor growth. The NICHD Neonatal Network is conducting a prospective trial of preterm infants randomized to two levels of baseline oxygen saturations. The effect of baseline saturations on pulmonary morbidity and ROP are the primary outcome measures. With respect to post-natal growth, there is a paucity of data relating alterations in baseline oxygen saturation and/or frequent deviations above or below the baseline to growth outcomes. We propose a secondary study to quantify short-term growth velocity in-hospital and long-term growth at 18-22 months of corrected age for infants enrolled in the SUPPORT Trial in relationship to oxygen saturation.

1.0.1 Primary Hypothesis:

1. Infants in the low oxygen saturation group (85-89%) will have better in-hospital and long-term (18-22 months corrected age) growth.

2. Trajectories of growth in hospital will be better for infants in the low oxygen saturation group.

1.0.2 Secondary Hypothesis:

1. Growth will be greater in infants who spend > 50% of the time with daily median oxygen saturation between 85% -95% while on supplemental oxygen, independent of randomization to low or high oxygen saturation.

2. Infants with BPD will have poorer in-hospital and long-term growth than infants without BPD, independent of the saturation randomization arm.

3. Better long-term growth will be positively related to neuro-developmental outcome, independent of the saturation randomization arm.

1.1 Specific Study Aims

a. To determine anthropometric measurements (wt, HC, length) in infants randomized to low and high oxygen saturation arms, from birth to hospital discharge and again at 18-22 months corrected age.
b. To determine nutritional intake (parenteral and enteral) during hospital stay.
c. To determine the percentage of infants with growth <10 percentile at 36 weeks PMA or discharge, whichever comes first.
d. To determine the percentage of infants with growth <10 percentile at 18-22 months corrected age.
e. To determine growth in relation to the proportion of time spent with oxygen saturation
    1. <85% and >95%
    2. 85%-95%
f. To determine growth in relation to infants' median oxygen saturation while in supplemental oxygen
    1. median oxygen saturation > 95%
    2. median oxygen saturation 85% - 95%
    3. median oxygen saturation < 85%
g. To relate incidence of BPD in low and high saturation arms to growth.
h. To determine in-hospital growth velocity/trajectory in low and high saturation arms.
i. To determine long-term growth velocity/trajectory, from hospital discharge to follow up at 18-22 months corrected age in low and high saturation arms.
j. To relate neuro-developmental outcome at 18-22 months corrected age to long-term growth in low and high saturation arms.

1.2 Study Design

This is an Observational Secondary study to the SUPPORT trial. Anthropometric measurements, clinical data, interventional data and follow-up data will be collected.

1.2.1 Anthropometric Measures

Weight, length and head circumference will be measured at birth, postnatal age 7, 14, 21, and 28 days, 32 weeks postmenstrual age and 36 weeks postmenstrual age ~~and~~ or discharge whichever comes first.

1. Weight – using standard digital electronic scales (c/o infant's nurse)
2. Length – using the Premie Length Board (average of two values, c/o research staff). If length can not be obtained at birth, measurements obtained within the first week of life should be recorded.
3. Head circumference – using paper measurement tape (average of c/o research staff)

1.2.2 Clinical Data

1. Date when the infant regains birth weight.
2. Date of first enteral feed.

3. Date of full enteral feed > 120ml/kg/d.
4. Total number of days on parenteral nutrition.
5. 24 hour intake 'snapshots' (parenteral, enteral) – postnatal age 7, 14, 21, and 28 day, 32 weeks postmenstrual age and 36 weeks postmenstrual age ~~and~~ or discharge whichever comes first.
6. Presence of BPD.

1.2.3 Intervention Data

1. Duration of time spent in target saturation ranges of interest (already part of SUPPORT‡).
2. Median values for unmasked oxygen saturation while still on supplemental oxygen therapy‡.
3. Highest daily FiO_2‡.
4. Duration of supplemental oxygen exposure‡.
5. Documentation of post-discharge oxygen use.

1.2.4 Follow Up data

1. Anthropometric measurements at 18-22months corrected age.
2. Neuro-developmental follow up at 18-22 months corrected age.

1.3 Sample Size

Given the importance of using an RCT to establish the impact of different levels of oxygen saturation from birth on short and long term growth, and recognizing the wealth of oxygen saturation data that will be available for analysis combined with the absence of comparable data in the literature, all infants in the SUPPORT Trial as of the start date of the secondary should be recruited **(n=1320)**. This sample size will be adequate to detect subtle differences in growth between the two groups with adequate (≥80%) power. For example, this sample size will have at least 80% power to detect a difference in means between the two saturation groups of less than 40 g (assuming a mean weight of 1000 g in the control group and a standard deviation of 250 g) using a two group t-test with a 0.05 two-sided significance level.

1.4 Study Outcomes

1.4.1 Primary Outcome

Growth in-hospital and at 18-22 months corrected age and in-hospital growth trajectories in high and low saturation arms.

Chapter 2

Administration

2.1 Organizational Structure

Post-natal Growth of Infants Enrolled in the NICHD Neonatal Network Oxygen Saturation (SUPPORT) Study is being conducted by the NICHD Neonatal Research Network. The Network is funded by the NICHD under cooperative agreements with sixteen institutions comprised of twenty clinical centers and a data coordinating center. The Steering committee for the Network consists of the Principal Investigator from each clinical center, the data center, and the NICHD project officer. The Steering Committee Chairman is appointed by NICHD and is not a Principal Investigator from any of the Clinical Centers. The Post-natal Growth Secondary Protocol Subcommittee is responsible for the preparation and maintenance of the protocol, data forms, and manual of operations. This subcommittee will monitor the overall study performance (including protocol compliance) and will report the progress of the trial to the Steering Committee. The Post-natal Growth subcommittee members are:

Cristina Navarrete
Shahnaz Duara
Richard A. Ehrenkranz
Ruth Everett
Neil Finer
Brenda Poindexter
Abhik Das
Rosemary Higgins

2.2 Participating Centers

Centers from the NICHD Neonatal Research Network participating in the trial are listed with NICHD center numbers in parenthesis and principal investigators listed in the right column.

PARTICIPATING CENTERS	NRN PI	SUPPORT STUDY PI
Case Western Reserve Univ. (3) Rainbow Babies and Children's Hospital	Michele Walsh, MD	Michele Walsh, MD
University of Texas-Dallas (4)	Charles Rosenfeld, MD	Walid Salhab, MD
Wayne State University (5) Children's Hospital of Michigan	Seetha Shankaran, MD	Seetha Shankaran, MD
University of Miami (8) Jackson Memorial Hospital	Shahnaz Duara, MD	Cristina Navarrete MD
Emory University (9) Grady Memorial Hospital	Barbara J. Stoll, MD	Susie Buchter, MD
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Yale University (13) The Children's Hospital at Yale – New Haven	Richard A. Ehrenkranz, MD	Vineet Bhandari, MD
Brown University (14) Women and Infant's Hospital	William Oh, MD	Abbot Laptook, MD
Stanford University (15) Stanford University Med Center	David K. Stevenson, MD	Krisa Van Meurs, MD
University of Alabama (16) University of Alabama at Birmingham	Waldemar A. Carlo, MD	Waldemar A. Carlo, MD
University of Texas- Houston (18)	Jon E. Tyson, MD	Brenda Morris, MD
Duke University (19)	Ronald Goldberg, MD	C. Michael Cotten, MD
Wake Forest University (20)	Michael O'Shea, MD	Michael O'Shea, MD
Children's Hospital at Strong (21)	Dale L. Phelps, MD	Nirupama Laroia, MD
University of California-San Diego (22)	Neil Finer, MD	Neil Finer, MD

2.3 Responsibilities of the Clinical Centers

The minimum staff required for network participation at each clinical center is the physician Principal Investigator (PI), the Research Coordinator and/or research nurse. The responsibilities of these individuals are described briefly in this chapter.

The **PI** or designee is responsible for ensuring the proper conduct of the trial at his or her clinical center (including recruitment and treatment of patients as specified in the protocol), accurate collection of data and transmission of information to the Data Coordinating Center (DCC). Other specific duties include the following:

- Presenting an in-service to the other physicians
- Applying for IRB approval
- Introducing the study to the parents of prospective patients, and obtaining signed informed consent from the parents of eligible infants (in some centers this responsibility may be delegated)
- Reviewing all infants for whom informed consent has been obtained to confirm their eligibility
- Informing the IRB of the study progress.

The **Research Coordinator** will be responsible for the day-to-day operations of the study at the clinical center, including data collection and management. This responsibility includes the following:

- Presenting an in-service to the appropriate nursing and ancillary staff detailing the study protocol.
- Collecting information necessary to complete the data collection forms, and coordinating data entry
- Training and certifying the staff in the use of the network microcomputer

- Controlling access to the network microcomputer and ensuring that required back-up, security and confidentiality are maintained
- Responding to edit messages and other communications from the data enter
- Distributing updates of the protocol and of the manual of operations to clinical center staff
- Reporting protocol deviations (including unmasking) by monitoring the respiratory therapy worksheets

2.4 Responsibilities of the Data Coordinating Center

The DCC is responsible for all aspects of statistical design and analysis as well as data management of the study. In particular, this includes:

- Processing, updating and distributing the protocol and manual of operations
- Developing, printing and distributing the data forms, including periodic updates as necessary
- Developing, testing and implementing the database and other software. Ensuring that data are correct and complete by implementing editing and auditing procedures
- Monitoring the progress and quality of the study
- Preparing interim and final analyses and reports
- Participating in the preparation of presentations and publications relating to the study.

2.5 Responsibilities of NICHD

In addition to its role as a funding agency, the NICHD participates in the activities of the cooperative agreement by being represented on the Steering Committee. The Program Official also participates in the development of protocol and in assisting the Steering committee in the coordination of the studies conducted by the Network. The NICHD Program Official, in conjunction with the RTI Principal Investigator is responsible for monitoring site performance of all participating centers. The Program Official has the following responsibilities:

- Assistance in the development of the study protocol.
- Assistance in the development of capitation-based budgets, including the identification of study costs and special institutional needs.
- Allocation of network resources to meet study needs including pharmacies, study drug supply, and other special requirements of the study.
- Facilitation of training meetings, site visits, and subcommittee meetings.
- Participating in preparation of publications.

Chapter 3

Study Forms

3.1 Nutritional Intake Form: (GRO-01)

"This form will be completed on all enrolled infants on days 1, 7, 14, 21 and 28, and on postmenstrual age 32 and 36 weeks ~~and~~ or discharge whichever comes first (all measurement time points may be +/- 4 days with the exception of day 1). The clinical team (attending, fellow, or nurse) should assess ~~Plus/minus one day (±1) will entail assessing~~ the infant 24 hours before actual data collection day for severity of illness. Severe illness may ~~as per clinical team (attending, fellow, or nurse) that would~~ preclude anthropometric measurements. If the infant is too ill for measurements, re-assessments are to be made for the next 48 hours."

3.1.1 Instructions for Completing Form GRO-01 (Nutritional Intake Form)

- **Center Number**
  Each study center has been assigned a Network center number.

- **Site**
  The center assigns these to their various hospitals. If applicable, any site letter or number is acceptable.

- **Network Number**
  The Network number is made up of a four digit Family (Pregnancy) Number plus the Birth Order Number. Therefore the Network Number is 5 digits.

- **Birth Number**
  This code distinguishes between siblings in the NICU. A single birth or first born of a multiple birth will be coded '1', '2', etc. It does not necessarily have to conform to strict birth order from a multiple birth, but must be kept consistent for each baby.

- **Mother's Initials**
  The Mother's normal initials (first, middle and last). If there is no middle initial, record the two initials. **This information is optional.**

- **Report Number**
  The Report Number is a sequential number, starting with number 1, documenting the number of times this form has been completed. (i.e., DOL 1 = report number 1; DOL 7 = report number 2 etc.)

1. Date
Record the date in MM/DD/YYYY format in which the day of life and the information correspond.

2. Day of life
Day one of life is the day that the baby is born. All data will be entered under the corresponding day of life.

3. Is the infant medically stable to obtain anthropometrics?
If coding "No", re-assess within the next 48 hours for clinical stability. If in the opinion of the treating physician, the infant is deemed unstable for handling by the end of the 48 hour time frame, Code "*" for the unavailable anthropometric measurements.

4. Today's New Weight
Weight should be obtained on day of life 1, 7, 14, 21 and 28, corrected ages 32 and 36 weeks ~~and~~ or discharge whichever comes first. Document weight in grams as recorded by the bedside nurse.

5. New Length
Length should be obtained on day of life 1, 7, 14, 21 and 28, corrected ages 32 weeks, 36 weeks, ~~and~~ or discharge whichever comes first. If length can not be obtained on DOL 1, measurements obtained within the first week of life should be recorded. If the infants first length measurement is obtained on day 7, record "*" for the DOL 1 measurement and record the length obtained on DOL 7 for that time point.

Document length in centimeters, rounded off to the nearest tenth. Measurements should be obtained by the research staff using the Premie Length Board, the infant is placed supine on the board (without a diaper). One examiner holds the infant's head horizontal and aligned to the spine so that there is no lateral tilt of the head or rotation of the chin from the midline. Gentle traction is applied to bring the top of the head into contact with the fixed headboard. The second examiner holds the infant's feet, toes pointing directly upward, and applies gentle traction to straighten the legs. The moveable footboard is brought to the feet and a measurement is taken when it is pressed firmly against the infant's heels. The length must be documented to the nearest tenth. Two measurements are taken and if they are within 1 cm of each other, the average is recorded. If the measurements are not within 1 cm of each other, a third measure should be taken and the median of the three is recorded.

6. Today's New Head Circumference

Head circumference should be obtained on day of life 1, 7, 14, 21 and 28, corrected ages 32 weeks, 36 weeks, ~~and~~ or discharge whichever comes first. Document head circumference in centimeters rounded off to the nearest tenth. Measurements should be obtained by the research staff by applying a measuring tape firmly around the head above the supraorbital ridge (most prominent part of the forehead), and over the occiput to give the maximum circumference. Two measurements should be taken, if the measurements are within 0.5 cm of each other, record the average. If they are not within 0.5 cm of each other, a third measure should be taken and the median of the three should be recorded (to the nearest tenth).

SECTION A. PARENTERAL NUTRITIONAL INTAKE

1. Was there parenteral intake?

If yes, complete question 2

2. For each 24-hour period record the following information for each bag of parenteral nutrition.

- Percent dextrose: Record the percent dextrose solution of the given bag of parenteral nutrition
- Amino acids: Record the number of grams/kg/day (AA Ordered) of amino acids as ordered by the physician for this bag of parenteral nutrition (record to the nearest tenth) **OR** record the concentration of amino acids in grams per liter (AA Concentration) in a given bag
- Record PN volume received: Enter the volume in cc of parenteral nutrition the infant received from the given bag during the 24 hour period
- Intralipids: Enter the percent solution used (10 or 20%) and the total volume in cc of intralipids that the infant received during the same 24 hour period

SECTION B. ENTERAL INTAKE

1. Was there enteral intake?

If yes, record the following for each:

- Type:
  Record the type code from the Enteral Nutrition Key table (found at the bottom right corner of the form), corresponding to the type given during the 24 hour period. If infant was NPO for the 24 hour time period, record "00" and the remainder of this section should be left blank for the given day
- Caloric Density:
  Document the total caloric density per ounce of the feeding type given. See Appendix.
- Volume received:
  Record the total amount of the particular feeding type given in the 24 hour time period (in cc's to the tenth).
- Nutrient additives:

Use the codes listed in the Enteral Nutrition Key table to document the use of MCT or other oil, Polycose, human milk fortifier, or liquid or powder formula added to the feeding.

APPENDIX A

Caloric density:

Milk Formula	Full strength (kcal/oz)	½ strength (kcal/oz)
Expressed breast milk Enfamil Premature Formula 20 Similac Special Care 20 Pregestimil 20 Nutramigen Similac 60/40 Isomil/ProSobee Alimentum Neocate	20	10
Enfamil Premature Formula 24 Similac Special Care 24 Pregestimil 24	24	12
Neosure Enfamil 22 (Enfacare)	22	11
Pedialyte	3	

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1. Anthropometric measurements at 18-22months corrected age.
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1.4 Study Outcomes

1.4.1 Primary Outcome

Growth in-hospital and at 18-22 months corrected age and in-hospital growth trajectories in high and low saturation arms.

Chapter 2

Administration

2.1 Organizational Structure

Post-natal Growth of Infants Enrolled in the NICHD Neonatal Network Oxygen Saturation (SUPPORT) Study is being conducted by the NICHD Neonatal Research Network. The Network is funded by the NICHD under cooperative agreements with sixteen institutions comprised of twenty clinical centers and a data coordinating center. The Steering committee for the Network consists of the Principal Investigator from each clinical center, the data center, and the NICHD project officer. The Steering Committee Chairman is appointed by NICHD and is not a Principal Investigator from any of the Clinical Centers. The Post-natal Growth Secondary Protocol Subcommittee is responsible for the preparation and maintenance of the protocol, data forms, and manual of operations. This subcommittee will monitor the overall study performance (including protocol compliance) and will report the progress of the trial to the Steering Committee. The Post-natal Growth subcommittee members are:

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- Reporting protocol deviations (including unmasking) by monitoring the respiratory therapy worksheets

2.4 Responsibilities of the Data Coordinating Center

The DCC is responsible for all aspects of statistical design and analysis as well as data management of the study. In particular, this includes:

- Processing, updating and distributing the protocol and manual of operations
- Developing, printing and distributing the data forms, including periodic updates as necessary
- Developing, testing and implementing the database and other software. Ensuring that data are correct and complete by implementing editing and auditing procedures
- Monitoring the progress and quality of the study
- Preparing interim and final analyses and reports
- Participating in the preparation of presentations and publications relating to the study.

2.5 Responsibilities of NICHD

In addition to its role as a funding agency, the NICHD participates in the activities of the cooperative agreement by being represented on the Steering Committee. The Program Official also participates in the development of protocol and in assisting the Steering committee in the coordination of the studies conducted by the Network. The NICHD Program Official, in conjunction with the RTI Principal Investigator is responsible for monitoring site performance of all participating centers. The Program Official has the following responsibilities:

- Assistance in the development of the study protocol.
- Assistance in the development of capitation-based budgets, including the identification of study costs and special institutional needs.
- Allocation of network resources to meet study needs including pharmacies, study drug supply, and other special requirements of the study.
- Facilitation of training meetings, site visits, and subcommittee meetings.
- Participating in preparation of publications.

Chapter 3

Study Forms

3.1 Nutritional Intake Form: (GRO-01)

"This form will be completed on all enrolled infants on days 1, 7, 14,, 21 and 28, and on postmenstrual age 32 and 36 weeks or discharge whichever comes first (all measurement time points may be +/- 4 days with the exception of day 1). The clinical team (attending, fellow, or nurse) should assess the infant 24 hours before actual data collection day for severity of illness. Severe illness may preclude anthropometric measurements. If the infant is too ill for measurements, re-assessments are to be made for the next 48 hours."

3.1.1 Instructions for Completing Form GRO-01 (Nutritional Intake Form)

- **Center Number**
  Each study center has been assigned a Network center number.

- **Site**
  The center assigns these to their various hospitals. If applicable, any site letter or number is acceptable.

- **Network Number**
  The Network number is made up of a four digit Family (Pregnancy) Number plus the Birth Order Number. Therefore the Network Number is 5 digits.

- **Birth Number**
  This code distinguishes between siblings in the NICU. A single birth or first born of a multiple birth will be coded '1', '2', etc. It does not necessarily have to conform to strict birth order from a multiple birth, but must be kept consistent for each baby.

- **Mother's Initials**
  The Mother's normal initials (first, middle and last). If there is no middle initial, record the two initials. **This information is optional.**

- **Report Number**
  The Report Number is a sequential number, starting with number 1, documenting the number of times this form has been completed. (i.e., DOL 1 = report number 1; DOL 7 = report number 2 etc.)

1. Date
Record the date in MM/DD/YYYY format in which the day of life and the information correspond.

2. Day of life
Day one of life is the day that the baby is born. All data will be entered under the corresponding day of life.

3. Is the infant medically stable to obtain anthropometrics?
If coding "No", re-assess within the next 48 hours for clinical stability. If in the opinion of the treating physician, the infant is deemed unstable for handling by the end of the 48 hour time frame, Code "*" for the unavailable anthropometric measurements.

4. Today's New Weight
Weight should be obtained on day of life 1, 7, 14, 21 and 28, corrected ages 32 weeks, 36 weeks, or discharge whichever comes first. Document weight in grams as recorded by the bedside nurse.

5. New Length
Length should be obtained on day of life 1, 7, 14, 21 and 28, corrected ages 32 weeks, 36 weeks, or discharge whichever comes first. If length can not be obtained on DOL 1, measurements obtained within the first week of life should be recorded. If the infants first length measurement is obtained on day 7, record "*" for the DOL 1 measurement and record the length obtained on DOL 7 for that time point.

Document length in centimeters, rounded off to the nearest tenth. Measurements should be obtained by the research staff using the Premie Length Board, the infant is placed supine on the board (without a diaper). One examiner holds the infant's head horizontal and aligned to the spine so that there is no lateral tilt of the head or rotation of the chin from the midline. Gentle traction is applied to bring the top of the head into contact with the fixed headboard. The second examiner holds the infant's feet, toes pointing directly upward, and applies gentle traction to straighten the legs. The moveable footboard is brought to the feet and a measurement is taken when it is pressed firmly against the infant's heels. The length must be documented to the nearest tenth. Two measurements are taken and if they are within 1 cm of each other, the average is recorded. If the measurements are not within 1 cm of each other, a third measure should be taken and the median of the three is recorded.

6. Today's New Head Circumference
Head circumference should be obtained on day of life 1, 7, 14, 21 and 28, corrected ages 32 weeks, 36 weeks, or discharge whichever comes first. Document head circumference in centimeters rounded off to the nearest tenth. Measurements should be obtained by the research staff by applying a measuring tape firmly around the head above the supraorbital ridge (most prominent part of the forehead), and over the occiput to give the maximum circumference. Two measurements should be taken, if the measurements are within 0.5 cm of each other, record the average. If they are not within 0.5 cm of each other, a third measure should be taken and the median of the three should be recorded (to the nearest tenth).

SECTION A. PARENTERAL NUTRITIONAL INTAKE

1. Was there parenteral intake?
If yes, complete question 2

2. For each 24-hour period record the following information for each bag of parenteral nutrition.

- Percent dextrose: Record the percent dextrose solution of the given bag of parenteral nutrition
- Amino acids: Record the number of grams/kg/day (AA Ordered) of amino acids as ordered by the physician for this bag of parenteral nutrition (record to the nearest tenth) **OR** record the concentration of amino acids in grams per liter (AA Concentration) in a given bag
- Record PN volume received: Enter the volume in cc of parenteral nutrition the infant received from the given bag during the 24 hour period
- Intralipids: Enter the percent solution used (10 or 20%) and the total volume in cc of intralipids that the infant received during the same 24 hour period

SECTION B. ENTERAL INTAKE

1. Was there enteral intake?
If yes, record the following for each:

- Type:
  Record the type code from the Enteral Nutrition Key table (found at the bottom right corner of the form), corresponding to the type given during the 24 hour period. If infant was NPO for the 24 hour time period, record "00" and the remainder of this section should be left blank for the given day
- Caloric Density:
  Document the total caloric density per ounce of the feeding type given. See Appendix.
- Volume received:
  Record the total amount of the particular feeding type given in the 24 hour time period (in cc's to the tenth).
- Nutrient additives:

Use the codes listed in the Enteral Nutrition Key table to document the use of MCT or other oil, Polycose, human milk fortifier, or liquid or powder formula added to the feeding.

APPENDIX A

Caloric density:

Milk Formula	Full strength (kcal/oz)	½ strength (kcal/oz)
Expressed breast milk Enfamil Premature Formula 20 Similac Special Care 20 Pregestimil 20 Nutramigen Similac 60/40 Isomil/ProSobee Alimentum Neocate	20	10
Enfamil Premature Formula 24 Similac Special Care 24 Pregestimil 24	24	12
Neosure Enfamil 22 (Enfacare)	22	11
Pedialyte	3	

NICU Network	SUPPORT Trial: Growth Secondary Nutritional Intake Form	GRO-01 version 1.1 Final January 26, 2006 Revised April 6, 2007

Center: __ __ Site No. ___ Network No: __ __ __ __ Birth No: ___ Mother's Initials: __ __ __ Report No. ___

This form should be completed on day of life 1, 7, 14, 21 and 28, days, 32 weeks PMA, 36 weeks PMA or discharge whichever comes first. Data should be collected for each time point (+/- 4 days). If length can not be obtained on DOL 1, measurements obtained within the first week of life should be recorded.

1. Date: __ __ / __ __ / __ __ __ __ (Month / Day / Year) **2. Day of Life:** __ __ __

3. Is the infant medically stable to obtain anthropometrics Y N

4. Today's New Weight (gms): __ __ __ __

5 New Length (cm): __ __ . __ **5a. Date:** __ __ / __ __ / __ __ __ __ (MM DD YYYY)

6. Today's New Head Circumference (cm): __ __ . __

A. PARENTERALNUTRITIONAL INTAKE

1. Was there parenteral Intake? Y N

If Yes,

2. PN	% Dextrose	AA Ordered (gm/kg/d)	PN Volume Received (cc's)	AA Concentration (gms/liter)	% Lipid Solution	Intralipid Volume Received (cc's)
a. Today's 1st Bag	__ __ . __	__ . __	__ __ __ . __	____ . __	__ __	__ __ . __
b. Today's 2nd Bag	__ __ . __	__ . __	__ __ __ . __	____ . __	__ __	__ __ . __
c. Today's 3rd Bag	__ __ . __	__ . __	__ __ __ . __	____ . __	__ __	__ __ . __

B. ENTERAL INTAKE

1. Was there enteral Intake? Y N

a. If Yes, record information below:

Type	Caloric Density (Kcal/ounce)	Volume Received (cc's)	Nutrient Additives
1. __ __	__ __	__ __ __ . __	__, __, __, __
2. __ __	__ __	__ __ __ . __	__, __, __, __
3. __ __	__ __	__ __ __ . __	__, __, __, __
4. __ __	__ __	__ __ __ . __	__, __, __, __

Enteral Nutrition Key

Type:		Nutrient Additives:
00= none	17. Donor Breast Milk	2= MCT or other oil
01= breast milk (full strength)	18. Neocate	4= polycose
02= Similac Special Care		6= human milk fortifier
03= Enfamil Premature Formula		8= formula powder or liquid
04= Similac (regular term infant formula)		9= Promod
05= Enfamil (regular term infant formula)		7= other
06= Pregestimil		
07= Nutramigen		
08= Alimentum		
09= Prosobee		
10= Isomil		
11= Similac 60/40		
12= Similac Natural Care		
13= Neosure		
14= Enfamil 22		
15= Other		
16= Pedialyte		

Initials of person completing this form: __ __ __

This form should be completed on day of life 1, 7, 14, 21 and 28, days, 32 weeks PMA, 36 weeks PMA or discharge whichever comes first. Data should be collected for each time point (+/- 4 days). If length can not be obtained on DOL 1, measurements obtained within the first week of life should be recorded.

1. Date: __ __/__ __/__ __ __ __ (Month Day Year) **2. Day of Life:** __ __ __

3. Is the infant medically stable to obtain anthropometrics Y N

4. Today's New Weight (gms): __ __ __ __

5 New Length (cm): __ __ . __ **5a. Date:** __ __/__ __/__ __ __ __ (MM DD YYYY)

6. Today's New Head Circumference (cm): __ __ . __

A. PARENTERALNUTRITIONAL INTAKE

1. Was there parenteral Intake? Y N

If Yes,

2. PN	**% Dextrose**	**AA Ordered (gm/kg/d)**	**PN Volume Received (cc's)**	**AA Concentration (gms/liter)**	**% Lipid Solution**	**Intralipid Volume Received (cc's)**
a. Today's 1st Bag	__ __ . __	__ . __	__ __ __ . __	__ __ . __	__ __	__ __ . __
b. Today's 2nd Bag	__ __ . __	__ . __	__ __ __ . __	__ __ . __	__ __	__ __ . __
c. Today's 3rd Bag	__ __ . __	__ . __	__ __ __ . __	__ __ . __	__ __	__ __ . __

B. ENTERAL INTAKE

1. Was there enteral Intake? Y N

a. If Yes, record information below:

Type	**Caloric Density (Kcal/ounce)**	**Volume Received (cc's)**	**Nutrient Additives**
1. __ __	__ __	__ __ __ . __	__, __, __, __
2. __ __	__ __	__ __ __ . __	__, __, __, __
3. __ __	__ __	__ __ __ . __	__, __, __, __
4. __ __	__ __	__ __ __ . __	__, __, __, __

Enteral Nutrition Key

Type:		Nutrient Additives:
00= none	17. Donor Breast Milk	2= MCT or other oil
01= breast milk (full strength)	18. Neocate	4= polycose
02= Similac Special Care		6= human milk fortifier
03= Enfamil Premature Formula		8= formula powder or liquid
04= Similac (regular term infant formula)		9= Promod
05= Enfamil (regular term infant formula)		7= other
06= Pregestimil		
07= Nutramigen		
08= Alimentum		
09= Prosobee		
10= Isomil		
11= Similac 60/40		
12= Similac Natural Care		
13= Neosure		
14= Enfamil 22		
15= Other		
16= Pedialyte		

Initials of person completing this form: __ __ __

From:	Pablo Sanchez
To:	japickett@rti.org
Cc:	Higgins, Rosemary (NIH/NICHD) [E]; adas@rti.org; Brandon Blasingame; Nancy Miller; Steve Wallace; Walid Salhab
Subject:	NICHD Neonatal Research Network Computer Support
Date:	Wednesday, March 28, 2007 9:03:18 PM

James: All of the suggested changes have been made on our end, and we are still not able to transmit data from the "new" computer. What's next--do you or someone else need to come here and see what is the problem? I am at a loss....thanks--pablo

Pablo J. Sanchez, M.D.
Professor of Pediatrics
University of Texas Southwestern Medical Center
Dept. of Pediatrics
5323 Harry Hines Blvd. (Room E3.508)
Dallas, TX 75390-9063
214-648-3753
214-648-2481 (fax)
972-206-9021 (beeper)
Pablo.Sanchez@UTSouthwestern.edu

From:	Newman, Jamie
To:	drficmd@aol.com; bss5@cwru.edu; amt24@case.edu; Roy.Heyne@UTSouthwestern.edu; JANET.MORGAN@childrens.com; Jackie.Hickman@Childrens.com; apappas@med.wayne.edu; sshankar@med.wayne.edu; kathymw@wayne.edu; CBauer@med.miami.edu; reverett@med.miami.edu; MNeri@med.miami.edu; SEguaras@med.miami.edu; ira_adams-chapman@oz.ped.emory.edu; ellen_hale@oz.ped.emory.edu; steichji@email.uc.edu; Teresa.Gratton@uc.edu; Kimberly.Yolton@cchmc.org; adusick@iupui.edu; ldrichar@iupui.edu; richard.ehrenkranz@yale.edu; Elaine.Romano@Yale.Edu; joanne.williams@yale.edu; BVohr@WIHRI.org; lnoel@wihri.org; AHensman@WIHRI.org; srhintz@stanford.edu; mbball@leland.stanford.edu; MPeralta@peds.uab.edu; VPhillips@peds.uab.edu; jon.e.tyson@uth.tmc.edu; Brenda.H.Morris@uth.tmc.edu; Georgia.E.McDavid@uth.tmc.edu; Nora.I.Alaniz@uth.tmc.edu; Charles.Green@uth.tmc.edu; Patricia.W.Evans@uth.tmc.edu; Sharon.Wright@uth.tmc.edu; golds005@mc.duke.edu; auten002@mc.duke.edu; lohme001@mc.duke.edu; rdillard@wfubmc.edu; npeters@wfubmc.edu; gary_myers@urmc.rochester.edu; diane_hust@urmc.rochester.edu; Rosemary_Jensen@URMC.Rochester.edu; dale_phelps@urmc.rochester.edu; yvaucher@ucsd.edu; wrich@ucsd.edu; mgfuller@ucsd.edu; cbackstrom@salud.unm.edu; kwatterberg@salud.unm.edu; Rohls@salud.unm.edu; JaFuller@salud.unm.edu; bradley.yoder@hsc.utah.edu; karen.osborne@hsc.utah.edu; karen-johnson@uiowa.edu; diane-eastman@uiowa.edu; michael-acarrequi@uiowa.edu; edward-bell@uiowa.edu; pchurch@tufts-nemc.org; bmackinnon@tufts-nemc.org
Cc:	Das, Abhik; Higgins, Rosemary (NIH/NICHD) [E]; Cunningham, Meg; Neil Finer; Gantz, Marie; Bann, Carla M.; Emrich, Steven L.; Hansen, Nellie I.; Kendrick, Douglas E. (in StatEpi); Perritt, Rebecca (Kitty); Saha, Shampa; Taylor, Sarah; Yao, Qing; Wrage, Lisa Ann; Auman, Jeanette O.; Yost, Patricia A.
Subject:	Updated SUPPORT Follow-up Form - SF10A (Status Form)
Date:	Monday, March 26, 2007 3:42:10 PM
Attachments:	SF10_A_03_22_07.pdf

Attached is an updated SF10A (Status Form) for the 18 month follow-up visit for SUPPORT patients that are NOT eligible for the ELBW Follow-up Study (i.e., those greater than 1000g). SUPPORT patients 401-1000g will be followed up with the regular ELBW 18 month follow-up forms (NF01, NF03, etc). The section concerning the Bayley II (2) items has been removed from this form since all SUPPORT patients will be followed up with the Bayley III (3). We are currently working to update this form in the data entry system.

This updated form will be posted on the private gateway of the NRN website under:
Protocols – SUPPORT – Secondary Studies – 18 month follow up – Forms – SF10A

Please let me know if you have any questions concerning the follow-up of SUPPORT patients.

Thanks, Jamie

Jamie E. Newman, MPH
Statistics and Epidemiology
RTI International
Telephone: (919) 485-5719
Fax: (919) 485-7762
newman@rti.org

NICU Network | FOLLOW-UP STUDY - SUPPORT > 1kg | Form SF10A Rel 1.1

STATUS FORM (SF10 - A) | March 22, 2007

Center: __ __ Site No: __ Network No: __ __ __ __ Birth Order: __ Mother's Initials: __ __ __ | Page 1 of 1

This form should be completed if any of the items listed below are missing on the SF05 or SF09A.

*Only complete reason for any **incomplete** items (leave all other items blank).*

A. SF05 Items:

1. B6-Current Gross Motor Function
Indicate reason:_____

2. A1-Weight
Indicate reason:_____

3. A2-Recumbent Length
Indicate reason:_____

4. B1a-Strabismus Right and/or Left
Indicate reason:_____

5. B1b-Nystagmus Right and/or Left
Indicate reason:_____

6. B1c-Roving Eye Right and/or Left
Indicate reason:_____

7. B1d-Tracks Right and/or Left
Indicate reason:_____

8. B1e-Vision Right and/or Left
Indicate reason:_____

9. B2b-Hearing Impaired
Indicate reason:_____

10. B3a-Swallowing
Indicate reason:_____

11. B4a-Abnormal Movements at Rest
Indicate reason:_____

12. C8a-Motor Skill: Axis Head and Neck
Indicate reason:_____

13. C8b-Motor Skill: Axis-Trunk
Indicate reason:_____

14. C8c-Motor Skill: Lower Limb function
Indicate reason:_____

15. C8d-Motor Skill: Upper Limb Function
Indicate reason:_____

16. C8e-Hand Function Right and/or Left
Indicate reason:_____

17. C9a-Normal Neurologic/Motor
Indicate reason:_____

18. C10-Does Child Have Cerebral Palsy
Indicate reason:_____

19. C11-Congenital/Acquired Abnormalities
Indicate reason:_____

B. SF09A Items:

1. A1a1-Unsuccessfully Tested for Cognitive or not tested because of reason 1, 2, 3 or 9?
Indicate reason:_____

2. A1b1-Unsuccessfully Tested for Receptive Communication or not tested because of reason 1, 2, 3 or 9?
Indicate reason:_____

3. A1c1-Unsuccessfully Tested for Expressive Communication or not tested because of reason 1, 2, 3 or 9?
In dicate reason:_____

C. Reason approved by NICHD? Yes No

D. Compliant visit? Yes No

E. Form Completion

1. Date form completed: __ __/__ __/__ __ __ __
Month Day Year

2. Initials of person completing this form: __ __ __

From: Walsh, Michele
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT SITE VISIT
Date: Friday, March 23, 2007 6:38:47 PM

No: Kristi emailed 2 weeks and wants me to come NOW
(after a long delay when I offered repeatedly to come)- when I had
a long research block. I am now in a many month block of service and can not go probably
until end of June. I suggest that Neil go as the closest if he is willing/able to travel,
or perhaps Wally?
Michele

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, March 23, 2007 12:53 PM
To: mcw3@case.edu; Kristi Watterberg
Subject: SUPPORT SITE VISIT

HI Were you folks able to get a date for a SUPPORT SITE visit?
Let me know.

Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Neil Finer
To:	Higgins, Rosemary (NIH/NICHD) [E]; alaptook@WIHRI.org; Abhik Das; ambal@uab.edu; aaf2@po.cwru.edu; Bradley.yoder@hsc.utah.edu; Brenda Poindexter; Carlo Waldemar (E-mail); Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz; Kennedy, Kathleen A; Krisa VanMeurs (VanMeurs, Krisa); Kristi Watterberg; kurt.schibler@cchmc.org; cotte010@mc.duke.edu; Michelle Walsh; MIckey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald GOldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); walid.salhab@UTSouthwestern.edu
Cc:	Cunningham, Meg; Huitema, Carolyn Petrie; Zaterka-Baxter, Kristin; Susan Hintz
Subject:	RE: Hintz slides.ppt
Date:	Friday, March 23, 2007 12:57:33 PM

These look fine to me.
Neil

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, March 23, 2007 6:00 AM
To: Neil Finer; alaptook@WIHRI.org; Abhik Das; ambal@uab.edu; aaf2@po.cwru.edu; Bradley.yoder@hsc.utah.edu; Brenda Poindexter; Carlo Waldemar (E-mail); Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz; Kennedy, Kathleen A; Krisa VanMeurs (VanMeurs, Krisa); Kristi Watterberg; kurt.schibler@cchmc.org; cotte010@mc.duke.edu; Michelle Walsh; MIckey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald GOldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); walid.salhab@utsouthwestern.edu
Cc: Cunningham, Meg; Huitema, Carolyn Petrie; Zaterka-Baxter, Kristin; Susan Hintz
Subject: Hintz slides.ppt

HI
Attached are two slides that Susan Hintz will use in an upcoming scientific presentation at the University of Cincinnati that describe the NRN SUPPORT Neuroimaging secondary study. The bulk of this is available on the website. Let me know if there are any comments.

Thanks
Rose

From: Zaterka-Baxter, Kristin
To: Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik
Subject: RE: Support dsmc
Date: Tuesday, March 20, 2007 2:48:14 PM

Hi,
The minutes and the additional materials are still under review by all the committee members. I will send out an email today asking for all comments to be sent by this coming Monday. I'm not sure if they would like to schedule a conference call to discuss anything further but will ask that as well in the email.
Thanks,
Kris

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tue 3/20/2007 11:05 AM
To: Zaterka-Baxter, Kristin
Subject: Support dsmc

Kris -
When will we have the support dsmc meeting document? I would like to begin scheduling conference calls with sites with low recruitment.

Thanks
Rose

Sent from my BlackBerry Wireless Handheld

From: Shankaran, Seetha
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT Adverse Events 01-04-07
Date: Wednesday, March 14, 2007 3:42:29 PM

Thanks Rose
Seetha

Seetha Shankaran, M.D.
Professor of Pediatrics
Wayne State University School of Medicine
Director, Neonatal-Perinatal Medicine
Children's Hospital of Michigan and
Hutzel Women's Hospital

Tel 313-745-1436
Fax 313-745-5867

Email sshankar@med.wayne.edu

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@MAIL.NIH.GOV]
Sent: Wednesday, March 14, 2007 11:25 AM
To: Shankaran, Seetha
Subject: SUPPORT Adverse Events 01-04-07

Seetha
Here is the document that Neil presented at the January SC meeting. This has the AE's thus far in the study and the table for reference from 2002-2004.

Let me know if you need more information for the IRB.

Thanks
Rose
<<SUPPORT Adverse Events 01-04-07.doc>>

From: Shankaran, Seetha
To: Higgins, Rosemary (NIH/NICHD) [E]; Neil; Carolyn; Zaterka-Baxter, Kristin
Subject: DSMB minutes
Date: Wednesday, March 14, 2007 10:30:27 AM

Hi all
We are doing our SUPPORT IRB continuation ---have there been any memos from DSMB since April 2006 that you have
Thanks
Seetha

Seetha Shankaran, M.D.
Professor of Pediatrics
Wayne State University School of Medicine
Director, Neonatal-Perinatal Medicine
Children's Hospital of Michigan and
Hutzel Women's Hospital

Tel 313-745-1436
Fax 313-745-5867

Email sshankar@med.wayne.edu

From: Neil Finer
To: Edmund Hey
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Those discussions about the NeOProM collaboration
Date: Thursday, March 08, 2007 10:29:14 PM

Hi Edmund
The Chairman of our DSMC is Gordon Avery. We had previously discussed that the DSMCs of the various trials could and should talk to each other if issues arise. We have just completed a DSMC review and we have been told to continue. I will copy Rose Higgins with this email.
The SUPPORT trial made recommendations regarding possible stopping and we are monitoring a number of issues for which we know the background occurrence.
I am hopeful that we will be able to continue to full recruitment.
If any trial is contemplating for any safety issue, in view of the similarity of the oximeters intervention, I would hope that this would be shared with all DSMC chairs and PIs
Yes I am looking at an individual patient meta analysis for all the INO trials for Preterm Infants. We have funding, and are trying to get all the PIs to agree to contribute their data. This will be done with Lisa and The University of Sydney group. This is taking time and getting their data etc is proving interesting. I will let you know how things progress. I can say that getting agreement up front is much easier than trying to get it after the fact.
Are you enrolling?
Best
Neil

From: Edmund Hey [mailto:shey@easynet.co.uk]
Sent: Thursday, March 08, 2007 3:05 PM
To: Neil Finer
Subject: Those discussions about the NeOProM collaboration

Dear Neil,

It sounds as though nearly everybody has now backed the bid that Lisa Askie needs to lodge with the Australian NHMRC in the next few days for money to support the meta-analysis we have all pledged to support when our individual trials are over. There has been quite a bit of discussion as to when the data merging should take place, and I suspect that this is something that is only going to finally get sorted when everybody gets to Toronto. There will be pressure however for at least a small sample of data to be merged fairly soon now, so we can all be sure that we are really are collecting similar data, are defining key items in a uniform way, and have found a way of doing the reprogramming needed to get all the anonymised data into a uniform format. If we can get all this done and debugged well before all the separate trials close then the whole merging process will be able to move ahead much faster and much more smoothly when this stage is reached.

Rumour tells me you are busy on a rather similar exercise yourself trying to merge data from individual patients retrospectively from another cluster of trials. Is that true ? Is it data from some of the nitric oxide trials ? How is it going ? Are there lessons we should be learing from your experience ? What have you done to reassure those who ran the various trials that they have not handed the 'ownership' of their data over to others, and can still control what is done with it ?

The Data Montiroing Committee for the UK BOOST trial is already thinking ahead to what it would need to do if they saw a significant trend emerging in one of the arms of the trial for which they are responsible. There is no question of their even thinking of stopping the trial because of a signifcant difference in a short term outcome (other than death) before we ever get round to finding out thwt the long term (18-24 month) outcome is like. However it is just possible that early mortality among UK chldren turns out to be significantly higher in one trial group. Should that happen they would feel that they had a duty to check and see whether other trials are starting to see a similar trend. It is difficult to think of any other

trend that might trigger a similar request, but DMCs are, of course, there to watch for unpredicted trends as well as predicted ones Sir Iain Chalmers has agreed to chair our DMC. If he reached the point of wanting to raise a question of this sort with those monitoring SUPPORT can you tell me who he would need to contact ? I presume the membership of your DMC is public knowledge. Where would I look to find a list of who the members are ?

Edmund

From:	Maynard Rasmussen, MD
To:	Higgins, Rosemary (NIH/NICHD) [E]
Subject:	RE: Supplement approval
Date:	Tuesday, March 06, 2007 6:47:45 PM

Hi Rose,
Thanks for the excellent news!
Maynard Rasmussen, MD

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, March 06, 2007 10:13 AM
To: Neil; Maynard Rasmussen, MD
Cc: Wade Rich
Subject: Supplement approval

Hi,
The request for a supplement for the SUPPORT Trial has been approved at NICHD for inclusion of the UCSD site (including Sharp Hospital) to enroll children into the trial. A Notice of Grant Award is in process and should be released shortly.
Let me know if you need additional information.

Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Shankaran, Seetha
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: when I am away
Date: Monday, March 05, 2007 5:10:52 PM

Rose
Yes, I will do that before I leave
Good news---got our first Inositol today and in Feb enrolled 2 SUPPORT
Seetha

Seetha Shankaran, M.D.
Professor of Pediatrics
Wayne State University School of Medicine
Director, Neonatal-Perinatal Medicine
Children's Hospital of Michigan and
Hutzel Women's Hospital

Tel 313-745-1436
Fax 313-745-5867

Email sshankar@med.wayne.edu

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, March 05, 2007 3:28 PM
To: Shankaran, Seetha
Subject: Re: when I am away

Can you send us your agenda and any handouts for your subcommittee meetings for the NRN meeting. April 12 is the deadline.
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

----- Original Message -----
From: Shankaran, Seetha <sshankar@med.wayne.edu>
To: Higgins, Rosemary (NIH/NICHD) [E]; Hammond, Jane <hammond@rti.org>; Barry Lester <BLester@WIHRI.ORG>
Sent: Mon Mar 05 15:04:08 2007
Subject: when I am away

Rose, Jane and Barry
I want you to know that I will be out of the country from March 28 to

April 12th. Let me know if anything I need Thanks Seetha

Seetha Shankaran, M.D.
Professor of Pediatrics
Wayne State University School of Medicine Director, Neonatal-Perinatal Medicine Children's Hospital of Michigan and Hutzel Women's Hospital

Tel 313-745-1436
Fax 313-745-5867

Email sshankar@med.wayne.edu

From: Susan Hintz
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: page 29, SUPPORT MRI
Date: Wednesday, February 28, 2007 4:48:48 PM

Hi Rose,

The information on page 29 of the report looks fine. I just want to make sure you know that I will still be sending q 3 month or so queries to the sites to get more complete information. I also think sending those queries also acts as a bit of a reminder to send in the MRIs and US. Pat and I have picked up a few issues on reviewing the MRI's that we have been able to address with the sites that I believe will result in better studies.

Thanks again. By the way, I will keep you in the loop about the J Peds PiNO FU paper stuff - hopefully I will hear "definitively" after the final authorship agreement forms are received by the journal.

Susan

--

Susan R. Hintz, M.D., M.S. Epi
Assistant Professor of Pediatrics
Division of Neonatal and Developmental Medicine
Stanford University School of Medicine
750 Welch Road, Suite 315
Palo Alto, CA 94304
ph: 650-723-5711
fax: 650-725-8351

From: Zaterka-Baxter, Kristin
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: Support DSMC (WIRB)
Date: Monday, February 26, 2007 3:57:50 PM
Importance: High

Hi,
A letter signed by Dr. Avery was scanned and emailed to Ms. Henson today indicating the latest DSMC review of the Support Trial was favorable and the trail will continue. We will send the WIRB the DSMC minutes when available.
Thanks,

Kris

From: Bette Henson [mailto:Bhenson@wirb.com]
Sent: Thursday, February 22, 2007 12:46 PM
To: Poole, W. Kenneth
Cc: higginsr@mail.nih.gov; Huitema, Carolyn Petrie
Subject: URGENT DSMB report request for protocol see title below WIRB protocol # 20050156 6 03-02-2007
Importance: High

Kenneth Poole, Ph.D.
poo@rti.org
Research Triangle Institute

Sponsor: National Institute of Child Health and Human Development (NICHD)
Sponsor Pr #: The SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants
WIRB Pr #: 20050156
Panel 6 agenda 03-02-2007
Annual Continuing Protocol Review

RE: URGENT – INFORMATION NECESSARY FOR REAPPROVAL OF RESEARCH

Dear Kenneth Poole, Ph.D.:

Western Institutional Review Board (WIRB) is conducting continuing review of the above-referenced protocol. As part of that review, we are charged with determining if the risk/benefit ratio remains acceptable, and if the consent form continues to adequately reflect the possible risks of the study.

It was noted at the time of initial protocol review that a Data Safety Monitoring Board (DSMB) or equivalent was to be established for this research. We therefore request that you provide WIRB with the most recent findings of the DSMB to assist with our review.

Please provide the information within the next 7 days so that it can be included in the Board's next review of the protocol. Without the information, the Board may be unable to determine whether the research remains acceptable, and **may be unable to reapprove the research.** The information can be sent to WIRB via e-mail (bhenson@wirb.com), fax (360-252-2495) attn: [Bette Henson].

Thank you for your assistance. If you have any questions, please contact us.

Sincerely,
Bette Henson
Western Institutional Review Board
3535 7th Ave SW, Olympia, WA 98502
P: 1-800-562-4789 ext. [3176] F: 360-252-2495

cc: Rose Higgins, MD, NICHD, higginsr@mail.nih.gov
Carolyn Petri, Medical Monitor, petrie@rti.org

From:	Zaterka-Baxter, Kristin
To:	Karen Osborne RN
Cc:	mbball@leland.stanford.edu; Higgins, Rosemary (NIH/NICHD) [E]
Subject:	Support oximeters
Date:	Tuesday, February 20, 2007 3:46:00 PM
Importance:	High

Thanks Karen!
Please send 2 BLUE masimo oximeters to Beth at Stanford; contacts below:

M Bethany Ball, B.S.
Stanford Univ. Division of Neonatolgy
750 Welch Road, Suite 315
Palo Alto CA 94304
(650) 725-8342
mbball@leland.stanford.edu

Thanks,
Kris

Kris Zaterka-Baxter, RN, CCRP
RTI International
4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From:	Neil Finer
To:	Higgins, Rosemary (NIH/NICHD) [E]
Cc:	Wade Rich
Subject:	RE: Common core Masimo trials data items - just one more supplementary question please
Date:	Tuesday, February 20, 2007 3:45:36 PM

Hi Rose
That would be great and will avoid future issues.
The group should include all the associated trials – Australia, New Zealand, Canada, Europe and England.
Many thanks
Neil

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, February 20, 2007 12:42 PM
To: Neil Finer
Subject: RE: Common core Masimo trials data items - just one more supplementary question please

Neil
Would you like me to see if the Steering Committee is ok with sharing the GDB forms (and MOP) with this group? We have shared them previously with VON and others who have inquired. This way, the group can plan data collections prospectively in trials that are just getting started. Let me know
Thanks
Rose

From: Neil Finer [mailto:nfiner@ucsd.edu]
Sent: Monday, February 19, 2007 10:59 AM
To: Edmund Hey
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Common core Masimo trials data items - just one more supplementary question please

Hi Edmund
The GDB asks for the type of steroid given – betamethasone or dexamethasone, if a complete course was given within 7 days of delivery, and the total number of courses that were given.
If labor was present, the time and date of the onset is recorded, the mode of delivery is noted as vaginal vertex, vaginal breech and Cesarean. Thus if all the entries are complete, you can tell if labor occurred prior to delivery.
Neil

From: Edmund Hey [mailto:shey@easynet.co.uk]
Sent: Sunday, February 18, 2007 1:41 AM
To: Neil Finer
Subject: Common core Masimo trials data items - just one more supplementary question please

Thank you for that. I had as good as deduced that that must be the case. The one question I would like to ask of this generic data base is how does it recordt the antenatal use of steroids ? Is it just yes/no, or does it probe a little deeper to find if treatment might have been given so long ago, or only started such a short time before delivery, that it was unlikely to have had any beneficial effect ? A note as to how mode of delivery is reported would also be of help. Can the data base distinguish between a Caesarean delivery undertaken before labour has started from one undertaken in a woman already in active labour ?
E

From: Neil Finer [mailto:nfiner@ucsd.edu]
Sent: 17 February 2007 17:40
To: Edmund Hey
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Common core data items for the various Masimo monitor trials

Hi Edmund
The NRN has a Generic Data Base completed on every infant born in any of the participating units. .All the information that you have asked about is recorded, and is available for all SUPPORT infants.
Sorry I missed this question.
Neil

From: Edmund Hey [mailto:shey@easynet.co.uk]
Sent: Saturday, February 17, 2007 7:57 AM
To: Neil Finer
Subject: FW: Common core data items for the various Masimo monitor trials

Neil,
Thank you for confirming that you would be going to Toronto in May (and that someone to represent SUPPORT would be there is you can't in the end make it yourself). This means that we can now be confident that all the neonatal trials currently using (or planning to use) Masimo off-set monitors will be at the meeting and I know that Lisa Askie is now going to push ahead with a meeting for all these people..
We need to try and get agreement at, or before, this meeting as to what the common core data items should be for this, and I attach now an annotated list of the items that might be collected before or shortly after randomisation. Only a minority of these probably need to be made available for any merged mata-analysis but we do need to decide what these items ought to be just as quickly as possible now.
In that connection, while you were good enough to let me see, in confidence, copies of all the report forms that SUPPORT will be using there were, as I mentioned in an earlier message, several key facts not recorded on those documents, and this led me to believe that the SUPPORT documents must be linked in some way to a larger Network data set. I *don't* need to see what that is, but we do obviously need confirmation that SUPPORT is collecting information on birthweight, sex , antenatal steroid use, mode of delivery and multiple birth that can be provided when a summary data set is eventually made available for the NeOProM meta-analysis.
Edmund

From: Edmund Hey [mailto:shey@easynet.co.uk]
Sent: 17 February 2007 15:31
To: Barbara Schmidt (schmidt@mcmaster.ca)
Subject: Common core data items for the various Masimo monitor trials

Barbara,

Here is my annotated list of the items that the various neonatal trials currently planning to use off-set Masimo monitors are collecting at or soon after randomisation. I suspect that we will only need to merge information on a small number of these variables when the NeOProM meta-analysis comes to be done, and I have marked the ones that I think are important with an asterisk. However this is a debate that we clearly need to have NOW. I am not yet entirely sure exactly what information is being collected in SUPPORT because, while Neil has let me have a copy of all the key trial documents, there are clearly a few data items such as sex, birthweight, mode of delivery, and information on multiple birth, that are not on these forms because, I presume, they are on some other generic form used by all units contributing to the NIH funded Neonatal Network,

I will produce a second list summarising the information being collected at 36 weeks, at discharge, and at 18-24 months, sometime in the next few days and let you see this too.

E

From: Gantz, Marie
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Das, Abhik
Subject: RE: ROP Missing Report
Date: Thursday, February 15, 2007 12:37:54 PM

OK, I will do that. Thanks!

Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-6255

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, February 15, 2007 12:37 PM
To: Gantz, Marie
Cc: Das, Abhik
Subject: RE: ROP Missing Report

Yes, keep sending them monthly so we track missing data for outcomes as we go (as opposed to waiting to the end of the trial)

Thanks
Rose

From: Gantz, Marie [mailto:mgantz@rti.org]
Sent: Thursday, February 15, 2007 12:30 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Das, Abhik
Subject: ROP Missing Report

Hi Rose,

Attached is the list of SUPPORT infants missing an ROP diagnosis this month. Do you to continue to send these out on a monthly basis?

Thanks,
Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-6255

From: Maynard Rasmussen, MD
To: Higgins, Rosemary (NIH/NICHD) [E]; Wade Rich
Cc: Neil Finer; Paul Wozniak, MD
Subject: RE: support enrollment
Date: Tuesday, February 13, 2007 10:06:45 AM

Good Morning,
Thank-you for the update.
Maynard Rasmussen, MD

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, February 12, 2007 10:41 AM
To: Wade Rich
Cc: Maynard Rasmussen, MD; Neil Finer
Subject: RE: support enrollment

HI,
I am awaiting consideration of an administrative supplement and issuance of a notice of grant award.
Thanks for your patience!!

-----Original Message-----
From: Wade Rich [mailto:wrich@ucsd.edu]
Sent: Friday, February 09, 2007 1:49 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Maynard Rasmussen, MD
Subject: support enrollment

Rose,
Maynard asked me to check again and see if it would be possible to get a letter from you stating that we have been requested to
start enrolling in support again for his IRB.
Wade

Wade Rich, BSHS,RRT,CCRC
Clinical Research Coordinator
Division of Neonatology
UCSD Medical Center
200 W Arbor Dr
San Diego, CA 92103-8774
619-543-5375
pgr 290-5230

From: Zaterka-Baxter, Kristin
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUpport reactivation letter
Date: Monday, February 12, 2007 11:15:17 AM
Attachments: Dr. Alexander.pdf
SUP05.doc

Please see attached. I'll have Dr. Alexander's letter posted along with the technical memo on the NRN web under the Support study.
Thanks,
Kris

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

National Institutes of Health
National Institute of Child Health
and Human Development
Bethesda, Maryland 20892

January 31, 2006

To: NICHD Neonatal Research Network SUPPORT Trial Centers

From: Dr. Duane Alexander
Director, NICHD

Following review of the Data Safety and Monitoring Committee meeting minutes from January 24, 2006, I concur that the SUPPORT Trial may be resumed at the NICHD NRN sites.

Duane Alexander

RTI INTERNATIONAL | Memorandum

February 9, 2006

SUPPORT TECHNICAL MEMO # 5

TO: Network Coordinators
Network PIs

FROM: The Data Coordinating Center

SUBJECT: Reactivating Enrollment into the SUPPORT Trial

The DSMC for the NICHD Neonatal Research Network SUPPORT trial met with the Principle Investigator and Data Coordinating Center staff on January 24th 2006 in Washington D.C. After reviewing the data presented to the DSMC, the consensus was to restart the SUPPORT Trial. The DSMC took Dr. Finer's 8 points of proposed changes as inherent in making its recommendation to continue the trial. The DSMC also emphasized that the current protocol should be resumed and that the DSMC was not changing the protocol. The proposed changes are as follows:

1. Require documentation that the oximeters alarm limits are functional per protocol every 4-6 hours.
2. Change our data collection for FiO2 to ensure that subsequent interval reports more accurately reflect whether the infant was receiving Oxygen or room air.
3. Further training and in-service at all the sites to stress the importance of keeping the SpO2 alarms functional and at the limits of 84% and 96%. We will use a training model based on the OWL (Oxygen with Love Program) developed at Oschner.
4. Develop guidelines for managing desaturations such that the increase in oxygen is proportional to the desaturation.
5. Place bedside cards to indicate the desired target range.
6. Initiate compliance monitoring visits coordinated by RTI to visit random sites.
7. Reanalyze group differences after an additional 100 -150 infants have been enrolled.
8. Utilize only actual SpO2 values for assessment of safety in subsequent analyses i.e.; SpO2 < 84% and > 96%, and analyze only actual time in oxygen.

The official start date for reactivating enrollment in the SUPPORT Trial is February 6, 2006. This is the date that the official notification letter from Dr. Duane Alexander, Director of the NICHD, was sent to the sites.

Please Note: Some of the above steps are in the process of being implemented and any form and Manual of Operations changes will be forthcoming. However, in the interest of time and to keep the momentum for this trial going, please resume enrollment as soon as you have IRB approval. Manual and form changes incorporating the 8 points above will be communicated to you and reflected on the web site and the DMS as soon as possible.

From: Richard Ehrenkranz
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Happy New Year and Updates
Date: Wednesday, February 07, 2007 10:49:43 AM
Attachments: Page 2-IRB approval dates rev 7Feb07.doc

Rose:
Here is a revised list. The SUPPORT trial and Candidiasis study have been recently reapproved.
Richard

At 10:39 AM 2/6/2007, you wrote:

> You can simply send us a table via email with the expiration date of each protocol.
>
> Thanks
> Rose

From: Richard Ehrenkranz [mailto:richard.ehrenkranz@yale.edu]
Sent: Tuesday, February 06, 2007 10:35 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: Happy New Year and Updates

Rose:
I just realized that I used my own table in the non-competing renewal which did not include the expiration date of each protocol. Should I send you a revised version?
Richard

At 02:16 PM 1/3/2007, you wrote:

> HI,
> Happy New Year to everyone.
>
> I have a few updates:
> Dr. Brenda Poindexter has been elected by the Protocol Review Subcommittee to serve as their Vice Chair.
> Dr. Edward Bell has been elected by the Generic Database Subcommittee to be their Vice Chair.
> Karen Johnson (Iowa) has been approved by the Genomics Subcommittee to serve as a member.
>
> **For the non-competing renewals (due February 1, 2007), please complete one of the attached IRB approval tables for all studies at your site.**
> This will facilitate the award process. If you have your own table that you prefer to use, that will be fine. We need each project with approval and expiration dates.
>
> Thanks
> Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
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Richard A. Ehrenkranz, MD
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The information contained in this email may be privileged and confidential. If you are the intended recipient,
you must maintain this message in a secure and confidential manner. If you are not the intended recipient,
please notify the sender immediately and destroy this message. Thank you.

Yale IRB#:	Approval Date:	Expiration Date:	Title of Protocol:
9503007879	10/25/06	10/25/07	Follow-up of Extremely Low Birth Weight Infants from 401 to 1000 grams
9907011067	06/20/06		Randomized Controlled Trial of Induced Hypothermia for Hypoxic-Ischemic Encephalopathy in Term Infants
	06/23/06	06/23/07	Extended Follow-up for Hypothermia Trial Survivors (Amendment)
0205016634	06/04/06	06/04/07	A Randomized Trial of Aggressive or Conservative Phototherapy to Extremely Low Birth Weight Infants
0304025158	4/10/06	4/10/07	Survey of Morbidity and Mortality in Very Low Birth Weight Infants
0311026123	02/20/07*	02/20/08	Early Diagnosis of Nosocomial Candidiasis
0402026453	06/02/06	06/02/07	Neurodiagnostic Evaluation that Assist in the Prediction of Adverse Outcome Following Acute Perinatal Asphyxia
0410027163	02/22/07*	02/22/08	The Surfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight infants (the SUPPORT Trial); includes Breathing Outcomes and Growth secondaries
0506000108	08/07/06	08/07/08	Early-Onset Sepsis Surveillance Study (This is an amendment to an ongoing study of entitled Neonatal Sepsis Review)
0503027540	06/08/06	06/08/07	Serum Inositol Status Among Neonates in 2005
0602001091	04/12/06	04/12/07	Pharmacokinetic Studies of Inositol in Premature Infants (Administrative Amendment approved 07/27/06)

*[Updated February 7, 2007]

From: Zaterka-Baxter, Kristin
To: Timothy_Stevens@URMC.Rochester.edu
Cc: Newman, Jamie; Das, Abhik; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: support breathing outcomes secondary
Date: Thursday, February 01, 2007 4:18:27 PM

Hi,
Be happy to; please let me know what studies you would like the tables for; GDB, active trials, Breathing Outcomes, all Follow-Up studies etc? If the latter two we will need to generate them so it may not be until early next week, would that be alright or are they needed quickly? Only for Rochester correct, or if for Breathing Outcomes, do you need all centers?
Thanks,
Kris

Kris Zaterka-Baxter, RN, CCRP
RTI International
4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, February 01, 2007 3:55 PM
To: Zaterka-Baxter, Kristin; Newman, Jamie
Cc: Timothy_Stevens@URMC.Rochester.edu
Subject: support breathing outcomes secondary

Can you generate a race/ethnicity table for Time Stevens for his non-competing K23 renewal?
Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Das, Abhik
To:	Higgins, Rosemary (NIH/NICHD) [E]
Cc:	Zaterka-Baxter, Kristin; Huitema, Carolyn Petrie
Subject:	FW: DSMC Meeting Agenda (Support Trial)
Date:	Thursday, February 01, 2007 9:06:30 AM
Attachments:	DSMC AGENDA20070206.doc

Here is the agenda. You are scheduled for 3 pm; but it may move faster than that. We can call and let you know if that happens.

Thanks

Abhik

From: Zaterka-Baxter, Kristin
Sent: Tuesday, January 30, 2007 3:19 PM
To: 'Gordon Avery'; 'Robert J. Boyle MD (rjb6j@hscmail.mcc.virginia.edu)'; 'cgleason@u.washington.edu'; [SCRN] Willinger, Marian; 'tclemons@emmes.com'; 'mikeross@ucla.edu'; 'kant@unc.edu'; 'merran.thomson@ic.ac.uk'; 'Marilee Allen'; 'GailD@nih.gov'
Cc: Das, Abhik; Gantz, Marie; Poole, W. Kenneth; Huitema, Carolyn Petrie; 'Price, Bonnie'
Subject: DSMC Meeting Agenda (Support Trial)

Hi everyone,
Please find attached the Agenda as promised.
Thanks,
Kris

Kris Zaterka-Baxter, RN, CCRP
RTI International
4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From: Zaterka-Baxter, Kristin
Sent: Tuesday, January 30, 2007 3:00 PM
To: 'Gordon Avery'; 'Robert J. Boyle MD (rjb6j@hscmail.mcc.virginia.edu)'; 'cgleason@u.washington.edu'; [SCRN] Willinger, Marian; 'tclemons@emmes.com'; 'mikeross@ucla.edu'; 'kant@unc.edu'; 'merran.thomson@ic.ac.uk'; 'Marilee Allen'; 'GailD@nih.gov'
Cc: Das, Abhik; Gantz, Marie; Poole, W. Kenneth; Huitema, Carolyn Petrie; 'Price, Bonnie'
Subject: NICHD NRN Support Study Materials for DSMC Review

Dear DSMC members,

Please find attached the following Support Trial study materials for review prior to the scheduled DSMC meeting Tuesday February 6, 2007 in Rockville, MD:

1. Support DSMC Report
2. NICHD NRN Support Protocol and the NRN website link to a one page study summary for your reference; https://neonatal.rti.org/pdf/StudySummary/summ_SUPPORT.pdf

Please note the agenda is forthcoming. Please also don't hesitate to let me know if you have any questions at all.
Thanks,

Kris

Kris Zaterka-Baxter, RN, CCRP
RTI International
4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From: Zaterka-Baxter, Kristin
Sent: Monday, December 18, 2006 12:21 PM
To: 'Gordon Avery'; 'Robert J. Boyle MD (rjb6j@hscmail.mcc.virginia.edu)'; 'cgleason@u.washington.edu'; [SCRN] Willinger, Marian; ' (tclemons@emmes.com)'; 'mikeross@ucla.edu'; 'kant@unc.edu'; 'merran.thomson@ic.ac.uk'; 'Marilee Allen'; 'GailD@nih.gov'; Das, Abhik; Gantz, Marie
Cc: 'Higgins, Rosemary (NIH/NICHD) [E]'; Huitema, Carolyn Petrie; 'Monica Bocaner'; Webb, Robin E.
Subject: NICHD NRN DSMC Support Study Mtg (02/06/07)

Dear DSMC members,
The meeting date for the first planned DSMC review of the NICHD NRN study titled "The SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants (SUPPORT Trial)" has been scheduled for **Tuesday February 6, 2007 in Rockville, MD.** Please find attached the DSMC roster and logistics memo including contacts should you have any questions regarding the meeting. Approximately one week prior to the meeting date, we will be sending out study reports to be reviewed during the meeting. We will have a conference line set up for those who will be joining us by phone. Instructions for the call will be sent closer to the meeting date.

Thanks,
Kris

Kris Zaterka-Baxter, RN, CCRP
RTI International
4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

NICHD Neonatal Research Network

Data Safety and Monitoring Committee (DSMC)

The SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants
(The SUPPORT Trial)

The February 6, 2007 DSMC meeting to review first interim analyses results for the SUPPORT Trial will be held in the Rockville, MD offices of RTI at 6110 Executive Boulevard, Suite 902, 9th Floor Conference Room. The meeting will start at 8:30 AM and will finish by 3:30 PM. Materials to be discussed are enclosed. Below is the agenda and participant list for this meeting.

AGENDA

CLOSED SESSION		
8:30 - 8:40	Introductions	Dr. Avery
8:40 - 9:00	Presentation of the SUPPORT Trial	Dr. Das and Dr. Gantz
9:00 – 10:30	Presentation of SUPPORT Interim Monitoring Data	Dr. Das and Dr. Gantz
10:30 – 12:00	Discussion of Presentation	DSMC
12:00 – 1:00	Lunch	
1:00 – 2:00	*Question- Answer Session	DSMC, Dr. Das and Dr. Gantz
2:00 – 3:00	Final Discussions and Recommendations for SUPPORT	DSMC
OPEN SESSION		
3:00 – 3:30	Communication of Action Recommended	DSMC and Dr. Higgins
3:30	Meeting Adjourned	

* Dr. Rosemary Higgins, NICHD Program Scientist available upon request

Participants:
DSMC:
Gordon Avery, MD, Chair
Robert J. Boyle, MD
Christine A. Gleason, MD
Marian Willinger, Ph.D.
Traci Clemons, Ph.D
Michael G. Ross, M.D., M.P.H. (by teleconference)
Shrikant Bangdiwala, Ph.D (by teleconference)
Marilee C. Allen, MD
Merran A. Thomson, MD
Dorothy Gail, PhD

Data Center:
Abhik Das, Ph.D.
Marie Gantz, Ph.D.
Carolyn Petrie Huitema
Kris Zaterka-Baxter

NICHD:
Rosemary Higgins, MD (Open Session)

From:	Zaterka-Baxter, Kristin
To:	Nancy Newman; Nancy.Miller@UTSouthwestern.edu; rbara@med.wayne.edu; ellen_hale@oz.ped.emory.edu; grisbyca@email.uc.edu; ldw@iupui.edu; monica.konstantino@yale.edu; Angelita Hensman; mbball@leland.stanford.edu; mcollins@peds.uab.edu; Georgia E McDavid; Kathy J Auten; Mackinnon, Brenda; Johnson, Karen; Karen Osborne; Conra Lacy; linda_reubens@urmc.rochester.edu
Cc:	sshankar@med.wayne.edu; Higgins, Rosemary (NIH/NICHD) [E]; Huitema, Carolyn Petrie
Subject:	Support study oximeters
Date:	Thursday, January 25, 2007 5:45:10 PM

Hi all,
If you anticipate needing additional Support study oximeters over the weekend or Monday please contact me by noon tomorrow.
Thanks,
Kris

Kris Zaterka-Baxter, RN, CCRP
RTI International
4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Wade Rich
Subject: RE: SUPPORT GROWTH SECONDARY RESULTS
Date: Monday, January 22, 2007 3:53:59 PM

Thanks Rose
This sounds fine
Neil

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, January 22, 2007 10:26 AM
To: Neil Finer; CNavarrete@med.miami.edu; Duara, Shahnaz
Cc: Wade Rich; Nancy Newman; mcw3@case.edu; wacarlo@uab.edu; Bradley.yoder@hsc.utah.edu; alaptook@WIHRI.org; kurt.schibler@cchmc.org; Adas@rti.org; Marie Gantz; Zaterka-Baxter, Kristin; Huitema, Carolyn Petrie
Subject: SUPPORT GROWTH SECONDARY RESULTS

Hi,
The vote is in and folks have voted +/- 4 days to be the range for obtaining the growth parameters.

Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Duara, Shahnaz
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT GROWTH SECONDARY RESULTS
Date: Monday, January 22, 2007 3:03:57 PM

Ok - thanks
Shahnaz

Sent from my BlackBerry Wireless Handheld

----- Original Message -----
From: Higgins, Rosemary (NIH/NICHD) [E] <higginsr@mail.nih.gov>
To: Neil Finer <nfiner@ucsd.edu>; Navarrete, Cristina; Duara, Shahnaz
Cc: Wade Rich <wrich@ucsd.edu>; Nancy Newman <nxs5@cwru.edu>; mcw3@case.edu <mcw3@case.edu>; wacarlo@uab.edu <wacarlo@uab.edu>; Bradley.yoder@hsc.utah.edu <Bradley.yoder@hsc.utah.edu>; alaptook@WIHRI.org <alaptook@WIHRI.org>; kurt.schibler@cchmc.org <kurt.schibler@cchmc.org>; Adas@rti.org <Adas@rti.org>; Marie Gantz <mgantz@rti.org>; Zaterka-Baxter, Kristin <kzaterka@rti.org>; Huitema, Carolyn Petrie <petrie@rti.org>
Sent: Mon Jan 22 13:25:55 2007
Subject: SUPPORT GROWTH SECONDARY RESULTS

Hi,

The vote is in and folks have voted +/- 4 days to be the range for obtaining the growth parameters.

Thanks

Rose

Rosemary D. Higgins, M.D.

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

NICHD, NIH

6100 Executive Blvd., Room 4B03B

MSC 7510

Bethesda, MD 20892

(For overnight delivery, use Rockville, MD 20852)

301-435-7909

301-496-3790 (FAX)

higginsr@mail.nih.gov

From: Zaterka-Baxter, Kristin
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT GROWTH SECONDARY RESULTS
Date: Monday, January 22, 2007 1:40:32 PM

Thanks – I'll update the form and MOP. I also have that the subcom voted in favor of having the last measurement be 36 weeks or discharge whichever comes first but Dr. Navarette was not present; should I go ahead and make this change as well?
Thanks,
Kris

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, January 22, 2007 1:26 PM
To: Neil Finer; CNavarrete@med.miami.edu; Duara, Shahnaz
Cc: Wade Rich; Nancy Newman; mcw3@case.edu; wacarlo@uab.edu; Bradley.yoder@hsc.utah.edu; alaptook@WIHRI.org; kurt.schibler@cchmc.org; Das, Abhik; Gantz, Marie; Zaterka-Baxter, Kristin; Huitema, Carolyn Petrie
Subject: SUPPORT GROWTH SECONDARY RESULTS

Hi,
The vote is in and folks have voted +/- 4 days to be the range for obtaining the growth parameters.

Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Shankaran, Seetha
To: Susan Hintz; Neil
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT MRI
Date: Monday, January 22, 2007 10:30:45 AM

Susan and Neil
Can you please send me the following
a) # enrolled in MRI secondary and % done without sedation
b) total amount of radiation exposure in rads/millirads and lay terms--I am sure you have sent this earlier but will be faster if you do so again!
thanks a million
Seetha

Seetha Shankaran, M.D.
Professor of Pediatrics
Wayne State University School of Medicine
Director, Neonatal-Perinatal Medicine
Children's Hospital of Michigan and
Hutzel Women's Hospital

Tel 313-745-1436
Fax 313-745-5867

Email sshankar@med.wayne.edu

From: Wade Rich
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Maynard Rasmussen, MD
Subject: RE: Inhalded Nitric Oxide in Premature Infants
Date: Thursday, January 18, 2007 4:57:16 PM

Rose,
Maynard at Sharp Mary Birch needs a letter from you for his IRB stating that you would like them to begin enrolling in SUPPORT again. His email address is maynard.rasmussen@sharp.com
Thanks !

Wade

Wade Rich, BSHS,RRT,CCRC
Clinical Research Coordinator
Division of Neonatology
UCSD Medical Center
200 W Arbor Dr
San Diego, CA 92103-8774
619-543-5375
pgr 290-5230

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, January 08, 2007 6:55 AM
To: Wade Rich
Subject: RE: Inhalded Nitric Oxide in Premature Infants

No problem at all, the steering committee had approved the request pending specific details of what is needed. Let me know if you need more than the data sheets at this point. For instance, if there is a particular piece of data of interest and you need to know how complete our data set is for a given item, we can help you in advance.

Thanks
Rose

-----Original Message-----
From: Wade Rich [mailto:wrich@ucsd.edu]
Sent: Monday, January 08, 2007 9:58 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Inhalded Nitric Oxide in Premature Infants

Rose,
These early calls are to establish just that. Until we can see what data is available from each study, we won't be able to determine what we can reasonably extract.
Thanks,
Wade

Wade Rich, BSHS,RRT,CCRC
Clinical Research Coordinator
Division of Neonatology
UCSD Medical Center

200 W Arbor Dr
San Diego, CA 92103-8774
619-543-5375
pgr 290-5230

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Sunday, January 07, 2007 1:57 PM
To: vanmeurs@stanford.edu; Wade Rich
Subject: Re: Inhalded Nitric Oxide in Premature Infants

Krisa
This request was "in principle" previously approved by the steering committee. We were awaiting a detailed list of data items. Let me know what we can do to expedite the process.

Thanks
Rose

Sent from my BlackBerry Wireless Handheld

----- Original Message -----
From: Krisa Van Meurs <vanmeurs@stanford.edu>
To: Wade Rich <wrich@ucsd.edu>
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Sun Jan 07 14:49:22 2007
Subject: Re: Inhalded Nitric Oxide in Premature Infants

Hi Wade,

I would be happy to participate of behalf of the NRN. I am available on Jan 23, 25, Feb 1, 5 and 8.

Thank you,

Krisa

>Dear Collaborators,
>
> INO Therapeutics has provided funding for the individual patient
>meta-analysis of Inhaled Nitric Oxide in Premature Infants, and we are
>ready to proceed. We would like to set up a conference call with the
>investigators to discuss how we would plan to move ahead with this
>project. It is our intent that the Principal Investigators at each site
>will be participants in the process, as well as authors on any
>published papers. We would like to discuss the proposed process for
>gathering the data, as well as the plans for the subsequent analyses
>during a conference call that we would try to schedule for either late
>January or early Februrary.
> We have spoken in the past informally, and several of you have already
>sent study forms, for which we are grateful. We would like to take
>this opportunity to formally invite you to participate in this process.
>Please respond to our study coordinator, Wade Rich at wrich@ucsd.edu to
>let us know which individual at your center will be the designated
>participant, and indicate to us which of the following dates would be
>appropriate for a conference call.
>

>Mon 1/22
>Tue 1/23
>Thu 1/25
>Mon 1/29
>Tue 1/30 AM
>Thu 2/1
>Mon 2/5
>Thu 2/8
>
>Thank you.
>
>Sincerely,
>
>Wade Rich, BS, RRT, CCRC
>Study Coordinator
>for
>Neil Finer, MD
>Lisa Askie, PhD, MPH
>Keith Barrington, MD
>Richard Ehrenkranz, MD
>
>
>cc:
>richard.ehrenkranz@yale.edu
>keith.barrington@mcgill.ca
>jean-christophe.mercier@rdb.ap-hop-paris.fr
>jm.hascoet@maternite.chu-nancy.fr
>vanmeurs@stanford.edu
>John.Kinsella@UCHSC.edu
>Personal Email
>david.field@uhl-tr.nhs.uk

From: Barbara Stoll
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT GROWTH SECONDARY STUDY
Date: Wednesday, January 17, 2007 4:43:39 PM

"Higgins, Rosemary \(NIH/NICHD\) [E]" <higginsr@mail.nih.gov> on Wednesday, January 17, 2007 at 4:05 PM -0500 wrote:

I have had a couple of requests to include +/- 3 days, so here is a new ballot.

_____ +/- 1 day

_____ +/- 3 days

__***____ +/- 4 days

For those that voted, you may cast another vote if you prefer the new choice.

Thanks
Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wednesday, January 17, 2007 1:42 PM
To: Abbot Laptook (alaptook@WIHRI.org); 'Abhik Das'; Ambal (ambal@uab.edu); Av [redacted]off (aaf2@po.cwru.edu); Brad Yoder (Bradley.Yoder@hsc.utah.edu); Brenda Poindexter; Carl [redacted]demar (E-mail); 'Ed Bell'; Ed Donovan; 'Ehrenkranz Richard (E-mail)'; 'Ivan Frantz'; Kennedy, Kathleen A; Krisa VanMeurs (VanMeurs, Krisa); 'Kristi Watterberg'; Kurt Schibler (Kurt Schibler [kurt.schibler@cchmc.org]); Michael Cotten (cotte010@mc.duke.edu); 'Michelle Walsh'; M[redacted]aplan; 'Oh William (E-mail)'; 'Pablo Sanchez'; papile@unm.edu; Poole Kenneth (E-mail); 'Roger Fa[redacted]; Ronald GOldberg'; 'Seetha Shankaran'; 'Stevenson David (E-mail)'; 'Stoll Barbara (E-mail)'; 'Tyson Jo[redacted]mail)'; Walid Salhab (walid.salhab@utsouthwestern.edu); (Karen.Osborne@hsc.utah.edu); Angelita [redacted]sman; Anne Furey (afurey@tufts-nemc.org); Becky bara; Bethany Ball; Cathy Grisby; Conra Backstrom; Diane Wilson; Ellen Hale; Georgia McDavid; Karen Johnson (karen-johnson@uiowa.edu); Kathy [redacted]; Leslie Wilson; Monica Collins; monica.konstantino@yale.edu; Nancy Miller; Nancy Newman; susan.tepper@hsc.utah.edu
Cc: Zaterka-Baxter, Kristin; Huitema, Carolyn Petrie; 'Duara, Shahnaz'; CNavarrete@med.miami.edu; 'Neil Finer'
Subject: SUPPORT GROWTH SECONDARY STUDY

HI,

For the SUPPORT GROWTH SECONDARY Study, there was significant discussion at the Steering Committee regarding the specific days for measurements. Please send me a vote by **January 22** on whether you think the measurements should be on the day with either of the following parameter choices:

_____ +/- 1 day

_____ +/- 4 days

ONLY 1 VOTE PER SITE

Thanks

Rose

Rosemary D. Higgins, M.D.

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

NICHD, NIH

6100 Executive Blvd., Room 4B03B

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Bethesda, MD 20892

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301-435-7909

301-496-3790 (FAX)

higginsr@mail.nih.gov

Barbara J. Stoll, MD
George W. Brumley, Jr., Professor and Chair, Department of Pediatrics
Medical Director, Children's Healthcare of Atlanta at Egleston
Office: 404-727-2456 Fax: 404-727-5737
barbara_stoll@oz.ped.emory.edu

From: Abbot Laptook
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT GROWTH SECONDARY STUDY
Date: Wednesday, January 17, 2007 4:37:15 PM

I will abstain since we are not participating. AL

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, January 17, 2007 1:42 PM
To: Abbot Laptook; Abhik Das; ambal@uab.edu; aaf2@po.cwru.edu; Bradley.yoder@hsc.utah.edu; Brenda Poindexter; Carlo Waldemar (E-mail); Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz; Kennedy, Kathleen A; Krisa VanMeurs (VanMeurs, Krisa); Kristi Watterberg; kurt.schibler@cchmc.org; cotte010@mc.duke.edu; Michelle Walsh; MIckey Caplan; Oh William (E-mail); Pablo Sanchez; papile@unm.edu; Poole Kenneth (E-mail); Roger Faix; Ronald GOldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); walid.salhab@utsouthwestern.edu; Karen.Osborne@hsc.utah.edu; Angelita Hensman; afurey@tufts-nemc.org; Becky bara; Bethany Ball; Cathy Grisby; Conra Backstrom; Diane Wilson; Ellen Hale; Georgia McDavid; karen-johnson@uiowa.edu; Kathy Auten; Leslie Wilson; Monica Collins; monica.konstantino@yale.edu; Nancy Miller; Nancy Newman; susan.tepper@hsc.utah.edu
Cc: Zaterka-Baxter, Kristin; Huitema, Carolyn Petrie; Duara, Shahnaz; CNavarrete@med.miami.edu; Neil Finer
Subject: SUPPORT GROWTH SECONDARY STUDY

HI,
For the SUPPORT GROWTH SECONDARY Study, there was significant discussion at the Steering Committee regarding the specific days for measurements. Please send me a vote by **January 22** on whether you think the measurements should be on the day with either of the following parameter choices:

_____ +/- 1 day

_____ +/- 4 days

ONLY 1 VOTE PER SITE

Thanks
Rose
Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Neil Finer
To:	Zaterka-Baxter, Kristin; sduara@miami.edu; CNavarrete@med.miami.edu
Cc:	Das, Abhik; Higgins, Rosemary (NIH/NICHD) [E]; Huitema, Carolyn Petrie
Subject:	RE: Growth (Support Secondary)
Date:	Wednesday, January 17, 2007 1:28:57 PM

Hi Kris
I would send this to all the coordinators and PIs and ask that they reply as to the width of the window – ie +/- 1day, 3days 4 days or other. If they would respond, then we can move ahead with this issue. I can be on the call and briefly discuss this.
Neil

From: Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]
Sent: Wednesday, January 17, 2007 6:28 AM
To: Neil Finer; sduara@miami.edu; CNavarrete@med.miami.edu
Cc: Das, Abhik; Rosemary (NIH/NICHD) [E] Higgins; Huitema, Carolyn Petrie
Subject: Growth (Support Secondary)

Hi Neil,
For the Growth secondary, as we discussed during the Support subcommittee, here is the revised text for the GRO-1 form and MOP regarding the last measurement time point (i.e. 36 weeks or D/C whichever comes first) and noting that infants who are in hospital >120 days, or if death occurs after 36 wks PMA but prior to 120 days of hospitalization, will have growth measures per GDB.

"...measurements at birth, postnatal age 7, 14, 21, and 28 days, 32 weeks postmenstrual age, 36 weeks postmenstrual age or discharge whichever comes first."

Please also note we need to decide on a reasonable 'window' of time to obtain each measurement on day 7 through 36 weeks (i.e. +/- 1d, +/-3d etc). We can talk about it on the coordinators conference call tomorrow if you'd like.

Thanks, and please let me know if you need anything further.
Kris

From: Wade Rich
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: 041069_2006_12_19_AMEND.PDF
Date: Wednesday, January 17, 2007 10:22:35 AM
Attachments: 041069_2006_12_19_AMEND.PDF

Here is our Support approval.
wade

UNIVERSITY OF CALIFORNIA, SAN DIEGO
HUMAN RESEARCH PROTECTIONS PROGRAM

Date: December 19, 2006

To: Dr. Neil Finer Mailcode: 8774

Re: Project #041069
The Surfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants The SUPPORT Trial of the NICHD Neonatal Research Network

Dear Dr. Finer:

Your November 27, 2006 request to amend Project 041069 has been reviewed and approved by the IRB Committee at the December 14, 2006 meeting. This amends the above-referenced research study to include the following: this previously approved protocol was closed to UCSD for new patient enrollment when UCSD was deleted from the NIH Network. The institution has now been re-instated and permission has been granted to enroll an additional 30 infants.

Copies of your revised and re-approved consent forms are enclosed.

On behalf of the UCSD Institutional Review Board,

/nm

Michael Caligiuri, Ph.D.
Director, Clinical Research Protections Program
Mailcode: 0052 Phone: 858-455-5050

From: Zaterka-Baxter, Kristin
To: nfiner@ucsd.edu; sduara@miami.edu; CNavarrete@med.miami.edu
Cc: Das, Abhik; Higgins, Rosemary (NIH/NICHD) [E]; Huitema, Carolyn Petrie
Subject: Growth (Support Secondary)
Date: Wednesday, January 17, 2007 9:28:29 AM

Hi Neil,
For the Growth secondary, as we discussed during the Support subcommittee, here is the revised text for the GRO-1 form and MOP regarding the last measurement time point (i.e. 36 weeks or D/C whichever comes first) and noting that infants who are in hospital >120 days, or if death occurs after 36 wks PMA but prior to 120 days of hospitalization, will have growth measures per GDB.

"...measurements at birth, postnatal age 7, 14, 21, and 28 days, 32 weeks postmenstrual age, 36 weeks postmenstrual age or discharge whichever comes first."

Please also note we need to decide on a reasonable 'window' of time to obtain each measurement on day 7 through 36 weeks (i.e. +/- 1d, +/-3d etc). We can talk about it on the coordinators conference call tomorrow if you'd like.

Thanks, and please let me know if you need anything further.
Kris

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Thanks
Date: Sunday, January 14, 2007 11:48:20 AM

Hi Rose
Ginny and I appreciate your support. I am delighted that there will be a visit to New Mexico. I want to push to finish SUPPORT within the next 16-18 months.
Be well and all the best for the New Year.
Neil

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, January 12, 2007 8:05 PM
To: Neil Finer
Subject: Thanks

Neil
As always, thanks for your commitment to the SUPPORT trial. I truly appreciate all of your efforts!!!
I hope you and Ginny are remaining healthy!
Take care
Rose

Sent from my BlackBerry Wireless Handheld

From: Gail, Dorothy (NIH/NHLBI) [E]
Subject: SUPPORT
Date: Friday, January 12, 2007 10:48:55 AM

Rose- Thanks so much for the invitation to attend the meeting yesterday. It was helpful to me to hear the issues and see the players. Neil Finer sounds terrific and I can see why you want him on the proejct. Let me know if you need anything on this end - sounds like you have it well under control.

Dorothy

Dorothy B. Gail, Ph.D
Chief
Lung Biology and Disease Branch
Division of Lung Diseases, NHLBI
(301) 435-0222 phone
(301) 480-3557 fax
gaild@mail.nih.gov

From: Das, Abhik
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT site monitoring
Date: Wednesday, January 10, 2007 12:19:36 PM

Rose:

We were thinking of sending the final report from the UAB visit to you, Dr. Avery, Neil and Wally. Does that sound alright?

Thanks

Abhik

Abhik Das, Ph.D.
Senior Research Statistician
RTI International
6110 Executive Blvd., Suite 902
Rockville, MD 20852-3903
e-mail: adas@rti.org
Phone: 301-770-8214
Fax: 301-230-4646

From: Zaterka-Baxter, Kristin
To: Phelps, Dale
Cc: Higgins, Rosemary (NIH/NICHD) [E]; Auman, Jeanette O.
Subject: RE: SUPP09 ROP question
Date: Wednesday, January 10, 2007 11:46:42 AM

Hi,
I think we can add this to the form easily because it's not adding or changing a question so it really doesn't affect the DMS; it is just an instruction so can do and can bring a copy if you'd like to the meeting?
Thanks,
Kris

Kris Zaterka-Baxter, RN, CCRP
RTI International
4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From: Phelps, Dale [mailto:Dale_Phelps@URMC.Rochester.edu]
Sent: Wednesday, January 10, 2007 10:30 AM
To: Zaterka-Baxter, Kristin
Cc: Higgins, Rosemary (NIH/NICHD) [E]; Auman, Jeanette O.
Subject: RE: SUPP09 ROP question

I think the issue is that some of the coordinators are interpreting Q.C.1 = No as that they do not have to report any eye exams. The comment there says 'if =yes, complete the SUPPORT10 (ROP) form.
As you say, I think the correct things are being done, it is just a 'mind-block' for some of the coordinators when they fill in the 'no'... they think maybe they should stop. You and Jenny don't let them, but would it be easier to make a small edit on the form?
I think your answer is "no, it would not be easier!" :-)

I would want to fix this before we use the form next (in INS-2)

Dale

From: Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]
Sent: Wednesday, January 10, 2007 10:24 AM
To: Phelps, Dale
Cc: Higgins, Rosemary (NIH/NICHD) [E]; Auman, Jeanette O.
Subject: RE: SUPP09 ROP question

Hi,
I talked to Jenny Auman about this and the only thing that stops an eye exam from being expected is if the patient died per the GDB information, prior to the 50 week date (we also check to see if the transfer status was death – if so, we don't expect an eye exam). It doesn't matter if the patient transferred, we still expect eye exams. So even if Q.C.1 = No on the Supp09 (No ROP exam done), the sites will still get a missing forms edit/query for a Supp10 unless the criteria above are met or you have specifically excused the case. I don't think we need to add a question to the Supp09 but if you would like too we can.
Thanks,
Kris

From: Phelps, Dale [mailto:Dale_Phelps@URMC.Rochester.edu]
Sent: Monday, January 08, 2007 10:22 AM
To: Zaterka-Baxter, Kristin
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPP09 ROP question

Kris,
I'm cleaning up e-mail. Did we ever fix this? You have probably taken care of it, but I wanted to be sure.
We should bring this up at the Subcommittee meeting and also in a co-ordinator's call.

I think adding to the SUPP09 form, question C would cover it....
Add
"If no and the infant survived, complete the SUPP10 (ROP) form based on subsequent exams (including back-transfer hospital and/or outpatient visits)."

Dale

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, November 16, 2006 2:36 PM
To: Zaterka-Baxter, Kristin
Cc: Phelps, Dale; Das, Abhik
Subject: SUPP09 ROP question

Kris
For infants in SUPPORT, If a child is transferred prior to any eye exams, but has exams at the second institution, we need to have a mechanism to obtain the exams – The study nurses answer NO on SUPP09. Which means SUPP10 doesn't get filled – but we need it _ can you fix this?
Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Zaterka-Baxter, Kristin
To:	Shankaran, Seetha; Bara, Rebecca; KATHLEEN F ABRAMCZYK
Cc:	Huitema, Carolyn Petrie; Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik; Sood, Beena
Subject:	RE: Support Oximeter Data 01/08/07
Date:	Wednesday, January 10, 2007 9:36:26 AM

Absolutely; have it noted.
Thanks!
Kris

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Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From: Shankaran, Seetha [mailto:sshankar@med.wayne.edu]
Sent: Wednesday, January 10, 2007 9:35 AM
To: Zaterka-Baxter, Kristin; Bara, Rebecca; KATHLEEN F ABRAMCZYK
Cc: Huitema, Carolyn Petrie; higginsr@mail.nih.gov; Das, Abhik; Sood, Beena
Subject: RE: Support Oximeter Data 01/08/07

Kris
Can you also include Dr Beena Sood in all correspondence re SUPPORT---she is PI of SUPPORT at Wayne
Thanks
SS

Seetha Shankaran, M.D.
Professor of Pediatrics
Wayne State University School of Medicine
Director, Neonatal-Perinatal Medicine
Children's Hospital of Michigan and
Hutzel Women's Hospital

Tel 313-745-1436
Fax 313-745-5867

Email sshankar@med.wayne.edu

From: Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]
Sent: Tuesday, January 09, 2007 4:23 PM
To: Shankaran, Seetha; Bara, Rebecca; KATHLEEN F ABRAMCZYK
Subject: Support Oximeter Data 01/08/07

Hi,

Please find attached the center specific Support study oximeter report through December 2006. This oximeter data was processed as of 01/08/07 to capture more of the December downloads (the last data processed was mid December 2006). Please note your site specific data will be added to this report when sufficient oximeter downloads have been completed. Please contact Marie Gantz (mgantz@rti.org) for any questions you may have regarding this report.

Thanks,

Kris

Kris Zaterka-Baxter, RN, CCRP
RTI International
4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From: Newman, Jamie
To: Neil Finer; Higgins, Rosemary (NIH/NICHD) [E]; Stevens, Timothy
Cc: Huitema, Carolyn Petrie
Subject: RE: SUPPORT SUBCOMMITTEE MEETING
Date: Tuesday, January 09, 2007 1:04:59 PM

Thanks for the last minute shuffle. Jenny Auman, the programmer for the Breathing Outcomes reports, will also be available from 2-2:30. I have not received any comments or questions from coordinators in recent months concerning the reports or the study procedures.

Thanks, Jamie

Jamie E. Newman, MPH
Statistics and Epidemiology
RTI International
Telephone: (919) 485-5719
Fax: (919) 485-7762
newman@rti.org

-----Original Message-----
From: Neil Finer [mailto:nfiner@ucsd.edu]
Sent: Tuesday, January 09, 2007 12:12 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; Newman, Jamie; Stevens, Timothy
Cc: Huitema, Carolyn Petrie
Subject: RE: SUPPORT SUBCOMMITTEE MEETING

This is fine with me.
Neil

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, January 09, 2007 6:20 AM
To: Newman, Jamie; Stevens, Timothy
Cc: Huitema, Carolyn Petrie; Neil Finer
Subject: RE: SUPPORT SUBCOMMITTEE MEETING

Yes, we can as long as it is ok with Neil

Neil- is this ok?
Rose

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]; Newman, Jamie; Stevens, Timothy
Cc: Huitema, Carolyn Petrie
Subject: RE: SUPPORT SUBCOMMITTEE MEETING
Date: Tuesday, January 09, 2007 12:10:58 PM

This is fine with me.
Neil

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, January 09, 2007 6:20 AM
To: Newman, Jamie; Stevens, Timothy
Cc: Huitema, Carolyn Petrie; Neil Finer
Subject: RE: SUPPORT SUBCOMMITTEE MEETING

Yes, we can as long as it is ok with Neil

Neil- is this ok?
Rose

-----Original Message-----
From: Newman, Jamie [mailto:newman@rti.org]
Sent: Tuesday, January 09, 2007 9:15 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; Stevens, Timothy
Cc: Huitema, Carolyn Petrie; Neil Finer
Subject: RE: SUPPORT SUBCOMMITTEE MEETING

I have a required doctoral seminar that starts at 2:30 so I am available until then. There are only 7 students in my cohort so it would be disruptive if I arrived late. Would it be possible to start the hour with Breathing Outcomes update?
Thanks, Jamie

Jamie E. Newman, MPH

Statistics and Epidemiology

RTI International

Telephone: (919) 485-5719

Fax: (919) 485-7762

newman@rti.org

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tue 1/9/2007 8:44 AM
To: Stevens, Timothy
Cc: Newman, Jamie; Huitema, Carolyn Petrie; Neil Finer
Subject: RE: SUPPORT SUBCOMMITTEE MEETING

Tim

We would want you to give a brief update. I am copying Jamie to see if she can also join.

Thanks

Rose

From: Stevens, Timothy [mailto:Timothy_Stevens@URMC.Rochester.edu]
Sent: Monday, January 08, 2007 9:19 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT SUBCOMMITTEE MEETING

Hi Rose,

I'm free at that time. What is my role during the subcommittee meeting and call-in? Can the call-in be a conference call so that the Breathing Outcomes coordinator can listen in?

Thanks

Tim

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, January 08, 2007 2:15 PM
To: Stevens, Timothy
Cc: Huitema, Carolyn Petrie
Subject: SUPPORT SUBCOMMITTEE MEETING

Tim

Are you joining the SUPPORT SUBCOMMITTEE on Jan. 11 at 2 PM? Let us know as we are arranging call-in lines.

Thanks
Rose

Rosemary D. Higgins, M.D.

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

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301-496-3790 (FAX)

higginsr@mail.nih.gov

From: Auman, Jeanette O.
To: Angelita Hensman; Pickett, James
Cc: Das, Abhik; Higgins, Rosemary (NIH/NICHD) [E]; Abbot Laptook
Subject: RE: SUPPORT study revised forms/data entry
Date: Monday, January 08, 2007 2:01:48 PM

Hi Angelita,

If you have Claudia transmit now, she'll be able to pick up the corrected version of Support for you to key the older versions of the other forms.

Thanks,
Jenny

From: Angelita Hensman [mailto:AHensman@WIHRI.org]
Sent: Monday, January 08, 2007 11:53 AM
To: Pickett, James; Auman, Jeanette O.
Cc: Das, Abhik; Higgins, Rosemary (NIH/NICHD) [E]; Abbot Laptook
Subject: RE: SUPPORT study revised forms/data entry

Jenny and James,

We were only able to enter the old version of the SUPP04, and SUPP05 forms. All the other forms say enter the new form. I thought the system was set up to allow us to enter the old forms for babies born before 12/29/06? We need to have this taken care of ASAP so that we have enough time to enter forms from 11/01 to 12/29/06 before transmission tomorrow.

Thanks
Angelita

From: Pickett, James [mailto:japickett@rti.org]
Sent: Tuesday, January 02, 2007 3:44 PM
To: Auman, Jeanette O.; Angelita Hensman
Subject: RE: SUPPORT study revised forms.

Hi Angelita,
I've setup the system so your infants start on the new forms as of 12/29. Have Claudia do a transmission to get the update. Let me know if you have any trouble with it.

J

James Pickett - Programmer / Analyst
(919) 541-1253 * 4E13A 800 Park * japickett@rti.org
RTI International * 3040 Cornwallis Road * P.O. Box 12194 * Research Triangle Park, NC 27709-2194

From: Auman, Jeanette O.
Sent: Tuesday, January 02, 2007 2:51 PM
To: 'Angelita Hensman'
Cc: Pickett, James
Subject: RE: SUPPORT study revised forms.

Angelita,

James is going to give Claudia a call in about 15-20 minutes, I'm tied up fixing another site's data.

From: Angelita Hensman [mailto:AHensman@WIHRI.org]
Sent: Tuesday, January 02, 2007 2:13 PM
To: Auman, Jeanette O.
Subject: RE: SUPPORT study revised forms.

Hi Jenny,
Claudia has called you a couple of times but your line is busy. Can you give here a call when you are free? We would like to enter the outstanding forms before we transmit today.
Thanks
Angelita

From: Auman, Jeanette O. [mailto:joa@rti.org]
Sent: Tuesday, January 02, 2007 1:21 PM
To: Angelita Hensman
Cc: Das, Abhik; Abbot Laptook; Pickett, James; Neil Finer; Higgins, Rosemary (NIH/NICHD) [E]; Zaterka-Baxter, Kristin
Subject: RE: SUPPORT study revised forms.

Hi Angelita,

Sure, I can just change the version shift in your version of Support data entry and the forms will come up as the old version for those patients born prior to 12/29/2006. Have Claudia give me a call and I'll take care of it.

Please key the relevant forms for the patients born between 11/1/2006 and 12/29/2006 as soon as possible. If the Support data entry system is updated (nothing is currently scheduled) then the special version date for your center will get overwritten with the date all the other centers have, 11/1/2006 and you will no longer be able to key new forms of the old version, pre-existing forms will be displayed in the version they were keyed, unless I change the version date again.

Thanks,
Jenny

From: Angelita Hensman [mailto:AHensman@WIHRI.org]
Sent: Tuesday, January 02, 2007 11:56 AM
To: Auman, Jeanette O.
Cc: Das, Abhik; Abbot Laptook; Pickett, James; Neil Finer; Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT study revised forms.

Hi Jenny,
We received the IRB approval letter to use the Nov 1st revision of the SUPPORT forms on 12/29/06. We had asked the IRB if we could use them on babies born after November 1st but they only approved this for the new SUPP05B form and not the others. They will not approve a retroactive date. This means that we can use the new forms for any patient born after 12/29/06. We have several forms we have been unable to enter (older version) . I believe you were going to discuss this with Abhik and get back to us. Please let me know when and how we should enter them.
Thanks
Angleita

From: Susan Hintz
To: BMackinnon@tufts-nemc.org
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: FW: SUPPORT MRI SECONDARY
Date: Wednesday, January 03, 2007 11:55:05 AM

Thanks so much Brenda. Congratulations on a great job so far!

Susan

Susan R. Hintz, M.D., M.S.
Assistant Professor of Pediatrics
Division of Neonatal and Developmental Medicine
Stanford University School of Medicine
750 Welch Road, Suite 315
Palo Alto, CA 94304
ph: 650-723-5711
fax: 650-725-8351

From: Mackinnon, Brenda [mailto:BMackinnon@tufts-nemc.org]
Sent: Wednesday, December 27, 2006 9:01 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; Frantz, Ivan
Subject: RE: SUPPORT MRI SECONDARY

Hi Dr. Higgins,

I have attached the neuroimaging data for Tufts.

Thanks,

Brenda

Content-Type: application/msword;
name="HUS report.doc"
Content-Description: HUS report.doc
Content-Disposition: attachment;

filename="HUS report.doc"

Attachment converted: Macintosh HD:HUS report.doc (WDBN/«IC») (000CE729)

--

From:	Zaterka-Baxter, Kristin
To:	mcw3@cwru.edu; Nancy Newman
Cc:	Das, Abhik; Wade Rich; Pickett, James; Higgins, Rosemary (NIH/NICHD) [E]
Subject:	Support Monitoring Visit (Case Western)
Date:	Tuesday, January 02, 2007 4:02:38 PM

Hi Dr. Walsh and Nancy,

RTI recently began site monitoring visits for the Support Trial as directed by the DSMC. As one of the highest enrolling centers, we would like to visit your site next. We would like to schedule a two day visit sometime between February 12th and the 23rd if possible. This is a preliminary request for availability; once the visit has been scheduled, we will send out a randomly generated list of approximately 10% of infants enrolled for case review. Please let me know what dates would be most convenient.

Thanks and please let me know if you have any questions.
Kris

Kris Zaterka-Baxter, RN, CCRP
RTI International
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Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From:	Zaterka-Baxter, Kristin
To:	Das, Abhik
Cc:	Higgins, Rosemary (NIH/NICHD) [E]; Schaefer, Scott E.
Subject:	FW: Support Study ROP Exam Tracking
Date:	Wednesday, May 17, 2006 4:53:16 PM
Attachments:	Template ROP_EXAM_TRACKING_22.doc

Hi,
Attached is a template of what Scott sent to all the sites requesting the missing ROP final exam data. He wanted me to forward this on just in case it is discussed during the coordinators conference all tomorrow.
Thanks,
Kris

From: Schaefer, Scott E.
Sent: Thursday, May 11, 2006 5:23 PM
To:
Cc: Zaterka-Baxter, Kristin
Subject: Support Study ROP Exam Tracking

Attached you will find a Word Doc that explains the new tracking of ROP exams that I have just implemented. ROP status is a primary outcome of the Support Study so entering the eye exams until final status is reached in both eyes is very important.

Included in the document is the list of cases that you have reached final eye exam status for and those that are still pending.

Scott *8-)

P.S. I will be out of the office tomorrow (Friday May 12th)

NICHD
NEONATAL RESEARCH NETWORK
SUPPORT TRIAL ROP EXAM TRACKING

From: Scott E. Schaefer
Date: 05/10/2006
Subj.: New tracking of ROP exams for final status reached in both eyes.

INTRODUCTION:

As all of you are aware, one of the Support Trial's primary outcomes is ROP status of the infant's eyes. The SUPP10 form is provided to allow you to record the results of each eye exam until a favorable or unfavorable outcome is reached for both eyes. This new tracking system has been created to alert you of the subject's that have not reached final status and still require additional eye exams to be recorded.

At the end of this message, you will find a list of all subjects that are requiring additional SUPP10 forms. These are listed by Network Number. After this preliminary listing, these messages will be included in the *Missing Forms Report* that Jenny Auman generates.

METHODS USED:

The tracking is for all subjects that were randomized into the Support Trial. Subjects that are known to have died early are automatically excused from the tracking, though you are allowed to enter SUPP10 forms for them if they were in fact examined. ROP exams are normally expected at 31 weeks PMA or after 4 weeks of life. Any subject that died up to 4 weeks after this time point has been reached is automatically excused.

Question C1 on the SUPP09 form states, "Was an exam performed for ROP?" If this is 'N' (No), the infant is also excused from ROP tracking.

For infants with SUPP10 forms, each eye is tracked across forms until final status is reached for both eyes. The rules for the favorable and unfavorable outcomes are listed in the MOP Section 15.2. If the Threshold (New Type 1) question is 'Y' (Yes), the outcome is unfavorable. How I have interpreted the other outcomes as they relate to the SUPP10 form's codes is listed below (**codes not listed do not contribute to final status**):

Zone Codes:

Code Value	Code Description	Outcome Status
3	Zone III	Favorable if two exams in a row.
4	Mature	Favorable
5	Status Post laser/cryo	Unfavorable

Stage Codes:

Code Value	Code Description	Outcome Status
4	Stage 4a or 4b	Unfavorable
5	Stage 5	Unfavorable
6	Post laser/cryo	Unfavorable

Surgery Codes:

Code Value	Code Description	Outcome Status
1	Laser	Unfavorable
2	Cryotherapy	Unfavorable
3	Both laser/cryo	Unfavorable
4	Scleral Buckle	Unfavorable
5	Vitrectomy	Unfavorable
6	Other	Unfavorable

Retinal Detachment Codes:

Code Value	Code Description	Outcome Status
3	Partial, not involving macula (stage 4a)	Unfavorable
4	Partial, does involve macula (stage 4b)	Unfavorable
5	Complete	Unfavorable

MESSAGE TYPES:

A grace period of 50 weeks PMA is used before the listing of the non-final subjects. This hopefully will allow most subjects to first reach final status. These messages will be reported in the *Missing Forms Report* generated by Jenny Auman.

Error Message	Occurrence
No SUPP10 forms have been entered though 50 weeks PMA has been reached and the infant did not die early.	No SUPP09 or SUPP10 forms have been keyed.
No SUPP10 records have been entered even though SUPP09 Question C1 indicates that an exam for ROP was performed.	SUPP09 Question C1 (Was an exam performed for ROP?) is 'Y' (Yes), but no SUPP10 forms exist.
SUPP10 records have been entered even though SUPP09 Question C1 indicates that no exam for ROP was performed.	SUPP10 forms exist, but SUPP09 Question C1 incorrectly indicates otherwise.
50 weeks PMA has been reached and final ROP exam status has not been reported on the SUPP10 for either eye.	SUPP10 forms exist but final status has not been reached.
50 weeks PMA has been reached and final	Same as previous.

Error Message	Occurrence
ROP exam status has not been reported on the SUPP10 for the left eye.	
50 weeks PMA has been reached and final ROP exam status has not been reported on the SUPP10 for the right eye.	Same as previous.

EXCUSING SUBJECTS:

Understanding that some of the subjects will die before final status is reached, or the parents may refuse any more contact, a mechanism is built into the ROP tracking program to allow non-final subjects to be excused from the reporting. Since the ROP status is so important to the Support Study, excused cases will be entered here at RTI once they have been approved. Please inform Scott Schaefer of any cases that need to be excused and why.

All efforts should be taken to record every eye exam possible for non-final subjects, even for the excused cases.

LIST OF YOUR CENTER'S PENDING CASES:

LIST OF YOUR CENTER'S COMPLETED CASES:

From: Neil Finer
To: Lisa Askie
Cc: wcarlo@peds.uab.edu; Higgins, Rosemary (NIH/NICHD) [E]
Date: Thursday, April 20, 2006 6:03:49 PM

Hi Lisa
Please add Wally Carlo as the Co-PI for SUPPORT and Rose Higgins as the Neonatal Network Representative for SUPPORT.
Thanks for the call
Neil

From: Ellen Hale
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Susie Buchter; Anthony Piazza; Barbara Stoll
Subject: SUPPORT
Date: Monday, March 13, 2006 4:04:06 PM

Dear Rose,

We began screening for SUPPORT at both our sites this morning. We have two moms we have approached (one at each site) for consent and both are considering whether or not to consent. We will let you know when we enroll our first patient.

Ellen

From:	Wade Rich
To:	Higgins, Rosemary (NIH/NICHD) [E]
Cc:	nfiner@ucsd.edu; "Petrie, Carolyn"
Subject:	FW: SUPPORT training in April
Date:	Monday, March 13, 2006 11:09:34 AM

Rose,

We will be losing at least 1 "storage site" for oximeters. Will one of the new centers be involved, and if so should we make this a brief agenda item?

wade

From: Petrie, Carolyn [mailto:petrie@rti.org]
Sent: Monday, March 13, 2006 7:37 AM
To: higginsr@mail.nih.gov; nfiner@ucsd.edu; edward.donovan@chmcc.org; wcarlo@peds.uab.edu
Cc: Zaterka-Baxter, Kristin; wrich@ucsd.edu; nxs5@cwru.edu; Petrie, Carolyn; Hastings, Betty J.
Subject: SUPPORT training in April

Hi Everyone-

At the next Steering committee meeting, we have a 1-hr session of SUPPORT training for the entire group. Immediately afterwards, there is a 2 hour session of continued training. Please send us your comments and suggestions.

1-Hr Session
Normal SUPPORT Subcommittee meeting (Dr. Finer)
DSMC Meeting
IRB/Screening/Enrollment
OWL

2Hr Session
Oximeters/Oximeter Transport
Randomizations
Forms and Manual
Physiologic Definition (Ms. Newman)

Carolyn Petrie Huitema
Neonatal Research Network Coordinator
RTI International
6110 Executive Blvd
Suite 902
Rockville, MD 20852
ph. (301) 230-4648
fx. (301) 230-4646

From: Susan Hintz
To: kristin zaterka
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: update re: SUPPORT secondary
Date: Friday, March 10, 2006 5:55:32 PM
Attachments: SiteMRISecondaryquestionsJan06.xls

Hi Kristin,

Rose Higgins told me that she thought there were several more sites with IRB approval for the SUPPORT secondary. The last update I have from you is from January when we were querying sites prior to the Network Steering committe meeting - at that time, only 4 sites had DEFINITE approval. Could you send me an updated spreadsheet? I would like to send out a few emails to the sites to either re-query about IRB approval, or to remind them about the procedures involving getting and sending in the MRIs and US if they already have approval.

Thanks so much! Attached is the January version of the spreadsheet.

Susan
--
Susan R. Hintz, M.D.
Assistant Professor of Pediatrics
Division of Neonatal and Developmental Medicine
Stanford University School of Medicine
750 Welch Road, Suite 315
Palo Alto, CA 94304
ph: 650-723-5711
fax: 650-725-8351

SITES	1. Has your site received IRB approval for the SUPPORT Neuroimaging secondary? **YES/NO**	2. Will your site be using a separate consent for the Neuroimaging secondary, or will the consent be embedded in the overall study consent? **Separate/Embedded**	3.If your site has not received IRB approval, has your site applied for IRB approval for the SUPPORT Neuroimaging secondary?	If not, does your site intend to participate in the	Approval
Alabama	Yes	unanswered	N/A	N/A	**Approved**
Case	No	Embedded	Has submitted but is on Hold d/t the Hold on SUPPORT	Yes	Pending
Dallas					
Wayne					
Miami	No	unanswered	Will do so once agreement has been reached for federal rates for MRIs	Yes	Pending
Emory					
CinA					
CinB					
CinC					
Indiana					
Yale					
Brown					
Stanford	Yes	Embedded	N/A	N/A	**Approved 09/27/05**
Houston					
Duke					
WF (1) Bowman Gray					
WF (2) Forsyth					
Roch	Yes	Embedded	N/A	N/A	**Approved 12/2005**
UCSD#1	Yes	Separate	N/A	N/A	**Approved 08/18/05**
UCSD#2					

From:	Petrie, Carolyn
To:	poo@rti.org; barbara_stoll@oz.ped.emory.edu; Charles.Rosenfeld@UTSouthwestern.edu; dale_phelps@urmc.rochester.edu; Das, Abhik; dstevenson@stanford.edu; edward.donovan@chmcc.org; goldb008@mc.duke.edu; Higgins, Rosemary (NIH/NICHD) [E]; jlemons@iupui.edu; jon.e.tyson@uth.tmc.edu; alaptook@WIHRI.org; mcw3@cwru.edu; moshea@wfubmc.edu; nfiner@ucsd.edu; richard.ehrenkranz@yale.edu; sduara@miami.edu; sshankar@med.wayne.edu; wcarlo@peds.uab.edu; WOh@wihri.org; Nancy.Miller@UTSouthwestern.edu; ae5357@wayne.edu; ahensman@wihri.org; auten002@mc.duke.edu; ellen_hale@oz.ped.emory.edu; Georgia.E.McDavid@uth.tmc.edu; grisbyca@email.uc.edu; linda_reubens@urmc.rochester.edu; lucmille@iupui.edu; mbball@leland.stanford.edu; mcollins@peds.uab.edu; Monica.konstantino@yale.edu; nxs5@cwru.edu; npeters@wfubmc.edu; reverett@med.miami.edu; wrich@ucsd.edu; Janet.Morgan@childrens.com; SEguaras@med.miami.edu; bjacksn@wfubmc.edu; bss5@cwru.edu; diane_hust@urmc.rochester.edu; dkennedy@dmc.org; joanne williams; ldrichar@iupui.edu; lnoel@wihri.org; lohme001@mc.duke.edu; mgfuller@ucsd.edu; elaine.romano@yale.edu; Teresa.Gratton@uc.edu; "Vivien Phillips " (E-mail); Roy.Heyne@utsouthwestern.edu; ira_adams-chapman@oz.ped.emory.edu; adusick@iupui.edu; apappas@med.wayne.edu; Brenda.H.Morris@uth.tmc.edu; bvohr@wihri.org; cbauer@peds.med.miami.edu; gary_myers@urmc.rochester.edu; golds005@mc.duke.edu; drfjcmd@aol.com; MPeralta@PEDS.UAB.EDU; rdillard@wfubmc.edu; srhintz@stanford.edu; steichji@email.uc.edu; yvaucher@ucsd.edu
Cc:	Price, Jeffrey M.; Auman, Jeanette O.; Newman, Jamie; Zaterka-Baxter, Kristin; Petrie, Carolyn; Hastings, Betty J.
Subject:	Tech memo for SUPPORT FU babies >1,000g
Date:	Wednesday, March 08, 2006 1:06:28 PM
Attachments:	SUPPORT FU tech memo1.doc

Dear All-

Please find the technical memo attached to this email, pertaining to the 18-22 month Follow Up visit for infants enrolled in SUPPORT and greater than 1000g.

Follow-up at 18 months should be completed for all patients enrolled in the SUPPORT Trial. The SUPPORT Trial Follow-up will be as follows:

1. All Network patients, eligible for the 18+4 month follow-up should have the GDB ELBW Follow-up forms completed (NF01, NF02, etc.). These forms are entered into the regular GDB Follow-up program.
2. All SUPPORT Trial study patients NOT eligible for the ELBW Network Follow-up Study, such as patients >1000 g, should complete the SUPPORT Follow-up Study forms (e.g., SF01, SF02, etc.). These forms will be entered into the SUPPORT Trial database.

Because the content of the follow-up is the same, the ELBW Follow-up study manual will be used for the additional SUPPORT Trial study patients, using the following substitutions: NF01 = SF01, NF02 = SF02, NF03 = SF03, Etc.

The NF13 (BITSEA) will not be done for SUPPORT Trial patients unless they are in the ELBW Follow-up Study. The SUPPORT patients not eligible for the ELBW Follow-up Study will use their Network number as the identifier. For patients that transfer to another center, the forms will need to be sent to the original center for keying.

The following forms will need to be completed for the SUPPORT Trial patients NOT eligible for ELBW Follow-up Study:

SF01 SES at Discharge
SF03 SES at 18 + 4 Months
SF04 Medical History Form
SF04A Readmission Form
SF05 Infant Examination Form

SF05A Gross Motor Function Work Sheet (will not be keyed)
SF09 Bayley Scales Summary Score Sheet
SF10 Status Form
SF10A Status Form
SF11 Summary of 18 Month Visit
SF12 Lost to Follow-up Questionnaire

These forms will be posted to the private gateway of the NRN website under: Protocols/SUPPORT/Secondary Studies/18 month Follow Up.

Please contact Jamie Newman at newman@rti.org or Carolyn Petrie Huitema at petrie@rti.org if you have any questions.

RTI INTERNATIONAL | Memorandum

SUPPORT FOLLOW-UP TECHNICAL MEMO # 1

DATE: March 8, 2006

TO: Network Follow-up PIs and Coordinators
SUPPORT Trial PIs and Coordinators

FROM: The Data Coordinating Center

SUBJECT: SUPPORT 18 month Follow-up

Follow-up at 18 months should be completed for all patients enrolled in the SUPPORT Trial. The SUPPORT Trial Follow-up will be as follows:

1. All Network patients, eligible for the 18+4 month follow-up should have the GDB ELBW Follow-up forms completed (NF01, NF02, etc.). These forms are entered into the regular GDB Follow-up program.
2. All SUPPORT Trial study patients NOT eligible for the ELBW Network Follow-up Study, such as patients >1000 g, should complete the SUPPORT Follow-up Study forms (e.g., SF01, SF02, etc.). These forms will be entered into the SUPPORT Trial database.

Because the content of the follow-up is the same, the ELBW Follow-up study manual will be used for the additional SUPPORT Trial study patients, using the following substitutions: NF01 = SF01, NF02 = SF02, NF03 = SF03, Etc.

The NF13 (BITSEA) will not be done for SUPPORT Trial patients unless they are in the ELBW Follow-up Study. The SUPPORT patients not eligible for the ELBW Follow-up Study will use their Network number as the identifier. For patients that transfer to another center, the forms will need to be sent to the original center for keying.

The following forms will need to be completed for the SUPPORT Trial patients NOT eligible for ELBW Follow-up Study:

SF01 SES at Discharge
SF03 SES at 18 + 4 Months
SF04 Medical History Form
SF04A Readmission Form
SF05 Infant Examination Form
SF05A Gross Motor Function Work Sheet (will not be keyed)
SF09 Bayley Scales Summary Score Sheet
SF10 Status Form
SF10A Status Form
SF11 Summary of 18 Month Visit
SF12 Lost to Follow-up Questionnaire

These forms will be posted to the private gateway of the NRN website under: Protocols/SUPPORT/Secondary Studies/18 month Follow Up.

Please contact Jamie Newman at newman@rti.org or Carolyn Petrie Huitema at petrie@rti.org if you have any questions.

Cc: Rosemary Higgins

From: Michael O`Shea
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Nancy Peters
Subject: RE: SUPPORT Masimo pulse oximeters
Date: Wednesday, March 08, 2006 12:17:02 PM

That's an excellent plan. We will probably have some that are not in use as of 3/31 and perhaps a few that come off of patients after that time. Where shall we mail them?
Thanks,
Mike

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, March 08, 2006 11:58 AM
To: Michael O`Shea
Cc: Nancy Peters
Subject: RE: SUPPORT Masimo pulse oximeters

Hi Mike,
At the end of the study, Masimo had agreed to "Unjigger" them for the sites for routine clinical/lab use. It would be great if you could make these available to sites with the agreement that you get them back when recruitment has ceased. Would that be OK?
thanks
Rose

From: Michael O`Shea [mailto:moshea@wfubmc.edu]
Sent: Tuesday, March 07, 2006 1:46 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Nancy Peters
Subject: SUPPORT Masimo pulse oximeters

Rose,
What should we do with the Masimo pulse oximeters which were purchased with the NICHD grant after we finish enrolling in SUPPORT?
Thank you,
Mike

From: Hastings, Betty J.
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT
Date: Tuesday, March 07, 2006 3:33:06 PM

Okay. I just sent the revised chapters but I will incorporate them into the MOP. We are also still working on a couple of the Appendices. We should have this ready by Thursday or Friday. I just wanted to get this out to the sites for their IRBs.

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, March 07, 2006 3:30 PM
To: Hastings, Betty J.; Zaterka-Baxter, Kristin
Subject: Re: SUPPORT

If these are final, we can send them to the 4 new sites. Let carolyn know when it goes to them. She has the support training videos and will ship them.
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Hastings, Betty J. <bkh@rti.org>
To: ahensman@wihri.org <ahensman@wihri.org>; mbball@leland.stanford.edu <mbball@leland.stanford.edu>; grisbyca@email.uc.edu <grisbyca@email.uc.edu>; ellen_hale@oz.ped.emory.edu <ellen_hale@oz.ped.emory.edu>; gaynelle.hensley@utsouthwestern.edu <gaynelle.hensley@utsouthwestern.edu>; Georgia E McDavid <Georgia.E.McDavid@uth.tmc.edu>; auten002@mc.duke.edu <auten002@mc.duke.edu>; linda_reubens@urmc.rochester.edu <linda_reubens@urmc.rochester.edu>; lucmille@iupui.edu <lucmille@iupui.edu>; mcollins@peds.uab.edu <mcollins@peds.uab.edu>; monica.konstantino@yale.edu <monica.konstantino@yale.edu>; Nancy.Miller@UTSouthwestern.edu <Nancy.Miller@UTSouthwestern.edu>; Nancy Newman <nxs5@cwru.edu>; npeters@wfubmc.edu <npeters@wfubmc.edu>; ae5357@wayne.edu <ae5357@wayne.edu>; rbridge@ucsd.edu <rbridge@ucsd.edu>; risa.demetrio@sharp.com <risa.demetrio@sharp.com>; kathy.arnell@sharp.com <kathy.arnell@sharp.com>; Reverett@med.miami.edu <Reverett@med.miami.edu>; wrich@ucsd.edu <wrich@ucsd.edu>; brenda.H.Morris@Uth.tmc.edu <brenda.H.Morris@Uth.tmc.edu>; cotte010@mc.duke.edu <cotte010@mc.duke.edu>; crosen@mednet.swmed.edu <crosen@mednet.swmed.edu>; vanmeurs@leland.stanford.edu <vanmeurs@leland.stanford.edu>; kurt.schibler@cchmc.org <kurt.schibler@cchmc.org>; alaptook@wihri.org <alaptook@wihri.org>; bpoindex@iupui.edu <bpoindex@iupui.edu>; edward.donovan@chmcc.org <edward.donovan@chmcc.org>; jlemons@iupui.edu <jlemons@iupui.edu>; moshea@wfubmc.edu <moshea@wfubmc.edu>; sshankar@med.wayne.edu <sshankar@med.wayne.edu>; sduara@miami.edu <sduara@miami.edu>; susie.buchter@oz.ped.emory.edu <susie.buchter@oz.ped.emory.edu>; wcarlo@peds.uab.edu <wcarlo@peds.uab.edu>; Maynard.Rasmussen@sharp.com <Maynard.Rasmussen@sharp.com>; mcw3@cwru.edu <mcw3@cwru.edu>;

Nirupama_Laroia@URMC.Rochester.edu <Nirupama_Laroia@URMC.Rochester.edu>;
Vineet.bhandari@yale.edu <Vineet.bhandari@yale.edu>;
vivek.Narendran@cchmc.org <vivek.Narendran@cchmc.org>;
Walid.Salhab@UTSouthwestern.edu <Walid.Salhab@UTSouthwestern.edu>;
dale_phelps@urmc.rochester.edu <dale_phelps@urmc.rochester.edu>;
richard.ehrenkranz@yale.edu <richard.ehrenkranz@yale.edu>;
Barbara.Alexander@cchmc.org <Barbara.Alexander@cchmc.org>; Estelle E.
Fischer <estelle.fischer@cchmc.org>; Holly Mincey
<minceyhl@email.uc.edu>; Jody Shively <jody.shively@cchmc.org>; Kate
Bridges, MD <Kathleen.Bridges@cchmc.org>; Lenora Jackson
<Lenora.Jackson@uc.edu>
CC: Higgins, Rosemary (NIH/NICHD) [E] <higginsr@mail.nih.gov>; Das,
Abhik <adas@rti.org>; Auman, Jeanette O. <joa@rti.org>; Poole, W.
Kenneth <poo@rti.org>; Zaterka-Baxter, Kristin <kzaterka@rti.org>;
nfiner@ucsd.edu <nfiner@ucsd.edu>
Sent: Tue Mar 07 15:21:43 2006
Subject: SUPPORT

Attached please find the following:

* Technical Memo SUP06
* Revised Chapter 10 and 16 of the Manual of Operations
* Revised SUPP05, SUPP05A and SUPP11.

Please let us know if you have questions about this material.
Thanks.
Betty <<SUP06.doc>> <<Chapter 16[Rev3-7-06].doc>> <<Chapter 10[Rev
3-7-06].doc>> <<SUPP11[Rev 3-7-06] .doc>>
<<SUPP05ASafetyMonitor[Rev3-7-06.doc>>
<<SUPP05SafetyMonitor[Rev3-7-06].doc>>

Betty Hastings

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Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7740
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bkh@rti.org <mailto:bkh@rti.org>

From:	Hastings, Betty J.
To:	ahensman@wihri.org; mbball@leland.stanford.edu; grisbyca@email.uc.edu; ellen_hale@oz.ped.emory.edu; gaynelle.hensley@utsouthwestern.edu; Georgia E McDavid; auten002@mc.duke.edu; linda_reubens@urmc.rochester.edu; mcollins@peds.uab.edu; monica.konstantino@yale.edu; Nancy.Miller@UTSouthwestern.edu; Nancy Newman; npeters@wfubmc.edu; ae5357@wayne.edu; risa.demetrio@sharp.com; jyhall@stanford.edu; kathy.arnell@sharp.com; Reverett@med.miami.edu; wrich@ucsd.edu; Barbara.Alexander@cchmc.org; Estelle E. Fischer; Holly Mincey; Jody Shively; Kate Bridges, MD; Lenora Jackson
Cc:	Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik; Zaterka-Baxter, Kristin
Subject:	SUPPORT
Date:	Thursday, March 02, 2006 2:12:23 PM

Just a reminder that we need your input regarding the revisions to the SUPPORT forms by tomorrow.
Thanks.
Betty

Betty Hastings

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P.O. Box 12194
Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7740
Fax: (919) 485-7762
bkh@rti.org

From: Zaterka-Baxter, Kristin
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Growth Secondary to Support
Date: Wednesday, March 01, 2006 4:29:23 PM

Hi Rose,
Are we gong to implement Growth Secondary to Support? Indiana and Houston have asked several times and I don't have an answer for them.
Thanks,
Kris

From:	Neil Finer
To:	Higgins, Rosemary (NIH/NICHD) [E]
Cc:	wrich@ucsd.edu; fmartinez@ucsd.edu
Subject:	RE: SUPPORT SUBCOMMITTEE and training
Date:	Thursday, February 23, 2006 8:58:49 PM

Hi Rose

Wade and I will take the early morning flight on the 6th. Even 4:00OM is too late to ensure that you will make the flight out of Dulles.
Thanks
Neil

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, February 23, 2006 11:40 AM
To: Neil
Cc: wrich@ucsd.edu; Petrie, Carolyn
Subject: SUPPORT SUBCOMMITTEE and training

Neil
We have scheduled the SUPPORT subcommittee and training meetings for April 4 from 1:30-4:30. The steering committee schedule has been shifted somewhat from the usual schedule as a one-time orientation meeting. Let me know if this time works for you and Wade. We have no SUPPORT activities scheduled for April 5 because we are requiring everyone to attend the first hour of the SUPPORT meeting.
FYI – I also check the flights into and out of Dulles to San Diego – the direct evening flight on United is now 6:20 PM – if you want to try to make that flight to get home, let Carolyn and I know and we could possibly shift things so that you would be done by 4 PM.

Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
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NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Wally Carlo, M.D.
To:	Higgins, Rosemary (NIH/NICHD) [E]; Monica Collins
Cc:	Hastings, Betty J.
Subject:	RE: oximeters
Date:	Thursday, February 23, 2006 5:08:21 PM

Rose: We have not received them. Monica is aware and is working with Vicky at Masimo. wally

---

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, February 23, 2006 2:32 PM
To: Wally Carlo, M.D.; Monica Collins
Cc: Hastings, Betty J.
Subject: oximeters

Hi
Did you receive your additional oximeters for SUPPORT? If so, Betty needs the serial numbers. If not, is there a problem with the ordering?
Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
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MSC 7510
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(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Neil Finer
To:	"Zaterka-Baxter, Kristin"; Higgins, Rosemary (NIH/NICHD) [E]
Cc:	"Hastings, Betty J."
Subject:	RE: Support re-activation
Date:	Tuesday, February 21, 2006 11:27:03 AM

Thanks Kristin
Neil

From: Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]
Sent: Tuesday, February 21, 2006 6:51 AM
To: nfiner@ucsd.edu; Higgins, Rosemary (NIH/NICHD) [E]
Cc: Hastings, Betty J.
Subject: Support re-activation

Hi,
Please see the attached spreadsheet for site re-activation status. Miami has not responded to date.
Thanks, and please note all the site comments for details.
Kris

Kris Zaterka-Baxter, RN, BSN, CCRP
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Durham, NC 27703
Telephone: (919) 485-7750
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kzaterka@rti.org

From:	Zaterka-Baxter, Kristin
To:	nfiner@ucsd.edu; Higgins, Rosemary (NIH/NICHD) [E]
Cc:	Hastings, Betty J.
Subject:	Support re-activation
Date:	Tuesday, February 21, 2006 9:51:46 AM
Attachments:	Support FiO2 Frequency and Reactivations.xls

Hi,
Please see the attached spreadsheet for site re-activation status. Miami has not responded to date.
Thanks, and please note all the site comments for details.
Kris

Kris Zaterka-Baxter, RN, BSN, CCRP
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4426 South Miami Blvd.
Durham, NC 27703
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Fax: (919) 485-7762
kzaterka@rti.org

SITES	FiO2 Frequency	Re-activation		
		Not submitted	Submitted	Approved
Alabama		Not submitted. Waiting for revisions		
Case	Q3hr		Submitted 02.17.06	
Dallas			Requiring Full Board as of 02.16.06	
Wayne				Approved: Actively screening
Miami	Q2hr			
Emory			Submitted	
CinA		About to Submit as of 02.17.06		
CinB				
CinC				
Indiana	Q2hr		Requiring Full Board	
Yale	Qhr (unitl stabel then Q2, Q3,..)		Submitted - IRB review sched 02.22.06	
Brown	Qhr		Submitted but need revised forms and MOP prior to receiving approval	
Stanford	minimum Q2hr (depending on change)			
Houston			Submitted	
Duke	Qhr (if on 02)		Submitted - Pending	
(1) Bowman	Qhr			Approved; however can not start enroll yet - possibly 02.22.06
WF (2) Forsyt			Submitted - Pending	
Roch	Qhr			Approved: Actively screening
UCSD#1	Q2hr (vent); Q4hr (nc)		Submitted - Pending	
UCSD#2				Approved: Actively screening
RTI	N/A			Approved 02.13.06

From:	Zaterka-Baxter, Kristin
To:	ahensman@wihri.org; mbball@leland.stanford.edu; grisbyca@email.uc.edu; ellen_hale@oz.ped.emory.edu; gaynelle.hensley@utsouthwestern.edu; Georgia E McDavid; auten002@mc.duke.edu; linda_reubens@urmc.rochester.edu; lucmille@iupui.edu; mcollins@peds.uab.edu; monica.konstantino@yale.edu; Nancy.Miller@UTSouthwestern.edu; Nancy Newman; npeters@wfubmc.edu; ae5357@wayne.edu; risa.demetrio@sharp.com; jyhall@stanford.edu; kathy.arnell@sharp.com; Reverett@med.miami.edu; wrich@ucsd.edu; charles.rosenfeld@utsouthwestern.edu; alaptook@wihri.org; Jobea0@chmcc.org; aaf2@po.cwru.edu; [SCRN] Stoll, Barbara; bpoindex@iupui.edu; dale_phelps@urmc.rochester.edu; dstevenson@stanford.edu; edward.donovan@chmcc.org; jlemons@iupui.edu; jon.e.tyson@uth.tmc.edu; moshea@wfubmc.edu; nfiner@ucsd.edu; richard.ehrenkranz@yale.edu; goldb008@mc.duke.edu; sshankar@med.wayne.edu; sduara@miami.edu; wcarlo@peds.uab.edu; woh@wihri.org; mcw3@cwru.edu; Walid.Salhab@UTSouthwestern.edu; Barbara.Alexander@cchmc.org; Lenora Jackson; Estelle E. Fischer; Holly Mincey; Jody Shively; Kate Bridges, MD
Cc:	Higgins, Rosemary (NIH/NICHD) [E]; Hastings, Betty J.; Phelps, Dale; Newman, Jamie
Subject:	Support Re-activation
Date:	Friday, February 17, 2006 12:47:24 PM

Hi all,
We have a quick follow up questions from the coordinators conference call yesterday regarding site IRB approvals for re-activation of the Support trial.
How many sites have obtained re-activation approval, how many sites have submitted and are waiting for approval and how many have not started the IRB submission process. Please send me a quick email with your sites status.
Very much appreciated as always,
Kris

Kris Zaterka-Baxter, RN, BSN, CCRP
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Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT DSMC Presentation
Date: Thursday, February 16, 2006 3:53:02 PM

I appreciate your sending them the presentation
Neil

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, February 16, 2006 8:37 AM
To: alaptook@WIHRI.org; Abhik Das; Brenda Poindexter; Carlo Waldemar (E-mail); Charles Rosenfeld; Dale Phelps; Ed Donovan; Ehrenkranz Richard (E-mail); Jobe Alan (E-mail); Krisa VanMeurs (VanMeurs, Krisa); Lemons Jim (E-mail); Michael O'Shea; Michelle Walsh; Neil Finer; Oh William (E-mail); Poole Kenneth (E-mail); Ronald GOldberg; Shahnaz Duara; Shankaran Seetha (E-mail); Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); walid.salhab@utsouthwestern.edu
Cc: Petrie, Carolyn; Hastings, Betty J.; Zaterka-Baxter, Kristin
Subject: SUPPORT DSMC Presentation

Hi,
I have enough yes votes to confidentially share our DSMC presentation with Drs. Barbara Schmidt and Dr. William Tarnow-Mordi, both of whom are leading pulse oximetry trials.

Thanks for the responses.

Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Berberich, Mary Anne (NIH/NHLBI) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT DSMC Minutes
Date: Thursday, February 09, 2006 1:52:21 PM

Thanks, Rose. Just returned to office after 3 days out for medical problem.

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wednesday, February 08, 2006 11:27 AM
To: Berberich, Mary Anne (NIH/NHLBI) [E]
Subject: Fw: SUPPORT DSMC Minutes

Here is the SUPPORT documentation.

Thanks
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Hastings, Betty J. <bkh@rti.org>
To: charles.rosenfeld@utsouthwestern.edu <charles.rosenfeld@utsouthwestern.edu>; alaptook@wihri.org <alaptook@wihri.org>; aaf2@po.cwru.edu <aaf2@po.cwru.edu>; [SCRN] Stoll, Barbara <barbara_stoll@oz.ped.emory.edu>; bpoindex@iupui.edu <bpoindex@iupui.edu>; dale_phelps@urmc.rochester.edu <dale_phelps@urmc.rochester.edu>; dstevenson@stanford.edu <dstevenson@stanford.edu>; edward.donovan@chmcc.org <edward.donovan@chmcc.org>; jlemons@iupui.edu <jlemons@iupui.edu>; jon.e.tyson@uth.tmc.edu <jon.e.tyson@uth.tmc.edu>; moshea@wfubmc.edu <moshea@wfubmc.edu>; nfiner@ucsd.edu <nfiner@ucsd.edu>; richard.ehrenkranz@yale.edu <richard.ehrenkranz@yale.edu>; goldb008@mc.duke.edu <goldb008@mc.duke.edu>; sshankar@med.wayne.edu <sshankar@med.wayne.edu>; sduara@miami.edu <sduara@miami.edu>; wcarlo@peds.uab.edu <wcarlo@peds.uab.edu>; woh@wihri.org <woh@wihri.org>; mcw3@cwru.edu <mcw3@cwru.edu>; ahensman@wihri.org <ahensman@wihri.org>; mbball@leland.stanford.edu <mbball@leland.stanford.edu>; grisbyca@email.uc.edu <grisbyca@email.uc.edu>; ellen_hale@oz.ped.emory.edu <ellen_hale@oz.ped.emory.edu>; gaynelle.hensley@utsouthwestern.edu <gaynelle.hensley@utsouthwestern.edu>; Georgia E McDavid <Georgia.E.McDavid@uth.tmc.edu>; auten002@mc.duke.edu <auten002@mc.duke.edu>; linda_reubens@urmc.rochester.edu <linda_reubens@urmc.rochester.edu>; lucmille@iupui.edu <lucmille@iupui.edu>; mcollins@peds.uab.edu <mcollins@peds.uab.edu>; monica.konstantino@yale.edu <monica.konstantino@yale.edu>; Nancy.Miller@UTSouthwestern.edu <Nancy.Miller@UTSouthwestern.edu>; Nancy Newman <nxs5@cwru.edu>; npeters@wfubmc.edu <npeters@wfubmc.edu>; ae5357@wayne.edu <ae5357@wayne.edu>; risa.demetrio@sharp.com <risa.demetrio@sharp.com>; jyhall@stanford.edu <jyhall@stanford.edu>; kathy.arnell@sharp.com <kathy.arnell@sharp.com>; Reverett@med.miami.edu <Reverett@med.miami.edu>; wrich@ucsd.edu <wrich@ucsd.edu>; Barbara.Alexander@cchmc.org <Barbara.Alexander@cchmc.org>; Lenora Jackson <Lenora.Jackson@uc.edu>; Estelle E. Fischer <estelle.fischer@cchmc.org>; Holly Mincey <minceyhl@email.uc.edu>; Jody Shively <jody.shively@cchmc.org>; Kate Bridges, MD <Kathleen.Bridges@cchmc.org>
CC: Higgins, Rosemary (NIH/NICHD) [E] <higginsr@mail.nih.gov>; Das, Abhik <adas@rti.org>; Poole, W. Kenneth <poo@rti.org>; Zaterka-Baxter, Kristin <kzaterka@rti.org>; Petrie, Carolyn <petrie@rti.org>
Sent: Mon Feb 06 12:40:40 2006
Subject: SUPPORT DSMC Minutes

Attached are the following documents:

* Letter from Dr. Duane Alexander concurring with the resumption of the SUPPORT Trial with the proposed modifications as summarized in the minutes
* Letter addressed to your local IRB
* Summary of the Minutes of January 24, 2006 DSMC meeting

Please note that the clarifications for the Manual of Operations and proposed form change will be forthcoming.

Thank you. <<Dr. Alexander.pdf>> <<DSMCMemosites[01-24-06].doc>> <<DSMC Min_SUPPORT[1-24-06].doc>>
Betty

Betty Hastings

RTI International
Statistics and Epidemiology
P.O. Box 12194
Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7740
Fax: (919) 485-7762
bkh@rti.org <mailto:bkh@rti.org>

From:	Hastings, Betty J.
To:	ahensman@wihri.org; mbball@leland.stanford.edu; grisbyca@email.uc.edu; ellen_hale@oz.ped.emory.edu; gaynelle.hensley@utsouthwestern.edu; Georgia E McDavid; auten002@mc.duke.edu; linda_reubens@urmc.rochester.edu; lucmille@iupui.edu; mcollins@peds.uab.edu; monica.konstantino@yale.edu; Nancy.Miller@UTSouthwestern.edu; Nancy Newman; npeters@wfubmc.edu; ae5357@wayne.edu; rbridge@ucsd.edu; risa.demetrio@sharp.com; kathy.arnell@sharp.com; Reverett@med.miami.edu; wrich@ucsd.edu; brenda.H.Morris@Uth.tmc.edu; cotte010@mc.duke.edu; crosen@mednet.swmed.edu; vanmeurs@leland.stanford.edu; kurt.schibler@cchmc.org; edward.donovan@chmcc.org; alaptook@wihri.org; bpoindex@iupui.edu; jlemons@iupui.edu; moshea@wfubmc.edu; nfiner@ucsd.edu; sshankar@med.wayne.edu; sduara@miami.edu; susie.buchter@oz.ped.emory.edu; wcarlo@peds.uab.edu; Maynard.Rasmussen@sharp.com; mcw3@cwru.edu; Nirupama_Laroia@URMC.Rochester.edu; Vineet.bhandari@yale.edu; vivek.Narendran@cchmc.org; Walid.Salhab@UTSouthwestern.edu; [SCRN] Stoll, Barbara; dale_phelps@urmc.rochester.edu; dstevenson@stanford.edu; jon.e.tyson@uth.tmc.edu; richard.ehrenkranz@yale.edu; goldb008@mc.duke.edu; woh@wihri.org; Barbara.Alexander@cchmc.org; Lenora Jackson; Estelle E. Fischer; Holly Mincey; Jody Shively; Kate Bridges, MD
Cc:	Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik; Petrie, Carolyn; Newman, Jamie; Zaterka-Baxter, Kristin
Subject:	SUPPORT Trial
Date:	Thursday, February 09, 2006 1:47:26 PM
Attachments:	SUP05.doc
Importance:	High

Attached is a Technical Memo #5. This memo is intended to help clarify some of the questions that have been raised about restarting the enrollment in the SUPPORT Trial. Namely, the official start date and changes to forms and MOP. The current protocol (dated 3/28/05) has not changed, however there will be some modifications to the MOP and possibly the SUPP05 form. These will be sent out to the sites just as soon as possible.

Thanks.
Betty

<<SUP05.doc>>

Betty Hastings

RTI International
Statistics and Epidemiology
P.O. Box 12194
Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7740
Fax: (919) 485-7762
bkh@rti.org

RTI INTERNATIONAL | Memorandum

February 9, 2006

SUPPORT TECHNICAL MEMO # 5

TO: Network Coordinators
Network PIs

FROM: The Data Coordinating Center

SUBJECT: Reactivating Enrollment into the SUPPORT Trial

The DSMC for the NICHD Neonatal Research Network SUPPORT trial met with the Principle Investigator and Data Coordinating Center staff on January 24th 2006 in Washington D.C. After reviewing the data presented to the DSMC, the consensus was to restart the SUPPORT Trial. The DSMC took Dr. Finer's 8 points of proposed changes as inherent in making its recommendation to continue the trial. The DSMC also emphasized that the current protocol should be resumed and that the DSMC was not changing the protocol. The proposed changes are as follows:

1. Require documentation that the oximeters alarm limits are functional per protocol every 4-6 hours.
2. Change our data collection for FiO2 to ensure that subsequent interval reports more accurately reflect whether the infant was receiving Oxygen or room air.
3. Further training and in-service at all the sites to stress the importance of keeping the SpO2 alarms functional and at the limits of 84% and 96%. We will use a training model based on the OWL (Oxygen with Love Program) developed at Oschner.
4. Develop guidelines for managing desaturations such that the increase in oxygen is proportional to the desaturation.
5. Place bedside cards to indicate the desired target range.
6. Initiate compliance monitoring visits coordinated by RTI to visit random sites.
7. Reanalyze group differences after an additional 100 -150 infants have been enrolled.
8. Utilize only actual SpO2 values for assessment of safety in subsequent analyses i.e.; SpO2 < 84% and > 96%, and analyze only actual time in oxygen.

The official start date for reactivating enrollment in the SUPPORT Trial is February 6, 2006. This is the date that the official notification letter from Dr. Duane Alexander, Director of the NICHD, was sent to the sites.

Please Note: Some of the above steps are in the process of being implemented and any form and Manual of Operations changes will be forthcoming. However, in the interest of time and to keep the momentum for this trial going, please resume enrollment as soon as you have IRB approval. Manual and form changes incorporating the 8 points above will be communicated to you and reflected on the web site and the DMS as soon as possible.

From: Hastings, Betty J.
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT DSMC Minutes
Date: Wednesday, February 08, 2006 8:55:43 AM

Thank you.

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, February 08, 2006 8:55 AM
To: Hastings, Betty J.; Das, Abhik; wrich@ucsd.edu
Cc: nfiner@ucsd.edu
Subject: Re: SUPPORT DSMC Minutes

Hi
The documents generated by the DSMC are considered confidential and should not go to Massimo. NICHD does not have an agreement with Massimo that would warranted their receipt of these documents. Let me know if there are other questions.

Thanks
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Hastings, Betty J. <bkh@rti.org>
To: Higgins, Rosemary (NIH/NICHD) [E] <higginsr@mail.nih.gov>
Sent: Wed Feb 08 08:22:35 2006
Subject: FW: SUPPORT DSMC Minutes

Rose,
Did you receive this? It didn't appear to go through.
Thanks.
Betty
-----Original Message-----
From: Hastings, Betty J.
Sent: Tuesday, February 07, 2006 1:38 PM
To: higginsr@mail.nih.gov
Cc: Das, Abhik
Subject: FW: SUPPORT DSMC Minutes

Rose,
What do you think about sending a copy of the minutes to Masimo? Thanks.
Betty -----Original Message-----
From: Wade Rich [mailto:wrich@ucsd.edu]
Sent: Tuesday, February 07, 2006 1:28 PM
To: Hastings, Betty J.
Subject: RE: SUPPORT DSMC Minutes

Are these minutes/letters public? Masimo would like to know what is up

with the study.
wade

Attached are the following documents:

* Letter from Dr. Duane Alexander concurring with the resumption of the SUPPORT Trial with the proposed modifications as summarized in the minutes
* Letter addressed to your local IRB
* Summary of the Minutes of January 24, 2006 DSMC meeting

Please note that the clarifications for the Manual of Operations and proposed form change will be forthcoming.

Thank you. <<Dr. Alexander.pdf>> <<DSMCMemosites[01-24-06].doc>> <<DSMC Min_SUPPORT[1-24-06].doc>>
Betty

Betty Hastings

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Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7740
Fax: (919) 485-7762
bkh@rti.org <mailto:bkh@rti.org>

From: Wade Rich
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: SUPPORT
Date: Tuesday, February 07, 2006 9:19:30 AM

Rose,
Can I forward the letters to Maribeth Sayre, or Masimo liaison?
wade

-----Original Message-----
From: Maribeth Sayre [mailto:MSayre@masimo.com]
Sent: Monday, February 06, 2006 4:16 PM
To: Wade Rich (E-mail)
Cc: Mike Petterson
Subject: SUPPORT

Hi Wade,

Is there any official word that you can share with us about the stop and restart of SUPPORT?
Is there an official restart date, or will each center restart at a different time?

Thanks for your help,
Maribeth

From: Neil Finer
To: "Colin Morley"
Cc: nfiner@ucsd.edu; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: G"day
Date: Thursday, February 02, 2006 11:45:10 PM

Hi Colin
Are you a part of the oximeter trial with Tarnow-Mordi? The issues with SUPPORT were related to the oximeters arm and we are willing to provide information to the PIs of those studies. Can you let me and Rose Higgins know?
Be well Mate
Neil

From: Colin Morley [mailto:colin.morley@rwh.org.au]
Sent: Wednesday, February 01, 2006 4:39 PM
To: Neil Finer
Subject: G'day

Hi Neil,

I hope you are well.
I hear the support trial is on hold. As you will appreciate i have considerable interest around this area with COIN, resuscitation and BOOST trial.
Would it be possible to tell me what the cause of the problem is so that we dont fall into any elephant traps ourselves?

Best wishes,

Colin

Colin Morley
Professor of Neonatal Medicine
Royal Women's and Royal Children's Hospitals
Melbourne, Australia
Tel Australia 03 9344 2524
Mobile 0417 036 188

Please note my old email address colin.morley@wch.org.au is now discontinued and any mail sent there will not get through to me. Please make sure you always use the email address above.

From: ccole@bidmc.harvard.edu
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: nfiner@ucsd.edu
Subject: RE: Update
Date: Thursday, February 02, 2006 10:23:38 AM

Dear Rose and Neil,
Thank you for your sharing the report.
I am sending this email to you before reading the report.
I will keep it strictly confidential.
Many thanks - Cindy

Cynthia H. Cole, MD, MPH
Director of Research
Department of Neonatology
Beth Israel Deaconess Medical Center
330 Brookline Avenue, Boston, MA 02215
phone: 00+1+ 617-667-3276
FAX: 00+1+ 617-667-1742
email: ccole@bidmc.harvard.edu

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, February 02, 2006 10:11 AM
To: Cole,Cynthia H. (HMFP - Neonatology)
Cc: Neil Finer
Subject: RE: Update

Hi Cindy,
It has taken us some time to get back to you. SUPPORT is about to restart recruitment. I am **confidentially** sharing with you a presentation that Neil made to the DSMC following detailed analyses of oximetry information collected for SUPPORT. This can be shared **confidentially** with your IRB and your Data Safety Monitoring Board. This information is not to be used for open scientific meetings or to be posted on any websites. Let us know if you have any questions.
Thanks for your patience.

Rose

From: ccole@bidmc.harvard.edu [mailto:ccole@bidmc.harvard.edu]
Sent: Tuesday, January 10, 2006 5:37 PM
To: nfiner@ucsd.edu
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Update
Importance: High

Hello, Neil,
I am writing again regarding requests from my IRB.
They understand the SUPPORT trial is 'on hold'.
The BIDMC IRB will not approve the US POST pilot study until they understand if the reason SUPPORT is 'on hold' is relevant to US POST.
I do not know if or what information you and or Rose can share.
Please advise.

As per my email to you and Rosemay in November, I believe the BIDMC IRB is still seeking information related to "are the SpO2 targeted ranges" above minimal risk compared to current care in NICUs. I (and you) relayed that the SpO2 range of 85-95% is within a range used by most NICUs in USA. Thus, this range per se is not above minimal risk. I explained that the two targeted ranges could have potential benefits, risks, and tradeoffs.

Many thanks for your help - Cindy

Cynthia H. Cole, MD, MPH
Director of Research
Department of Neonatology
Beth Israel Deaconess Medical Center
330 Brookline Avenue, Boston, MA 02215
phone: 00+1+ 617-667-3276
FAX: 00+1+ 617-667-1742
email: ccole@bidmc.harvard.edu

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: wrich@ucsd.edu
Subject: SUPPORT
Date: Wednesday, February 01, 2006 2:32:31 PM

Rose,

I wanted to let you know that our site is interested in continuing to participate in the SUPPORT trial and it's secondaries. In order to do so we would need to be able to continue to enroll subjects in the trial, and be paid capitation for those subjects. We understand that no base salaries would be available. I understand that there is significant co-funding of this trial by NHLBI might help facilitate this type of contract. As the originator of this trial and the number one enroller in this trial, and to our knowledge the only center enrolling in the MRI secondary, we feel we would be able to help the trial move forward. Under these circumstances, I would be willing to continue as PI. Please let me know if this is a something the Network would consider

Neil

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT
Date: Wednesday, February 01, 2006 2:29:20 PM

I see that is already done
Thanks
Neil

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, February 01, 2006 10:04 AM
To: Neil Finer
Subject: SUPPORT

Hi Neil,
I sent the powerpoint over to Dr. Alexander and he approves this going confidentially to the investigators, IRBs and DSMCs for the other oximetry trials. Since these data technically belong to the steering committee, I will send an email to obtain approval from the steering committee.
Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Barbara Stoll
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT
Date: Wednesday, February 01, 2006 11:19:24 PM

Can we share the DSMC slides with our colleagues at Emory?
BJS

Barbara J. Stoll, MD
George W. Brumley, Jr., Professor and Chair, Department of Pediatrics
Medical Director, Children's Healthcare of Atlanta at Egleston
Office: 404-727-2456 Fax: 404-727-5737
barbara_stoll@oz.ped.emory.edu

From: Ellen Hale
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT
Date: Tuesday, January 31, 2006 12:40:30 PM

Rose,

Thanks for calling me back. Our IRB knows that we are not enrolling but the renewal had to be made so we could follow current patients enrolled. Hope there won't be alot of work to get it back through our IRB's.

Ellen

From: Oh, William MD

To: Higgins, Rosemary (NIH/NICHD) [E]; "susie.buchter@oz.ped.emory.edu "; "kurt.schibler@cchmc.org "; "vineet.bhandari@yale.edu "; "Betty Vohr "; "Susan Hintz "; "ambal@sprynet.com "; "ambal@uab.edu "; "Brenda.H.Morris@uth.tmc.edu "; "Laroia, Nirupama "; "carl_dangio@URMC.Rochester.edu "; "Michael Cotten "; "maynard.rasmussen@sharp.com "; "alaptook@WIHRI.org "; "Abhik Das "; "Brenda Poindexter "; "Carlo Waldemar (E-mail) "; "Charles Rosenfeld "; "Dale Phelps "; "Ed Donovan "; "Ehrenkranz Richard (E-mail) "; "Jobe Alan (E-mail) "; "Krisa VanMeurs (VanMeurs, Krisa) "; "Lemons Jim (E-mail) "; "Michael O"Shea "; "Michelle Walsh "; "Neil Finer "; "Oh William (E-mail) "; "Poole Kenneth (E-mail) "; "Ronald GOldberg "; "Shahnaz Duara "; "Shankaran Seetha (E-mail) "; "Stevenson David (E-mail) "; "Stoll Barbara (E-mail) "; "Tyson Jon (E-mail) "; "walid.salhab@utsouthwestern.edu "; "Angelita Hensman "; "Becky bara "; "Bethany Ball "; "Cathy Grisby "; "Ellen Hale "; "Georgia McDavid "; "Kathy Auten "; "Linda Reubens "; "Lucy Miller "; "Monica Collins "; "monica.konstantino@yale.edu "; "Nancy Miller "; "Nancy Newman "; "Nancy Peters "; "Ruth Everett "; "Wade RIch "

Cc: "Betty Hastings "; "Zaterka-Baxter, Kristin "; "Petrie, Carolyn "

Subject: RE: SUPPORT TRIAL

Date: Thursday, January 26, 2006 7:01:48 AM

Great news and what a team work!

Bill

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E]

To: susie.buchter@oz.ped.emory.edu; kurt.schibler@cchmc.org; vineet.bhandari@yale.edu; Betty Vohr; Susan Hintz; ambal@sprynet.com; ambal@uab.edu; Brenda.H.Morris@uth.tmc.edu; Laroia, Nirupama; carl_dangio@URMC.Rochester.edu; Michael Cotten; maynard.rasmussen@sharp.com; alaptook@WIHRI.org; Abhik Das; Brenda Poindexter; Carlo Waldemar (E-mail); Charles Rosenfeld; Dale Phelps; Ed Donovan; Ehrenkranz Richard (E-mail); Jobe Alan (E-mail); Krisa VanMeurs (VanMeurs, Krisa); Lemons Jim (E-mail); Michael O'Shea; Michelle Walsh; Neil Finer; Oh William (E-mail); Poole Kenneth (E-mail); Ronald GOldberg; Shahnaz Duara; Shankaran Seetha (E-mail); Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); walid.salhab@utsouthwestern.edu; Angelita Hensman; Becky bara; Bethany Ball; Cathy Grisby; Ellen Hale; Georgia McDavid; Kathy Auten; Linda Reubens; Lucy Miller; Monica Collins; monica.konstantino@yale.edu; Nancy Miller; Nancy Newman; Nancy Peters; Ruth Everett; Wade RIch

Cc: Betty Hastings; Zaterka-Baxter, Kristin; Petrie, Carolyn

Sent: 1/25/2006 8:46 AM

Subject: SUPPORT TRIAL

Hi,

The DSMC met in person yesterday to review the additional data analyses for the SUPPORT trial. They recommended that the oximetry arm of the trial resume with some minor modifications. I have spoken with Dr. Alexander and once we have the documentation from the meeting and IRB information along with a revised protocol, we can get IRB approvals and continue the trial. Hopefully we can get these documents finalized in the next week.

Dr. Finer provided a superb overview of the data analyses and we thank him, the subcommittee, and RTI for all of the effort involved in this process. In addition, Dr. Carlo attended the meeting and was extremely helpful during the discussion period.

Thanks again to everyone for persistence and patience!!!

Rose

Rosemary D. Higgins, M.D.

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

NICHD, NIH

6100 Executive Blvd., Room 4B03B

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Bethesda, MD 20892

(For overnight delivery, use Rockville, MD 20852)

301-435-7909

301-496-3790 (FAX)

higginsr@mail.nih.gov <mailto:higginsr@mail.nih.gov>

From:	Charles Rosenfeld
To:	william_oh@brown.edu; edward.donovan@cchmc.org; kurt.schibler@cchmc.org; Jobea0@chmcc.org; nxs5@cwru.edu; grisbyca@email.uc.edu; bpoindex@iupui.edu; jlemons@iupui.edu; lucmille@iupui.edu; mbball@leland.stanford.edu; vanmeurs@leland.stanford.edu; Higgins, Rosemary (NIH/NICHD) [E]; auten002@mc.duke.edu; cotte010@mc.duke.edu; goldb008@mc.duke.edu; Reverett@med.miami.edu; sduara@miami.edu; barbara_stoll@oz.ped.emory.edu; ellen_hale@oz.ped.emory.edu; susie.buchter@oz.ped.emory.edu; mcollins@peds.uab.edu; wcarlo@peds.uab.edu; mcw3@po.cwru.edu; adas@rti.org; poo@rti.org; maynard.rasmussen@sharp.com; ambal@sprynet.com; dstevenson@stanford.edu; srhintz@stanford.edu; ambal@uab.edu; nfiner@ucsd.edu; wrich@ucsd.edu; carl_dangio@urmc.rochester.edu; dale_phelps@urmc.rochester.edu; linda_reubens@urmc.rochester.edu; Nirupama_Laroia@urmc.rochester.edu; Brenda.H.Morris@uth.tmc.edu; Georgia.E.McDavid@uth.tmc.edu; Jon.E.Tyson@uth.tmc.edu; Nancy Miller; Walid Salhab; ae5357@wayne.edu; s_shankaran@wayne.edu; moshea@wfubmc.edu; npeters@wfubmc.edu; ahensman@wihri.org; alaptook@wihri.org; BVohr@wihri.org; monica.konstantino@yale.edu; richard.ehrenkranz@yale.edu; vineet.bhandari@yale.edu
Cc:	bkh@rti.org; kzaterka@rti.org; petrie@rti.org
Subject:	Re: SUPPORT TRIAL
Date:	Wednesday, January 25, 2006 7:45:04 PM

excellent

Charles

Charles R. Rosenfeld, M.D.
George L. MacGregor Professor of Pediatrics
and Professor of Obstetrics and Gynecology
Director, Division of Neonatal-Perinatal Medicine
UT Southwestern Medical Center at Dallas
5323 Harry Hines Blvd.
Dallas, TX 75390-9063
Telephone: (214) 648-3903
FAX: (214) 648-2481
Email: charles.rosenfeld@utsouthwestern.edu

>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> 01/25/06 7:46 AM >>>
Hi,

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Rose

Rosemary D. Higgins, M.D.

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

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NICHD, NIH

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Bethesda, MD 20892

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301-435-7909

301-496-3790 (FAX)

higginsr@mail.nih.gov

From:	Shankaran, Seetha
To:	Higgins, Rosemary (NIH/NICHD) [E]; susie.buchter@oz.ped.emory.edu; kurt.schibler@cchmc.org; vineet.bhandari@yale.edu; Betty Vohr; Susan Hintz; ambal@sprynet.com; ambal@uab.edu; Brenda.H.Morris@uth.tmc.edu; Laroia, Nirupama; carl_dangio@URMC.Rochester.edu; Michael Cotten; maynard.rasmussen@sharp.com; alaptook@WIHRI.org; Abhik Das; Brenda Poindexter; Carlo Waldemar (E-mail); Charles Rosenfeld; Dale Phelps; Ed Donovan; Ehrenkranz Richard (E-mail); Jobe Alan (E-mail); Krisa VanMeurs (VanMeurs, Krisa); Lemons Jim (E-mail); Michael O"Shea; Michelle Walsh; Neil Finer; Oh William (E-mail); Poole Kenneth (E-mail); Ronald GOldberg; Shahnaz Duara; Shankaran Seetha (E-mail); Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); walid.salhab@utsouthwestern.edu; Angelita Hensman; Becky bara; Bethany Ball; Cathy Grisby; Ellen Hale; Georgia McDavid; Kathy Auten; Linda Reubens; Lucy Miller; Monica Collins; monica.konstantino@yale.edu; Nancy Miller; Nancy Newman; Nancy Peters; Ruth Everett; Wade RIch
Cc:	Betty Hastings; Zaterka-Baxter, Kristin; Petrie, Carolyn
Subject:	RE: SUPPORT TRIAL
Date:	Wednesday, January 25, 2006 11:33:05 AM

Neil, Abhik, Ken, Rose
Congrats to you and subcommittee
Seetha

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, January 25, 2006 8:47 AM
To: susie.buchter@oz.ped.emory.edu; kurt.schibler@cchmc.org; vineet.bhandari@yale.edu; Betty Vohr; Susan Hintz; ambal@sprynet.com; ambal@uab.edu; Brenda.H.Morris@uth.tmc.edu; Laroia, Nirupama; carl_dangio@URMC.Rochester.edu; Michael Cotten; maynard.rasmussen@sharp.com; alaptook@WIHRI.org; Abhik Das; Brenda Poindexter; Carlo Waldemar (E-mail); Charles Rosenfeld; Dale Phelps; Ed Donovan; Ehrenkranz Richard (E-mail); Jobe Alan (E-mail); Krisa VanMeurs (VanMeurs, Krisa); Lemons Jim (E-mail); Michael O'Shea; Michelle Walsh; Neil Finer; Oh William (E-mail); Poole Kenneth (E-mail); Ronald GOldberg; Shahnaz Duara; Shankaran Seetha (E-mail); Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); walid.salhab@utsouthwestern.edu; Angelita Hensman; Becky bara; Bethany Ball; Cathy Grisby; Ellen Hale; Georgia McDavid; Kathy Auten; Linda Reubens; Lucy Miller; Monica Collins; monica.konstantino@yale.edu; Nancy Miller; Nancy Newman; Nancy Peters; Ruth Everett; Wade RIch
Cc: Betty Hastings; Zaterka-Baxter, Kristin; Petrie, Carolyn
Subject: SUPPORT TRIAL

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Thanks again to everyone for persistence and patience!!!

Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510

Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Duara, Shahnaz
To:	Higgins, Rosemary (NIH/NICHD) [E]; susie.buchter@oz.ped.emory.edu; kurt.schibler@cchmc.org; vineet.bhandari@yale.edu; Betty Vohr; Susan Hintz; ambal@sprynet.com; ambal@uab.edu; Brenda.H.Morris@uth.tmc.edu; Laroia, Nirupama; carl_dangio@urmc.rochester.edu; Michael Cotten; maynard.rasmussen@sharp.com; alaptook@WIHRI.org; Abhik Das; Brenda Poindexter; Carlo Waldemar (E-mail); Charles Rosenfeld; Dale Phelps; Ed Donovan; Ehrenkranz Richard (E-mail); Jobe Alan (E-mail); Krisa VanMeurs (VanMeurs, Krisa); Lemons Jim (E-mail); Michael O"Shea; Michelle Walsh; Neil Finer; Oh William (E-mail); Poole Kenneth (E-mail); Ronald GOldberg; Shahnaz Duara; Shankaran Seetha (E-mail); Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); walid.salhab@utsouthwestern.edu; Angelita Hensman; Becky bara; Bethany Ball; Cathy Grisby; Ellen Hale; Georgia McDavid; Kathy Auten; Linda Reubens; Lucy Miller; Monica Collins; monica.konstantino@yale.edu; Nancy Miller; Nancy Newman; Nancy Peters; Everett, Ruth; Wade RIch
Cc:	Betty Hastings; Zaterka-Baxter, Kristin; Petrie, Carolyn
Subject:	RE: SUPPORT TRIAL
Date:	Wednesday, January 25, 2006 9:20:46 AM

Hi,

This is great news. Neil and Wally, a big round of applause and thanks so much for all your hard work.

Shahnaz

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, January 25, 2006 8:47 AM
To: susie.buchter@oz.ped.emory.edu; kurt.schibler@cchmc.org; vineet.bhandari@yale.edu; Betty Vohr; Susan Hintz; ambal@sprynet.com; ambal@uab.edu; Brenda.H.Morris@uth.tmc.edu; Laroia, Nirupama; carl_dangio@urmc.rochester.edu; Michael Cotten; maynard.rasmussen@sharp.com; alaptook@WIHRI.org; Abhik Das; Brenda Poindexter; Carlo Waldemar (E-mail); Charles Rosenfeld; Dale Phelps; Ed Donovan; Ehrenkranz Richard (E-mail); Jobe Alan (E-mail); Krisa VanMeurs (VanMeurs, Krisa); Lemons Jim (E-mail); Michael O'Shea; Michelle Walsh; Neil Finer; Oh William (E-mail); Poole Kenneth (E-mail); Ronald GOldberg; Shahnaz Duara; Shankaran Seetha (E-mail); Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); walid.salhab@utsouthwestern.edu; Angelita Hensman; Becky bara; Bethany Ball; Cathy Grisby; Ellen Hale; Georgia McDavid; Kathy Auten; Linda Reubens; Lucy Miller; Monica Collins; monica.konstantino@yale.edu; Nancy Miller; Nancy Newman; Nancy Peters; Everett, Ruth; Wade RIch
Cc: Betty Hastings; Zaterka-Baxter, Kristin; Petrie, Carolyn
Subject: SUPPORT TRIAL

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(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Richard Ehrenkranz
To:	Higgins, Rosemary (NIH/NICHD) [E]; susie.buchter@oz.ped.emory.edu; kurt.schibler@cchmc.org; vineet.bhandari@yale.edu; Betty Vohr; Susan Hintz; ambal@sprynet.com; ambal@uab.edu; Brenda.H.Morris@uth.tmc.edu; Laroia, Nirupama; carl_dangio@URMC.Rochester.edu; Michael Cotten; maynard.rasmussen@sharp.com; alaptook@WIHRI.org; Abhik Das; Brenda Poindexter; Carlo Waldemar (E-mail); Charles Rosenfeld; Dale Phelps; Ed Donovan; Jobe Alan (E-mail); Krisa VanMeurs (VanMeurs, Krisa); Lemons Jim (E-mail); Michael O"Shea; Michelle Walsh; Neil Finer; Oh William (E-mail); Poole Kenneth (E-mail); Ronald GOldberg; Shahnaz Duara; Shankaran Seetha (E-mail); Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); walid.salhab@utsouthwestern.edu; Angelita Hensman; Becky bara; Bethany Ball; Cathy Grisby; Ellen Hale; Georgia McDavid; Kathy Auten; Linda Reubens; Lucy Miller; Monica Collins; monica.konstantino@yale.edu; Nancy Miller; Nancy Newman; Nancy Peters; Ruth Everett; Wade RIch
Cc:	Betty Hastings; Zaterka-Baxter, Kristin; Petrie, Carolyn
Subject:	Re: SUPPORT TRIAL
Date:	Wednesday, January 25, 2006 9:09:41 AM

Great! Way to go Neil!!!
Richard

At 08:46 AM 1/25/2006, Higgins, Rosemary (NIH/NICHD) [E] wrote:

> Hi,
> The DSMC met in person yesterday to review the additional data analyses for the SUPPORT trial. They recommended that the oximetry arm of the trial resume with some minor modifications. I have spoken with Dr. Alexander and once we have the documentation from the meeting and IRB information along with a revised protocol, we can get IRB approvals and continue the trial. Hopefully we can get these documents finalized in the next week.
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> Thanks again to everyone for persistence and patience!!!
>
> Rose
>
> Rosemary D. Higgins, M.D.
> Program Scientist for the Neonatal Research Network
> Pregnancy and Perinatology Branch
> Center for Developmental Biology and Perinatal Medicine
> NICHD, NIH
> 6100 Executive Blvd., Room 4B03B
> MSC 7510
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> 301-496-3790 (FAX)
> higginsr@mail.nih.gov

Richard A. Ehrenkranz, MD
Department of Pediatrics
Yale University School of Medicine
333 Cedar Street
PO Box 208064
New Haven, CT 06520-8064
tele: 203-688-2320
fax: 203-688-5426

From: Michael Cotten
To: Higgins, Rosemary (NIH/NICHD) [E]; Neil Finer; Wally Carlo, M.D.
Subject: Re: SUPPORT TRIAL
Date: Wednesday, January 25, 2006 9:08:35 AM

---

thanks Rose, Neil and Wally!

mc

C. Michael Cotten, MD
Assistant Clinical Professor of Pediatrics
Clinical Research Director, Duke Neonatology
Director Special Care Nursery, Durham Regional Hospital
Box 3179 DUMC
Durham, NC 27710
(919) 681-6025
fax: (919) 681-6065
pager: (919) 970-4381

"Higgins, Rosemary \(NIH/NICHD\) [E]" <higginsr@mail.nih.gov>
01/25/2006 08:46 AM

To: <susie.buchter@oz.ped.emory.edu>, <kurt.schibler@cchmc.org>, <vineet.bhandari@yale.edu>, "Betty Vohr" <BVohr@WIHRI.org>, "Susan Hintz" <srhintz@stanford.edu>, <ambal@sprynet.com>, <ambal@uab.edu>, <Brenda.H.Morris@uth.tmc.edu>, "Laroia, Nirupama" <Nirupama_Laroia@URMC.Rochester.edu>, <carl_dangio@URMC.Rochester.edu>, "Michael Cotten" <cotte010@mc.duke.edu>, <maynard.rasmussen@sharp.com>, <alaptook@WIHRI.org>, "Abhik Das" <adas@rti.org>, "Brenda Poindexter" <bpoindex@iupui.edu>, "Carlo Waldemar \(E-mail\)" <wcarlo@peds.uab.edu>, "Charles Rosenfeld" <crosen@mednet.swmed.edu>, "Dale Phelps" <dale_phelps@URMC.Rochester.edu>, "Ed Donovan" <edward.donovan@cchmc.org>, "Ehrenkranz Richard \(E-mail\)" <richard.ehrenkranz@yale.edu>, "Jobe Alan \(E-mail\)" <Jobea0@chmcc.org>, "Krisa VanMeurs \(VanMeurs, Krisa\)" <vanmeurs@leland.stanford.edu>, "Lemons Jim \(E-mail\)" <jlemons@iupui.edu>, "Michael O'Shea" <moshea@wfubmc.edu>, "Michelle Walsh" <mcw3@po.cwru.edu>, "Neil Finer" <nfiner@ucsd.edu>, "Oh William \(E-mail\)" <william_oh@brown.edu>, "Poole Kenneth \(E-mail\)" <poo@rti.org>, "Ronald GOldberg" <goldb008@mc.duke.edu>, "Shahnaz Duara" <sduara@miami.edu>, "Shankaran Seetha \(E-mail\)" <s_shankaran@wayne.edu>, "Stevenson David \(E-mail\)" <dstevenson@stanford.edu>, "Stoll Barbara \(E-mail\)" <barbara_stoll@oz.ped.emory.edu>, "Tyson Jon \(E-mail\)" <Jon.E.Tyson@uth.tmc.edu>,

<walid.salhab@utsouthwestern.edu>, "Angelita Hensman" <ahensman@WIHRI.org>, "Becky
bara" <ae5357@wayne.edu>, "Bethany Ball" <mbball@leland.stanford.edu>, "Cathy Grisby"
<grisbyca@email.uc.edu>, "Ellen Hale" <ellen_hale@oz.ped.emory.edu>, "Georgia McDavid"
<Georgia.E.McDavid@uth.tmc.edu>, "Kathy Auten" <auten002@mc.duke.edu>, "Linda Reubens"
<linda_reubens@URMC.Rochester.edu>, "Lucy Miller" <lucmille@iupui.edu>, "Monica
Collins" <mcollins@peds.uab.edu>, <monica.konstantino@yale.edu>, "Nancy Miller"
<Nancy.Miller@utsouthwestern.edu>, "Nancy Newman" <nxs5@cwru.edu>, "Nancy Peters"
<npeters@wfubmc.edu>, "Ruth Everett" <Reverett@med.miami.edu>, "Wade RIch"
<wrich@ucsd.edu>
cc: "Betty Hastings" <bkh@rti.org>, "Zaterka-Baxter, Kristin" <kzaterka@rti.org>, "Petrie, Carolyn" <petrie@rti.org>
Subject: SUPPORT TRIAL

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301-435-7909
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higginsr@mail.nih.gov

From: Michele Walsh
To: Wade RIch; Ruth Everett; Nancy Peters; Nancy Newman; Nancy Miller; monica.konstantino@yale.edu; Monica Collins; Lucy Miller; Linda Reubens; Kathy Auten; Georgia McDavid; Ellen Hale; Cathy Grisby; Bethany Ball; Becky bara; Angelita Hensman; walid.salhab@utsouthwestern.edu; Tyson Jon (E-mail); Stoll Barbara (E-mail); Stevenson David (E-mail); Shankaran Seetha (E-mail); Shahnaz Duara; Ronald GOldberg; Poole Kenneth (E-mail); Oh William (E-mail); Neil Finer; Michelle Walsh; Michael O"Shea; Lemons Jim (E-mail); Krisa VanMeurs (VanMeurs, Krisa); Jobe Alan (E-mail); Ehrenkranz Richard (E-mail); Ed Donovan; Dale Phelps; Charles Rosenfeld; Carlo Waldemar (E-mail); Brenda Poindexter; Abhik Das; alaptook@WIHRI.org; maynard.rasmussen@sharp.com; Michael Cotten; carl_dangio@urmc.rochester.edu; Laroia, Nirupama; Brenda.H.Morris@uth.tmc.edu; ambal@uab.edu; ambal@sprynet.com; Susan Hintz; Betty Vohr; vineet.bhandari@yale.edu; kurt.schibler@cchmc.org; susie.buchter@oz.ped.emory.edu; Higgins, Rosemary (NIH/NICHD) [E]
Cc: Fanaroff, Avroy; Petrie, Carolyn; Zaterka-Baxter, Kristin; Betty Hastings
Subject: Re: SUPPORT TRIAL
Date: Wednesday, January 25, 2006 9:05:08 AM

Congratulations! Let the game (re-) begin. Thank you Neil, Wally, Rose and Abhik for representing us so ablely. Michele

----- Original Message -----
From: Higgins, Rosemary (NIH/NICHD) [E]
To: susie.buchter@oz.ped.emory.edu ; kurt.schibler@cchmc.org ; vineet.bhandari@yale.edu ; Betty Vohr ; Susan Hintz ; ambal@sprynet.com ; ambal@uab.edu ; Brenda.H.Morris@uth.tmc.edu ; Laroia, Nirupama ; carl_dangio@urmc.rochester.edu ; Michael Cotten ; maynard.rasmussen@sharp.com ; alaptook@WIHRI.org ; Abhik Das ; Brenda Poindexter ; Carlo Waldemar (E-mail) ; Charles Rosenfeld ; Dale Phelps ; Ed Donovan ; Ehrenkranz Richard (E-mail) ; Jobe Alan (E-mail) ; Krisa VanMeurs (VanMeurs, Krisa) ; Lemons Jim (E-mail) ; Michael O'Shea ; Michelle Walsh ; Neil Finer ; Oh William (E-mail) ; Poole Kenneth (E-mail) ; Ronald GOldberg ; Shahnaz Duara ; Shankaran Seetha (E-mail) ; Stevenson David (E-mail) ; Stoll Barbara (E-mail) ; Tyson Jon (E-mail) ; walid.salhab@utsouthwestern.edu ; Angelita Hensman ; Becky bara ; Bethany Ball ; Cathy Grisby ; Ellen Hale ; Georgia McDavid ; Kathy Auten ; Linda Reubens ; Lucy Miller ; Monica Collins ; monica.konstantino@yale.edu ; Nancy Miller ; Nancy Newman ; Nancy Peters ; Ruth Everett ; Wade RIch
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Sent: Wednesday, January 25, 2006 8:46 AM
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301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]; wcarlo@peds.uab.edu
Subject: RE: Thanks
Date: Tuesday, January 24, 2006 10:26:26 PM

Thanks Rose and Wally for your support and encouragement.
Neil

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, January 24, 2006 2:26 PM
To: nfiner@ucsd.edu; wcarlo@peds.uab.edu
Subject: Thanks

Hi,
Thanks to both of you, especially Neil for all the hard work, effort,
and genuine persistence with the SUPPORT trial!!!
I spoke with Dr. Alexander this afternoon and pending the receipt of the
DSMC recommendation from RTI, we will be able to get restarted.
Your dedication is truly appreciated!
Thanks again!
Rose

Sent from my BlackBerry Wireless Handheld

From: Wally Carlo, M.D.
To: Higgins, Rosemary (NIH/NICHD) [E]; nfiner@ucsd.edu
Subject: Re: Thanks
Date: Tuesday, January 24, 2006 5:28:07 PM

Neil: you did a terrific job.
Rose: you were a great guiding force.

What a team! Thanks a lot.
Wally

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] <higginsr@mail.nih.gov>
To: nfiner@ucsd.edu <nfiner@ucsd.edu>; Wally Carlo, M.D. <WCarlo@peds.uab.edu>
Sent: Tue Jan 24 16:25:42 2006
Subject: Thanks

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Sent from my BlackBerry Wireless Handheld

From: Das, Abhik
To: Zaterka-Baxter, Kristin
Cc: Higgins, Rosemary (NIH/NICHD) [E]; Hastings, Betty J.
Subject: RE: DSMC Support Meeting
Date: Tuesday, January 17, 2006 9:26:21 AM

I would give him a call and then proceed with the arrangements.

-----Original Message-----
From: Zaterka-Baxter, Kristin
Sent: Monday, January 16, 2006 5:34 PM
To: Das, Abhik
Cc: 'higginsr@mail.nih.gov'; Hastings, Betty J.
Subject: FW: DSMC Support Meeting

Hi,

I've not heard from Dr. Avery whether it is alright to proceed with the DSMC mtg with Dr. D'Alton only available in the afternoon by teleconference (this confirmed via email sent by her secretary). Please let me know if you think we can move forward and confirm hotel reservation and things of this nature.
Thanks,
Kris

Kristin Zaterka-Baxter, RN, BSN, CCRP
RTI International
Statistics and Epidemiology
4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From: Zaterka-Baxter, Kristin
Sent: Wednesday, January 11, 2006 10:26 AM
To: 'gavery@cnmc.org'
Cc: Das, Abhik; 'Higgins, Rosemary (NIH/NICHD) [E]'; Hastings, Betty J.
Subject: DSMC Support Meeting

Dr. Avery,

Dr. D'Alton will not be available to come to the DSMC Support meeting on January 24th, 2006. She will however be available to call in to the meeting in the afternoon, perhaps around 1 p.m. We can easily set up a phone conference line for her to call during this time. Please let me know if we need to revise the agenda to accommodate Dr. D'Alton or if other arrangements will need to be made.

Thank you,
Kris

Kristin Zaterka-Baxter, RN, BSN, CCRP
RTI International
Statistics and Epidemiology
4426 South Miami Blvd.

Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From: Zaterka-Baxter, Kristin
To: Das, Abhik
Cc: Higgins, Rosemary (NIH/NICHD) [E]; Hastings, Betty J.
Subject: FW: DSMC Support Meeting
Date: Monday, January 16, 2006 5:33:57 PM
Attachments: DSMC AGENDA 1 24 06.doc

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Durham, NC 27703
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Fax: (919) 485-7762
kzaterka@rti.org

From: Zaterka-Baxter, Kristin
Sent: Wednesday, January 11, 2006 10:26 AM
To: 'gavery@cnmc.org'
Cc: Das, Abhik; 'Higgins, Rosemary (NIH/NICHD) [E]'; Hastings, Betty J.
Subject: DSMC Support Meeting

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Thank you,
Kris

Kristin Zaterka-Baxter, RN, BSN, CCRP
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Statistics and Epidemiology
4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

NICHD Neonatal Research Network

Data Safety and Monitoring Committee (DSMC)

Meeting to discuss the protocol for The SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants
(The SUPPORT Trial)

The January 24, 2006, meeting of the SUPPORT DSMC will be held at 6110 Executive Boulevard, Suite 902, 9th Floor Conference Room, Rockville, MD. The meeting will start at 8:30 AM and will finish by 3:30 PM. The material to be discussed has been previously sent to the committee. Below is the agenda and participant list for this meeting.

AGENDA

OPEN SESSION		
8:30 - 8:40	Introductions	Drs. Higgins and Avery
8:40 - -8:50	Role of the DSMC	Dr. Avery
8:50 - 9:10	Presentation of the SUPPORT Trial	Dr. Finer
9:10 to 9:30	Discussion of Presentation	DSMC, Dr. Finer and Dr. Higgins
CLOSED SESSION		
09:30 – 11:00	Presentation of SUPPORT Interim Monitoring Data	Dr. Das and Dr. Gantz
11:00 – 1:30	Discussion and Working Lunch	DSMC
1:30 – 2:00	Final Discussions and Recommendations for SUPPORT	DSMC
2:00 – 2:30 Open Session	Communication of Actions Recommended	DSMC, Dr. Finer and Dr. Higgins
2:30 – 3:30	Discussion of Pilot $IPGE_1$ Study (time permitting)	DSMC
3:30	Meeting Adjourned	

Participants:
Gordon Avery, MD, Chair
Robert Boyle, MD
Carl Hunt, MD
Merran A. Thomson, MD
Christine A. Gleason, MD
Carol Redmond, Ph.D.
Marilee C. Allen, MD
Marian Willinger, Ph.D.
Traci Clemons, Ph.D
Neil Finer, MD (Open Session)
Waldemar A. Carlo, MD (Open Session)
Rosemary Higgins, MD (Open Session)
Mary Ann Berberich, MD (NHLBI) (Open Session)
Abhik Das, Ph.D.
Kenneth Poole, Ph.D. (via phone conference)
Marie Gantz, Ph.D.
Carolyn Petrie Huitema
Kris Zaterka-Baxter (via phone conference)

From:	Neil Finer
To:	ccole@bidmc.harvard.edu
Cc:	Higgins, Rosemary (NIH/NICHD) [E]
Subject:	RE: Update
Date:	Tuesday, January 10, 2006 8:30:26 PM

Hi Cindy

We meet with the DSMC on Jan 24th. I will be in contact with you immediately after that. I did speak to the IRB Chair who reviewed your proposal. I'm sorry that we cannot discuss this in any depth till then, and we are all very frustrated with the delay.
I also reiterated the points about minimal risk and the SpO2 ranges.

If you do not hear from me by Jan 26th, please call or check that I am still breathing etc!!!!!!!!!!!
Be well
Neil

From: ccole@bidmc.harvard.edu [mailto:ccole@bidmc.harvard.edu]
Sent: Tuesday, January 10, 2006 2:37 PM
To: nfiner@ucsd.edu
Cc: higginsr@mail.nih.gov
Subject: Update
Importance: High

Hello, Neil,
I am writing again regarding requests from my IRB.
They understand the SUPPORT trial is 'on hold'.
The BIDMC IRB will not approve the US POST pilot study until they understand if the reason SUPPORT is 'on hold' is relevant to US POST.
I do not know if or what information you and or Rose can share.
Please advise.
As per my email to you and Rosemay in November, I believe the BIDMC IRB is still seeking information related to "are the SpO2 targeted ranges" above minimal risk compared to current care in NICUs. I (and you) relayed that the SpO2 range of 85-95% is within a range used by most NICUs in USA. Thus, this range per se is not above minimal risk. I explained that the two targeted ranges could have potential benefits, risks, and tradeoffs.

Many thanks for your help - Cindy

Cynthia H. Cole, MD, MPH
Director of Research
Department of Neonatology
Beth Israel Deaconess Medical Center
330 Brookline Avenue, Boston, MA 02215
phone: 00+1+ 617-667-3276
FAX: 00+1+ 617-667-1742
email: ccole@bidmc.harvard.edu

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT
Date: Tuesday, January 10, 2006 7:21:00 PM

I won't spill the beans
Neil

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, January 10, 2006 2:12 PM
To: nfiner@ucsd.edu
Subject: Re: SUPPORT

Yes, but he doesn't know that!
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Neil Finer <nfiner@ucsd.edu>
To: Higgins, Rosemary (NIH/NICHD) [E] <higginsr@mail.nih.gov>
Sent: Tue Jan 10 16:56:25 2006
Subject: RE: SUPPORT

I am intending to come to dinner - isn't that Alan's farewell??

Neil

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, January 10, 2006 1:01 PM
To: nfiner@ucsd.edu
Subject: SUPPORT

Hi Neil,

For the SUPPORT Subcommittee, we have your agenda and the powerpoint presentation. For the secondary studies, Dale will update folks on the pulmonary outcomes study. Krisa will fill in for Susan Hintz for the MRI secondary. I also looked up the capitation for this study. There are 2 hours of research nurse time ($64), $250 for a 36 week ultrasound and $1000 for a 36 week MRI. The growth study hasn't gotten going since recruitment has been halted for the time-being.

Let me know if there are any issues that have been left out so that they can be included.

Also, are you coming to the dinner on Thursday night at the Bolger Center??

Have a safe trip.

Rose

Rosemary D. Higgins, M.D.

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

NICHD, NIH

6100 Executive Blvd., Room 4B03B

MSC 7510

Bethesda, MD 20892

(For overnight delivery, use Rockville, MD 20852)

301-435-7909

301-496-3790 (FAX)

higginsr@mail.nih.gov

From: Susan Hintz
To: kristin zaterka
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT MRI secondary IRB approval
Date: Tuesday, January 10, 2006 10:55:42 AM

Hi Kristin,

I count four sites that have IRB approval for the MRI secondary (Stanford, UCSD#1, Alabama, Rochester) - does that jive with your numbers? Clearly, several of the other sites that are seeking IRB approval got hung up when the main trial was put on hold

Let me know

Thanks

Susan
--
Susan R. Hintz, M.D.
Assistant Professor of Pediatrics
Division of Neonatal and Developmental Medicine
Stanford University School of Medicine
750 Welch Road, Suite 315
Palo Alto, CA 94304
ph: 650-723-5711
fax: 650-725-8351

From:	Neil Finer
To:	Higgins, Rosemary (NIH/NICHD) [E]; "Petrie, Carolyn"
Cc:	"Avroy A. Fanaroff, M.D."; "Betty Hastings"; Das, Abhik; "Ed Donovan"; "Ken Poole"; "Maynard Rasmussen"; "Michele"; "Neil Finer"; "Shahnaz Duara"; "Wade Rich"; "Wally Carlo"
Date:	Monday, January 09, 2006 1:52:25 PM

Hi Rose and Carolyn
The agenda for the SUPPORT Committee

1. Review the response to the DSMC – 40 minutes with discussion
2. Review Status of Secondaries, including MRI – Each PI for the Secondaries to give a 5 minute update
3. Closing Prayer

Please ask for any additions.
Many thanks
Neil

From:	Zaterka-Baxter, Kristin
To:	nfiner@ucsd.edu
Cc:	Das, Abhik; Higgins, Rosemary (NIH/NICHD) [E]; Hastings, Betty J.
Subject:	DSMC Support mtg.
Date:	Friday, January 06, 2006 1:22:58 PM
Attachments:	DSMC AGENDA 1 24 06.doc

Hi. Dr. Finer,

Please find attached the agenda for the upcoming DSMC Support meeting scheduled for January 24th 2006 from 8:30am to 3:30pm. We will provide copies of the materials you sent Betty in preparation for the conference call. Please also find below logistical information for this meeting.

DATE & LOCATION The meeting is scheduled for Tuesday January 24, 2006, at RTI's Rockville office, located at 6110 Executive Blvd—9th Floor, Rockville, MD 20852.

SCHEDULE The meeting will begin Tuesday morning at 8:30 am. The meeting will conclude by 3:30 pm however discussion of the Support study will end by 3:00pm (the agenda has the support discussions ending by 2:30 hopefully).

HOTEL RTI is providing hotel accommodations for the DSMC members at the Doubletree Rockville, located at 1750 Rockville Pike, Rockville, MD 20852. This hotel is approximately 1.5 miles from the RTI Rockville office.

TAXIS AND METRO The DoubleTree is located approximately forty-five minutes from Washington Reagan National Airport or Dulles International Airport. Taxis from National Airport cost approximately $45. Taxis from Dulles are approximately $52 and from BWI, $63.

Super Shuttle is available and recommended for groups traveling together. Fares are approximately $25 for the first passenger and $8 for each additional passenger. Reservations may be made online at http://www.supershuttle.com/htm/cities/dca.htm.

You may also take the Metro from Reagan National Airport to the hotel. Take the Yellow Line from the airport towards Mt. Vernon Square. Get off at the Gallery Place/Chinatown stop and change to a Red Line train towards ShadyGrove. The DoubleTree is located right on the Twinbrook stop on the RedLine.

Hope this is helpful and please let me know if you have any questions.
Thanks,

Kristin Zaterka-Baxter, RN, BSN, CCRP
RTI International
Statistics and Epidemiology
4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

NICHD Neonatal Research Network

Data Safety and Monitoring Committee (DSMC)

Meeting to discuss the protocol for The SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants
(The SUPPORT Trial)

The January 24, 2006, meeting of the SUPPORT DSMC will be held at 6110 Executive Boulevard, Suite 902, 9th Floor Conference Room, Rockville, MD. The meeting will start at 8:30 AM and will finish by 3:30 PM. The material to be discussed has been previously sent to the committee. Below is the agenda and participant list for this meeting.

AGENDA

OPEN SESSION		
8:30 - 8:40	Introductions	Drs. Higgins and Avery
8:40 - -8:50	Role of the DSMC	Dr. Avery
8:50 - 9:10	Presentation of the SUPPORT Trial	Dr. Finer
9:10 to 9:30	Discussion of Presentation	DSMC, Dr. Finer and Dr. Higgins
CLOSED SESSION		
09:30 – 11:00	Presentation of SUPPORT Interim Monitoring Data	Dr. Das and Dr. Gantz
11:00 – 1:30	Discussion and Working Lunch	DSMC
1:30 – 2:00	Final Discussions and Recommendations for SUPPORT	DSMC
2:00 – 2:30 Open Session	Communication of Actions Recommended	DSMC, Dr. Finer and Dr. Higgins
2:30 – 3:30	Discussion of Pilot IPGE$_1$ Study (time permitting)	DSMC
3:30	Meeting Adjourned	

Participants:
Gordon Avery, MD, Chair
Robert Boyle, MD
Carl Hunt, MD
Merran A. Thomson, MD
Christine A. Gleason, MD
Marilee C. Allen, MD
Marian Willinger, Ph.D.
Traci Clemons, Ph.D
Neil Finer, MD (Open Session)
Waldemar A. Carlo, MD (Open Session)
Rosemary Higgins, MD (Open Session)
Mary Ann Berberich, MD (NHLBI) (Open Session)
Abhik Das, Ph.D.
Kenneth Poole, Ph.D. (via phone conference)
Marie Gantz, Ph.D.
Carolyn Petrie Huitema
Kris Zaterka-Baxter (via phone conference)

From:	Zaterka-Baxter, Kristin
To:	Higgins, Rosemary (NIH/NICHD) [E]
Subject:	RE: DSMC agenda
Date:	Friday, January 06, 2006 12:02:51 PM

Yup, will do and change the time the mtg is adjourned to 3pm.
Thanks

Kristin Zaterka-Baxter, RN, BSN, CCRP
RTI International
Statistics and Epidemiology
4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, January 06, 2006 12:01 PM
To: Zaterka-Baxter, Kristin
Subject: RE: DSMC agenda

If we need to be available at the end of the meting, you can put that in the agenda – Neil wants to leave for the airport at 3PM – can it end by then? Otherwise it is fine
Rose

From: Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]
Sent: Friday, January 06, 2006 12:00 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: DSMC agenda

Hi,
Abhik made a few changes to the agenda and left the IPGE as tentative. He added a support safety data discussion and said that the DSMC might want an open session at the end to discuss findings but will leave that unsaid for now. He knows you wanted a ½ for Neil to answer any of the DSMC questions but I think Abhik is under the impression Neil will be available the whole day just in case this is the fact. Wanted to let you know the particulars before I sent this out. Still have not heard from Dr. Avery.
Thanks,
Kris

Kristin Zaterka-Baxter, RN, BSN, CCRP
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4426 South Miami Blvd.
Durham, NC 27703
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From:	Neil Finer
To:	Higgins, Rosemary (NIH/NICHD) [E]
Subject:	RE: Network meeting
Date:	Thursday, January 05, 2006 4:21:39 PM

Great

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, January 05, 2006 12:53 PM
To: nfiner@ucsd.edu
Subject: RE: Network meeting

Neil
I looked this over and have no suggestions. I sent it to the steering committee.

See you soon.
Rose

From: Neil Finer [mailto:nfiner@ucsd.edu]
Sent: Wednesday, January 04, 2006 7:55 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Network meeting

Hi Rose
This is the PowerPoint response for the DSMC. I will present to the SUPPORT Subcommittee and then in brief to the Steering Committee. I think it should be circulated to the Steering Committee before our meeting.
Thanks
Neil

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, January 03, 2006 12:32 PM
To: Sood, Beena; Betty_Vohr@brown.edu; Susan Hintz; Kennedy, Kathleen A; Maynard Rasmussen, MD; Brenda Poindexter; Morris, Brenda H; D'Angio, Carl; Guillet, Ronnie; Stevens, Timothy; Michael Cotten; Daniel K Benjamin; alaptook@WIHRI.org; Abhik Das; Carlo Waldemar (E-mail); Charles Rosenfeld; Dale Phelps; Ed Donovan; Ehrenkranz Richard (E-mail); Jobe Alan (E-mail); Krisa VanMeurs (VanMeurs, Krisa); Lemons Jim (E-mail); Michael O'Shea; Michelle Walsh; Neil Finer; Oh William (E-mail); Poole Kenneth (E-mail); Ronald GOldberg; Shahnaz Duara; Shankaran Seetha (E-mail); Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); walid.salhab@utsouthwestern.edu
Cc: Petrie, Carolyn; Zaterka-Baxter, Kristin; Betty Hastings
Subject: Network meeting

Hi,
Please send all materials for the steering committee next week by Monday January 9, 2006.

Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B

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301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Webb, Robin E.
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: SUPPORT Trial Mtg.
Date: Thursday, December 29, 2005 9:43:41 AM

Rose,

Dr. D'Alton will be able to call into the meeting around 1pm (see email below). Is that ok?

Thanks,
Robin

-----Original Message-----
From: Brandy Davis-James [mailto:brd2116@columbia.edu]
Sent: Wednesday, December 28, 2005 8:02 AM
To: Webb, Robin E.
Subject: Re: SUPPORT Trial Mtg.

Thanks for your consideration. Dr. D'Alton is available to call in the afternoon, perhaps around 1 p.m. Please advise if this would be suitable.

Thanks for your help.

Sincerely,
Brandi James

Webb, Robin E. wrote:

>Brandi,
>
>I was asked to see if Dr. D'Alton would be available to call into the
>meeting at any time during the day. The meeting is from 8am-3pm
>approximately.
>
>Thanks,
>Robin
>
>-----Original Message-----
>From: Brandy Davis-James [mailto:brd2116@columbia.edu]
>Sent: Wednesday, December 21, 2005 8:17 AM
>To: Webb, Robin E.
>Subject: SUPPORT Trial Mtg.
>
>
>Hi Robin,
>
>This is to advice that Dr. Mary D'Alton will not be able to attend the
>above meeting taking place on January 24th due to a schedule conflict.
>
>Thank you,
>
>Brandi James

>For Dr. Mary D'Alton
>(212) 305-2377
>
>

From: Barbara Stoll
To: Higgins, Rosemary (NIH/NICHD) [E]; Ellen Hale
Subject: Re: SUPPORT ANCILLARY -Emory
Date: Thursday, December 22, 2005 8:43:20 PM

Will do
Will include nursing budget for screeining, collecting, processing and shipping samples and separate Lab Budget.

I assumed that NIH would not cover the lab costs-- Is this correct?
BJS**"Higgins, Rosemary \(NIH/NICHD\) [E]" <higginsr@mail.nih.gov> writes:**
Barbara

Can we get a budget estimate for this project?
Thanks

Rose

From: Barbara Stoll [mailto:barbara.stoll@oz.ped.emory.edu]
Sent: Friday, December 16, 2005 4:13 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT ANCILLARY -Emory

Pkease send the attached to the SUPPORT Subcommittee-- Perhaps need to wait until restarted-- but can share with Neil FIner
BJS

Barbara J. Stoll, MD
George W. Brumley, Jr., Professor and Chair, Department of Pediatrics
Medical Director, Children's Healthcare of Atlanta at Egleston
Office: 404-727-2456 Fax: 404-727-5737
barbara_stoll@oz.ped.emory.edu

----- Original Message -----

Friday, December 16, 2005 12:09:56 PM
Urgent Message
From: [redacted] Theresa Gauthier

Subject: SUPPORT ANCILLARY ? FINAL DRAFT
To: Barbara Stoll
Susie Buchter
Anthony Piazza
LouAnn Brown
Attachments: final Protocol outline NICH.doc 152K

I have attached the ? Final outline for the proposed ancillary study to evaluate the tracheal aspirates, alveolar macrophage from the infants enrolled in SUPPORT trial- Anthony, I apologize for not including you in the earlier email about this proposal- Please review. Barbara please get this to them before their January meeting.

Thanks everybody

TG

Barbara J. Stoll, MD
George W. Brumley, Jr., Professor and Chair, Department of Pediatrics
Medical Director, Children's Healthcare of Atlanta at Egleston
Office: 404-727-2456 Fax: 404-727-5737
barbara_stoll@oz.ped.emory.edu

From:	Webb, Robin E.
To:	ckr3+@pitt.edu; cgleason@u.washington.edu; gavery123@hotmail.com; Willinger, Marian (NIH/NICHD) [E]; rjb6j@hscmail.mcc.viriginia.edu; Hunt, Carl (NIH/NHLBI) [E]; mcallen@jhmi.edu; merran.thomson@lc.ac.uk; nfiner@ucsd.edu; Das, Abhik; Poole, W. Kenneth
Cc:	csd12@columbia.edu; mck6@pitt.edu; milhil@u.washington.edu; poppoff@u.washington.edu; Hastings, Betty J.; Higgins, Rosemary (NIH/NICHD) [E]
Subject:	SUPPORT Trial Meeting
Date:	Thursday, December 22, 2005 11:47:56 AM

Dear DSMC Members,

The meeting to discuss the SUPPORT Trial has been scheduled for January 24, 2006. This meeting will take place in RTI's Rockville, MD office. We will be contacting you regarding your requirements for hotel accommodations. The meeting is tentatively scheduled from 8:30am to 3:00pm. The agenda and all of the particulars regarding this meeting will be forthcoming.

Thank you,

Robin Webb
RTI International
6110 Executive Blvd., Suite 902
Rockville, MD 20853
301-770-8204

From: Webb, Robin E.
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT Trial Meeting
Date: Thursday, December 22, 2005 11:40:16 AM

I'll check with Dr. D'Alton about be available by phone. Meanwhile, I I'll let everyone know that the meeting is set for the 24th.

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, December 22, 2005 11:34 AM
To: Webb, Robin E.
Subject: RE: SUPPORT Trial Meeting

Can Mary D'Alton be available by phone?
Otherwise this is fine.

Thanks for all your help!!

Rose

From: Webb, Robin E. [mailto:rwebb@rti.org]
Sent: Thursday, December 22, 2005 11:32 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT Trial Meeting

Rose,

I just heard back from Dr. Hunt's assistant. He will be able to attend the meeting on the 24th. I also heard from Dr. D'Alton she will not be able to attend the 24th. Is that ok? Should I send out an email confirming the meeting for the 24th?

Thanks,
Robin

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, December 22, 2005 8:38 AM
To: Webb, Robin E.
Subject: RE: SUPPORT Trial Meeting

Robin – can you re-contact him today both by email and phone?
Thanks
Rose

From: Webb, Robin E. [mailto:rwebb@rti.org]
Sent: Thursday, December 22, 2005 7:20 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT Trial Meeting

Hi Rose,

Just wanted to let you know that I still haven't heard from Dr. Hunt

or his assistant. I've called and sent emails but no response. I will be going out of town tomorrow through Wednesday, 12/28. What would you like me to do at this point?

Thanks,
Robin

Robin Webb
RTI International
6110 Executive Blvd., Suite 902
Rockville, MD 20853
301-770-8204

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: OWL
Date: Monday, December 19, 2005 5:49:48 PM

Hi Rose
We have permission to use the OWL documents for SUPPORT.
Neil

-----Original Message-----
From: Margaret Thibodeaux [mailto:mthibodeaux@ochsner.org]
Sent: Monday, December 19, 2005 11:26 AM
To: nfiner@ucsd.edu
Subject: RE: OWL

Thank you and you are welcome to use and/or reproduce any of the materials.

>>> "Neil Finer" <nfiner@ucsd.edu> 12/15/05 03:32PM >>>
Hello Margaret
Many thanks for this.
I congratulate you for developing this program. May we use this and reproduce the materials for the Network Sites?
Regards
Neil Finer

-----Original Message-----
From: Margaret Thibodeaux [mailto:mthibodeaux@ochsner.org]
Sent: Thursday, December 15, 2005 7:24 AM
To: nfiner@ucsd.edu
Subject: OWL

Enclosed is the information that you requested from Dr. Goldsmith. Attached are the documents we used to get started. There is the Potentially Better Practice Sheet, The contract we had each employee sign, a copy of the Logo, the worksheet for data collection, a copy of the bedside summary, (was laminated and placed at each OWL's bedside), and the form used to do the q shift walk throughs for compliance.

We did not have any special materials for the family. There was a copy of the protocol guidelines attached to each OWL's bedside, and for those who asked, an explanation of the protocol was given.
We did not get any negative feedback from the staff in relation to the families, just a sense of a greater need of awareness for the nurses and therapists at the bedside.
When we initiated the protocol all babies under 1500 gms were but on the protocol, even those that had been with us prior to the date of initiation.
We did not experience any complaints or major problems with the implementation or the families awareness of it.
I also attached a power point presentation that we used to initiate the education to the unit.We started with the Neo Docs and had them all agree that this would be a change of policy and unit protocol to be followed by all unless an order was written with a substantiated reason for not following the protocol.
The frequent alarms and frequent changes in the o2 sats and requirements are part of the deal. We found there is a period of time that all of the micro

premies experience this and it stops with time. It can be very challenging for the bedside nurse. You may find the contract helpful. We also found the nurses took personal responsibility for making sure their primary did not need cryo.
We also have a large amount of very senior staff. We did have small amount of trouble with compliance in the beginning.
We did a large amount of education prior to initiating the change. We published (in the unit) our numbers compared to the national average, (our numbers were much worse). I kept the staff updated with current data, what their compliance was as well as our ongoing ROP numbers.

From: Webb, Robin E.
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT Trial Meeting
Date: Monday, December 19, 2005 1:12:21 PM

I called his assistant but haven't heard back yet.

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, December 19, 2005 9:53 AM
To: Webb, Robin E.
Subject: Re: SUPPORT Trial Meeting

We need to have Dr. Hunt - can you contact him by phone?
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Webb, Robin E. <rwebb@rti.org>
To: Higgins, Rosemary (NIH/NICHD) [E] <higginsr@mail.nih.gov>
Sent: Mon Dec 19 09:50:34 2005
Subject: SUPPORT Trial Meeting

Hi Rose,

I still haven't heard whether Dr. Hunt will be able to attend the meeting on the 24th. Should I send out an email to the rest of the members confirming the date so they'll have it on their calendars? Or do you want to wait to hear from Dr. Hunt?

Thanks,
Robin

Robin Webb
RTI International
6110 Executive Blvd., Suite 902
Rockville, MD 20853
301-770-8204

From: Berberich, Mary Anne (NIH/NHLBI) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT DSMC
Date: Monday, December 19, 2005 12:49:20 PM

At this point in time : YES

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Friday, December 16, 2005 10:54 AM
To: Berberich, Mary Anne (NIH/NHLBI) [E]
Cc: 'bkh@rti.org'
Subject: SUPPORT DSMC

Hi Mary Ann

It looks the the SUPPORT DSMC will meet on 1/24/06 in person in Rockville - can you attend the open portion of the meeting? Thanks Rose

---

Sent from my BlackBerry Wireless Handheld

From:	Neil Finer
To:	"Brenda Poindexter"; timothy_stevens@urmc.rochester.edu; "Dale Phelps"
Cc:	Higgins, Rosemary (NIH/NICHD) [E]; "Carolyn Petrie"
Subject:	RE: SUPPORT - pulmonary outcomes study
Date:	Tuesday, December 13, 2005 11:58:37 AM

Hi Everyone
Sorry for the delay, now extended probably till the New Year.
I am hopeful that we can proceed. We need to present our case as soon as possible.
All the best for the Holidays
Neil

-----Original Message-----
From: Brenda Poindexter [mailto:bpoindex@iupui.edu]
Sent: Monday, December 12, 2005 11:31 AM
To: timothy_stevens@urmc.rochester.edu; Dale Phelps; Neil Finer
Cc: Rosemary Higgins; Carolyn Petrie
Subject: SUPPORT - pulmonary outcomes study

Tim,
Our research coordinator, Lucy Miller, told me this morning that you are requesting that we proceed with IRB submission for your secondary study. Unfortunately, with the main trial currently on hold pending Neil's response to the DSMC, we will not be able to submit any of the secondary studies to our IRB until we have the official word that we can resume enrollment in SUPPORT. In the meantime, we will get everything ready for submission, working under the assumption that we will resume enrollment in the near future - but until we get the official green light from the DSMC and NICHD, the IRB will not be able to even consider any proposals for secondary or ancillary studies. Please let me know if you have any questions regarding this.
Brenda

From:	Hastings, Betty J.
To:	Hastings, Betty J.; ckr3+@pitt.edu; cgleason@u.washington.edu; Personal Email D'Alton, Mary (NIH/NICHD); Willinger, Marian (NIH/NICHD) [E]; Hunt, Carl (NIH/NHLBI) [E]; mcallen@jhmi.edu; merran.thomson@ic.ac.uk; rjb6j@hscmail.mcc.virginia.edu; Higgins, Rosemary (NIH/NICHD) [E]; nfiner@ucsd.edu; Berberich, Mary Anne (NIH/NHLBI) [E]
Cc:	mck6@pitt.edu; milhil@u.washington.edu; poppoff@u.washington.edu; Simon, Malinda (NIH/NHLBI) [C]; Perez, Tania (NIH/NHLBI) [C]; zlv2102@columbia.edu; Das, Abhik; Poole, W. Kenneth; Zaterka-Baxter, Kristin; Gantz, Marie
Subject:	RE: SUPPORT Conference Call
Date:	Monday, December 12, 2005 2:37:32 PM
Importance:	High

Dear DSMC Members,
Due to the complexity of the SUPPORT Trial, the Chair of the DSMC has appropriately requested a face-to-face meeting with the members. Therefore, the conference call has been cancelled for tomorrow. We are in the process of trying to schedule a meeting and will be in touch with you regarding your availability to attend a meeting sometime in January.

Thank you.
Betty

Betty Hastings
RTI International
Statistic Research Division
P.O. Box 12194
Research Triangle Park, NC 7709-2194
Telephone: (919) 485-7740
Fax: (919) 485-7762
e-mail: bkh@rti.org

From: Neil Finer
To: "Petrie, Carolyn"
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Draft SC agenda
Date: Monday, December 12, 2005 12:18:18 PM

Hi Carolyn
I will need to attend the "Emergency Research in Children" meeting being held on the same 2 days at the Bethesda Marriott as the Steering Committee
Could I ask that The SUPPORT Subcommittee meeting be held at 7:00 AM on the Thursday till 8:30AM and that I be the first presenter for the Friday meeting at 7:30 AM. I will then need to leave to be at the other meeting.
I hope you can accommodate this request.
Many thanks
Neil

From: Petrie, Carolyn [mailto:petrie@rti.org]
Sent: Monday, December 12, 2005 6:43 AM
To: bsood@med.wayne.edu; Brenda.H.Morris@uth.tmc.edu; bpoindex@iupui.edu; Carl_Dangio@urmc.rochester.edu; BENJA005@dcri.duke.edu; vanmeurs@leland.stanford.edu; kurt.schibler@cchmc.org; mblakely@utmem.edu; ambal@sprynet.com; cotte010@mc.duke.edu; Ronnie_Guillet@urmc.rochester.edu; poo@rti.org; barbara_stoll@oz.ped.emory.edu; Charles.Rosenfeld@UTSouthwestern.edu; dale_phelps@urmc.rochester.edu; Das, Abhik; dstevenson@stanford.edu; edward.donovan@chmcc.org; goldb008@mc.duke.edu; higginsr@mail.nih.gov; jlemons@iupui.edu; Jobea0@chmcc.org; jon.e.tyson@uth.tmc.edu; alaptook@WIHRI.org; mcw3@cwru.edu; moshea@wfubmc.edu; nfiner@ucsd.edu; richard.ehrenkranz@yale.edu; sduara@miami.edu; sshankar@med.wayne.edu; wcarlo@peds.uab.edu; WOh@WIHRI.org; Nancy.Miller@UTSouthwestern.edu; ae5357@wayne.edu; ahensman@WIHRI.org; auten002@mc.duke.edu; ellen_hale@oz.ped.emory.edu; Georgia.E.McDavid@uth.tmc.edu; grisbyca@email.uc.edu; linda_reubens@urmc.rochester.edu; lucmille@iupui.edu; mbball@leland.stanford.edu; mcollins@peds.uab.edu; Monica.konstantino@yale.edu; nxs5@cwru.edu; npeters@wfubmc.edu; reverett@med.miami.edu; wrich@ucsd.edu
Cc: Hastings, Betty J.; Poole, W. Kenneth; Zaterka-Baxter, Kristin; Auman, Jeanette O.; Gantz, Marie; bking@mednet.swmed.edu; Pagliaro, Susan (NIH/NICHD); Petrie, Carolyn
Subject: Draft SC agenda

Attached is the draft agenda for the January 12-13 NRN Steering Committee.

Carolyn Petrie Huitema
Neonatal Research Network Coordinator
RTI International
6110 Executive Blvd
Suite 902
Rockville, MD 20852
ph. (301) 230-4648
fx. (301) 230-4646

From: Barbara Stoll
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT
Date: Sunday, December 11, 2005 12:07:19 PM

Thanks Rose
I had a nice conversation with Neil Finer-- who really does deserve to be thanked for his professional approach
BJS"Higgins, Rosemary \(NIH/NICHD\) [E]" <higginsr@mail.nih.gov> writes:
>Barbara
>Thanks for taking the time for speaking to me about the SUPPORT issue
>and, above all, your professional approach!
>Have a nice weekend!
>Rose
>----------
>Sent from my BlackBerry Wireless Handheld

Barbara J. Stoll, MD
George W. Brumley, Jr., Professor and Chair, Department of Pediatrics
Medical Director, Children's Healthcare of Atlanta at Egleston
Office: 404-727-2456 Fax: 404-727-5737
barbara_stoll@oz.ped.emory.edu

From:	Neil Finer
To:	"Hastings, Betty J."
Cc:	Higgins, Rosemary (NIH/NICHD) [E]; wrich@ucsd.edu
Subject:	RE:
Date:	Monday, December 05, 2005 5:00:17 PM

Betty
I have spoken to Rose
Please hold sending anything to the DSMC till the morning. I will get all the newer info to you by then
Many thanks
Neil

From: Hastings, Betty J. [mailto:bkh@rti.org]
Sent: Monday, December 05, 2005 7:38 AM
To: nfiner@ucsd.edu
Subject: RE:

Great. So are we waiting for anything else? Here is what I plan
to send:

Marie's table-12-2-05
Your letter to the DSMC--Dated 11-30-05
The response to the DSMC -Dated 12-4-05
The UCSD1 file
Late Breaker abstract
Askie NEJM paper
STOP_ROP paper
The SUPPORT protocol

If you want to send the power point presentation, I can send that later by e-mail.
I plan to send this Fed-Ex so if you need to have any additional material sent, please let me know. I'll wait until tomorrow send it.
Thanks.
Betty
-----Original Message-----
From: Neil Finer [mailto:nfiner@ucsd.edu]
Sent: Monday, December 05, 2005 10:27 AM
To: Hastings, Betty J.
Cc: Das, Abhik; 'Higgins, Rosemary (NIH/NICHD)'
Subject: RE:

> Hi Betty
> I would think that we should send Marie's latest Table which I have attached.
> Thanks
> Neil
>
> ---
>
> **From:** Hastings, Betty J. [mailto:bkh@rti.org]
> **Sent:** Monday, December 05, 2005 5:39 AM
> **To:** Neil Finer
> **Cc:** Das, Abhik
> **Subject:** RE:
> **Importance:** High
>
> Neil,
> I will use your latest response to the DSMC (dated 12-4) but please let me know if I should send

this latest table:

Percent of time spent at each SpO2 value (data processed as of 12/02/2005).

I wanted to make sure that I send the latest versions to the DSMC.

Thanks.

Betty

-----Original Message-----

From: Neil Finer [mailto:nfiner@ucsd.edu]

Sent: Sunday, December 04, 2005 10:51 PM

To: "Higgins, Rosemary (NIH/NICHD)' '; 'Avroy A. Fanaroff, M.D.'; Hastings, Betty J.; Das, Abhik; 'Ed Donovan'; Poole, W. Kenneth; Maynard Rasmussen; 'Michele'; 'Neil Finer'; 'Shahnaz Duara'; 'Wade Rich'; 'Wally Carlo'

Subject:

Hi Rose and Everyone

I have asked Marie to do some analyses for FiO2. I think that our response as written in the attached revision - - Dec 4 – is the one that should go forward to the DSMC

I prepared a PowerPoint presentation. Once we see the FiO2 data, we can decide how or if to use them. I would like your opinions as to whether I should use this with the DSMC during the phone call by circulating it to them in advance.

I will be on service this week but will keep close to the email and phone.

Be well

Neil

From: Hastings, Betty J.
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: DSMC SUPPORT Conference Call
Date: Friday, December 02, 2005 9:09:20 AM

Sorry, but one more question. Will there be any other PI besides Neil on the call? I wanted to make sure that Robin reserved enough lines.

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Friday, December 02, 2005 9:08 AM
To: Hastings, Betty J.
Subject: RE: DSMC SUPPORT Conference Call

I am checking with Neil, though it is only 6 AM in California
Rose

From: Hastings, Betty J. [mailto:bkh@rti.org]
Sent: Friday, December 02, 2005 9:06 AM
To: Higgins, Rosemary (NIH/NICHD)
Cc: Das, Abhik
Subject: RE: DSMC SUPPORT Conference Call

Yes, I believe Neil sent them. I'll plan to send them the following:
Agenda and list of participants
List of members with their specialty, etc.
SUPPORT Protocol
Letter of Response from the Steering Committee
The two abstracts.

Anything else?

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Friday, December 02, 2005 9:00 AM
To: Hastings, Betty J.
Subject: RE: DSMC SUPPORT Conference Call

The PI's had until last night to weight in – Neil will do it today.

Can we also send the Hagadorn abstract and the Case Western Abstract to them? Do you have the files for both?
Thanks
Rose

From: Hastings, Betty J. [mailto:bkh@rti.org]
Sent: Friday, December 02, 2005 8:58 AM
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE: DSMC SUPPORT Conference Call

Do you know when the letter will be ready to send out to the DSMC?

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Friday, December 02, 2005 8:56 AM

To: Hastings, Betty J.
Subject: RE: DSMC SUPPORT Conference Call

Yes,
Neonatology, bioethics

From: Hastings, Betty J. [mailto:bkh@rti.org]
Sent: Friday, December 02, 2005 8:55 AM
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE: DSMC SUPPORT Conference Call

Thanks so much. Do you have this for Robert Boyle?

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Friday, December 02, 2005 8:54 AM
To: Hastings, Betty J.
Subject: RE: DSMC SUPPORT Conference Call

Avery – Neonatology, Clinical trials
D'Alton – Obstetrics, maternal fetal medicine, antenatal screening
Gleason- Neonatology, cerebral-vascular physiology
Carol Redmond – biostatistics
Marian Willinger – control of breathing, SIDS

Merrin Tompson – Neonatology, Respiratory physiology
Carl Hunt – Neonatology, Sleep, sleep apnea
Marilee Allen – Neonatology, high risk infant follow up, neurodevelopment

---

From: Hastings, Betty J. [mailto:bkh@rti.org]
Sent: Friday, December 02, 2005 8:41 AM
To: Higgins, Rosemary (NIH/NICHD)
Subject: FW: DSMC SUPPORT Conference Call

Rose,
Could you help me with this? The DSMC members could also be characterized as to specialty. I not sure that I have this.
Thank you.
Betty
-----Original Message-----
From: Gordon Avery [mailto:Personal Email
Sent: Friday, December 02, 2005 8:35 AM
To: Webb, Robin E.
Cc: Hastings, Betty J.
Subject: Re: DSMC SUPPORT Conference Call

I have the Dec 13 call on my calendar. Please send, ahead of time, the current roster of DSMC Committee, NIH rep, RTI major players, with e-mail and phone numbers. The DSMC members could also be characterized as to specialty. This will aid us all in being present to one another under the current practice of no meetings, all conference calls. In light of what we will be discussing, we should also have, in advance of the call, the SUPPORT protocol and the Steering Committee proposal for continuing, if there is such. We need to do reading and thinking in advance of the call. Thanks. Gordon

----- Original Message -----

From: Webb, Robin E.
To: cgleason@u.washington.edu ; ckr3+@pitt.edu ; gavery123@hotmail.com ; md511@columbia.edu ; [SCRN] Willinger, Marian ; rjb6j@hscmail.mcc.virginia.edu ; huntc@nhlbi.nih.gov ; mcallen@jhmi.edu ; merran.thomson@ic.ac.uk ; nfiner@ucsd.edu ; Das, Abhik ; Poole, W. Kenneth
Cc: csd12@columbia.edu ; mck6@pitt.edu ; milhil@u.washington.edu ; poppoff@u.washington.edu ; Hastings, Betty J.
Sent: Friday, December 02, 2005 7:57 AM
Subject: DSMC SUPPORT Conference Call

The DSMC SUPPORT conference call is scheduled for Tuesday, December 13 from 2pm-3:30pm ET. An email with all the details will be sent out soon.

Thanks,
Robin

Robin Webb
RTI International
6110 Executive Blvd., Suite 902
Rockville, MD 20853
301-770-8204

From: Das, Abhik
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: DSMC SUPPORT Conference Call
Date: Friday, December 02, 2005 8:59:00 AM

Not sure whether you got this...

-----Original Message-----

From: Webb, Robin E.

Sent: Friday, December 02, 2005 7:57 AM

To: cgleason@u.washington.edu; ckr3+@pitt.edu; M. D. Gordon Avery Personal Email; md511@columbia.edu; [SCRN] Willinger, Marian; rjb6j@hscmail.mcc.viriginia.edu; Carl E. Hunt (huntc@nhlbi.nih.gov); Marilee C. Allen (mcallen@jhmi.edu); Merran A. Thomson (merran.thomson@ic.ac.uk); Neil Finer (nfiner@ucsd.edu); Das, Abhik; Poole, W. Kenneth

Cc: Chef Davis (csd12@columbia.edu); mck6@pitt.edu; milhil@u.washington.edu; Sean Poppoff (poppoff@u.washington.edu); Hastings, Betty J.

Subject: DSMC SUPPORT Conference Call

The DSMC SUPPORT conference call is scheduled for Tuesday, December 13 from 2pm-3:30pm ET. An email with all the details will be sent out soon.

Thanks,
Robin

Robin Webb
RTI International
6110 Executive Blvd., Suite 902
Rockville, MD 20853
301-770-8204

From: Hastings, Betty J.
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: DSMC SUPPORT Conference Call
Date: Friday, December 02, 2005 8:41:56 AM

You much have read my mind!

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Friday, December 02, 2005 8:39 AM
To: Hastings, Betty J.
Subject: RE: DSMC SUPPORT Conference Call

Betty
Let me know if you need any help with this, especially the expertise areas.

Rose

From: Hastings, Betty J. [mailto:bkh@rti.org]
Sent: Friday, December 02, 2005 8:38 AM
To: Gordon Avery
Cc: Higgins, Rosemary (NIH/NICHD)
Subject: RE: DSMC SUPPORT Conference Call

Dr. Avery,
I will get the requested material to you by early next week. Thanks so much.
Betty

-----Original Message-----
From: Gordon Avery [mailto Personal Email]
Sent: Friday, December 02, 2005 8:35 AM
To: Webb, Robin E.
Cc: Hastings, Betty J.
Subject: Re: DSMC SUPPORT Conference Call

I have the Dec 13 call on my calendar. Please send, ahead of time, the current roster of DSMC Committee, NIH rep, RTI major players, with e-mail and phone numbers. The DSMC members could also be characterized as to specialty. This will aid us all in being present to one another under the current practice of no meetings, all conference calls. In light of what we will be discussing, we should also have, in advance of the call, the SUPPORT protocol and the Steering Committee proposal for continuing, if there is such. We need to do reading and thinking in advance of the call. Thanks. Gordon

----- Original Message -----
From: Webb, Robin E.
To: cgleason@u.washington.edu ; ckr3+@pitt.edu ; gavery123@hotmail.com ; md511@columbia.edu ; [SCRN] Willinger, Marian ; rjb6j@hscmail.mcc.viriginia.edu ; huntc@nhlbi.nih.gov ; mcallen@jhmi.edu ; merran.thomson@ic.ac.uk ; nfiner@ucsd.edu ; Das, Abhik ; Poole, W. Kenneth
Cc: csd12@columbia.edu ; mck6@pitt.edu ; milhil@u.washington.edu ; poppoff@u.washington.edu ; Hastings, Betty J.
Sent: Friday, December 02, 2005 7:57 AM
Subject: DSMC SUPPORT Conference Call

The DSMC SUPPORT conference call is scheduled for Tuesday, December 13 from 2pm-3:30pm ET. An email with all the details will be sent out soon.

Thanks,
Robin

Robin Webb
RTI International
6110 Executive Blvd., Suite 902
Rockville, MD 20853
301-770-8204

From: Petrie, Carolyn
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: SUPPORT conference call
Date: Tuesday, November 29, 2005 9:30:52 AM
Importance: High

From: Alan Jobe [mailto:Alan.Jobe@cchmc.org]
Sent: Thursday, November 24, 2005 8:08 AM
To: Petrie, Carolyn
Subject: Re: SUPPORT conference call
Importance: High

On 11/23/05 9:58 AM, "Petrie, Carolyn" <petrie@rti.org> wrote:

Please send your availably for this urgent and important conference call regarding the SUPPORT trial.

I will schedule a SUPPORT subcommittee call first (Mon or Tues) and then a second call with the NRN PIs (Wed or Thurs).

If you are unable, please send the availability for the Alt-PI or trial PI at the site.

Mon Nov 28 –OK – except 10-11, after 5

Tues Nov 29 – OK before 130

Wed Dec 1 Out of town

Thurs Dec 2 OK except 12-1

--

Alan H Jobe MD Phd
Prof of Pediatrics/Neonatology
Cincinnati Childrens Hospital
3333 Burnet Ave, Cincinnati OH, 45229
Ph - 5136368563
Fax - 5136368691
Alan.jobe@cchmc.org

Thank you!

Carolyn Petrie Huitema

Neonatal Research Network Coordinator

RTI International

6110 Executive Blvd

Suite 902

Rockville, MD 20852

ph. (301) 230-4648

fx. (301) 230-4646

From: Shankaran, Seetha
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: SUPPORT conference call
Date: Thursday, November 24, 2005 1:40:12 PM
Importance: High

Rose
when I talked to you, I was so exhausted I forgot to ask why the DSMB wanted it stopped---only because of lack of separation of 2 oxygen saturation levels?
Have a wonderful Thanksgiving---take it easy on the turkey and football
Thanks
Seetha

-----Original Message-----
From: Petrie, Carolyn [mailto:petrie@rti.org]
Sent: Wednesday, November 23, 2005 9:59 AM
To: poo@rti.org; barbara_stoll@oz.ped.emory.edu; Charles.Rosenfeld@UTSouthwestern.edu; dale_phelps@urmc.rochester.edu; Das, Abhik; dstevenson@stanford.edu; edward.donovan@chmcc.org; goldb008@mc.duke.edu; higginsr@mail.nih.gov; jlemons@iupui.edu; Jobea0@chmcc.org; jon.e.tyson@uth.tmc.edu; alaptook@WIHRI.org; mcw3@cwru.edu; moshea@wfubmc.edu; nfiner@ucsd.edu; richard.ehrenkranz@yale.edu; sduara@miami.edu; Shankaran, Seetha; wcarlo@peds.uab.edu; WOh@WIHRI.org
Cc: Alice.J.Reardon@uth.tmc.edu; aellison@med.miami.edu; echaisso@iupui.edu; Personal Email diane.timmer@cchmc.org; fmartinez@ucsd.edu; Karen.Kirby@UTSouthwestern.edu; debra.camputaro@yale.edu; Townsend, Katrice; KGilley@CareNE.org; lisa.joo@stanford.edu; msumner@peds.uab.edu; mazie_tinsley@oz.ped.emory.edu; renee.dunbar-scott@oz.ped.emory.edu; Jensen, Rosemary; gonza025@mc.duke.edu; Wendy Holcomb; Hastings, Betty J.; Zaterka-Baxter, Kristin; Petrie, Carolyn; Gantz, Marie; wrich@ucsd.edu
Subject: SUPPORT conference call
Importance: High

Please send your availably for this urgent and important conference call regarding the SUPPORT trial. I will schedule a SUPPORT subcommittee call first (Mon or Tues) and then a second call with the NRN PIs (Wed or Thurs).

If you are unable, please send the availability for the Alt-PI or trial PI at the site.

Mon Nov 28
Tues Nov 29
Wed Dec 1
Thurs Dec 2

Thank you!

Carolyn Petrie Huitema
Neonatal Research Network Coordinator
RTI International
6110 Executive Blvd
Suite 902
Rockville, MD 20852
ph. (301) 230-4648
fx. (301) 230-4646

From: Tyson, Jon E
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT PI CALL
Date: Wednesday, November 23, 2005 3:47:00 PM

No though I really want to be. (I believe Alice told Carolyn when I would be unavailable- please let me know if there was a mix up).

Jon E. Tyson, MD, MPH
Center for Clinical Research & Evidence-Based Medicine
UT Medical School at Houston
6431 Fannin St., MSB 2.106
Houston, TX 77030
voice 713-500-5651
fax 713-500-0519

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, November 23, 2005 1:41 PM
To: Tyson, Jon E
Subject: SUPPORT PI CALL

Jon
Would you be available on Wed. Nov 30 from 9:30-1030 AM EST (8:30-9:30 CST)?
Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Barbara Stoll
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Renee Dunbar-Scott
Subject: Re: FW: SUPPORT conference call
Date: Wednesday, November 23, 2005 2:01:05 PM

Nov 30-- OK after 3:45
Dec 1-- OK after 4
BJS

Barbara J. Stoll, MD
George W. Brumley, Jr., Professor and Chair, Department of Pediatrics
Medical Director, Children's Healthcare of Atlanta at Egleston
Office: 404-727-2456 Fax: 404-727-5737
barbara_stoll@oz.ped.emory.edu

From:	William Oh
To:	Petrie, Carolyn; poo@rti.org; barbara_stoll@oz.ped.emory.edu; Charles.Rosenfeld@UTSouthwestern.edu; dale_phelps@urmc.rochester.edu; Das, Abhik; dstevenson@stanford.edu; edward.donovan@chmcc.org; goldb008@mc.duke.edu; Higgins, Rosemary (NIH/NICHD) [E]; jlemons@iupui.edu; Jobea0@chmcc.org; jon.e.tyson@uth.tmc.edu; Abbot Laptook; mcw3@cwru.edu; moshea@wfubmc.edu; nfiner@ucsd.edu; richard.ehrenkranz@yale.edu; sduara@miami.edu; sshankar@med.wayne.edu; wcarlo@peds.uab.edu
Cc:	Alice.J.Reardon@uth.tmc.edu; aellison@med.miami.edu; echaisso@iupui.edu; cdg2749@yahoo.com; diane.timmer@cchmc.org; fmartinez@ucsd.edu; Karen.Kirby@UTSouthwestern.edu; debra.camputaro@yale.edu; Ktownsen@med.wayne.edu; Kellye Gilley; lisa.joo@stanford.edu; msumner@peds.uab.edu; mazie_tinsley@oz.ped.emory.edu; renee.dunbar-scott@oz.ped.emory.edu; Jensen, Rosemary; gonza025@mc.duke.edu; Wendy Holcomb; Hastings, Betty J.; Zaterka-Baxter, Kristin; Gantz, Marie; wrich@ucsd.edu
Subject:	RE: SUPPORT conference call
Date:	Wednesday, November 23, 2005 11:30:23 AM

Carolyn:I am available all next week

Bill

From: Petrie, Carolyn [mailto:petrie@rti.org]
Sent: Wednesday, November 23, 2005 9:59 AM
To: poo@rti.org; barbara_stoll@oz.ped.emory.edu; Charles.Rosenfeld@UTSouthwestern.edu; dale_phelps@urmc.rochester.edu; Das, Abhik; dstevenson@stanford.edu; edward.donovan@chmcc.org; goldb008@mc.duke.edu; higginsr@mail.nih.gov; jlemons@iupui.edu; Jobea0@chmcc.org; jon.e.tyson@uth.tmc.edu; Abbot Laptook; mcw3@cwru.edu; moshea@wfubmc.edu; nfiner@ucsd.edu; richard.ehrenkranz@yale.edu; sduara@miami.edu; sshankar@med.wayne.edu; wcarlo@peds.uab.edu; William Oh
Cc: Alice.J.Reardon@uth.tmc.edu; aellison@med.miami.edu; echaisso@iupui.edu; [redacted]; diane.timmer@cchmc.org; fmartinez@ucsd.edu; Karen.Kirby@UTSouthwestern.edu; debra.camputaro@yale.edu; Ktownsen@med.wayne.edu; Kellye Gilley; lisa.joo@stanford.edu; msumner@peds.uab.edu; mazie_tinsley@oz.ped.emory.edu; renee.dunbar-scott@oz.ped.emory.edu; Jensen, Rosemary; gonza025@mc.duke.edu; Wendy Holcomb; Hastings, Betty J.; Zaterka-Baxter, Kristin; Petrie, Carolyn; Gantz, Marie; wrich@ucsd.edu
Subject: SUPPORT conference call
Importance: High

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Mon Nov 28
Tues Nov 29
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Thank you!

Carolyn Petrie Huitema
Neonatal Research Network Coordinator
RTI International
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Rockville, MD 20852
ph. (301) 230-4648
fx. (301) 230-4646

From:	Petrie, Carolyn
To:	poo@rti.org; barbara_stoll@oz.ped.emory.edu; Charles.Rosenfeld@UTSouthwestern.edu; dale_phelps@urmc.rochester.edu; Das, Abhik; dstevenson@stanford.edu; edward.donovan@chmcc.org; goldb008@mc.duke.edu; Higgins, Rosemary (NIH/NICHD) [E]; jlemons@iupui.edu; Jobea0@chmcc.org; jon.e.tyson@uth.tmc.edu; alaptook@WIHRI.org; mcw3@cwru.edu; moshea@wfubmc.edu; nfiner@ucsd.edu; richard.ehrenkranz@yale.edu; sduara@miami.edu; sshankar@med.wayne.edu; wcarlo@peds.uab.edu; WOh@wihri.org
Cc:	Alice.J.Reardon@uth.tmc.edu; aellison@med.miami.edu; echaisso@iupui.edu; cdg2749@yahoo.com; diane.timmer@cchmc.org; fmartinez@ucsd.edu; Karen.Kirby@UTSouthwestern.edu; debra.camputaro@yale.edu; Ktownsen@med.wayne.edu; KGilley@CareNE.org; lisa.joo@stanford.edu; msumner@peds.uab.edu; mazie_tinsley@oz.ped.emory.edu; renee.dunbar-scott@oz.ped.emory.edu; Jensen, Rosemary; gonza025@mc.duke.edu; Wendy Holcomb; Hastings, Betty J.; Zaterka-Baxter, Kristin; Petrie, Carolyn; Gantz, Marie; wrich@ucsd.edu
Subject:	SUPPORT conference call
Date:	Wednesday, November 23, 2005 9:58:37 AM
Importance:	High

Please send your availably for this urgent and important conference call regarding the SUPPORT trial. I will schedule a SUPPORT subcommittee call first (Mon or Tues) and then a second call with the NRN PIs (Wed or Thurs).

If you are unable, please send the availability for the Alt-PI or trial PI at the site.

Mon Nov 28
Tues Nov 29
Wed Dec 1
Thurs Dec 2

Thank you!

Carolyn Petrie Huitema
Neonatal Research Network Coordinator
RTI International
6110 Executive Blvd
Suite 902
Rockville, MD 20852
ph. (301) 230-4648
fx. (301) 230-4646

From: Kathy J Auten
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Ronald N Goldberg; cotte010@mc.duke.edu
Subject: Re: SUPPORT
Date: Tuesday, November 22, 2005 3:25:31 PM

Duke is fine. Have a good holiday.
Kathy

Kathy J. Auten, BA, MSHS
Neonatal Research Coordinator
Duke University Medical Center
Box 3179
Durham, NC 27710 USA
919-681-5859 tel
919-681-4868 fax
kathy.auten@duke.edu

"Higgins, Rosemary \(NIH/NICHD\)" <higginsr@mail.nih.gov> wrote on 11/22/2005 11:26:11 AM:

> Hi everyone,
> Since Thanksgiving may be a four day holiday at many institutions,
> please assess your SUPPORT oximeters TODAY. If you think you may
> need additional oximeters over the long holiday weekend, let me know
> ASAP so that we insure time for shipping.
>
> Happy Thanksgiving to Everyone!!!
> Rose
>
> Rosemary D. Higgins, M.D.
> Program Scientist for the Neonatal Research Network
> Pregnancy and Perinatology Branch
> Center for Developmental Biology and Perinatal Medicine
> NICHD, NIH
> 6100 Executive Blvd., Room 4B03B
> MSC 7510
> Bethesda, MD 20892
> (For overnight delivery, use Rockville, MD 20852)
> 301-435-7909
> 301-496-3790 (FAX)
> higginsr@mail.nih.gov
>

From: Newman, Jamie
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT Breathing Outcomes Study
Date: Tuesday, November 22, 2005 1:18:51 PM

Hi Rose,
Is there any reason why I should not send out the final versions of the Breathing Outcomes Manual and Forms as I had planned to later today? Also, it looks like that Friday Dec 9 and either Dec 12 or Dec 13 will work for the coordinators for the two Breathing Outcomes interview trainings to be conducted by telephone.

Thanks, Jamie

Jamie E. Newman, MPH
Statistics and Epidemiology
RTI International
Telephone: (919) 485-5719
Fax: (919) 485-7762
newman@rti.org

From:	Michele Walsh
To:	Phelps, Dale; Higgins, Rosemary (NIH/NICHD) [E]
Cc:	Williams, Angelia; Siner, Bonnie; Newman, Nancy; Wilson-Costello, Dee; Hack, Maureen
Subject:	Pulmonary Outcome Secondary to SUPPORT
Date:	Monday, November 21, 2005 11:06:29 AM

HI:
After much discussion, the Case follow-up team has decided that it will be best for
our site to do the interviews here in clinic. Please correct your records, and let us know what, if any, training will need to be done. How will we track when someone is due for their interviews? Will a schedule be generated with the monthly reports?
Thanks
Michele Walsh
Dale: pls forward to Tim Stevens, I do not have his email.

From: Ellen Hale
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT death
Date: Sunday, November 13, 2005 2:21:40 AM

From:	Newman, Jamie
To:	Betty Vohr
Cc:	Higgins, Rosemary (NIH/NICHD) [E]
Subject:	Study title for SUPPORT Pulmonary Outcomes Study
Date:	Thursday, November 03, 2005 12:29:22 PM

Betty,

We (mostly Tim Stevens) have made all the changes discussed on Tuesday's conference call except for the change in study title. After we hung up, we were unsure whether the title of the study should change on all study documents (protocol, MOP, sample consents and forms) or only on the sample consent forms that are submitted to the IRBs. You described the need for a two syllable study title and 8th grade reading level for your consent forms. Did you mean that the two syllable title should be applied to all documents or only those that are read by families? The title that was agreed on during the call was "Breathing Outcomes Study". Should this be the official title for all study documents?

Would it be possible to have the follow-up coordinators join a portion of the regularly scheduled Coordinators' call on Thurs Nov 17 to discuss the "Breathing Outcomes Study" as we previously discussed on the last coordinators' call? I am waiting to confirm Tim Stevens' availability that day.

Thanks, Jamie

Jamie E. Newman, MPH
Statistics Research Division
RTI International
Telephone: (919) 485-5719
Fax: (919) 485-7762
newman@rti.org

From:	Neil Finer
To:	"Abbot Laptook"; "Hastings, Betty J."; Wade Rich
Cc:	"Angelita Hensman"; Higgins, Rosemary (NIH/NICHD) [E]
Subject:	RE: Masimo oximeters--Display Range
Date:	Thursday, October 27, 2005 5:54:47 PM

Hi Abbot
This is the easiest way for use to look at the data. We use any oxygen that resulted in coding the infant on oxygen for that day.
Neil

From: Abbot Laptook [mailto:ALaptook@WIHRI.org]
Sent: Thursday, October 27, 2005 5:19 AM
To: Hastings, Betty J.; nfiner@ucsd.edu; wrich@ucsd.edu
Cc: Angelita Hensman; HigginsR@mail.nih.gov
Subject: RE: Masimo oximeters--Display Range

Betty, Neil, Wade
This summary is very helpful but it is not limited to infants receiving supplemental oxygen. It includes time in room air and supplemental oxygen. AL

From: Hastings, Betty J. [mailto:bkh@rti.org]
Sent: Wednesday, October 26, 2005 11:07 AM
To: Abbot Laptook; Angelita Hensman
Subject: Masimo oximeters--Display Range

Attached is the monthly table for the SUPPORT Study. This table shows the percent of time infants receiving supplemental oxygen spend in the target SPO2 range as displayed on the Masimo oximeters. The report includes data for infants at your center, broken out by month, as well as center totals and the total across all of the study centers to date.

<<Center 14 pct in display range (10-26-05).rtf>>

Betty Hastings

RTI International
Statistic Research Division
P.O. Box 12194
Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7740
Fax: (919) 485-7762
bkh@rti.org

From:	Nancy Peters
To:	wrich@ucsd.edu; nfiner@ucsd.edu
Cc:	Hastings, Betty J.; Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik; Auman, Jeanette O.; Poole, W. Kenneth; Zaterka-Baxter, Kristin; Gantz, Marie; Schaefer, Scott E.; ahensman@wihri.org; mbball@leland.stanford.edu; grisbyca@email.uc.edu; ellen_hale@oz.ped.emory.edu; gaynelle.hensley@utsouthwestern.edu; Georgia E McDavid; auten002@mc.duke.edu; linda_reubens@urmc.rochester.edu; mcollins@peds.uab.edu; monica.konstantino@yale.edu; Nancy.Miller@UTSouthwestern.edu; ae5357@wayne.edu; risa.demetrio@sharp.com; kathy.arnell@sharp.com; Reverett@med.miami.edu; Nancy Newman
Subject:	SUPPORT oximeters & time change
Date:	Wednesday, October 26, 2005 4:03:56 PM

Wade,

At Wake Forest we will go on "Daylight Savings Time" this weekend. I know that this change may not affect all centers, but how will this affect the SUPPORT Trial study oximeters and analysis of the downloaded information and correlation to data that might be collected on data forms? Do we do a download from all study oximeters on Monday morning and change the time then or just change the time when we do the next scheduled download?

Thanks. (not something I can take the credit for thinking of....a question from one of our research staff, and I did not know the answer)

Nancy P.

From: Wade Rich
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: support protocol for parent
Date: Monday, October 24, 2005 3:00:30 PM

I have it. I just needed permission to give it to them. Thanks. Sorry to bother you while traveling.
wade

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Monday, October 24, 2005 11:43 AM
To: wrich@ucsd.edu
Subject: Re: support protocol for parent

Wade
Go into the private website and you should be able to find the protocol.

Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
To: 'wrich@ucsd.edu' <wrich@ucsd.edu>
Sent: Mon Oct 24 14:34:21 2005
Subject: Re: support protocol for parent

Wade
Sorry for the delay as I am travelling . You may share the protocol with the parents. Do they have a medical baxkground?

Thanks
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Wade Rich <wrich@ucsd.edu>
To: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
Sent: Mon Oct 24 12:08:27 2005
Subject: support protocol for parent

Rose,
Can I provide the protocol for SUPPORT to an parent or grandparent? I know some of the
info is posted on trials.gov., but the full protocol is not so I wanted to make sure of the regs. Neil is in-flight, which is why I am asking you.

Wade

From: Scholl, Diane (NIH/OD/DEAS)
To: "Petrie, Carolyn"
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Wade Rich called RE: Support Trial for non signatory
Date: Monday, October 24, 2005 2:40:56 PM

Hi Carolyn, Please call Wade Rich at USD, San Diego Medical Center. He is asking for a copy of the "support trial." He thinks it is posted. He wants to give it to a non signatory. I think this is for you to handle. His number is 619-543-5375. THANKS!! ☺

Diane H. Scholl
Extramural Staff Assistant
NIH/OD/OER/NICHD/DEAS/Hub A
6100 Executive Blvd. Room 4B-03
Rockville, MD 20852
Tele: 301-435-6907
Fax: 301-496-3790
E-mail: scholld@mail.nih.gov

From: Spong, Catherine (NIH/NICHD)
To: Higgins, Rosemary (NIH/NICHD)
Subject: Re: support protocol for parent
Date: Monday, October 24, 2005 2:33:03 PM

I would think so - if they are in the trial they should be able to see it if they want to
---
Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
To: Spong, Catherine (NIH/NICHD) <spongc@dir49.nichd.nih.gov>
Sent: Mon Oct 24 13:42:10 2005
Subject: Fw: support protocol for parent

Is this allowable?
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Wade Rich <wrich@ucsd.edu>
To: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
Sent: Mon Oct 24 12:08:27 2005
Subject: support protocol for parent

Rose,
Can I provide the protocol for SUPPORT to an parent or grandparent? I know some of the
info is posted on trials.gov., but the full protocol is not so I wanted to make sure of the
regs. Neil is in-flight, which is why I am asking you.

Wade

From: Nancy Peters
To: Zaterka-Baxter, Kristin
Cc: Higgins, Rosemary (NIH/NICHD) [E]; Susan Hintz; Hastings, Betty J.
Subject: RE: SUPPORT MRI Secondary
Date: Monday, October 24, 2005 12:56:50 PM

Mail just arrived....U-turn from other IRB. Needless to say we will not be ready to start this secondary study anytime soon.

Nancy P.

From: Nancy Peters
Sent: Monday, October 24, 2005 12:26 PM
To: 'Zaterka-Baxter, Kristin'
Cc: Higgins, Rosemary (NIH/NICHD); Susan Hintz; Hastings, Betty J.
Subject: RE: SUPPORT MRI Secondary

At one site, our submission is making a U-turn. They are strongly suggesting that we add this as an addendum (received phone call just before I left for vacation last week). Their IRB meets only once a month so I am waiting to receive their letter of suggestions for an acceptable form of submission. I have not heard back from the board of the other hospital. They have weekly IRB meetings but only 2 boards can review pediatric applications so that drives the timeline for that IRB.

Nancy P.

From: Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]
Sent: Wednesday, October 19, 2005 1:09 PM
To: Rebecca Bara; mcollins@peds.uab.edu; Everett, Ruth; CATHY A. GRISBY; ellen_hale@oz.ped.emory.edu; Gaynelle Hensley; Kathy J Auten; linda_reubens@urmc.rochester.edu; Georgia E McDavid; Miller, Lucy C.; monica.konstantino@yale.edu; Nancy Peters; Nancy Newman; wrich@ucsd.edu; Kathy Arnell
Cc: Higgins, Rosemary (NIH/NICHD); Susan Hintz; Hastings, Betty J.
Subject: SUPPORT MRI Secondary

Dear All,

Please send a quick email to let us know what your IRB submission status is for the SUPPORT MRI Secondary. If you have received approval, please fax a copy to RTI at 919-485-7762.

As always, it's very much appreciated.

Kris

Kristin Zaterka-Baxter
RTI International
Statistic Research Division
P.O. Box 12194
Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From: Zaterka-Baxter, Kristin
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: SUPPORT Growth Secondary Study
Date: Wednesday, October 19, 2005 1:11:24 PM

Hi Rose,
Should I add Drs. Navarette and Finer to the SUPPORT Growth Secondary Conference Call (see below)
Thanks,
Kris

Kristin Zaterka-Baxter
RTI International
Statistic Research Division
P.O. Box 12194
Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From: Duara, Shahnaz [mailto:SDuara@med.miami.edu]
Sent: Wednesday, October 19, 2005 1:07 PM
To: Zaterka-Baxter, Kristin
Cc: Ellison, Amanda
Subject: RE: SUPPORT Growth Secondary Study

Kris,

Cristina Navarette needs to be on the call, as she is PI of this secondary. Her email address is cnavarrete@med.miami.edu . Also, as PI of SUPPORT, shouldn't Neil be on the call?

My availability is

Wednesday Oct. 26 - all day except 12-1:30
Thursday Oct. 27- all day
Friday Oct. 28- all day except 1-2

Monday Oct. 31- all day
Tuesday Nov. 1 - after 1 PM
Wednesday Nov. 2 -after 1 PM
Thursday Nov. 3 - after 1 PM
Friday Nov. 4 - after 2 PM

Shahnaz

> -----Original Message-----
> **From:** Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]
> **Sent:** Wednesday, October 19, 2005 11:24 AM
> **To:** sduara@miami.edu; richard.ehrenkranz@yale.edu; bpoindex@iupui.edu; Das, Abhik
> **Cc:** Higgins, Rosemary (NIH/NICHD); Hastings, Betty J.; Petrie, Carolyn
> **Subject:** SUPPORT Growth Secondary Study
>
> Dear All
>
> Please send me your availability for a conference call to discuuss the SUPPORT secondary study. Attached for your review is the Nutritional Intake Form (GRO-01)

Monday Oct. 24
Tuesday Oct. 25
Wednesday Oct. 26
Thursday Oct. 27
Friday Oct. 28

Monday Oct. 31
Tuesday Nov. 1
Wednesday Nov. 2
Thursday Nov. 3
Friday Nov. 4

Monday Nov. 7
Tuesday Nov. 8
Wednassday Nov. 9
Thursday Nov. 10
Friday Nov. 11

Thanks,
Kris

Kristin Zaterka-Baxter
RTI International
Statistic Research Division
P.O. Box 12194
Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7750
Fax: (919) 485-7762
kzaterka@rti.org

From:	Ira Adams-Chapman
To:	Newman, Jamie
Cc:	Timothy_Stevens@URMC.Rochester.edu; richard.ehrenkranz@yale.edu; jon.e.tyson@uth.tmc.edu; MPeralta@PEDS.UAB.EDU; Roy.Heyne@utsouthwestern.edu; cbauer@peds.med.miami.edu; apappas@med.wayne.edu; sshankar@med.wayne.edu; srhintz@stanford.edu; yvaucher@ucsd.edu; golds005@mc.duke.edu; rdillard@wfubmc.edu; gary_myers@URMC.Rochester.edu; bvohr@wihri.org; adusick@iupui.edu; steichji@email.uc.edu; drficmd@aol.com; Higgins, Rosemary (NIH/NICHD) [E]; Betty Vohr; Das, Abhik; maegan.c.currence@uth.tmc.edu; SEguaras@med.miami.edu; MNeri@med.miami.edu; Reverett@med.miami.edu; Janet.Morgan@childrens.com; VPhillips@PEDS.UAB.EDU; mgfuller@ucsd.edu; lnoel@wihri.org; ldrichar@iupui.edu; lohme001@mc.duke.edu; bjacksn@wfubmc.edu; diane_hust@URMC.Rochester.edu; mbball@leland.stanford.edu; elaine.romano@yale.edu; Teresa.Gratton@uc.edu; Ellen Hale; dkennedy@dmc.org; Jackie.Hickman@childrens.com; bss5@cwru.edu; joanne.williams@yale.edu
Subject:	Re: Please respond: SUPPORT Conf Call - Tues Nov 1
Date:	Tuesday, October 18, 2005 6:00:14 PM

Jamie- this will work for me.

Ira Adams-Chapman, MD
Director, Developmental Progress Clinic
Assistant Professor of Pediatrics
Emory University School of Medicine
Department of Pediatrics/Division of Neonatology

404-778-1450 (O)
ira_adams-chapman@oz.ped.emory.edu

From: Shankaran, Seetha
To: Newman, Jamie
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Please respond: SUPPORT Conf Call - Tues Nov 1
Date: Tuesday, October 18, 2005 4:18:45 PM

Jamie
Nov 1 is probably going to be very hard---first day of the month and first day on the clinical service. Would have preferred any other day!
Thanks
Seetha

-----Original Message-----
From: Newman, Jamie [mailto:newman@rti.org]
Sent: Tuesday, October 18, 2005 11:41 AM
To: Timothy_Stevens@URMC.Rochester.edu; richard.ehrenkranz@yale.edu; jon.e.tyson@uth.tmc.edu; MPeralta@PEDS.UAB.EDU; Roy.Heyne@utsouthwestern.edu; ira_adams-chapman@oz.ped.emory.edu; cbauer@peds.med.miami.edu; Pappas, Athina; Shankaran, Seetha; srhintz@stanford.edu; yvaucher@ucsd.edu; golds005@mc.duke.edu; rdillard@wfubmc.edu; gary_myers@URMC.Rochester.edu; bvohr@wihri.org; adusick@iupui.edu; steichjj@email.uc.edu; Personal Email
Cc: higginsr@mail.nih.gov; Betty Vohr; Das, Abhik; maegan.c.currence@uth.tmc.edu; SEguaras@med.miami.edu; MNeri@med.miami.edu; Reverett@med.miami.edu; Janet.Morgan@childrens.com; VPhillips@PEDS.UAB.EDU; mgfuller@ucsd.edu; lnoel@wihri.org; ldrichar@iupui.edu; lohme001@mc.duke.edu; bjacksn@wfubmc.edu; diane_hust@URMC.Rochester.edu; mbball@leland.stanford.edu; elaine.romano@yale.edu; Teresa.Gratton@uc.edu; ellen_hale@oz.ped.emory.edu; Kennedy, Deborah (DMC); Jackie.Hickman@childrens.com; bss5@cwru.edu; joanne.williams@yale.edu
Subject: Please respond: SUPPORT Conf Call - Tues Nov 1

Dear Follow-up PI's,
I apologize for the multiple messages but it has been difficult finding a day/time that works for a good number of people for the conference call to review the SUPPORT Follow-up documents. **Tuesday, November 1 from 2 - 3pm EST** seems to work the best for a considerable number of PIs. Please indicate whether you will be able to attend this call by 5pm tomorrow so that we can have a head count of who to expect on the call. If you are not available at this time, please indicate whether your coordinator can serve as your proxy.

Attached is the respiratory diary that is discussed in the Manual of Operations (MOO). It was not included in Appendix E of the MOO.

Thank you,

Jamie E. Newman, MPH
Statistics Research Division
RTI International
Telephone: (919) 485-5719
Fax: (919) 485-7762
newman@rti.org

From: Jean Steichen
To: "Newman, Jamie"; Timothy_Stevens@URMC.Rochester.edu; richard.ehrenkranz@yale.edu; jon.e.tyson@uth.tmc.edu; MPeralta@PEDS.UAB.EDU; Roy.Heyne@utsouthwestern.edu; ira_adams-chapman@oz.ped.emory.edu; cbauer@peds.med.miami.edu; apappas@med.wayne.edu; sshankar@med.wayne.edu; srhintz@stanford.edu; yvaucher@ucsd.edu; golds005@mc.duke.edu; rdillard@wfubmc.edu; gary_myers@urmc.rochester.edu; bvohr@wihri.org; adusick@iupui.edu; steichjj@email.uc.edu; Personal Email
Cc: Higgins, Rosemary (NIH/NICHD) [E]; "Betty Vohr"; "Das, Abhik"; maegan.c.currence@uth.tmc.edu; SEguaras@med.miami.edu; MNeri@med.miami.edu; Reverett@med.miami.edu; Janet.Morgan@childrens.com; VPhillips@peds.uab.edu; mgfuller@ucsd.edu; lnoel@wihri.org; ldrichar@iupui.edu; lohme001@mc.duke.edu; bjacksn@wfubmc.edu; diane_hust@urmc.rochester.edu; mbball@leland.stanford.edu; elaine.romano@yale.edu; Teresa.Gratton@uc.edu; ellen_hale@oz.ped.emory.edu; dkennedy@dmc.org; Jackie.Hickman@Childrens.com; bss5@cwru.edu; joanne.williams@yale.edu
Subject: RE: Please respond: SUPPORT Conf Call - Tues Nov 1
Date: Tuesday, October 18, 2005 12:06:41 PM

Hi Fellow PIs
I have Infant follow-up clinic on Tuesdays 'afternoons .I will try to join in as my clinic schedule permits
Thank you
Jean J. Steichen

-----Original Message-----
From: Newman, Jamie [mailto:newman@rti.org]
Sent: Tuesday, October 18, 2005 11:41 AM
To: Timothy_Stevens@URMC.Rochester.edu; richard.ehrenkranz@yale.edu; jon.e.tyson@uth.tmc.edu; MPeralta@PEDS.UAB.EDU; Roy.Heyne@utsouthwestern.edu; ira_adams-chapman@oz.ped.emory.edu; cbauer@peds.med.miami.edu; apappas@med.wayne.edu; sshankar@med.wayne.edu; srhintz@stanford.edu; yvaucher@ucsd.edu; golds005@mc.duke.edu; rdillard@wfubmc.edu; gary_myers@urmc.rochester.edu; bvohr@wihri.org; adusick@iupui.edu; steichjj@email.uc.edu; Personal Email
Cc: higginsr@mail.nih.gov; Betty Vohr; Das, Abhik; maegan.c.currence@uth.tmc.edu; SEguaras@med.miami.edu; MNeri@med.miami.edu; Reverett@med.miami.edu; Janet.Morgan@childrens.com; VPhillips@peds.uab.edu; mgfuller@ucsd.edu; lnoel@wihri.org; ldrichar@iupui.edu; lohme001@mc.duke.edu; bjacksn@wfubmc.edu; diane_hust@urmc.rochester.edu; mbball@leland.stanford.edu; elaine.romano@yale.edu; Teresa.Gratton@uc.edu; ellen_hale@oz.ped.emory.edu; dkennedy@dmc.org; Jackie.Hickman@Childrens.com; bss5@cwru.edu; joanne.williams@yale.edu
Subject: Please respond: SUPPORT Conf Call - Tues Nov 1

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Attached is the respiratory diary that is discussed in the Manual of Operations (MOO). It was not included in Appendix E of the MOO.

Thank you,

Jamie E. Newman, MPH
Statistics Research Division
RTI International
Telephone: (919) 485-5719
Fax: (919) 485-7762
newman@rti.org

From:	Newman, Jamie
To:	Timothy_Stevens@URMC.Rochester.edu; richard.ehrenkranz@yale.edu; jon.e.tyson@uth.tmc.edu; MPeralta@PEDS.UAB.EDU; Roy.Heyne@utsouthwestern.edu; ira_adams-chapman@oz.ped.emory.edu; cbauer@peds.med.miami.edu; apappas@med.wayne.edu; sshankar@med.wayne.edu; srhintz@stanford.edu; yvaucher@ucsd.edu; golds005@mc.duke.edu; rdillard@wfubmc.edu; gary_myers@urmc.rochester.edu; bvohr@wihri.org; adusick@iupui.edu; steichji@email.uc.edu; drfjcmd@aol.com
Cc:	Higgins, Rosemary (NIH/NICHD) [E]; Betty Vohr; Das, Abhik; maegan.c.currence@uth.tmc.edu; SEguaras@med.miami.edu; MNeri@med.miami.edu; Reverett@med.miami.edu; Janet.Morgan@childrens.com; VPhillips@peds.uab.edu; mgfuller@ucsd.edu; lnoel@wihri.org; ldrichar@iupui.edu; lohme001@mc.duke.edu; bjacksn@wfubmc.edu; diane_hust@urmc.rochester.edu; mbball@leland.stanford.edu; elaine.romano@yale.edu; Teresa.Gratton@uc.edu; ellen_hale@oz.ped.emory.edu; dkennedy@dmc.org; Jackie.Hickman@Childrens.com; bss5@cwru.edu; joanne.williams@yale.edu
Subject:	Please respond: SUPPORT Conf Call - Tues Nov 1
Date:	Tuesday, October 18, 2005 11:42:02 AM
Attachments:	Breathing Diary10_18.doc

Dear Follow-up PI's,

I apologize for the multiple messages but it has been difficult finding a day/time that works for a good number of people for the conference call to review the SUPPORT Follow-up documents. **Tuesday, November 1 from 2 - 3pm EST** seems to work the best for a considerable number of PIs. Please indicate whether you will be able to attend this call by 5pm tomorrow so that we can have a head count of who to expect on the call. If you are not available at this time, please indicate whether your coordinator can serve as your proxy.

Attached is the respiratory diary that is discussed in the Manual of Operations (MOO). It was not included in Appendix E of the MOO.

Thank you,

Jamie E. Newman, MPH
Statistics Research Division
RTI International
Telephone: (919) 485-5719
Fax: (919) 485-7762
newman@rti.org

Thank you for participating.

Neonatal Continuing Care Program
At Golisano Children's Hospital at Strong

PO Box 651
601 Elmwood Avenue
Rochester, NY 14642

Telephone: (585) 275-8373

My Baby's Breathing Book

Golisano Children's Hospital at Strong
University of Rochester

Created for:

Born:

Birth Weight:

Length:

Home from NICU:

Space for Baby Photo Below

The table below is designed to help families remember events that might happen with their baby's breathing.

If one of the breathing events along the left happens, please write the date that the event occurred along the top and make a check mark in the box below the date which corresponds to that baby's breathing problem or treatment.

1. Wheeze Today																											
No																											
Yes, 2 times or less																											
Yes, more than 2 times																											
Yes, all the time																											
2. Cough Today																											
No																											
Yes, 2 times or less																											
Yes, more than 2 times																											
Yes, all the time																											
3. Medical Visit for a Breathing Problem																											
Doctor's Office																											
Emergency Room																											
Hospitalization																											
4. Medications for breathing																											
Name:																											
Name:																											
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The table below is designed to help families remember events that might happen with their baby's breathing.

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NICHD NEONATAL RESEARCH NETWORK

NICHD SUPPORT Trial
Pulmonary Outcomes Follow Up Study

Premature babies are more likely than full term babies to have breathing problems after discharge from the NICU. The purpose of this study is to see whether the treatment your baby received as part of the SUPPORT Study improves your baby's breathing in the 18-22 months following the baby's due date.

As part of this study, we will contact you every 6 months or so to ask you questions about your baby's breathing. The questions will be about your baby's breathing symptoms, especially wheezing and coughing, and about your baby's need for medical visits and treatments for breathing problems.

Wheezing can mean different sounds to different people. By wheezing, we mean an expiratory sound (a sound that is made when breathing out, not in) that comes from the chest, sometimes described as whistling or musical.

We have prepared a diary for you to help you keep track of your baby's breathing, especially breathing problems or treatments.

To complete the diary, please record how often your baby has wheezing or coughing, whether your baby visited a doctor's office, emergency room or was hospitalized for breathing problems and what medications your baby needs.

When we call, we'd like you to gather the diary and any medications or other information about your baby's breathing. As with all information we collect, the answers to these questions will be kept confidential.

The table below is designed to help families remember events that might happen with their baby's breathing.

If one of the breathing events along the left happens, please write the date that the event occurred along the top and make a check mark in the box below the date which corresponds to that baby's breathing problem or treatment.

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From:	Betty Vohr
To:	Higgins, Rosemary (NIH/NICHD) [E]; Newman, Jamie
Cc:	Joyce Rose
Subject:	RE: Call for SUPPORT Follow-up - Thurs afternoon?
Date:	Tuesday, October 18, 2005 11:29:42 AM

Fine with me

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, October 18, 2005 10:44 AM
To: Betty Vohr; Newman, Jamie
Cc: Joyce Rose
Subject: RE: Call for SUPPORT Follow-up - Thurs afternoon?

Betty
Thursday afternoon is not good for me – Jamie is looking at Nov. 1. We have not had an overwhelming response to the request for availability, so Jamie will remind folks again today.
Thanks
Rose

From: Betty Vohr [mailto:BVohr@WIHRI.org]
Sent: Tuesday, October 18, 2005 10:39 AM
To: Newman, Jamie
Cc: Joyce Rose; Higgins, Rosemary (NIH/NICHD)
Subject: RE: Call for SUPPORT Follow-up - Thurs afternoon?

I could do 3:30 to 5.

Yes in some cases it would be appropriate to have coordinators if the PI cannot be on the call. I note that Roy Heyne has a lot of comments. As long as we have some representation from the majority of sites we should have the call. We do have to move ahead with this.
Thanks for working on this I know it is difficult.

From: Newman, Jamie [mailto:newman@rti.org]
Sent: Tuesday, October 18, 2005 10:04 AM
To: Betty Vohr; higginsr@mail.nih.gov
Cc: Timothy_Stevens@URMC.Rochester.edu
Subject: Call for SUPPORT Follow-up - Thurs afternoon?

Not yet, I'm still working on a time that maximizes participation. In case your schedules have changed since I originally queried you, how does Thursday afternoon after the coordinator's call work? Starting at 3:30? This time seems to work for a good number of PI's. Would it be possible for the coordinators to jump on for the PI's that can't make it?

Thanks, Jamie

Jamie E. Newman, MPH
Statistics Research Division
RTI International
Telephone: (919) 485-5719
Fax: (919) 485-7762
newman@rti.org

From: Betty Vohr [mailto:BVohr@WIHRI.org]
Sent: Tuesday, October 18, 2005 8:45 AM
To: Newman, Jamie; higginsr@mail.nih.gov
Subject: RE: Availability for call to review SUPPORT Follow-up Forms

Jamie or Rose
Has the time been set for the conference call for Support ?

From: Newman, Jamie [mailto:newman@rti.org]
Sent: Tuesday, October 11, 2005 5:01 PM
To: Timothy_Stevens@URMC.Rochester.edu; higginsr@mail.nih.gov; richard.ehrenkranz@yale.edu; jon.e.tyson@uth.tmc.edu; MPeralta@PEDS.UAB.EDU; Roy.Heyne@utsouthwestern.edu; ira_adams-chapman@oz.ped.emory.edu; cbauer@peds.med.miami.edu; apappas@med.wayne.edu; sshankar@med.wayne.edu; srhintz@stanford.edu; yvaucher@ucsd.edu; golds005@mc.duke.edu; rdillard@wfubmc.edu; gary_myers@urmc.rochester.edu; Betty Vohr; adusick@iupui.edu; steichjj@email.uc.edu; Personal Email
Cc: adas@email.unc.edu; sshankar@med.wayne.edu
Subject: Availability for call to review SUPPORT Follow-up Forms

Dear Follow-up PIs,
Please let me know your availability for a conference call to finalize the SUPPORT Follow-up forms.

Thursday morning Oct 20
Friday morning Oct 21
Monday afternoon Oct 24
Tuesday afternoon Oct 25
Thursday afternoon Oct 27

Study documents will be distributed to you later this week.

Thank you,

Jamie E. Newman, MPH
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RTI International
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newman@rti.org

From:	Newman, Jamie
To:	Betty Vohr
Cc:	Joyce Rose; Higgins, Rosemary (NIH/NICHD) [E]
Subject:	RE: Call for SUPPORT Follow-up - Thurs afternoon?
Date:	Tuesday, October 18, 2005 10:43:59 AM

I just spoke with Rose and then Joyce. Rose has meetings on Thursday and the next day that looks promising is Tues Nov 1 at 2pm. Are you free then?

Jamie E. Newman, MPH
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Telephone: (919) 485-5719
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newman@rti.org

From: Betty Vohr [mailto:BVohr@WIHRI.org]
Sent: Tuesday, October 18, 2005 10:39 AM
To: Newman, Jamie
Cc: Joyce Rose; higginsr@mail.nih.gov
Subject: RE: Call for SUPPORT Follow-up - Thurs afternoon?

I could do 3:30 to 5.

Yes in some cases it would be appropriate to have coordinators if the PI cannot be on the call. I note that Roy Heyne has a lot of comments. As long as we have some representation from the majority of sites we should have the call. We do have to move ahead with this.
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From: Newman, Jamie [mailto:newman@rti.org]
Sent: Tuesday, October 18, 2005 10:04 AM
To: Betty Vohr; higginsr@mail.nih.gov
Cc: Timothy_Stevens@URMC.Rochester.edu
Subject: Call for SUPPORT Follow-up - Thurs afternoon?

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Thanks, Jamie

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Telephone: (919) 485-5719
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newman@rti.org

From: Betty Vohr [mailto:BVohr@WIHRI.org]
Sent: Tuesday, October 18, 2005 8:45 AM
To: Newman, Jamie; higginsr@mail.nih.gov

Subject: RE: Availability for call to review SUPPORT Follow-up Forms

Jamie or Rose
Has the time been set for the conference call for Support ?

From: Newman, Jamie [mailto:newman@rti.org]
Sent: Tuesday, October 11, 2005 5:01 PM
To: Timothy_Stevens@URMC.Rochester.edu; higginsr@mail.nih.gov; richard.ehrenkranz@yale.edu; jon.e.tyson@uth.tmc.edu; MPeralta@PEDS.UAB.EDU; Roy.Heyne@utsouthwestern.edu; ira_adams-chapman@oz.ped.emory.edu; cbauer@peds.med.miami.edu; apappas@med.wayne.edu; sshankar@med.wayne.edu; srhintz@stanford.edu; yvaucher@ucsd.edu; golds005@mc.duke.edu; rdillard@wfubmc.edu; gary_myers@urmc.rochester.edu; Betty Vohr; adusick@iupui.edu; steichjj@email.uc.edu; Personal Address
Cc: adas@email.unc.edu; sshankar@med.wayne.edu
Subject: Availability for call to review SUPPORT Follow-up Forms

Dear Follow-up PIs,
Please let me know your availability for a conference call to finalize the SUPPORT Follow-up forms.

Thursday morning Oct 20
Friday morning Oct 21
Monday afternoon Oct 24
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Study documents will be distributed to you later this week.

Thank you,

Jamie E. Newman, MPH
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RTI International
Telephone: (919) 485-5719
Fax: (919) 485-7762
newman@rti.org

From:	Richard Ehrenkranz
To:	Higgins, Rosemary (NIH/NICHD) [E]; Poindexter, Brenda B
Cc:	Duara, Shahnaz; nfiner@ucsd.edu
Subject:	Re: SUPPORT GROWTH Secondary
Date:	Monday, October 17, 2005 3:49:55 PM

Absolutely.
Richard

At 03:25 PM 10/17/2005, Higgins, Rosemary (NIH/NICHD) wrote:

> Hi Brenda and Richard,
> The SUPPORT growth secondary study was approved and Shahnaz has asked that you serve as consultants for this secondary study. We will work out the authorship issues when we have out first call (hopefully in the next 2-3 weeks to go over the form). Let me know if you are interested.
>
> Thanks
> Rose
>
> Rosemary D. Higgins, M.D.
> Program Scientist for the Neonatal Research Network
> Pregnancy and Perinatology Branch
> Center for Developmental Biology and Perinatal Medicine
> NICHD, NIH
> 6100 Executive Blvd., Room 4B03B
> MSC 7510
> Bethesda, MD 20892
> (For overnight delivery, use Rockville, MD 20852)
> 301-435-7909
> 301-496-3790 (FAX)
> higginsr@mail.nih.gov

Richard A. Ehrenkranz, MD
Department of Pediatrics
Yale University School of Medicine
333 Cedar Street
PO Box 208064
New Haven, CT 06520-8064
tele: 203-688-2320
fax: 203-688-5426

From: Poindexter, Brenda B
To: Higgins, Rosemary (NIH/NICHD) [E]; Richard Ehrenkranz
Cc: Duara, Shahnaz; nfiner@ucsd.edu
Subject: RE: SUPPORT GROWTH Secondary
Date: Monday, October 17, 2005 3:45:12 PM

That sounds great - Thanks for thinking of me, Shahnaz. I would be happy to help.
Brenda

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Mon 10/17/2005 2:25 PM
To: Richard Ehrenkranz; Poindexter, Brenda B
Cc: Duara, Shahnaz; nfiner@ucsd.edu
Subject: SUPPORT GROWTH Secondary

Hi Brenda and Richard,

The SUPPORT growth secondary study was approved and Shahnaz has asked that you serve as consultants for this secondary study. We will work out the authorship issues when we have out first call (hopefully in the next 2-3 weeks to go over the form). Let me know if you are interested.

Thanks
Rose

Rosemary D. Higgins, M.D.

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

NICHD, NIH

6100 Executive Blvd., Room 4B03B

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higginsr@mail.nih.gov

From: Betty Vohr
To: newman@RTI.org
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Support
Date: Thursday, October 13, 2005 6:15:09 PM

I think we should schedule the call with as many as we can. If someone can not be on the call, we can ask them to have a representative from their site.

From: Newman, Jamie
To: Joyce Rose; Betty Vohr; Higgins, Rosemary (NIH/NICHD) [E]
Subject: Additional availability for SUPPORT FU call
Date: Thursday, October 13, 2005 3:38:59 PM

Betty and Rose,
I am having difficulty finding a day/time that fits the Follow-up PI's schedules for the SUPPORT Follow-up form/MOO review. I will be sending out the forms/MOO to the group later today.

Tim Stevens tells me that he is now available on the afternoons of:
Thurs 10/20
Friday 10/21 (Rose has already said 12-3)
Also, please indicate your availability the afternoons of the week of Oct 31.

Thanks, Jamie

Jamie E. Newman, MPH
Statistics Research Division
RTI International
Telephone: (919) 485-5719
Fax: (919) 485-7762
newman@rti.org

From: Wade Rich
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SAE-Support
Date: Thursday, October 13, 2005 9:38:28 AM

It is exactly the same form. The only difference is that you guys put the header on it which has site number, subject number, etc.
If we put the study number and site # in the ID box it will give you everything the other one does. Just seems easier for you to read text than my writing !!
Wade

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Thursday, October 13, 2005 6:35 AM
To: wrich@ucsd.edu; 'Hastings, Betty J.'
Subject: RE: SAE-Support

This seems appropriate - is it consistent with the manual of operations?
Thanks
Rose

-----Original Message-----
From: Wade Rich [mailto:wrich@ucsd.edu]
Sent: Thursday, October 13, 2005 9:18 AM
To: 'Hastings, Betty J.'; Higgins, Rosemary (NIH/NICHD)
Subject: FW: SAE-Support

Sorry guys. Here it is. The question still applies.
wade

-----Original Message-----
From: Wade Rich [mailto:wrich@ucsd.edu]
Sent: Wednesday, October 12, 2005 2:53 PM
To: 'Higgins, Rosemary (NIH/NICHD)'; 'Hastings, Betty J.'; 'Zaterka-Baxter, Kristin'
Subject: SAE-Support

Attached is a support MedWatch. The one on line can be filled out. Is it OK to use it if I identify the study in the Patient Identifier section?
wade

From:	Newman, Jamie
To:	Timothy_Stevens@URMC.Rochester.edu; Higgins, Rosemary (NIH/NICHD) [E]; richard.ehrenkranz@yale.edu; jon.e.tyson@uth.tmc.edu; MPeralta@PEDS.UAB.EDU; Roy.Heyne@utsouthwestern.edu; ira_adams-chapman@oz.ped.emory.edu; cbauer@peds.med.miami.edu; apappas@med.wayne.edu; sshankar@med.wayne.edu; srhintz@stanford.edu; yvaucher@ucsd.edu; golds005@mc.duke.edu; rdillard@wfubmc.edu; gary_myers@urmc.rochester.edu; bvohr@wihri.org; adusick@iupui.edu; steichji@email.uc.edu; drfjcmd@aol.com
Cc:	adas@email.unc.edu; sshankar@med.wayne.edu
Subject:	Availability for call to review SUPPORT Follow-up Forms
Date:	Tuesday, October 11, 2005 5:01:27 PM

Dear Follow-up PIs,
Please let me know your availability for a conference call to finalize the SUPPORT Follow-up forms.

Thursday morning Oct 20
Friday morning Oct 21
Monday afternoon Oct 24
Tuesday afternoon Oct 25
Thursday afternoon Oct 27

Study documents will be distributed to you later this week.

Thank you,

Jamie E. Newman, MPH
Statistics Research Division
RTI International
Telephone: (919) 485-5719
Fax: (919) 485-7762
newman@rti.org

Blansfield, Earl (NIH/NICHD) [E]

From: Monica Collins <MCollins@peds.uab.edu>
Sent: Thursday, September 29, 2005 11:44 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Oximeters

Rose,
Just to make sure--this is for 10 additional floaters, correct?
Monica

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Wed 9/28/2005 12:53 PM
To: Wally Carlo, M.D.; Monica Collins; Jon E Tyson; 'Georgia McDavid '; 'Neil Finer '; Abbot Laptook; Angelita Hensman; William Oh; Nancy Newman; Michele Walsh
Cc: Petrie, Carolyn; Zaterka-Baxter, Kristin; 'Hastings, Betty J. '
Subject: Oximeters

Hi,
You were one of five sites allocated additional money for oximeters. Please let me know if you have the additional oximeters at your sites at this time. We are asked from time to time to provide sites oximeters if they are running low.

Thanks very much!
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
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MSC 7510
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301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Das, Abhik
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Hastings, Betty J.; Zaterka-Baxter, Kristin
Subject: RE: ROP data and support
Date: Wednesday, September 28, 2005 4:24:45 PM

Rose:

We would need a similar data access agreement that we used for Susan Hintz, and then put it through our IRB. Kris will send the form to Dale that she needs to fill out and sign, and send back to us.

Thanks

Abhik

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, September 28, 2005 3:30 PM
To: Das, Abhik
Subject: ROP data and support

Abhik
How are we doing with the ROP forms getting to Dale for review??
Thanks
Rose
Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
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301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Petrie, Carolyn
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT pilot
Date: Wednesday, September 21, 2005 9:26:44 AM

---

so should they send a memo and include this information?

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Wed 9/21/2005 9:25 AM
To: Petrie, Carolyn
Subject: Re: SUPPORT pilot

We need to know how many are enrolled in the pilot.
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Petrie, Carolyn <petrie@rti.org>
To: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
Sent: Wed Sep 21 09:16:59 2005
Subject: FW: SUPPORT pilot

please advise. should we send a memo indicatingf the stopmdate of the support pilot?

-----Original Message-----
From: Hastings, Betty J.
Sent: Wed 9/21/2005 8:25 AM
To: Petrie, Carolyn
Subject: FW: SUPPORT pilot

Have you asked Wally, Neil or Rose about this? I didn't know if I should follow-up on it.
Thanks.
Betty
-----Original Message-----
From: Hastings, Betty J.
Sent: Monday, September 19, 2005 5:00 PM
To: Petrie, Carolyn
Subject: RE: SUPPORT pilot

There really wasn't one. I was just mentioned in passing.
We probably need to clarify that this is happening. -----Original Message-----
From: Petrie, Carolyn
Sent: Monday, September 19, 2005 4:39 PM
To: Hastings, Betty J.; Zaterka-Baxter, Kristin
Subject: FW: SUPPORT pilot

Help. I have not found one.

-----Original Message-----
From: CATHY A. GRISBY [mailto:grisbyca@email.uc.edu]
Sent: Monday, September 19, 2005 4:38 PM
To: Petrie, Carolyn
Subject: SUPPORT pilot

Hi Carolyn,

Was there an official stop date/memo for the SUPPORT pilot?

Thanks,

Cathy

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]; "Ken Poole"; "Das, Abhik"
Cc: Neil Finer; wrich@ucsd.edu
Date: Monday, September 12, 2005 10:40:35 AM

Hi Rose Abhik and Ken
In my request to you yesterday I believe that I omitted the most important question. I would need the outcome of death or NDI at 18-22 months for 23 – 276/7 and 28 to 32 6/7, and overall as this would be a co-primary and I would want to power the study for this outcome. I would use the same correction for multiples to the same arm of the study as did SUPPORT.
Many thanks for looking at this.
Neil

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]; Haverkos, Lynne (NIH/NICHD) [E]
Subject: Re: Clinical trials.gov
Date: Saturday, September 10, 2005 1:39:24 PM

Hi Rose and Lynne
I think I just sent you an email re Azithro study that was old, and probably worth ignoring
I have completed the entries for the SUPPORT Trial on the web site. The only deficiency is that I did not have all the U award numbers. I used those from the PINO paper but not all centers were on that study. Rose can you provide either me or Lynne or can you go into this site and add the missing U award numbers? I will await the review of the entries and make any additional changes as needed.
Sorry for having missed this - especially as I have been very concerned that we get the study online.
I will ensure that I remove Lynne's email address from my excluded recipients at work.
Be well
Neil
----- Original Message -----
From: "Higgins, Rosemary (NIH/NICHD)" <higginsr@mail.nih.gov>
To: <nfiner@ucsd.edu>; "Haverkos, Lynne (NIH/NICHD)" <haverkol@mail.nih.gov>
Sent: Friday, September 09, 2005 6:20 PM
Subject: Re: Clinical trials.gov

> Lynne
> Can you resend Dr. Finer his information to access the SUPPORT trial in
> clinicaltrials.gov?
> Thanks
> Rose
> ----------
> Sent from my BlackBerry Wireless Handheld
>
>
> -----Original Message-----
> From: Neil Finer <nfiner@ucsd.edu>
> To: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
> Sent: Fri Sep 09 21:08:15 2005
> Subject: Re: Clinical trials.gov
>
> Rose
> How do I access this account?
> Thanks
> Neil
> ----- Original Message -----
> From: "Higgins, Rosemary (NIH/NICHD)" <higginsr@mail.nih.gov>
> To: <nfiner@ucsd.edu>
> Sent: Friday, September 09, 2005 3:27 PM
> Subject: Clinical trials.gov
>
>
>> Neil
>> Did you complete the clinicaltrials.gov record for the support trial? We

>> have a record of an account created for you, but no entry.
>> Let me know ASAP.
>> Thanks
>> Rose
>> ----------
>> Sent from my BlackBerry Wireless Handheld
>>
>

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]; Haverkos, Lynne (NIH/NICHD) [E]
Subject: Re: Clinical trials.gov
Date: Friday, September 09, 2005 11:40:13 PM

Hi Rose
I found an email from Lynne to me in Jan of this year. Somehow, I suspect it got placed in my junk mail at work, because I could only find it at home using the name in this email. She had sent instructions, which I will follow and complete the site. Looks like a problem at my end for which I apologize. Please let Lynne know that I found this and I will follow her instructions.
Thanks again.
Neil
----- Original Message -----
From: "Higgins, Rosemary (NIH/NICHD)" <higginsr@mail.nih.gov>
To: <nfiner@ucsd.edu>; "Haverkos, Lynne (NIH/NICHD)" <haverkol@mail.nih.gov>
Sent: Friday, September 09, 2005 6:20 PM
Subject: Re: Clinical trials.gov

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> To: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
> Sent: Fri Sep 09 21:08:15 2005
> Subject: Re: Clinical trials.gov
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> Rose
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> From: "Higgins, Rosemary (NIH/NICHD)" <higginsr@mail.nih.gov>
> To: <nfiner@ucsd.edu>
> Sent: Friday, September 09, 2005 3:27 PM
> Subject: Clinical trials.gov
>
>
>> Neil
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>> have a record of an account created for you, but no entry.
>> Let me know ASAP.
>> Thanks
>> Rose
>> ----------
>> Sent from my BlackBerry Wireless Handheld
>>

From: Haverkos, Lynne (NIH/NICHD)
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE: SUPPORT Trial
Date: Friday, September 09, 2005 6:26:53 PM

Rose,
Thanks

Lynne

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD)
Sent: Friday, September 09, 2005 6:26 PM
To: Haverkos, Lynne (NIH/NICHD)
Subject: Re: SUPPORT Trial

I will ask him.
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Haverkos, Lynne (NIH/NICHD) <haverkol@mail.nih.gov>
To: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
Sent: Fri Sep 09 18:22:19 2005
Subject: RE: SUPPORT Trial

Hi Rose,

I created an account for Neil but don't see the record in the system. Are you sure he created a record?

Lynne
Lynne M. Haverkos, MD, MPH
Program Director,
Behavioral Pediatrics and Health Promotion Research
http://www.nichd.nih.gov/crmc/cdb/p_behave.htm <http://www.nichd.nih.gov/crmc/cdb/p_behave.htm>
NICHD/NIH
6100 Executive Blvd. Room 4B05 MSC 7510
Bethesda, MD. 20892-7510
For Fed Ex use: Rockville, MD. 20852
phone: 301-435-6881
fax: 301-480-0230
email: haverkol@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD)
Sent: Friday, September 09, 2005 10:39 AM

To: Haverkos, Lynne (NIH/NICHD)
Subject: SUPPORT Trial

Hi Lyn

One of our investigators was asking about the SUPPORT trial – it is not yet posted on clinicaltrials.gov. Do you know where we are in the process for this one? Neil Finer is the PI.
Thanks

Rose

Rosemary D. Higgins, M.D.

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

NICHD, NIH

6100 Executive Blvd., Room 4B03B

MSC 7510

Bethesda, MD 20892

(For overnight delivery, use Rockville, MD 20852)

301-435-7909

301-496-3790 (FAX)

higginsr@mail.nih.gov

From: Neil Finer
To: "Edmund Hey"; "Hastings, Betty J."
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT Manual & Protocol
Date: Friday, September 09, 2005 3:16:26 PM

Hi Edmund
The following is the best description of how you should use the materials regarding SUPPORT
As you know, this is an ongoing trial and we recommend appropriate discretion in discussions with scientific colleagues. We agree that common endpoints are important, but request that the information be used judiciously.

Be well
Neil Finer

From: Edmund Hey [mailto:shey@easynet.co.uk]
Sent: Friday, September 09, 2005 1:58 AM
To: Hastings, Betty J.
Cc: Finer, Neil
Subject: Re: SUPPORT Manual & Protocol

In connection with my last message it would probably help if I could see copies of the report forms that study recruiting units are using when submitting outcome data once the baby is ready for discharge bhome as well as the manual (unless copies of these are in, or come with, the study Manual).
More importantly it would be particularly helpful to see what sort of charts you are planning to use to document the ophthalmic outcomes.

E

> ----- Original Message -----
> **From:** Hastings, Betty J.
> **To:** shey@easynet.co.uk
> **Sent:** Wednesday, September 07, 2005 9:39 PM
> **Subject:** SUPPORT Manual & Protocol
>
> Dr. Hey,
> I will be glad to mail you a copy of the SUPPORT Manual and Protocol. Could you please send me your Fed-Ex address.
> Thanks very much.
> Betty
>
> **Betty Hastings**
>
> RTI International
> Statistic Research Division
> P.O. Box 12194
> Research Triangle Park, NC 27709-2194
> Telephone: (919) 485-7740
> Fax: (919) 485-7762
> bkh@rti.org

From: Newman, Jamie
To: Stevens, Timothy
Cc: Petrie, Carolyn; Das, Abhik; Betty Vohr; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT Trial Follow-up
Date: Thursday, September 08, 2005 9:41:40 AM

Dr. Stevens,
In response to your questions below:

-RTI will be able to send out a reminder to each center when the respiratory questionnaire is due. We can send out a list of IDs each month that are due to have questionnaires conducted (at 6 mo, 12 mo, and 12-22 mo) along with acceptable windows for conducting the interviews.

-Rochester will be able to enter questionnaire data for interviews completed there. Mailing/faxing questionnaires to the local centers is not necessary. Are there any IRB/HIPPA issues that we may need to consider? This might be something that we will want to bring up for discussion at the meeting but maybe Rose and Betty can provide us with some guidance in the meantime. We will want to state very clearly that Rochester will be conducting the interviews for some of the sites in the Protocol/Manual that is given to the IRBs for review and also mention it in the consent form.

Please let me know if you have additional questions. I look forward to meeting you next week.

Thanks, Jamie

Jamie E. Newman, MPH
Statistics Research Division
RTI International
Telephone: (919) 485-5719
Fax: (919) 485-7762
newman@rti.org

From: Stevens, Timothy [mailto:Timothy_Stevens@URMC.Rochester.edu]
Sent: Tuesday, August 30, 2005 3:10 PM
To: Newman, Jamie
Cc: Petrie, Carolyn; Das, Abhik
Subject: RE: SUPPORT Trial Follow-up

Hi Ms. Newman,

Thank you for the note. Can I ask you a few questions?

For the SUPPORT Trial Pulmonary Outcomes Study, some centers chose to have the Rochester site administer the respiratory health questionnaires to their patients by telephone, long distance. To achieve this, since RTI does not collect personal identifiers, each center using Rochester will need to fax contact information to us in order to initiate the telephone contact.

Question 1: Will RTI be able to send a reminder, based on corrected age (post menstrual age), to each center when the respiratory questionnaire is due or will all tracking and reminding need to be handled locally?

For centers using Rochester to administer the telephone interviews to their patients, a completed telephone questionnaire form will be generated in Rochester. Currently, we do not have privileges to enter data directly for other centers.

Question 2: What is the best way to conduct data entry from questionnaires completed in Rochester for

sites other than our own? Should we mail or fax the completed form back to the local center for data entry or would you be able to grant privileges to our center to enter questionnaire data on behalf of the local center.

At the Network meeting on Sept 15th, I'd like to present answers to these questions.

Thanks for considering these issues.

Tim

From:	Neil Finer
To:	"Petrie, Carolyn"
Cc:	"Avroy A. Fanaroff, M.D."; "Betty Hastings"; "Ed Donovan"; Higgins, Rosemary (NIH/NICHD) [E]; "Ken Poole"; "Michele"; "Neil Finer"; "Shahnaz Duara"; "Wade Rich"; "Wally Carlo"
Subject:	Agenda for SUPPORT Committee
Date:	Tuesday, September 06, 2005 7:08:23 PM

Hi Carolyn
Here is an Agenda for the SUPPORT Meeting:

1. Review enrollments to date
2. Review issues with downloads and oximeters – Wade Rich and coordinators
3. Review Consent Study – Wade Rich and Coordinators
4. Review Status of Secondaries – MRI, Pulmonary, Genomics and Growth
5. Discuss feedback regarding oximeter ranges – Wally Carlo
6. Review any protocol issues from sites
7. Review of Oxygen challenge and diagnosis of BPD – form PHYS 02
8. Other business

See you next week
Regards
Neil Finer

From: Petrie, Carolyn [mailto:petrie@rti.org]
Sent: Tuesday, September 06, 2005 11:04 AM
To: WOh@wihri.org; adas@rti.org; barbara_stoll@oz.ped.emory.edu; ellen_hale@oz.ped.emory.edu; goldb008@mc.duke.edu; higginsr@mail.nih.gov; alaptook@wihri.org; mcw3@cwru.edu; nxs5@cwru.edu; sduara@miami.edu; sshankar@med.wayne.edu; dstevenson@stanford.edu; jlemons@iupui.edu; nfiner@ucsd.edu; rdillard@wfubmc.edu; adusick@iupui.edu; cbauer@peds.med.miami.edu; gary_myers@urmc.rochester.edu; golds005@mc.duke.edu; MPeralta@PEDS.UAB.EDU
Cc: Poole, W. Kenneth
Subject: Wilson Abstract attached.

Carolyn Petrie

Neonatal Research Network Coordinator
RTI International
6110 Executive Blvd
Suite 902
Rockville, MD 20852
ph. (301) 230-4648
fx. (301) 230-4646

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT
Date: Tuesday, September 06, 2005 3:25:44 PM

Thanks Rose
Neil

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, September 06, 2005 12:13 PM
To: 'nfiner@ucsd.edu'
Subject: SUPPORT

Neil
The DSMC will look at the data after 25 percent enrollment. Let me know if you have other questions.
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

From:	Neil Finer
To:	Higgins, Rosemary (NIH/NICHD) [E]
Subject:	RE: SUPPORT AND OXIMETERS
Date:	Friday, August 12, 2005 10:22:10 PM

Neil to Rose
Have a great trip and thanks for your support!!!
Neil

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Thursday, August 11, 2005 1:29 PM
To: Kurt Schibler (Kurt Schibler [kurt.schibler@cchmc.org]); (susie.buchter@oz.ped.emory.edu); (vineet.bhandari@yale.edu); Krisa VanMeurs (VanMeurs, Krisa); Brenda Morris (Brenda.H.Morris@uth.tmc.edu); Laroia, Nirupama; Michael Cotten; Maynard Rasmussen (maynard.rasmussen@sharp.com); (Vivek.Narendran@cchmc.org); Angelita Hensman; Becky bara; Bethany Ball; Cathy Grisby; Ellen Hale; Georgia McDavid; Kathy Auten; Linda Reubens; Lucy Miller; Monica Collins; monica.konstantino@yale.edu; Nancy Miller; Nancy Newman; Nancy Peters; Ruth Everett; Wade RIch; Abbot Laptook (alaptook@WIHRI.org); Abhik Das; Brenda Poindexter; Carlo Waldemar (E-mail); Charles Rosenfeld; Dale Phelps; Ed Donovan; Ehrenkranz Richard (E-mail); Jobe Alan (E-mail); Lemons Jim (E-mail); Michael O'Shea; Michelle Walsh; Neil Finer; Oh William (E-mail); Poole Kenneth (E-mail); Ronald GOldberg; Shahnaz Duara; Shankaran Seetha (E-mail); Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); Walid Salhab (Walid Salhab)
Cc: petrie@rti.org; 'Hastings, Betty J.'; Zaterka-Baxter, Kristin
Subject: SUPPORT AND OXIMETERS
Importance: High

HI,
I will be out of the office next week. If your site has an acute need for supplemental oximeters for the SUPPORT Trial, please contact Betty Hastings and she will assist you in procuring equipment from another site. Please keep in mind, that if weekend needs are anticipated, try to make the arrangements, if possible by **Thursday** preceding the weekend. Many institutions have no mechanism for overnight delivery which arrives on Saturday (and little to no Sunday deliveries are available).

I want to thank all of the sites for their effort so far for SUPPORT and want to be able to facilitate recruitment by insuring that equipment is available. I especially thank the sites who have notified us of need for equipment and sites who have responded with equipment so quickly!

Thanks again for the commitment and dedication!!!
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Michael Cotten
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT AND OXIMETERS
Date: Thursday, August 11, 2005 9:35:31 PM

---

thanks Rose...for this and helping w/ GDB proposal advice
mc

C. Michael Cotten, MD
Assistant Clinical Professor of Pediatrics
Clinical Research Director, Duke Neonatology
Director Special Care Nursery, Durham Regional Hospital
Box 3179 DUMC
Durham, NC 27710
(919) 681-6025
fax: (919) 681-6065
pager: (919) 970-4381

"Higgins, Rosemary (NIH/NICHD)" <higginsr@mail.nih.gov>

08/11/2005 04:28 PM

To: "Kurt Schibler (Kurt Schibler [kurt.schibler@cchmc.org])" <kurt.schibler@cchmc.org>, " (susie.buchter@oz.ped.emory.edu)" <susie.buchter@oz.ped.emory.edu>, " (vineet.bhandari@yale.edu)" <vineet.bhandari@yale.edu>, "Krisa VanMeurs (VanMeurs, Krisa)" <vanmeurs@leland.stanford.edu>, "Brenda Morris (Brenda.H.Morris@uth.tmc.edu)" <Brenda.H.Morris@uth.tmc.edu>, "Laroia, Nirupama" <Nirupama_Laroia@URMC.Rochester.edu>, Michael Cotten <cotte010@mc.duke.edu>, "Maynard Rasmussen (maynard.rasmussen@sharp.com)" <maynard.rasmussen@sharp.com>, " (Vivek.Narendran@cchmc.org)" <Vivek.Narendran@cchmc.org>, Angelita Hensman <ahensman@wihri.org>, Becky bara <ae5357@wayne.edu>, Bethany Ball <mbball@leland.stanford.edu>, Cathy Grisby <grisbyca@email.uc.el du>, Ellen Hale <ellen_hale@oz.ped.emory.edu>, Georgia McDavid <Georgia.E.McDavid@uth.tmc.edu>, Kathy Auten <auten002@mc.duke.edu>, Linda Reubens <linda_reubens@URMC.Rochester.edu>, Lucy Miller <lucmille@iupui.edu>, Monica Collins <mcollins@peds.uab.edu>, monica.konstantino@yale.edu, Nancy Miller <Nancy.Miller@UTSouthwestern.edu>, Nancy Newman <nxs5@cwru.edu>, Nancy Peters <npeters@wfubmc.edu>, Ruth Everett <Reverett@med.miami.edu>, Wade RIch <wrich@ucsd.edu>, "Abbot Laptook (alaptook@WIHRI.org)" <alaptook@wihri.org>, Abhik Das <adas@rti.org>, Brenda Poindexter <bpoindex@iupui.edu>, "Carlo Waldemar (E-mail)" <wcarlo@peds.uab.edu>, Charles Rosenfeld <crosen@mednet.swmed.edu>, Dale Phelps <dale_phelps@URMC.Rochester.edu>, Ed Donovan <edward.donovan@cchmc.org>, "Ehrenkranz Richard (E-mail)" <richard.ehrenkranz@yale.edu>, "Jobe I Alan (E-mail)" <Jobea0@chmcc.org>, "Lemons Jim (E-mail)" <jlemons@iupui.edu>, "Michael O'Shea" <moshea@wfubmc.edu>, Michelle Walsh <mcw3@po.cwru.edu>, Neil Finer <nfiner@ucsd.edu>, "Oh William (E-mail)" <william_oh@brown.edu>, "Poole Kenneth (E-mail)" <poo@rti.org>, Ronald GOldberg <goldb008@mc.duke.edu>, Shahnaz Duara <sduara@miami.edu>, "Shankaran Seetha (E-mail)" <s_shankaran@wayne.edu>, "Stevenson David (E-mail)" <dstevenson@stanford.edu>, "Stoll Barbara (E-mail)" <barbara_stoll@oz.ped.emory.edu>, "Tyson Jon (E-mail)" <Jon.E.Tyson@uth.tmc.edu>, "Walid Salhab (Walid Salhab)" <Walid.Salhab@UTSouthwestern.edu>

cc: petrie@rti.org, "'Hastings, Betty J.'" <bkh@rti.org>, "Zaterka-Baxter, Kristin" <kzaterka@rti.org>

Subject: SUPPORT AND OXIMETERS

HI,
I will be out of the office next week. If your site has an acute need for supplemental oximeters for the SUPPORT Trial, please contact Betty Hastings and she will assist you in procuring equipment from another site. Please keep in mind, that if weekend needs are anticipated, try to make the arrangements, if possible by **Thursday** preceding the weekend. Many institutions have no mechanism for overnight delivery which arrives on Saturday (and little to no Sunday deliveries are available).

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need for equipment and sites who have responded with equipment so quickly!

Thanks again for the commitment and dedication!!!
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Michele Walsh
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT AND OXIMETERS
Date: Thursday, August 11, 2005 5:46:25 PM

---

have fun Rose! Michele

----- Original Message -----
From: Higgins, Rosemary (NIH/NICHD)
To: Kurt Schibler (Kurt Schibler [kurt.schibler@cchmc.org]) ; (susie.buchter@oz.ped.emory.edu) ; (vineet.bhandari@yale.edu) ; Krisa VanMeurs (VanMeurs, Krisa) ; Brenda Morris (Brenda.H.Morris@uth.tmc.edu) ; Laroia, Nirupama ; Michael Cotten ; Maynard Rasmussen (maynard.rasmussen@sharp.com) ; (Vivek.Narendran@cchmc.org) ; Angelita Hensman ; Becky bara ; Bethany Ball ; Cathy Grisby ; Ellen Hale ; Georgia McDavid ; Kathy Auten ; Linda Reubens ; Lucy Miller ; Monica Collins ; monica.konstantino@yale.edu ; Nancy Miller ; Nancy Newman ; Nancy Peters ; Ruth Everett ; Wade RIch ; Abbot Laptook (alaptook@WIHRI.org) ; Abhik Das ; Brenda Poindexter ; Carlo Waldemar (E-mail) ; Charles Rosenfeld ; Dale Phelps ; Ed Donovan ; Ehrenkranz Richard (E-mail) ; Jobe Alan (E-mail) ; Lemons Jim (E-mail) ; Michael O'Shea ; Michelle Walsh ; Neil Finer ; Oh William (E-mail) ; Poole Kenneth (E-mail) ; Ronald GOldberg ; Shahnaz Duara ; Shankaran Seetha (E-mail) ; Stevenson David (E-mail) ; Stoll Barbara (E-mail) ; Tyson Jon (E-mail) ; Walid Salhab (Walid Salhab)
Cc: petrie@rti.org ; 'Hastings, Betty J.' ; Zaterka-Baxter, Kristin
Sent: Thursday, August 11, 2005 4:28 PM
Subject: SUPPORT AND OXIMETERS

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Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
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6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Ellen Hale
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: Pulmonary follow up secondary to SUPPORT
Date: Friday, August 05, 2005 11:17:36 AM

Yes, we will review.
Thanks,
Ellen

From: Charles Bauer, M.D.
To: Bada, Henrietta; Shankaran, Seetha; henrietta; barry; LINDA_LAGASSE@brown.edu; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Other Support
Date: Tuesday, July 26, 2005 12:26:08 PM

Henrietta,

You are right, I did NOT include this in my application.

Charlie

At 02:00 PM 7/20/2005 -0400, Bada, Henrietta wrote:

> Hi All, Charlie has submitted his. Doubt that this was included in Charlie's application.
>
> I looked up instruction son page 29 PHS398: Part1. ["other support" information is required for all applications that are selected to receive awards. NIH staff will request complete and up-to-date "other support" information from you after peer review.]
>
> Henrietta
>
> -----Original Message-----
> From: Shankaran, Seetha [mailto:sshankar@med.wayne.edu]
> Sent: Wednesday, July 20, 2005 1:37 PM
> To: henrietta; barry; LINDA_LAGASSE@brown.edu; Charlie; Rose
> Subject: FW: Other Support
>
> Hi all
> FYI re Other Support
> Seetha
>
> -----Original Message-----
> From: Robey, John Chris (NIH/NICHD) [mailto:robeyj@mail.nih.gov]
> Sent: Wednesday, July 20, 2005 12:38 PM
> To: 's_shankaran@wayne.edu'
> Cc: Higgins, Rosemary (NIH/NICHD)

Subject: RE: Other Support

Dr. Shankaran,

Unless the program is included under the "Just-In-Time" procedures the applicant does not need to include "Other Support" information for key personnel. However, it appears this is not the case for the MLS LOI. So yes, I would include it.

Sincerely,

-Chris

Christopher Robey
Grants Management Team Leader
National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd.
Room 8A17K, MSC 7510
Bethesda, Maryland 20892 (For Fed Ex/UPS Use 20852)
Telephone: (301) 435-6996
Fax: (301) 480-4783
E-Mail: robeyj@mail.nih.gov

==========

In support of NICHD electronic Grants Management, please use e-mail, NICHD e-Fax (301.451.5510) and the NIH eRA Commons. https://commons.era.nih.gov/commons Please note: All e-mail correspondence must be e-mail by the business official with a copy to the PI

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD)
Sent: Tuesday, July 19, 2005 5:31 PM
To: Robey, John Chris (NIH/NICHD); 's_shankaran@wayne.edu'
Subject: Fw: Other Support

Chris
Can you answer Dr. Shankaran's question?
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Shankaran, Seetha <sshankar@med.wayne.edu>
To: barry <barry_lester@brown.edu>; Charlie <cbauer@peds.med.miami.edu>; henrietta <hbada2@uky.edu>; Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
Sent: Tue Jul 19 16:42:07 2005
Subject: Other Support

Hi
Do we need the Other support pages for recompets? Current 398/2590 says no What are you doing? Rose? Rose, I did not get the answer to my question re my effort on MLS Seetha

From: Edward Donovan
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT Oximeter downloads
Date: Monday, July 25, 2005 10:27:48 AM

---

yes

Edward F. Donovan, M.D.
Director
Child Policy Research Center
Children's Hospital Medical Center
3333 Burnet Avenue, ML 7014
Cincinnati, OH 45229-3039
Phone 513-636-0182
Fax 513-636-0171
www.cprc-chmc.uc.edu

>>> "Higgins, Rosemary (NIH/NICHD)" <higginsr@mail.nih.gov> 07/25/2005 8:35:08 AM >>>
Neil and others,
Should we set up a call in the next few weeks to discuss?
Thanks
Rose

From: Neil Finer [mailto:nfiner@ucsd.edu]
Sent: Saturday, July 23, 2005 7:28 PM
To: 'Avroy A. Fanaroff, M.D.'; 'Betty Hastings'; 'Ed Donovan'; Higgins, Rosemary (NIH/NICHD); 'Ken Poole'; 'Michele'; 'Neil Finer'; 'Shahnaz Duara'; 'Wade Rich'; 'Wally Carlo'
Subject: SUPPORT Oximeter downloads

Hi Everyone
I would like to send out this 2 slide presentation with Maria's data to all centers
What do you think? Is it too early? I would like to have the sites aware that we are looking at the data, as it may help them educate their staffs.
Your thoughts
Thanks
Neil

From:	Neil Finer
To:	"Wally Carlo, M.D."
Cc:	"Avroy A. Fanaroff, M.D."; "Betty Hastings"; "Ed Donovan"; Higgins, Rosemary (NIH/NICHD) [E]; "Ken Poole"; "Michele"; "Neil Finer"; "Shahnaz Duara"; "Wade Rich"
Subject:	RE: SUPPORT Oximeter downloads
Date:	Sunday, July 24, 2005 10:24:41 PM

Thanks Wally
Before we send anything out we can ask Maria for the most recent data
Neil

From: Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]
Sent: Sunday, July 24, 2005 2:37 PM
To: Neil Finer; Avroy A. Fanaroff, M.D.; Betty Hastings; Ed Donovan; higginsr@mail.nih.gov; Ken Poole; Michele; Shahnaz Duara; Wade Rich
Subject: RE: SUPPORT Oximeter downloads

I think it would be useful to give some feedback. I will put together the suggestions for the figures. wally

---

From: Neil Finer [mailto:nfiner@ucsd.edu]
Sent: Saturday, July 23, 2005 6:28 PM
To: 'Avroy A. Fanaroff, M.D.'; 'Betty Hastings'; 'Ed Donovan'; higginsr@mail.nih.gov; 'Ken Poole'; 'Michele'; 'Neil Finer'; 'Shahnaz Duara'; 'Wade Rich'; Wally Carlo, M.D.
Subject: SUPPORT Oximeter downloads

Hi Everyone
I would like to send out this 2 slide presentation with Maria's data to all centers
What do you think? Is it too early? I would like to have the sites aware that we are looking at the data, as it may help them educate their staffs.
Your thoughts
Thanks
Neil

From: Estelle Fischer
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT
Date: Thursday, June 23, 2005 11:43:12 AM

Thank you

Estelle E. Fischer, MHSA, MBA
Clinical Research Manager
Division of Neonatology
Children's Hospital Medical Center (MLC 7009)
3333 Burnet Avenue
Cincinnati, OH 45229-3039
Phone: 513.558.0005 Fax: 513.558.7770

>>> "Higgins, Rosemary (NIH/NICHD)" <higginsr@mail.nih.gov> 06/23/05 11:08 AM >>>

The membership and disciplines are

Gordon Avery, M.D. – neonatology

Christine Gleason, M.D. – neonatology

Mary D'Alton, M.D. – OB/MFM

Carol Redmond, Ph.D. – statistician

Robert Boyle M.D.– ethics and neonatology

W. Kenneth Poole, Ph.D. – liaison from RTI

Marian Willinger M.D.– NICHD Representative

For the SUPPORT trial, we have ad hoc membership which includes:

Carl Hunt, M.D. - Neonatology and SIDS, NHLBI representative

Merran Thomson, M.D. – Neonatology (specific expertise with CPAP)

Marilee Allen, M.D. – neonatal follow up and long term outcomes

Let me know if you need additional information.

Thanks

Rose

From: Edward Donovan [mailto:Edward.Donovan@cchmc.org]
Sent: Thursday, June 23, 2005 11:00 AM
To: Higgins, Rosemary (NIH/NICHD)
Cc: Estelle Fischer
Subject: SUPPORT

Rose,
Although we will enroll no babies at Children's Hosp., some of our SUPPORT babies will be transferred for surgery, etc.
The Children's IRB has asked for the "composition" of the DSMB. I think disciplines represented would be fine.
Thanks,
Ed

Edward F. Donovan, M.D.
Director
Child Policy Research Center
Children's Hospital Medical Center
3333 Burnet Avenue, ML 7014
Cincinnati, OH 45229-3039
Phone 513-636-0182
Fax 513-636-0171
www.cprc-chmc.uc.edu

From: Shankaran, Seetha
To: henrietta; barry; LINDA_LAGASSE@brown.edu; Charlie; Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: Other Support
Date: Wednesday, July 20, 2005 1:37:13 PM

Hi all
FYI re Other Support
Seetha

-----Original Message-----
From: Robey, John Chris (NIH/NICHD) [mailto:robeyj@mail.nih.gov]
Sent: Wednesday, July 20, 2005 12:38 PM
To: 's_shankaran@wayne.edu'
Cc: Higgins, Rosemary (NIH/NICHD)
Subject: RE: Other Support

Dr. Shankaran,

Unless the program is included under the "Just-In-Time" procedures the applicant does not need to include "Other Support" information for key personnel. However, it appears this is not the case for the MLS LOI. So yes, I would include it.

Sincerely,

-Chris

Christopher Robey
Grants Management Team Leader
National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd.
Room 8A17K, MSC 7510
Bethesda, Maryland 20892 (For Fed Ex/UPS Use 20852)
Telephone: (301) 435-6996
Fax: (301) 480-4783
E-Mail: robeyj@mail.nih.gov

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In support of NICHD electronic Grants Management, please use e-mail, NICHD e-Fax (301.451.5510) and the NIH eRA Commons. https://commons.era.nih.gov/commons Please note: All e-mail correspondence must be e-mail by the business official with a copy to the PI

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD)
Sent: Tuesday, July 19, 2005 5:31 PM
To: Robey, John Chris (NIH/NICHD); 's_shankaran@wayne.edu'

Subject: Fw: Other Support

Chris
Can you answer Dr. Shankaran's question?
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Shankaran, Seetha <sshankar@med.wayne.edu>
To: barry <barry_lester@brown.edu>; Charlie <cbauer@peds.med.miami.edu>; henrietta <hbada2@uky.edu>; Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
Sent: Tue Jul 19 16:42:07 2005
Subject: Other Support

Hi
Do we need the Other support pages for recompets? Current 398/2590 says no What are you doing? Rose? Rose, I did not get the answer to my question re my effort on MLS Seetha

From: Shankaran, Seetha
To: barry; Charlie; henrietta; Higgins, Rosemary (NIH/NICHD) [E]
Subject: Other Support
Date: Tuesday, July 19, 2005 4:42:11 PM

Hi
Do we need the Other support pages for recompets? Current 398/2590 says no
What are you doing? Rose?
Rose, I did not get the answer to my question re my effort on MLS
Seetha

From: Higgins, Rosemary (NIH/NICHD)
To: "nfiner@ucsd.edu"
Subject: Re: support trial
Date: Monday, July 11, 2005 9:17:43 PM

Many times, these questions come to the PI, so I usually try to let the PI know the response.
take care
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Neil Finer <nfiner@ucsd.edu>
To: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
Sent: Mon Jul 11 19:55:46 2005
Subject: RE: support trial

Thanks for copying me Rose
Tony is one of my previous fellows
Regards
Neil

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Monday, July 11, 2005 1:47 PM
To: Tony Ryan
Subject: RE: support trial

Dr. Ryan
The SUPPORT Trial is being conducted in the NICHD Neonatal Research Network.
The need for continuous and active communication among sites dictates that
only institutions in the United States are eligible to apply. There is a
current Research Funding Announcement describing application which I have
attached.
Thank you for your interest.
Rose
Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

-----Original Message-----
From: Tony Ryan [mailto:ryant01@eircom.net]
Sent: Monday, July 11, 2005 4:33 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: support trial

I am interested in the SUPPORT trial. Are there any centres outside the US involved?

Tony Ryan
Department of Paediatrics & Child Health
University College Cork and
Cork University Hospitals, Cork, Ireland

From:	Higgins, Rosemary (NIH/NICHD)
To:	Tony Ryan
Bcc:	nfiner@ucsd.edu
Subject:	RE: support trial
Date:	Monday, July 11, 2005 4:46:00 PM
Attachments:	RFA-HD-04-010 NICHD Cooperative Multicenter Neonatal Research Network.htm

Dr. Ryan
The SUPPORT Trial is being conducted in the NICHD Neonatal Research Network. The need for continuous and active communication among sites dictates that only institutions in the United States are eligible to apply. There is a current Research Funding Announcement describing application which I have attached.
Thank you for your interest.
Rose
Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
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6100 Executive Blvd., Room 4B03B
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301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

-----Original Message-----
From: Tony Ryan [mailto:ryant01@eircom.net]
Sent: Monday, July 11, 2005 4:33 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: support trial

I am interested in the SUPPORT trial. Are there any centres outside the US involved?
Tony Ryan
Department of Paediatrics & Child Health
University College Cork and
Cork University Hospitals, Cork, Ireland

Part I Overview Information

Department of Health and Human Services

Participating Organizations
National Institutes of Health (NIH), (http://www.nih.gov/)

Components of Participating Organizations
National Institute of Child Health and Human Development (NICHD), (http://www.nichd.nih.gov/)

Title: NICHD Cooperative Multicenter Neonatal Research Network

Announcement Type
This announcement for the NICHD Neonatal Research Network (NRN) is a reissue with modifications of RFA-HD-00-010, released on April 3, 2000.

Request For Applications (RFA) Number: RFA-HD-04-010

Catalog of Federal Domestic Assistance Number(s)
93.865

Key Dates
Release Date: March 4, 2005
Letters of Intent Receipt Date(s): June 22, 2005
Application Receipt Dates(s): July 22, 2005
Peer Review Date(s): October/November 2005
Council Review Date(s): January 2006
Earliest Anticipated Start Date: April 1, 2006
Additional Information To Be Available Date May 16, 2005 (Url Activation Date): A workshop on the RFA will be held on May 16, 2005 in conjunction with the Pediatric Academic Societies Annual Meeting in Washington, DC. The presentation will be available at (http://www.nichd.nih.gov/RFA/HD-04-010/Workshop.htm).
Expiration Date: July 23, 2005

Due Dates for E.O. 12372
Not Applicable

Additional Overview Content

Executive Summary

- The National Institute of Child Health and Human Development (NICHD) invites applications from investigators willing to participate with the NICHD under a cooperative agreement in an ongoing multi-center clinical program designed to investigate problems in neonatal medicine, particularly those related to low birth weight, prematurity, and common neonatal medical problems.
- The NICHD intends to commit approximately $6.4 million in total costs [Direct plus Facilities and Administrative (F & A) costs] in FY 2006 to fund 13 to 16 new and/or competing continuation grants in response to this RFA.
- An applicant may request a project period of up to five years and a budget for direct costs up to $180,000 per year.
- This funding opportunity will use the NIH Cooperative Clinical Research (U10) award mechanism(s).
- Investigators may submit an application if their institution has any of the following characteristics: For-profit or non-profit organizations, Public or private institutions, such as universities, colleges, hospitals, and laboratories, Units of State and local governments, Eligible agencies of the Federal government.

- Eligible principal investigators include any individual with the skills, knowledge, and resources necessary to carry out the proposed research are invited to work with their institution to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH programs.
- An applicant institution may submit only one application in response to this RFA.
- Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 9/2004). The PHS 398 is available at http://grants.nih.gov/grants/funding/phs398/phs398.html in an interactive format. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: GrantsInfo@nih.gov. Applications must be received by the date listed under Key Dates, above.
- Telecommunications for the hearing impaired is available at: TTY 301-451-0088

Table of Contents

Part II - Full Text of Announcement

Section I. Funding Opportunity Description

1. Research Objectives

The National Institute of Child Health and Human Development (NICHD) invites applications from investigators willing to participate with the NICHD under a cooperative agreement in an ongoing multicenter clinical program designed to perform interventional and observational clinical studies in newborn infants, particularly low birth weight infants. The model of multi-site clinical centers for research is the gold standard for conducting clinical research. The objective of this program is to facilitate the advancement of neonatal care by establishing a network of academic centers that, by rigorous patient evaluation using common protocols, can study the required numbers of patients and can provide answers more rapidly that individual centers acting alone.

The infrastructure is set up for the ideal randomized double-blinded placebo controlled trial with the ability to follow short term (clinical effect) and long term (neurodevelopmental outcome) measures. The infrastructure is also set up for observational, longitudinal studies in the neonatal intensive care unit setting. Many randomized clinical trials involve the need for baseline information regarding disease incidence and outcome, which is available from the generic database of neonates < 1,500 grams birth weight in the current Neonatal Research Network. This initiative will foster conducting multicenter trials in the neonatal population.

The NICHD Program Staff will assist Principal Investigators of the Neonatal Research Network (NRN) and the Advisory Board in identifying research topics of high priority, and in designing and implementing protocols in the evaluation of optimum management in the areas targeted for research.

It is anticipated that approximately 13 to 16 clinical centers will be involved in the program.

Background

The primary objective of the Neonatal Research Network (NRN) is to advance the field of Neonatal-Perinatal Medicine by establishing and maintaining a network of academic centers that perform multi-center clinical protocols in a rigorous manner to investigate the safety and efficacy of treatment and management strategies to care for newborn infants, including low birth weight infants.

In an attempt to respond to the need for well-designed clinical trials in neonatal medicine, NICHD established a Neonatal Research Network in 1986. Seven university units were selected from among respondents to an RFA. The Network Steering Committee, which consists of representatives from each Clinical Center, NICHD staff, and data center staff, evaluated several controversial issues for study. It then selected certain priority areas in which to develop protocols for randomized clinical trials. Protocols on the prevention of sepsis, intraventricular hemorrhage, pulmonary hypertension, surfactant administration, and outcome and resource requirements for very low birth weight (VLBW) infants were initiated. In addition, the Network established a generic database of infants less than 1,500 grams at birth. During the second grant period of the Neonatal Research Network (1991-1996), clinical trials were initiated on the prevention or treatment of chronic lung disease (CLD), intraventricular hemorrhage, retinopathy of prematurity, and persistent pulmonary hypertension. Studies of VLBW maturity and postnatal growth, the sequelae of the fetal drug exposure, and a standardized follow-up program also were initiated. During the third Neonatal Research Network

funding period (1996 – 2001), intraventricular hemorrhage, retinopathy of prematurity, the treatment of persistent pulmonary hypertension, parenteral glutamine, indomethacin, erythropoietin, inhaled nitric oxide, postnatal steroids, ventilation management strategies, and outcome at follow-up were addressed. During the fourth cycle (2001-present), 16 clinical sites performed studies in the areas of necrotizing enterocolitis, inhaled nitric oxide, whole body cooling for asphyxia, benchmarking practices for bronchopulmonary dysplasia, phototherapy for extremely low birth weight infants, continuous positive airway pressure in the delivery room, candidal infections, neonatal infections, pneumococcal vaccine in very low birth weight infants, and follow up of high risk infants.

Scope

There are a number of controversial issues in neonatology that might be clarified by multicenter collaborative research. Funded Principal Investigators will cooperate with the NICHD Program Scientist in identifying research topics of high priority and in designing protocols appropriate to the evaluation of superior, or even optimal management in these areas. The participating Neonatal Research Network members will be designated as "Clinical Centers" which will recruit, assess and treat subjects under the supervision of the respective Clinical Center Principal Investigator. The data center, which is funded under a separate RFA, will have primary responsibility for data management and analysis for Network research in collaboration with the Steering Committee.

The NICHD expects to enable the Network to initiate new protocols within the first year of the next award period. The topics of these protocols will be decided cooperatively by the Steering Committee with advice from the Advisory Board. Areas of potential projects include but are not limited to:

- Trials of agents and strategies to improve short term and long term outcomes for infants (e.g. resuscitation strategies, medications, preventive measures and so forth)
- Observational studies of areas where little or no evidence is available for clinical management (e.g., infants born at the threshold of viability) or areas where there are gaps in knowledge

Ongoing protocols such as the generic data base and follow up study will continue.

See Section VIII. Other Information - Required Federal Citations, for policies related to this announcement.

Section II. Award Information

1. Mechanism(s) of Support

This funding opportunity will use the NIH Cooperative Clinical Research U10 award mechanism(s). As an applicant, you will be solely responsible for planning, directing, and executing the proposed project. The anticipated award date is April 1, 2006.

The NIH (U 10) is a cooperative agreement award mechanism. In the cooperative agreement mechanism, the Principal Investigator retains the primary responsibility and dominant role for planning, directing, and executing the proposed project, with NIH staff being substantially involved as a partner with the Principal Investigator, as described under the Section VI. 2. Administrative Requirements, "Cooperative Agreement Terms and Conditions of Award".

2. Funds Available

The NICHD intends to commit approximately $6.4 million in total costs [Direct plus Facilities and Administrative (F & A) costs] in FY 2006 to fund 13 to 16 new and/or competing continuation grants in response to this RFA. An applicant may request a project period of up to five years and a budget for direct costs up to $180,000 per year.

Because the nature and scope of the proposed research will vary from application to application, it is anticipated that the size and duration of each award will also vary. Although the financial plans of the IC(s) provide support for this program, awards pursuant to this funding opportunity are contingent upon the availability of funds and the receipt of a sufficient number of meritorious applications. At this time, it is not known if this RFA will be reissued.

Facilities and administrative costs requested by consortium participants are not included in the direct cost limitation,

see http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-004.html.

Section III. Eligibility Information

1. Eligible Applicants

1.A. Eligible Institutions

You may submit (an) application(s) if your organization has any of the following characteristics:

- For-profit organizations
- Non-profit organizations
- Public or private institutions, such as universities, colleges, hospitals, and laboratories
- Units of State government
- Units of local government
- Eligible agencies of the Federal government
- Domestic Institutions only

Clinical centers must have a minimum of 500 admissions per year in the neonatal intensive care unit. No more than 30 percent of the infants should be outborn. Large perinatal services will be given preference over combined services composed of a small inborn unit with a large transfer population s. Organizations should have academically oriented divisions of neonatology. The need for continuous and active communication among sites dictates that only institutions in the United States are eligible to apply. Racial/ethnic minority individuals, women, and persons with disabilities are encouraged to apply as Principal Investigators.

1.B. Eligible Individuals

Any individual with the skills, knowledge, and resources necessary to carry out the proposed research is invited to work with their institution to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH programs.

2. Cost Sharing or Matching

Not applicable

3. Other-Special Eligibility Criteria

The NICHD invites applications both from current members of the NRN Network (competing renewal applications) and from prospective members (new applications). The following items must be addressed satisfactorily for an applicant to be eligible for consideration as a Network site.

Academic Productivity

Provide evidence of research productivity by the clinical center in previous or ongoing clinical trials, especially those of a cooperative or multicenter design. Contributions in key areas of research development and design, patient recruitment, retention and study completion, data collection and analysis, and track record of publications should be included in the application.

Applicants who are current Neonatal Research Network members should describe their participation and contribution to the network in detail including patient enrollment in studies, involvement in trials and their particular contribution to the trials (principal investigator at site, trial subcommittee), standing subcommittee activities including chairmanship or vice chairmanship, and publications. New applicants must describe their recent experience and participation in randomized clinical trials. Specific roles (principal investigator, participating site, steering committee, writing committee, trial design and development) should be described for each study. Publications should be listed that resulted from participation in the studies.

Neonatology Staffing

Participants must be based at a level III/IV neonatal intensive care units that admits inborn and outborn infants. There must be at least four full time, board certified in neonatal perinatal medicine, academically oriented neonatologists. A complete description of the neonatal staff's training and qualifications in clinical care and research is required. Participation in clinical trials and clinical research should be highlighted. The principal investigator should be a practicing neonatologist and should describe their clinical, research, administrative and academic commitments. One neonatologist must be designated as an alternate principal investigator who is able to serve in the absence of the PI. Appropriate biographical sketches should be submitted with the application for the alternate PI and site neonatologists. Sites with neonatology staff at more than one clinical center must provide evidence of collaboration on recent trials including publications resulting from these studies.

Population Available for Clinical Trials

Applicant clinical centers must have at least 500 admissions per year. No more than 30 percent of admissions should be outborn. In order to provide peer reviewers with the specific neonatal population available for study at the clinical site (s), include information regarding admissions over the designated two-year period (2002-2003) in tabular format:

Number of births
Number of NICU admissions
NICU admissions < 1500 grams birth weight
NICU admissions < 1000 grams birth weight
NICU transport admissions
Average daily census for the NICU
Average daily census for intermediate care/special care nursery
Average NICU length of stay
Number of patients receiving CPAP only
Number of patients receiving ventilator care
Number of ECMO cases
Number of surgical cases

For sites with more than one clinical center, please include each site's information in a separate column. Large perinatal centers are ideal and may be given preference over multi-site arrangements. If a multi-site center has a long standing, well-documented collaboration and interaction among institutions, this should be clearly stated in the application. Eligibility and enrollment in previous clinical trials should be included in the application.

In addition, the patient population served by the NRN must be characterized by demographics, obstetric parameters, and payment status. Indications must be given of the proportions of various subgroups, including minorities, that have been eligible and actually have been randomized, in previous or current clinical trials. In addition, centers with ongoing clinical trials should report those patients eligible for NRN studies (not competing with institutional research).

Maternal Fetal Medicine Unit

The clinical center should be located in an institution with a maternal fetal medicine service for delivery of high-risk pregnancies. Perinatologists should be active in clinical research and a history of collaboration between neonatology and Perinatology towards excellent clinical care, database accessibility, and research productivity should be included in the application. The application should include a letter of collaboration along with a biographical sketch of a maternal fetal medicine collaborator. The application must include in tabular form the following information from 2002-2003 detailing maternal population for potential neonatal studies:

Number of deliveries
Number of C-sections
Number of multiple pregnancies delivered
Number of patients with diabetes (include gestational diabetes as well as patients with diabetes prior to pregnancy)
Number of patients with pregnancy induced hypertension or chronic Hypertension
Number of deliveries that are low birth weight (Number of antenatal consults performed by neonatalogy service (may include inpatient and outpatient consults)
Number of deliveries that are low birth weight: Number of antenatal consults performed by neonatalogy service (may include inpatient and outpatient consults).

Follow Up Program

An established neonatal follow up program with experience in tracking and retaining patients must be in place at the clinical site. The Neonatal Research Network strives for an 80 percent follow up rate at 18-22 months corrected gestational age. The number of clinic visits in 2001 and 2002 need to be included in the application, as well as criteria for follow up (e.g. LBW, ELBW, neurological issue, ECMO, etc.) and post conceptual age at which the children are seen in clinic visits. A designated facility for follow up must be in place at the clinical center. Applicants should describe in detail mechanisms in place to insure compliance and assistance with neonatal follow up including procedures for maintaining contact with families, scheduling appointments, actions taken for missed appointments, home visit appointments including staff participating in home visits, and creative measures instituted at the site to insure excellence in follow up rates and compliance with clinical research study protocols. There must be a follow up investigator (can be the PI) designated in the application with an included biosketch. The follow up portion of the clinical capabilities must include expertise in performing Bayley Developmental assessments, neurological examinations, and hearing and vision assessments. The current system of follow up assessment including data collection, population demographics, compliance rates, schedule of follow up visits, funding sources, policies and procedures for conducting research in the follow up setting and appropriate specialist involvement in the follow up program should be delineated in the application.

Perinatal Data System

An established electronic perinatal data system must be in place to collect and analyze patient information. A detailed description of variables collected, quality control, and management of the data system must be provided. An illustration of the use of the system for a recent clinical research application should be included in the application. All successful applications must provide complete, accurate and timely transmission of data to the Neonatal Research Network Data Coordinating Center.

Research Staff

A full time research nurse coordinator must be designated for the coordinator position. Additional research staff should be available, as many protocols require patient recruitment at night and on weekends. The individual staff training, experience, qualifications, and prior involvement in clinical research should be described in the application.

Intent to Participate

There must be a clearly expressed intent to participate in a cooperative manner with other NRN clinical centers, the NICHD and the data coordinating center in all aspect of research as outlined in this RFA. NRN projects are given priority at awarded clinical sites. Sites are expected to participate in all trials unless they describe trials that currently conflict with ongoing network trials as part of their application for this RFA.

Departmental and Institutional Commitment

The departmental and institutional commitments to participate in MFMU research should be clearly documented with letters of support from appropriate individuals. Evidence of past support can also be cited. Support in areas of grants management, personnel management; space allocation, procurement, equipment as well as general support of the research should be described as well as evidence of past research support.

Acceptance of the Budgetary Mechanism (see also budget preparation below)

Assurance of cooperation with the policy for capitation of research costs for each individual protocol, in addition to a base budget, should be provided from the departmental and institutional offices of sponsored research programs. The appropriate Federal cost policies and regulations governing NIH grant programs will be applied (see NIH Grants Policy Statement at http://grants.nih.gov/grants/policy/nihgps_2003/index.htm).

If the institution submits applications in response to both the Neonatal Research Network RFA and the Maternal Fetal Medicine Unit RFA (HD-04-023), the applicant must describe how the two research programs will be integrated.

Section IV. Application and Submission Information

1. Address to Request Application Information

The PHS 398 application instructions are available at http://grants.nih.gov/grants/funding/phs398/phs398.html in an interactive format. Applicants must use the currently approved version of the PHS 398. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: GrantsInfo@nih.gov.

Telecommunications for the hearing impaired: TTY 301-451-0088.

2. Content and Form of Application Submission

Applications must be prepared using the most current PHS 398 research grant application instructions and forms. Applications must have a D&B Data Universal Numbering System (DUNS) number as the universal identifier when applying for Federal grants or cooperative agreements. The D&B number can be obtained by calling (866) 705-5711 or through the web site at http://www.dnb.com/us/. The D&B number should be entered on line 11 of the face page of the PHS 398 form.

The title and number of this funding opportunity must be typed on line 2 of the face page of the application form and the YES box must be checked.

3. Submission Dates and Times

Applications must be received on or before the receipt date described below (Section IV.3.A). Submission times N/A.

3.A. Receipt, Review and Anticipated Start Dates

Letters of Intent Receipt Date(s): June 22, 2005
Application Receipt Date(s): July 22, 2005
Peer Review Date(s): October/November 2005
Council Review Date(s): January 2006
Earliest Anticipated Start Date: April 1, 2006

3.A.1. Letter of Intent

Prospective applicants are asked to submit a letter of intent that includes the following information:

- Descriptive title of proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Number and title of this funding opportunity

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows IC staff to estimate the potential review workload and plan the review.

The letter of intent is to be sent by the date listed at the beginning of this document.

The letter of intent should be sent to:

Rosemary D. Higgins, MD
Pregnancy and Perinatology Branch
National Institute of Child Health And Human Development
6100 Executive Boulevard, Room 4B03B, MSC 7510
Bethesda, MD 20892-7510
Rockville, MD 20852 (for express/courier service, non-USPS service)
Telephone: (301) 435-7909
FAX: (301) 496-3790

Email: mailto:spongc@mail.nih.gov

3.B. Sending an Application to the NIH

Applications must be prepared using the PHS 398 research grant application instructions and forms as described above. Submit a signed, typewritten original of the application, including the checklist, and three signed photocopies in one package to:

Center for Scientific Review
National Institutes of Health
6701 Rockledge Drive, Room 1040, MSC 7710
Bethesda, MD 20892-7710 (U.S. Postal Service Express or regular mail)
Bethesda, MD 20817 (for express/courier service; non-USPS service)

At the time of submission, two additional copies of the application and all copies of the appendix material must be sent to:

Robert Stretch, Ph.D.
Director, Division of Scientific Review
National Institute of Child Health and Human Development
6100 Executive Boulevard, Room 5B01, MSC 7510
Bethesda, MD 20892-7510
Rockville, MD 20852 (for express/courier service, non-USPS service)
Telephone: (301) 496-1485
FAX: (301) 402-4104
Email: stretchr@mail.nih.gov

Using the RFA Label: The RFA label available in the PHS 398 application instructions must be affixed to the bottom of the face page of the application. Type the RFA number on the label. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2 of the face page of the application form and the YES box must be marked. The RFA label is also available at: http://grants.nih.gov/grants/funding/phs398/labels.pdf. Personal deliveries of applications are no longer permitted.

3.C. Application Processing

Applications must be **received on or before the application receipt date(s)** described above (Section IV.3.A.). If an application is received after that date, it will be returned to the applicant without review. Upon receipt, applications will be evaluated for completeness by the CSR and responsiveness by the NICHD. Incomplete and non-responsive applications will not be reviewed.

The NIH will not accept any application in response to this funding opportunity that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. However, when a previously unfunded application, originally submitted as an investigator-initiated application, is to be submitted in response to a funding opportunity, it is to be prepared as a NEW application. That is, the application for the funding opportunity must not include an Introduction describing the changes and improvements made, and the text must not be marked to indicate the changes from the previous unfunded version of the application.

Although there is no immediate acknowledgement of the receipt of an application, applicants are generally notified of the review and funding assignment within eight (8) weeks.

4. Intergovernmental Review

This initiative is not subject to intergovernmental review.

5. Funding Restrictions

All NIH awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement. The Grants Policy Statement can be found at http://grants.nih.gov/grants/policy/policy.htm

(see also Section VI.3. Reporting).

Pre-Award Costs are allowable. A grantee may, at its own risk and without NIH prior approval, incur obligations and expenditures to cover costs up to 90 days before the beginning date of the initial budget period of a new or competing continuation award if such costs: are necessary to conduct the project, and would be allowable under the grant, if awarded, without NIH prior approval. If specific expenditures would otherwise require prior approval, the grantee must obtain NIH approval before incurring the cost. NIH prior approval is required for any costs to be incurred more than 90 days before the beginning date of the initial budget period of a new or competing continuation award.

The incurrence of pre-award costs in anticipation of a competing or non-competing award imposes no obligation on NIH either to make the award or to increase the amount of the approved budget if an award is made for less than the amount anticipated and is inadequate to cover the pre-award costs incurred. NIH expects the grantee to be fully aware that pre-award costs result in borrowing against future support and that such borrowing must not impair the grantee's ability to accomplish the project objectives in the approved time frame or in any way adversely affect the conduct of the project. See NIH Grants Policy Statement http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part6.htm.

6. Other Submission Requirements

In addition to the information under Section III. Eligibility Information 3. "Other Special Eligibility Criteria," applicants must include the following in their application:

Clinical Capabilities

The applicant clinical center is expected to have a full range of perinatal subspecialists, clinical capabilities and support staff including an active research coordinator. A detailed description of the clinical attributes of the NRN must be provided. This should include antenatal fetal testing, intrapartum diagnosis, laboratory testing, and perinatal pathology. Other institutional components related to the NRN must also be described. In particular, the ambulatory facilities for prenatal and postpartum care must be presented, including the established policies and procedures for conducting clinical research in these facilities, in both low risk and complicated pregnancies. Also, the availability of an institutional pharmacy capable of supporting clinical research must be documented. A description of whether, and how, policies and procedures may have been modified to support perinatal clinical research in the past must be provided.

A clinical research coordinator must be designated for a full time position.

Capabilities for patient recruitment on nights and weekends should be outlined in the application

Concept Proposal

To provide peer reviewers and the NICHD an idea of capabilities of investigators, a concept proposal for a project for the Neonatal Research Network submission should be described briefly (two to three pages maximum). A proposal including hypothesis, specific aim(s), background, methods, and data analysis (including a consideration of power) for potential conduct in the NRN must be provided in the application. The proposed "concept" will serve as an indicator of the applicant's ability to participate in the development and design of cooperative protocols in the network. The "concept" needs to be appropriate for the NRN in that it requires a multicenter design. The "concept" or another design on the same topic may or may not actually be performed in the network. It is anticipated that funded NRN centers will be invited to submit the "concepts" included in their application to the Steering Committee.

The "concept" should also demonstrate use of the applicant's perinatal data system to estimate numbers of available patients eligible for the protocol at the institution. In addition, the protocol should address relevant ethical issues and the appropriate inclusion of minorities as subjects.

Special Strengths of the PI or Institution

Applications are encouraged to describe special or unique strengths that may be relevant to NRN research. This can include state-of-the art scientific capabilities such as modern imaging techniques, proteomics, genomics, micro analysis, genetics, placental function, clinical pharmacology and so forth, which may be shared or may be available to develop and expand the scientific productivity of the NRN.

In addition special administrative strengths or experience as well as participation in administrative aspects of clinical

research (institutional review board, data safety monitoring committee, advisory board for clinical research, clinical research committees and so forth) should be highlighted. Level and support of clinical trials can be described.

Applications from institutions that have a General Clinical research Center (GCRC) funded by NIH or other funded perinatal research centers as resources for conducting the proposed research should provide a letter of agreement that identifies the level of support from the PI or the GCRC program director.

Budget Preparation

The instructions for the budget requests provided with the research grant application (PHS 398) should be followed. F&A costs will be awarded in the same manner as for research project grants. Budgets will be reviewed on the basis of appropriateness for the work proposed. Allowable costs and policies governing the research grants programs of the NIH will prevail. In planning the budget section of your application, each applicant should submit the base budget estimates for all years.

The first year budget at the time of application will be limited to a BASE BUDGET with maximum allowances as follows:

- Principal Investigator (PI): 10 percent effort
- Alternate PI, PI, or Follow Up PI: additional 10 percent effort
- Research Nurse: 100 percent effort
- Data Entry Clerk: 50 percent effort
- Supplies and small equipment (itemized and justified): Not to exceed $5,000
- Travel (a total of 10 trips to DC metro Area per network team): as appropriate
- Other costs (itemized and individually justified): Not to exceed $3,000

The base budget direct costs are limited to $180,000 for the first year.

When an application has been favorably recommended and is being considered for funding, the applicant will be required to complete protocol budgets for those studies underway in the network. These budgets will consist of specific protocol related allowances and will be capitated on the anticipated number of subjects to be enrolled in the study at the applicant NRN center.

Ongoing annual budgets of the NRN centers will be based on individual protocols that will be funded through a capitation system. Each NRN center will be given base costs (listed above), in addition to a flat fee for a patient successfully enrolled and completed for individual studies. For centers with GCRC funding, applicable capitation funds can be reduced relative to the amount of GCRC support. The Principal Investigator will be required to project patient enrollment for a specific protocol during a specified time frame; continuation and the level of funding will be based on actual enrollment. Each year, capitation budgets are rectified based on actual enrollment. Future years' base budgets should be limited to the first year base budget costs, with an annual increment of base salary and travel costs not to exceed 3 percent (the maximum amount available for equipment, supplies, and other costs will not increase). Federal agencies shall use the negotiated rates for F&A costs in effect at the time of the initial award throughout each competitive cycle of the project. Award levels for sponsored agreements may not be adjusted in future years as a result of changes in negotiated rates.

Plan for Sharing Research Data

The precise content of the data-sharing plan will vary, depending on the data being collected and how the investigator is planning to share the data. Applicants who are planning to share data may wish to describe briefly the expected schedule for data sharing, the format of the final dataset, the documentation to be provided, whether or not any analytic tools also will be provided, whether or not a data-sharing agreement will be required and, if so, a brief description of such an agreement (including the criteria for deciding who can receive the data and whether or not any conditions will be placed on their use), and the mode of data sharing (e.g., under their own auspices by mailing a disk or posting data on their institutional or personal website, through a data archive or enclave). Investigators choosing to share under their own auspices may wish to enter into a data-sharing agreement. References to data sharing may also be appropriate in other sections of the application.

The data sharing plan should be in accordance with current NRN Policies.

All applicants must include a plan for sharing research data in their application. The data sharing policy is available at http://grants.nih.gov/grants/policy/data_sharing. All investigators responding to this funding opportunity should include a description of how final research data will be shared, or explain why data sharing is not possible.

The reasonableness of the data sharing plan or the rationale for not sharing research data will be assessed by the reviewers. However, reviewers will not factor the proposed data sharing plan into the determination of scientific merit or the priority score.

Section V. Application Review Information

1. Criteria

Only the review criteria described below will be considered in the review process.

Applications recommended by the National Advisory Child Health and Human Development Council will be considered for award based primarily on scientific and technical merit, as determined by peer review. Program balance, that is, the scope and variety of research strengths to enable a successful collaborative program, will be considered. Final selection of Clinical Centers for funding may be partly based on the need for diversity including geography and special populations in the study population. Availability of funds may also determine the awards made.

The following will be considered in making funding decisions:

- Scientific merit of the proposed project as determined by peer review
- Availability of funds
- Relevance of program priorities

2. Review and Selection Process

Upon receipt, applications will be reviewed for completeness by the CSR and responsiveness by the NICHD. Incomplete and/or non-responsive applications will not be reviewed.

Applications that are complete and responsive to the RFA will be evaluated for scientific and technical merit by an appropriate peer review group convened by NICHD in accordance with the review criteria stated below.

As part of the initial merit review, all applications will:

- Undergo a selection process in which only those applications deemed to have the highest scientific merit, generally the top half of applications under review, will be discussed and assigned a priority score.
- Receive a written critique.
- Receive a second level of review by the National Advisory Child Health and Human Development Council (NACHHD).

The following review criteria will be applied:

Applications will be reviewed based on their ability to meet overall requirements of the RFA and to cooperatively participate as an NRN site. Review of the concept proposal is one component and is used to demonstrate the site's ability to formulate appropriate and timely scientific questions applicable to the network.

Qualifications and Commitment of Key Personnel:

- The scientific, administrative, clinical and academic qualifications of the principal investigator and the research team at the center, as well as the qualifications of the applicant institution and the institution's population to participate fully in the Neonatal Research Network
- Knowledge and experience in areas relevant to the conduct of collaborative clinical research, especially

randomized clinical trials, including experience in research design, in neonatology.
- Commitment of staff time for the satisfactory conduct of the studies.
- Experience and qualifications of team members who would be responsible for data quality and management activities.

Protocols and Procedures

- Quality of the unit's participation in a randomized clinical trial (new applicants) in the recent past or Network protocols during the current grant period (current Network members).
- Willingness to work and cooperate with other NRN sites and the NICHD in a manner summarized in this RFA.

Facilities and Management

- Adequacy of administrative, clinical, and data organizational management facilities as described in the requirements.
- Institutional assurance to provide support to the study in such areas as fiscal administration, personnel management, space allocation, procurement, planning, and budgeting.
- Optional administrative strengths, such as affiliations with other research units.

Scientific Review of Concept Proposal

Evaluation of the concept proposal for an interventional or observational study for potential implementation in the Neonatal Research Network in terms of the quality of proposed hypotheses, specific aim(s), background, methods, and data analysis (including a consideration of power).

2.A. Additional Review Criteria:

In addition to the above criteria, the following items will continue to be considered in the determination of scientific merit and the priority score:

Protection of Human Subjects from Research Risk: The involvement of human subjects and protections from research risk relating to their participation in the proposed research will be assessed (see the Research Plan, Section E on Human Subjects in the PHS Form 398).

Inclusion of Women, Minorities and Children in Research: The adequacy of plans to include subjects from both genders, all racial and ethnic groups (and subgroups), and children as appropriate for the scientific goals of the research will be assessed. Plans for the recruitment and retention of subjects will also be evaluated (see the Research Plan, Section E on Human Subjects in the PHS Form 398).

2.B. Additional Review Considerations

Budget: The reasonableness of the proposed budget and the requested period of support in relation to the proposed research. The priority score should not be affected by the evaluation of the budget.

2.C. Sharing Research Data

Data Sharing Plan: The reasonableness of the data sharing plan or the rationale for not sharing research data may be assessed by the reviewers. However, reviewers will not factor the proposed data sharing plan into the determination of scientific merit or the priority score. The funding organization will be responsible for monitoring the data sharing policy. http://grants.nih.gov/grants/policy/data_sharing.

2.D. Sharing Research Resources
Not applicable

3. Anticipated Announcement and Award Dates
Not applicable

Section VI. Award Administration Information

1. Award Notices

After the peer review of the application is completed, the Principal Investigator will also receive a written critique called a Summary Statement.

If the application is under consideration for funding, NIH will request "just-in-time" information from the applicant. For details, applicants may refer to the NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General (http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_part4.htm).

A formal notification in the form of a Notice of Grant Award (NGA) will be provided to the applicant organization. The NGA signed by the grants management officer is the authorizing document.

Selection of an application for award is not an authorization to begin performance. Any costs incurred before receipt of the NGA are at the recipient's risk. These costs may be reimbursed only to the extent considered allowable pre-award costs. See Also Section IV.5. Funding Restrictions.

Once all administrative and programmatic issues have been resolved, the Notice of Grant Award will be generated via e-mail notification from the awarding component to the grantee business official (designated in Item 14 on the Application Face Page). If a grantee is not e-mail enabled, a hard copy of the Notice of Grant Award will be mailed to the business official.

2. Administrative and National Policy Requirements

All NIH grant and cooperative agreement awards include the NIH Grants Policy Statement as part of the notice of grant award. For these terms of award, see the NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General (http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part4.htm) and Part II Terms and Conditions of NIH Grant Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Grantees, and Activities (http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_part9.htm).

The following Terms and Conditions will be incorporated into the award statement and will be provided to the Principal Investigator as well as to the appropriate institutional official, at the time of award.

2.A. Cooperative Agreement Terms and Conditions of Award

The following special terms of award are in addition to, and not in lieu of, otherwise applicable OMB administrative guidelines, HHS grant administration regulations at 45 CFR Parts 74 and 92 (Part 92 is applicable when State and local Governments are eligible to apply), and other HHS, PHS, and NIH grant administration policies.

The administrative and funding instrument used for this program will be the cooperative agreement (NIH Cooperative Clinical Research U10), an "assistance" mechanism (rather than an "acquisition" mechanism), in which substantial NIH programmatic involvement with the awardees is anticipated during the performance of the activities. Under the cooperative agreement, the NIH purpose is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the award recipients in a partnership role; it is not to assume direction, prime responsibility, or a dominant role in the activities. Consistent with this concept, the dominant role and prime responsibility resides with the awardees for the project as a whole, although specific tasks and activities may be shared among the awardees and the NICHD Program Scientist. Facilities and Administrative cost (indirect cost) award procedures apply to cooperative agreements in the same manner as for grants. Business management aspects of these awards will be administered by the NICHD Grants Management Branch in accordance with HHS and NIH grant administrative requirements.

2.A.1. Principal Investigator Rights and Responsibilities

The Principal Investigator will have the primary responsibility for:

- Identification of priority areas for research
- Developing and implementing the network protocols
- Collection and transmission of the data to the data-coordinating center
- Analysis of data and publication of results of the NRN trials

The Data Coordinating Center is funded through a separate solicitation as a cooperative agreement (U01).

All parties will agree to accept the coordinating role of the group and the participatory and cooperative nature of the group process.

The individual members will be required to project patient enrollment for a specific protocol during a specified time frame; continuation and level of funding will be based on actual recruitment.

The NRN Steering Committee will retain custody and have primary rights to the data developed under these awards, subject to Government rights of access consistent with current HHS, PHS, and NIH policies.

Awardees will retain custody of and have primary rights to the data and software developed under these awards, subject to Government rights of access consistent with current HHS, PHS, and NIH policies.

2.A.2. NIH Responsibilities

NICHD Program Scientist

An NICHD Program Scientist will have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below.

1. Assistance with the identification of important areas of study.

2. Assistance in the development of study protocols.

3. Assistance in the development and review of capitation-based budgets, including the identification of study costs and special institutional needs.

4. Assistance in the review and evaluation of each stage of the program before subsequent stages are started, in conjunction with the Steering Committee and the Advisory Board.

5. Assistance in reporting results in the community of investigators and health care recipients.

6. Assisting in the conduct of the trials, including ongoing review of progress; possible redirection of activities to improve performance and cooperation; and frequent communication with other members of the Steering Committee.

7. Participation on the Steering Committee and all active subcommittees.

NICHD Project Officer

Additionally, an agency program official or IC program director will be responsible for the normal scientific and programmatic stewardship of the award and will be named in the award notice.

Traditional program management/stewardship responsibility for review and oversight of the cooperative agreement award will reside with the NRN Project Officer. This role is separate from the Program Scientist and will include the following:

- Carry out continuous review of all activities to ensure that the objectives are being met and that all regulatory, fiscal, and administrative matters are handled according to NIH guidelines.
- Have the option to withhold support to a participating institution if technical performance requirements are not met.

- Perform other duties required for normal program stewardship of grants.
- Assurance of the scientific merit of the trials, including the option to withhold support of a participating center if technical performance requirements such as protocol compliance, enrollment targets, or randomization of subjects are not met.
- Initiation of a decision to modify or terminate a study based on the advice of the data center, Data Safety and Monitoring Committee, and/or Advisory Board with the mutual consent of the Steering Committee.

2.A.3. Collaborative Responsibilities

The management of the Neonatal Research Network includes committees with the following functions:

Steering Committee

A Steering Committee will be responsible for protocol development, assisted by the Advisory Board and the Data Safety and Monitoring Committee. The Steering Committee will have primary responsibility for the conduct of protocols and the preparation of publications. The Steering Committee will be composed of all Principal Investigators, one representative from the data center, and two NICHD staff. The Data Coordinating Center is supported through a separate cooperative agreement solicited in a separate RFA. Participating NICHD staff will include the Pregnancy and Perinatology Branch NRN Program Scientist. The NRN Program Scientist will be the only voting NICHD staff member of the Steering Committee. A member of the NICHD Grants Management Branch advises the Steering Committee on funding matters. An outside chairperson, who is not participating as a Principal Investigator, will be selected by the NICHD.

Advisory Board

The Advisory Board assists the Steering Committee in the identification and prioritization of topics for perinatal research. The advisory board is selected by the NICHD and consists of individuals with expertise in clinical trials, biostatistics, epidemiology, perinatology, and neonatology, and the Chairperson of the Steering Committee. Additional members will participate based on the need for specific expertise.

Data Safety and Monitoring Committee

A Data Safety and Monitoring Committee (DSMC) monitors the safety of ongoing clinical trials. The DSMC is established by the NICHD and reports to the Director of NICHD. The DSMC is composed of individuals with expertise in clinical trial design and conduct, perinatology, neonatology, basic science, and ethics.

In addition, the NICHD Neonatal Research Network has established policies and procedures that govern its operations, including publications. These policies and procedures can be amended by the Steering Committee and the NICHD.

Each full member will have one vote. Awardee members of the Steering Committee will be required to accept and implement policies approved by the Steering Committee.

2.A.4. Arbitration Process

Any disagreements that may arise in scientific or programmatic matters (within the scope of the award) between award recipients and the NIH may be brought to arbitration. An Arbitration Panel composed of three members will be convened. It will have three members: a designee of the Steering Committee chosen without NIH staff voting, one NIH designee, and a third designee with expertise in the relevant area who is chosen by the other two; in the case of individual disagreement, the first member may be chosen by the individual awardee. This special arbitration procedure in no way affects the awardee's right to appeal an adverse action that is otherwise appealable in accordance with PHS regulations 42 CFR Part 50, Subpart D and HHS regulations 45 CFR Part 16.

3. Reporting

Awardees will be required to submit the PHS Non-Competing Grant Progress Report, Form 2590 annually (http://grants.nih.gov/grants/funding/2590/2590.htm) and financial statements as required in the NIH Grants Policy Statement.

Section VII. Agency Contacts

We encourage your inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants. Inquiries may fall into three areas: scientific/research, peer review, and financial or grants management issues:

1. Scientific/Research Contacts:

Rosemary D. Higgins, MD
Pregnancy and Perinatology Branch
National Institute of Child Health And Human Development
6100 Executive Boulevard, Room 4B03B, MSC 7510
Bethesda, MD 20892-7510
Rockville, MD 20852 (for express/courier service, non-USPS service)
Telephone: (301) 435-7909
FAX: (301) 496-3790
Email: higginsr@mail.nih.gov

2. Peer Review Contacts:

Robert Stretch, Ph.D.
Director, Division of Scientific Review
National Institute of Child Health and Human Development
6100 Executive Boulevard, Room 5B01, MSC 7510
Bethesda, MD 20892-7510
Rockville, MD 20852 (for express/courier service, non-USPS service)
Telephone: (301) 496-1485
FAX: (301) 402-4104
Email: stretchr@mail.nih.gov

3. Financial or Grants Management Contacts:

Chris Robey
Grants Management Branch
National Institute of Child Health and Human Development
6100 Executive Boulevard, Room 8A01, MSC 7510
Bethesda, MD 20892-7510
Rockville, MD 20852 (for express/courier service, non-USPS service)
Telephone: (301) 435-6996
FAX: (301) 402-0915
Email: robeyj@mail.nih.gov

Section VIII. Other Information

Required Federal Citations

Human Subjects Protection:
Federal regulations (45CFR46) require that applications and proposals involving human subjects must be evaluated with reference to the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained (http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm).

Data and Safety Monitoring Plan:
Data and safety monitoring is required for all types of clinical trials, including physiologic toxicity and dose-finding studies (phase I); efficacy studies (Phase II); efficacy, effectiveness and comparative trials (Phase III). Monitoring

should be commensurate with risk. The establishment of data and safety monitoring boards (DSMBs) is required for multi-site clinical trials involving interventions that entail potential risks to the participants (NIH Policy for Data and Safety Monitoring, NIH Guide for Grants and Contracts, http://grants.nih.gov/grants/guide/notice-files/not98-084.html).

Inclusion of Women And Minorities in Clinical Research:
It is the policy of the NIH that women and members of minority groups and their sub-populations must be included in all NIH-supported clinical research projects unless a clear and compelling justification is provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43). All investigators proposing clinical research should read the "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html); a complete copy of the updated Guidelines is available at http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm. The amended policy incorporates: the use of an NIH definition of clinical research; updated racial and ethnic categories in compliance with the new OMB standards; clarification of language governing NIH-defined Phase III clinical trials consistent with the new PHS Form 398; and updated roles and responsibilities of NIH staff and the extramural community. The policy continues to require for all NIH-defined Phase III clinical trials that: a) all applications or proposals and/or protocols must provide a description of plans to conduct analyses, as appropriate, to address differences by sex/gender and/or racial/ethnic groups, including subgroups if applicable; and b) investigators must report annual accrual and progress in conducting analyses, as appropriate, by sex/gender and/or racial/ethnic group differences.

Inclusion of Children as Participants in Clinical Research:
The NIH maintains a policy that children (i.e., individuals under the age of 21) must be included in all clinical research, conducted or supported by the NIH, unless there are scientific and ethical reasons not to include them.

All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines" on the inclusion of children as participants in research involving human subjects (http://grants.nih.gov/grants/funding/children/children.htm).

Required Education on the Protection of Human Subject Participants:
NIH policy requires education on the protection of human subject participants for all investigators submitting NIH applications for research involving human subjects and individuals designated as key personnel. The policy is available at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html.

Public Access to Research Data through the Freedom of Information Act:
The Office of Management and Budget (OMB) Circular A-110 has been revised to provide public access to research data through the Freedom of Information Act (FOIA) under some circumstances. Data that are (1) first produced in a project that is supported in whole or in part with Federal funds and (2) cited publicly and officially by a Federal agency in support of an action that has the force and effect of law (i.e., a regulation) may be accessed through FOIA. It is important for applicants to understand the basic scope of this amendment. NIH has provided guidance at http://grants.nih.gov/grants/policy/a110/a110_guidance_dec1999.htm. Applicants may wish to place data collected under this PA in a public archive, which can provide protections for the data and manage the distribution for an indefinite period of time. If so, the application should include a description of the archiving plan in the study design and include information about this in the budget justification section of the application. In addition, applicants should think about how to structure informed consent statements and other human subjects procedures given the potential for wider use of data collected under this award.

Standards for Privacy of Individually Identifiable Health Information:
The Department of Health and Human Services (DHHS) issued final modification to the "Standards for Privacy of Individually Identifiable Health Information", the "Privacy Rule", on August 14, 2002. The Privacy Rule is a federal regulation under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 that governs the protection of individually identifiable health information, and is administered and enforced by the DHHS Office for Civil Rights (OCR).

Decisions about applicability and implementation of the Privacy Rule reside with the researcher and his/her institution. The OCR website (http://www.hhs.gov/ocr/) provides information on the Privacy Rule, including a complete Regulation Text and a set of decision tools on "Am I a covered entity?" Information on the impact of the HIPAA Privacy Rule on NIH processes involving the review, funding, and progress monitoring of grants, cooperative agreements, and research contracts can be found at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-025.html.

URLs in NIH Grant Applications or Appendices:
All applications and proposals for NIH funding must be self-contained within specified page limitations. Unless

otherwise specified in an NIH solicitation, Internet addresses (URLs) should not be used to provide information necessary to the review because reviewers are under no obligation to view the Internet sites. Furthermore, we caution reviewers that their anonymity may be compromised when they directly access an Internet site.

Healthy People 2010:
The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a PHS-led national activity for setting priority areas. This PA is related to one or more of the priority areas. Potential applicants may obtain a copy of "Healthy People 2010" at http://www.health.gov/healthypeople.

Authority and Regulations:
This program is described in the Catalog of Federal Domestic Assistance at http://www.cfda.gov/ and is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review. Awards are made under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and under Federal Regulations 42 CFR 52 and 45 CFR Parts 74 and 92. All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement. The NIH Grants Policy Statement can be found at http://grants.nih.gov/grants/policy/policy.htm.

The PHS strongly encourages all grant recipients to provide a smoke-free workplace and discourage the use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care, or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

Weekly TOC for this Announcement
NIH Funding Opportunities and Notices

Department of Health and Human Services

NIH National Institutes of Health (NIH)
9000 Rockville Pike
Bethesda, Maryland 20892

From: Higgins, Rosemary (NIH/NICHD)
To: VanMeurs, Krisa
Date: Monday, July 11, 2005 4:17:00 PM
Attachments: Protocol outline.doc

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

Protocol outline

A. Abstract

B. Statement of the Problem

C. Hypothesis

D. Specific Aims

E. Rationale/justification

F. Background / Previous Studies

G. Method/ Procedures

1. Description of study design (masked, randomized etc.)_
2. Definition of study population (with inclusion/exclusion criteria)
3. Description of study intervention
4. Precise definition of primary/secondary outcomes
5. Sample size estimate with some statistical support (including estimate of compliance and consent rates) based upon primary outcome.
6. Available population/compatibility with other ongoing protocols
7. Estimate of projected recruitment time

H, Risks/benefits, with estimate of frequency/severity of risks.

I. Budget estimate

From: Wade Rich
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Oxims
Date: Monday, July 11, 2005 2:23:49 PM

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not yet. I just emailed Betty to see if she has received the list of serial #s.
wade

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Monday, July 11, 2005 11:21 AM
To: 'wrich@ucsd.edu'
Subject: Re: Oxims

Thanks
I will check with betty hastings regarding the replenishment of the sites that you had borrowed from - also, are the codes and stickers on them?
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Wade Rich <wrich@ucsd.edu>
To: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
Sent: Mon Jul 11 14:19:22 2005
Subject: Oxims

Rose,
My 10 oximeters have arrived and are being checked in by Biomed if you get any frantic phone calls from other sites.
Wade

Wade Rich, BS,RRT-NPS
Clinical Research Coordinator
Division of Neonatology
UCSD Medical Center
200 W Arbor Dr
San Diego, CA 92103-8774
619-543-5375
pgr 290-5230

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Re: MRI"s at 36 weeks
Date: Monday, July 11, 2005 10:35:41 AM

Thanks Rose

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Monday, July 11, 2005 5:29 AM
To: nfiner@ucsd.edu
Subject: FW: Re: MRI's at 36 weeks

Neil
I also asked Jon Tyson to comment on the practice at UT Houston – I will let you know when I hear from him
Thanks
Rose

From: Susan Hintz [mailto:srhintz@stanford.edu]
Sent: Friday, July 08, 2005 7:19 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: Fwd: Re: MRI's at 36 weeks

Hi Rose,

1) If a child is ventilated, we do NOT get an MRI per our usual routine - it will be delayed until the infant is stable. This is part of the reason that I built in the 7 week "window" for the MRI to be done (i.e., 35-42 weeks PCA) - if a baby is unstable/intubated at 36 weeks, the study can be delayed.

2) When a stable baby has an MRI, IV access is NOT required at Stanford. This is because we do not routinely use sedation.

3) The "failure" rate for FIRST TIME try at conventional MRI with no sedation is a bit less than 20%. We will often try again with no sedation and get a good study, but we may just go to conscious sedation as the next step. With respect to who does the sedation, this will be different for each institution. At Stanford, it is a neonatal nurse practioner or physician who has gone through the formal "Conscious sedation training" and has been certified in this practice.

Let me know if you need any further information. Thanks,

Susan

Hi,

The SUPPORT Subcommittee met via phone conference today and would like to know the following:

1. If a child is ventilated at 36 weeks, do you get an MRI as per your usual routine.
2. When a stable baby has an MRI, is IV access required
3. What percent of the children get sedated at you site to have the MRI> Who does the sedation? Does the person doing the sedation have "Conscious sedation privileges?"

Thanks

Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
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301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

--

Susan R. Hintz, M.D.
Assistant Professor of Pediatrics
Division of Neonatal and Developmental Medicine
Stanford University School of Medicine
750 Welch Road, Suite 315
Palo Alto, CA 94304
ph: 650-723-5711
fax: 650-725-8351

From: Higgins, Rosemary (NIH/NICHD)
To: Poole, W. Kenneth
Subject: RE: SUPPORT Enrollment
Date: Friday, July 08, 2005 1:52:00 PM

OK THANKS
ROSE

From: Poole, W. Kenneth [mailto:poo@rti.org]
Sent: Friday, July 08, 2005 1:52 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE: SUPPORT Enrollment

Don't think so.

> -----Original Message-----
> **From:** Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
> **Sent:** Friday, July 08, 2005 12:59 PM
> **To:** Poole, W. Kenneth
> **Subject:** SUPPORT Enrollment
>
> Ken
> Any chance you could tell us how many kids are enrolled in SUPPORT for the call?
> Thanks
> Rose
>
> Rosemary D. Higgins, M.D.
> Program Scientist for the Neonatal Research Network
> Pregnancy and Perinatology Branch
> Center for Developmental Biology and Perinatal Medicine
> NICHD, NIH
> 6100 Executive Blvd., Room 4B03B
> MSC 7510
> Bethesda, MD 20892
> (For overnight delivery, use Rockville, MD 20852)
> 301-435-7909
> 301-496-3790 (FAX)
> higginsr@mail.nih.gov

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: oxygen saturation targetting
Date: Tuesday, July 05, 2005 12:03:12 PM

Not to my knowledge
Neil. I may have missed this but certainly there was no phone contact, and I do not think that I have received an email in this regard.
Neil

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, July 05, 2005 8:54 AM
To: nfiner@ucsd.edu
Subject: RE: oxygen saturation targetting

NO, You should have been contacted by Dr. Lynne Haverkos at NICHD to have a summary placed on the clinicaltrials.gov website which then fulfills the criteria for posting the protocol. DI she contact you?
Thanks
Rose

-----Original Message-----
From: Neil Finer [mailto:nfiner@ucsd.edu]
Sent: Tuesday, July 05, 2005 11:52 AM
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE: oxygen saturation targetting

Hi Rose
What is the requirement for posting a protocol re future publication? Is a summary adequate?
Thanks
Neil

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, July 05, 2005 5:51 AM
To: Neil Finer
Subject: RE: oxygen saturation targetting

Neil
Betty will post the summary this week. Do you want me to poll the steering committee (if they want the full protocol)?
Thanks
Rose

-----Original Message-----
From: Neil Finer [mailto:nfiner@ucsd.edu]
Sent: Saturday, July 02, 2005 1:15 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE: oxygen saturation targetting

Hi Rose
I thought that we had to put the Protocol on a Web site to satisfy newer CONSORT publication requirements Is that true and if so where is the Web

site?
I will ask Ben if he is working with Lisa Askie who has the protocol?
Thanks
Neil

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Friday, July 01, 2005 11:16 AM
To: Neil Finer
Cc: Hastings, Betty J.
Subject: RE: oxygen saturation targetting

Neil
Usually RTI posts a synopsis of the trial on the public website, but SUPPORT is not there. I will ask Betty when we will have this. If he needs to have the entire protocol, the steering committee needs to authorize the release (which we have done for others - Askie, Cole, etc).

Thanks
Rose

-----Original Message-----
From: Neil Finer [mailto:nfiner@ucsd.edu]
Sent: Friday, July 01, 2005 2:08 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: FW: oxygen saturation targetting

Rose
Can I send Ben the protocol, or refer him to the site where it is posted?
What is that site??
Thanks
Neil
-----Original Message-----
From: Stenson, Ben [mailto:Ben.Stenson@luht.scot.nhs.uk]
Sent: Friday, July 01, 2005 6:40 AM
To: nfiner@ucsd.edu
Subject: oxygen saturation targetting

Dear Neil
I understand that you are one of the investigators on the SUPPORT trial and that this will include randomisation of infants to different saturation targets. Is this trial now funded and recruiting and if so would you be be so kind as to e-mail me a copy of the protocol? I am involved in plans for a similar trial in the UK and from time to time I get asked to speak on the subject. It is helpful to know exactly what is already on the radar.

With best wishes and thanks for any help that you can offer.

Ben Stenson
Edinburgh

message is strictly forbidden.
****

From: Neil Finer
To: "Stenson, Ben"
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: oxygen saturation targetting
Date: Tuesday, July 05, 2005 11:49:49 AM

Hi Ben
Let me know if you don't get the protocol.
Good luck with your trial
Neil

-----Original Message-----
From: Stenson, Ben [mailto:Ben.Stenson@luht.scot.nhs.uk]
Sent: Tuesday, July 05, 2005 4:23 AM
To: Neil Finer
Subject: RE: oxygen saturation targetting

Thanks Neil
I am one of the applicants in the UK for the BOOST-II UK trial. This is under consideration by the MRC for funding (looking good) and one of the things they want to know is what other similar research is in progress elsewhere and whether outcome measures are sufficiently similar for future comparison. It is great to hear that you are recruiting. It would be great to see your protocol so that issues of definitions of outcomes in our study can be made as consistent as possible. I am particularly interested in precisely how you will define and measure pulmonary outcomes as we have to decide what to do about BPD. I will ask Lisa.

Cheers

Ben

-----Original Message-----
From: Neil Finer [mailto:nfiner@ucsd.edu]
Sent: Saturday, July 02, 2005 6:15 PM
To: Stenson, Ben
Subject: RE: oxygen saturation targetting

Hi Ben
The Network did previously send Lisa Askie the protocol. Can you get her to show you this? If not and you need this for a trial I will need to make a formal request from the Steering Committee. Please let me know and if you need a copy, please describe the trial that you are involved with.
Regards
Neil Finer

-----Original Message-----
From: Stenson, Ben [mailto:Ben.Stenson@luht.scot.nhs.uk]
Sent: Friday, July 01, 2005 6:40 AM
To: nfiner@ucsd.edu
Subject: oxygen saturation targetting

Dear Neil
I understand that you are one of the investigators on the SUPPORT trial and

that this will include randomisation of infants to different saturation targets. Is this trial now funded and recruiting and if so would you be be so kind as to e-mail me a copy of the protocol? I am involved in plans for a similar trial in the UK and from time to time I get asked to speak on the subject. It is helpful to know exactly what is already on the radar.

With best wishes and thanks for any help that you can offer.

Ben Stenson
Edinburgh

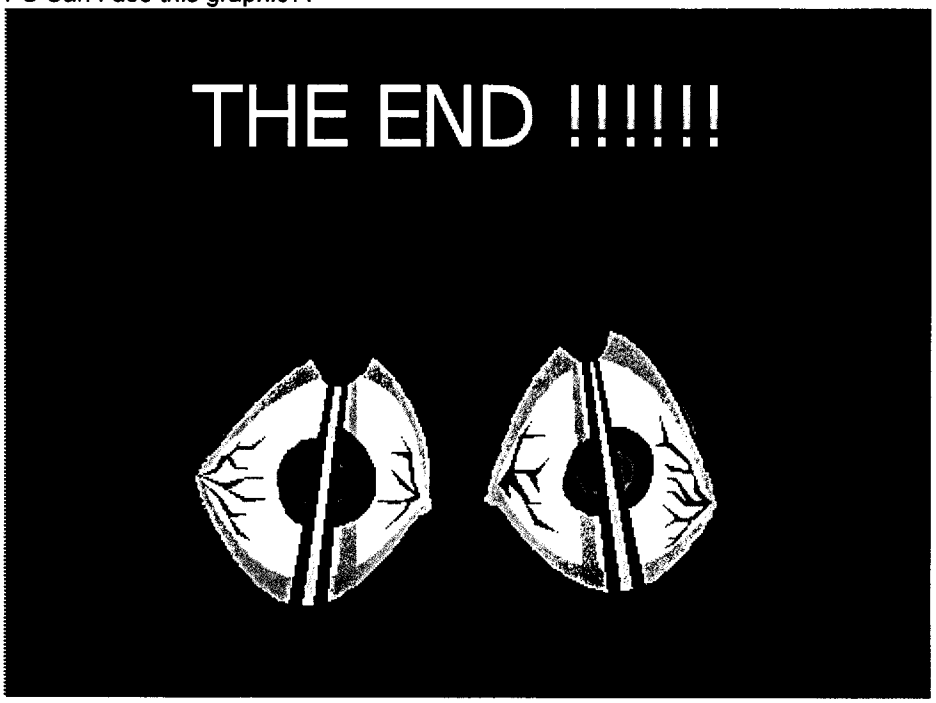
****
The information contained in this message may be confidential or legally privileged and is intended for the addressee only, If you have received this message in error or there are any problems please notify the originator immediately. The unauthorised use, disclosure, copying or alteration of this message is strictly forbidden.
****

From: Hastings, Betty J.
To: Neil Finer
Cc: wade rich; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT
Date: Tuesday, July 05, 2005 8:37:54 AM

Neil,
Wade did all the work, I just included it in the MOP! So he was the creative one.
Betty

-----Original Message-----
From: Neil Finer [mailto:nfiner@ucsd.edu]
Sent: Monday, July 04, 2005 9:22 PM
To: Hastings, Betty J.
Cc: 'wade rich'; higginsr@mail.nih.gov
Subject: RE: SUPPORT

Hi Betty and Wade
I just wanted you guys to know that I thought that the Appendix doc was very creative and instructive – I loved the graphics.
Nice work, and many thanks.
Neil
PS Can I use this graphic??



From: Hastings, Betty J. [mailto:bkh@rti.org]
Sent: Thursday, June 30, 2005 7:39 AM
To: ahensman@wihri.org; mbball@leland.stanford.edu; grisbyca@email.uc.edu; ellen_hale@oz.ped.emory.edu; gaynelle.hensley@utsouthwestern.edu; Georgia E McDavid;

auten002@mc.duke.edu; linda_reubens@urmc.rochester.edu; lucmille@iupui.edu; mcollins@peds.uab.edu; monica.konstantino@yale.edu; Nancy.Miller@utsouthwestern.edu; Nancy Newman; npeters@wfubmc.edu; ae5357@wayne.edu; rbridge@ucsd.edu; risa.demetrio@sharp.com; kathy.arnell@sharp.com; Reverett@med.miami.edu; brenda.H.Morris@uth.tmc.edu; cotte010@mc.duke.edu; crosen@mednet.swmed.edu; vanmeurs@leland.stanford.edu; kurt.schibler@cchmc.org; alaptook@wihri.org; bpoindex@iupui.edu; edward.donovan@chmcc.org; Jobea0@chmcc.org; jlemons@iupui.edu; moshea@wfubmc.edu; sshankar@med.wayne.edu; sduara@miami.edu; susie.buchter@oz.ped.emory.edu; wcarlo@peds.uab.edu; mcw3@cwru.edu; wcarlo@peds.uab.edu; Vineet.bhandari@yale.edu; vivek.Narendran@cchmc.org; Walid.Salhab@utsouthwestern.edu; Personal Email ; Lenora Jackson; Estelle E. Fischer; Holly Mincey; Jody Shively; Kate Bridges, MD
Cc: Das, Abhik; Poole, W. Kenneth; Zaterka-Baxter, Kristin; Gantz, Marie; higginsr@mail.nih.gov; nfiner@ucsd.edu; wrich@ucsd.edu; Petrie, Carolyn
Subject: SUPPORT

Attached please find the following material for the SUPPORT Trial

- Technical Memo SUP03
- A revised SUPP11 Form
- Revised Chapter 16
- New Chapter 17
- Appendix D (new)
- Appendix E (new)

Please note that there may be some additional (minor) changes that may need to be to the manual, however we wanted to get this material out to you so you can begin to use the revised SUPP11 form. The data entry software for this revised version was sent to you with the transmission on Tuesday. Please let Wade or me know if you have questions about these changes.

Thanks.
Betty

<<SUP03.doc>> <<SUPP11 6-27-05 .doc>> <<Chapter 17[6-27-05].doc>> <<RevChapter 16[6-27-05].doc>>
<<APPENDIX E.doc>> <<APPENDIX D.doc>>

Betty Hastings

RTI International
Statistic Research Division
P.O. Box 12194
Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7740
Fax: (919) 485-7762
bkh@rti.org

From: Higgins, Rosemary (NIH/NICHD)
To: Petrie, Carolyn
Subject: RE: growth prot June 30 2005.doc
Date: Thursday, June 30, 2005 3:48:00 PM

Both are open.
Thanks
Rose

-----Original Message-----
From: Petrie, Carolyn [mailto:petrie@rti.org]
Sent: Thursday, June 30, 2005 2:40 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE: growth prot June 30 2005.doc

We are looking at the afternoon of either, mon aug 1 or thur aug 4
Do you have any conflicts?

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Thursday, June 30, 2005 1:05 PM
To: Petrie, Carolyn
Subject: Fw: growth prot June 30 2005.doc

We wil likely need 2 hours for the protocol review call.

This one + probiotics!

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Duara, Shahnaz <SDuara@med.miami.edu>
To: richard.ehrenkranz@yale.edu <richard.ehrenkranz@yale.edu>
CC: Neil Finer <nfiner@ucsd.edu>; Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
Sent: Thu Jun 30 13:02:18 2005
Subject: growth prot June 30 2005.doc

<<growth prot June 30 2005.doc>> Hi Rich,

I wish to submit the Growth secondary to SUPPORT for protocol review on Cristina Navarrete's behalf. She has developed 3 scenarios of data collection, with input from Abhik, and matching budgets.

Look forward to the response from your committee.
Shahnaz
<<growth prot June 30 2005.doc>>

From: Higgins, Rosemary (NIH/NICHD)
To: Betty Vohr
Subject: RE: Pulmonary outcomes secondary study
Date: Thursday, June 30, 2005 11:14:00 AM

Thanks
Rose

From: Betty Vohr [mailto:BVohr@WIHRI.org]
Sent: Thursday, June 30, 2005 11:13 AM
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE: Pulmonary outcomes secondary study

I believe Abbot already responded for us. We would like to do it during our visits.

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, June 29, 2005 3:11 PM
Subject: FW: Pulmonary outcomes secondary study

Hi
Can you send me your preference for the administration of the questionnaires for the Pulmonary Follow up study to SUUPPORT?
Thanks
Rose

From: Higgins, Rosemary (NIH/NICHD)
Sent: Friday, June 17, 2005 10:07 AM
To: Abbot Laptook (alaptook@WIHRI.org); 'Abhik Das'; 'Brenda Poindexter'; 'Carlo Waldemar (E-mail)'; 'Charles Rosenfeld'; 'Dale Phelps'; 'Ed Donovan'; 'Ehrenkranz Richard (E-mail)'; 'Jobe Alan (E-mail)'; 'Lemons Jim (E-mail)'; 'Michael O'Shea'; 'Michelle Walsh'; 'Neil Finer'; 'Oh William (E-mail)'; 'Poole Kenneth (E-mail)'; 'Ronald GOldberg'; 'Shahnaz Duara'; 'Shankaran Seetha (E-mail)'; 'Stevenson David (E-mail)'; 'Stoll Barbara (E-mail)'; 'Tyson Jon (E-mail)'; Walid Salhab (Walid Salhab); Anna Dusick (adusick@iupui.edu); Betty Vohr ('Betty_Vohr@brown.edu'); Charlie Bauer (cbauer@peds.med.miami.edu); Dee WIlson Personal Email Gary Myers (Gary_myers@URMC.Rochester.edu); 'Ira Adams-Chapman'; Jean Steichen (steichjj@email.uc.edu); Myriam Peralta (mperalta@peds.uab.edu); Ricki Goldstein (golds005@mc.duke.edu); 'Robert Dillard'; 'Roy Heyne'; 'Susan Hintz'; Yvette Johnson (yjohnson@med.wayne.edu); Yvonne Vaucher (Yvonne Vaucher)
Cc: 'Hastings, Betty J.'; (kzaterka@rti.org); 'Petrie, Carolyn'
Subject: Pulmonary outcomes secondary study

Hi
Attached are documents and questionnaires associated with the pulmonary outcomes secondary study to the SUPPORT Trial. Please review the documents and send me a preference by June 27 indicating the following:

1. My site will do the Questionnaires
2. Rochester site to do questionnaires on my study subjects

I am checking on the issues regarding how the consents would be phrased in order that information could pass from your site to the Rochester site.

Thanks in advance for all your help!!
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Hastings, Betty J.
To:	ahensman@wihri.org; mbball@leland.stanford.edu; grisbyca@email.uc.edu; ellen_hale@oz.ped.emory.edu; gaynelle.hensley@utsouthwestern.edu; Georgia E McDavid; auten002@mc.duke.edu; linda_reubens@urmc.rochester.edu; lucmille@iupui.edu; mcollins@peds.uab.edu; monica.konstantino@yale.edu; Nancy.Miller@UTSouthwestern.edu; Nancy Newman; npeters@wfubmc.edu; ae5357@wayne.edu; rbridge@ucsd.edu; risa.demetrio@sharp.com; kathy.arnell@sharp.com; Reverett@med.miami.edu; brenda.H.Morris@Uth.tmc.edu; cotte010@mc.duke.edu; crosen@mednet.swmed.edu; vanmeurs@leland.stanford.edu; kurt.schibler@cchmc.org; alaptook@wihri.org; bpoindex@iupui.edu; edward.donovan@chmcc.org; Jobea0@chmcc.org; jlemons@iupui.edu; moshea@wfubmc.edu; sshankar@med.wayne.edu; sduara@miami.edu; susie.buchter@oz.ped.emory.edu; wcarlo@peds.uab.edu; mcw3@cwru.edu; wcarlo@peds.uab.edu; Vineet.bhandari@yale.edu; vivek.Narendran@cchmc.org; Walid.Salhab@UTSouthwestern.edu; balexanba@hotmail.com; Lenora Jackson; Estelle E. Fischer; Holly Mincey; Jody Shively; Kate Bridges, MD
Cc:	Das, Abhik; Poole, W. Kenneth; Zaterka-Baxter, Kristin; Gantz, Marie; Higgins, Rosemary (NIH/NICHD) [E]; nfiner@ucsd.edu; wrich@ucsd.edu; Petrie, Carolyn
Subject:	SUPPORT
Date:	Thursday, June 30, 2005 10:39:46 AM
Attachments:	SUP03.doc SUPP11 6-27-05 .doc Chapter 17[6-27-05].doc RevChapter 16[6-27-05].doc APPENDIX E.doc APPENDIX D.doc

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Attached please find the following material for the SUPPORT Trial

- Technical Memo SUP03
- A revised SUPP11 Form
- Revised Chapter 16
- New Chapter 17
- Appendix D (new)
- Appendix E (new)

Please note that there may be some additional (minor) changes that may need to be to the manual, however we wanted to get this material out to you so you can begin to use the revised SUPP11 form. The data entry software for this revised version was sent to you with the transmission on Tuesday. Please let Wade or me know if you have questions about these changes.

Thanks.
Betty

<<SUP03.doc>> <<SUPP11 6-27-05 .doc>> <<Chapter 17[6-27-05].doc>> <<RevChapter 16[6-27-05].doc>>
<<APPENDIX E.doc>> <<APPENDIX D.doc>>

Betty Hastings

RTI International
Statistic Research Division
P.O. Box 12194
Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7740
Fax: (919) 485-7762
bkh@rti.org

RTI INTERNATIONAL | Memorandum

June 30, 2005

SUPPORT TECHNICAL MEMO # 3

TO: Network Coordinators
Network PIs

FROM: The Data Coordinating Center
Neil Finer, MD
Wade Rich

SUBJECT: Revised SUPP11 Form, Chapter 16 and New Chapter 17

The SUPP11 form has been revised as follows:

This form should be completed from study day 15 through 36 weeks or status, whichever come first.

The following should be recorded for each day (**the study day is now printed on the form**)

- Date
- Oxygen - Yes/No
- Highest Level of Support
- Flow rate (Nasal Cannula only)

The revised Chapter 16 reflects these changes and provides the instructions for completing these questions.

There is a new Chapter 17, Oximeter Setup. This chapter provides detailed instructions for setting up the oximeter, as well as, who to contact at Masimo if you encounter problems with the oximeters.

Also attached is Appendix D, the Power Point presentation for the SUPPORT Down Load and Appendix E, a copy of the Return Material Authorization Form (RMA).

If you have questions about this material, please contact Wade Rich or Betty Hastings.

cc: Rosemary Higgins

NICU Network

The SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants

RESPIRATORY SUPPORT AFTER 14 DAYS

SUPP11 Rel 3.0
June 27, 2005

Center: __ __ Site No: __ Network No: __ __ __ __ Birth No: __ Mother's Initials: __ __ __

Complete this form daily from study day 15 through 36 weeks or status, whichever comes first.
Date of 36 weeks __ __ / __ __ / __ __ __ __

(a) Study Day	15	16	17	18	19	20
(b) Date	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year
(c) Highest Level of Support	__	__	__	__	__	__
(d) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(e) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(a) Study Day	21	22	23	24	25	26
(b) Date	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year
(c) Highest Level of Support	__	__	__	__	__	__
(d) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(e) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(a) Study Day	27	28	29	30	31	32
(b) Date	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year
(c) Highest Level of Support	__	__	__	__	__	__
(d) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(e) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(a) Study Day	33	34	35	36	37	38
(b) Date	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year
(c) Highest Level of Support	__	__	__	__	__	__
(d) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(e) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.

1= HFV 2= CV 3= Nasal SIMV 4= CPAP 5= NC 6=Hood 7= No Support

Complete this form daily from study day 15 through 36 weeks or status, whichever comes first.
Date of 36 weeks __ __ / __ __ / __ __ __ __

(a) Study Day	39	40	41	42	43	44
(b) Date	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year
(c) Highest Level of Support	__	__	__	__	__	__
(d) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(e) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(a) Study Day	45	46	47	48	49	50
(b) Date	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year
(c) Highest Level of Support	__	__	__	__	__	__
(d) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(e) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(a) Study Day	51	52	53	54	55	56
(b) Date	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year
(c) Highest Level of Support	__	__	__	__	__	__
(d) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(e) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(a) Study Day	57	58	59	60	61	62
(b) Date	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year
(c) Highest Level of Support	__	__	__	__	__	__
(d) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(e) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.

1= HFV 2= CV 3= Nasal SIMV 4= CPAP 5= NC 6=Hood 7= No Support

Complete this form daily from study day 15 through 36 weeks or status, whichever comes first.
Date of 36 weeks __ __ / __ __ / __ __ __ __

(a) Study Day	63	64	65	66	67	68
(b) Date	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year
(c) Highest Level of Support	__	__	__	__	__	__
(d) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(e) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(a) Study Day	69	70	71	72	73	74
(b) Date	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year
(c) Highest Level of Support	__	__	__	__	__	__
(d) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(e) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(a) Study Day	75	76	77	78	79	80
(b) Date	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year
(c) Highest Level of Support	__	__	__	__	__	__
(d) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(e) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.
(a) Study Day	81	82	83	84	85	86
(b) Date	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year	__ __/__ __/__ __ __ __ Month Day Year
(c) Highest Level of Support	__	__	__	__	__	__
(d) Oxygen	YES NO	YES NO	YES NO	YES NO	YES NO	YES NO
(e) Flow Rate (NC only)	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.	__ __ . __ __ __ Liters/Min.

1= HFV 2= CV 3= Nasal SIMV 4= CPAP 5= NC 6=Hood 7= No Support

Chapter 17

OXIMETER SETUP

17.1 Oximeter Setup – Masimo Radical

Review the following EACH TIME the oximeter is placed on a baby.

17.1.1 Power

If possible, units should remain plugged in between uses. Where this is not possible the oximeter should be plugged in as soon as possible after randomization.

17.1.2 Initial Settings – [Radical Manual pp. 30-42]

Date – Check to see that the date and time are correct. This must be done prior to gathering data. **Changing the date or time after data collection has started will erase the memory!**

Sensitivity – Set to Normal Mode
Averaging Time – Set to 16 seconds
Alarm Limits – Sat: Suggested between 85 and 95.
Audible Delay – 10 seconds
Trend Period – [43-45] - 10 Seconds **Note: Changing this setting during a recording will erase all data !!**

17.1.3 Help – If you can not find these settings using your oximeter manual, or if you have any problems with the Masimo masked oximeters used in the SUPPORT study, please contact:

1. The local Masimo Clinical Specialist who did the inservicing for your center
   Please identify yourself as one of the SUPPORT centers, with questions about a masked oximeter.

   and/or

2. Masimo Technical Support at 800-326-4890, option 2. tech@Masimo.com
   Please identify yourself as one of the SUPPORT centers, with questions about a masked oximeter. The techs are aware of SUPPORT and the masked oximeters.

   and/or

3. Dr Maribeth Sayre, Director of Medical Affairs for Masimo, and the Masimo liaison for the SUPPORT study. Her contact information is:
   msayre@Masimo.com cell phone 925-337-3856

If a masked oximeter is malfunctioning, it must be sent back to Masimo headquarters. First, a RMA # (Return Material Authorization number) is needed.

A copy of the form **is contained in Appendix E.** . Please identify the facility as one of the SUPPORT centers, and the product as a masked Radical handheld or docking station.

If there are questions relating to alarm parameters, they should be referred to Wade Rich.

PLEASE COPY DR. MARIBETH SAYRE ON ALL EMAILS RELATED TO THE MASKED OXIMETERS.

17.2 Downloading Data

17.2.1 Software

The software used to download the data is called TExtract. If you have not gotten a copy, it is available by email from wrich@ucsd.edu or it can be downloaded to your Network computer by RTI.

Using TExtract
A PowerPoint presentation showing how to use TExtract is included in the manual as Appendix D.

17.2.2 Cable

Data may be downloaded from the oximeter to a laptop using either a serial cable or a USB-to-Serial cable. A picture of a USB-Serial cable is included in the power-point presentation that was sent out to all the sites.

17.2.3 Preparing Masimo for Download

- Turn Oximeter on.
- Output should be Binary
- Select button
- Use arrow key to highlight "Output".
- Select button.
- Enter the Serial Menu by selecting the button.
- Use arrow key to select "Binary".
- Select ☑ button.
- Select ☒ button twice.

When to Download
Downloads should be done every 2 weeks, or earlier if a child reaches a study milestone (e.g. Off oxygen for 72 hrs, death, discharge, or 36 weeks PCA)

17.2.4 After the download:

Be sure to clear the memory of the Masimo after you have downloaded the data. Otherwise you will send RTI data which they already have along with the new data the next time you download. Clearing the memory is done as follows:

From the main screen when the Masimo is first turned on:

Select the → button.

Select the ▦ button.
Select the ▤ button twice.
Select the 🗑 icon.
Select the ☑ icon and the data will be dumped.

17.2.5 Uploading Data to Network Computer

Data can be transferred from the laptop to the network computer by way of a floppy disk or a USB Memory Stick. The USB device is preferable because it will hold many studies instead of just one.

To upload this data to your Network computer the USB stick must be put into the USB port on the computer. This is often in the back. A USB extension cable will help make this easier, as one end can just be placed on the desk for easy reach.

The SUPPORT data entry software program from RTI will take you through the process of uploading. The information regarding how to label the files is included in the TExtract Power point appendix D to this manual.

17.2.6 Masimo Technical Issues

It is recommended that the Radical Handheld be docked to the docking station and attached to an AC power source when it is not in use to ensure that the battery remains fully charged. All batteries lose capacity with age. When battery run time is significantly reduced, it is advisable to completely discharge and fully recharge the battery pack. Masimo does not give a recommended TIME FRAME for performing a discharge cycle since every environment is different.

17.2.7 How to Deep-Discharge the Radical Battery

The discharge cycle will take approximately 16 hours to complete for the handheld battery. The Docking Station battery will take approximately 30 hours to complete. A message will appear in the service screen when the discharge cycle is complete. The batteries will be fully charged after completion of the cycle.

Note: *In order for the discharge cycle to be properly completed, the Handheld must be docked to a Docking Station and supplied with AC power throughout the cycle.*

Warning: WHEN DEEP-DISCHARGING THE HANDHELD OR DOCKING STATION BATTERY, MAKE SURE THAT THE DEVICE HAS BEEN REMOVED FROM SERVICE UNTIL FULL BATTERY CAPABILITY CAN BE RESTORED.

1. Press the three page button to access the main menu screen
2. Highlight the Service menu and press the single page button
3. Enter password 2 – 3 – 1
4. Press single page button
5. Confirm by pressing the checkmark

6. Wait until message of "Discharge Cycle is Complete"

17.2.8 Defective Equipment

If you need to return defective Masimo equipment, please contact Technical Support at Masimo 1-800-326-4890 for a Return Merchandise Authorization #. You will need the device serial # when you call.

Chapter 16

Respiratory Support after 14 Days

16.1 Introduction

The purpose of this form is to document any respiratory support the infant receives after day 14.

16.1.1 Instructions for completing the Respiratory Support Form after 14 Days (SUPP11)

This form is to be completed daily from study day 15 through 36 weeks or status, whichever comes first.

Record the following for each day:

- **Date**
  Record the date corresponding to the Study day
- **Oxygen -Yes/No**
  Record "Yes" if the infant was on oxygen at any time during the day. Disregard any temporary increases in FiO_2 for desaturation episodes, apnea, bradycardia or procedures where the infant returns to his/her previous FiO_2 in a reasonable amount of time (≤ 30 minutes). Record "No" if the infant is not in oxygen on this day.
- **Highest Level of Support**
  Record the highest level of support the infant was in on this **STUDY** day. Enter 1= HFV, 2=CV, 3= Nasal SIMV, 4= CPAP, 5= NC, 6= Hood, 7= No Support
- **Flow rate (Nasal Cannula only)**
  Record the highest flow rate the infant was on at any time during the study day. Disregard any temporary increases in flow for desaturation episodes, apnea, bradycardia or procedures where the infant returns to his/her previous flow rate in a reasonable amount of time (≤ 30 minutes)***Flow rate should be recorded **only** if the infant was on a nasal cannula that day. For purposes of recording, Vapotherm is considered a cannula.

APPENDIX E

RETURN MATERIAL AUTHORIZATION FORM (RMA)

SHIP TO:

MASIMO®

40 Parker
Irvine, CA 92618 USA
Tel: 1 800 326-4890
Fax: 949-297-7499
Email tech@masimo.com

RETURNED MATERIAL AUTHORIZATION

xxxx

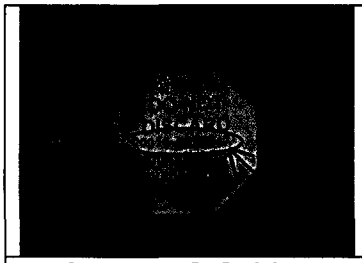
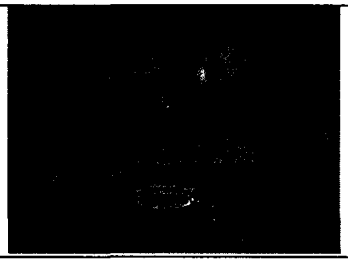
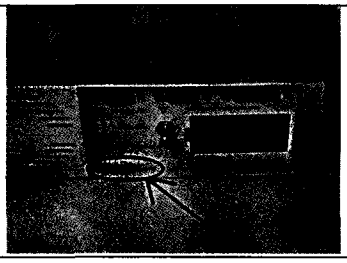
PLEASE ENSURE ALL RETURNED PRODUCTS ARE BIO HAZARD CLEANED

1. Complete this form.
2. Return this form with the product by affixing to the outside of the container with a clear shipper.

THANK YOU!

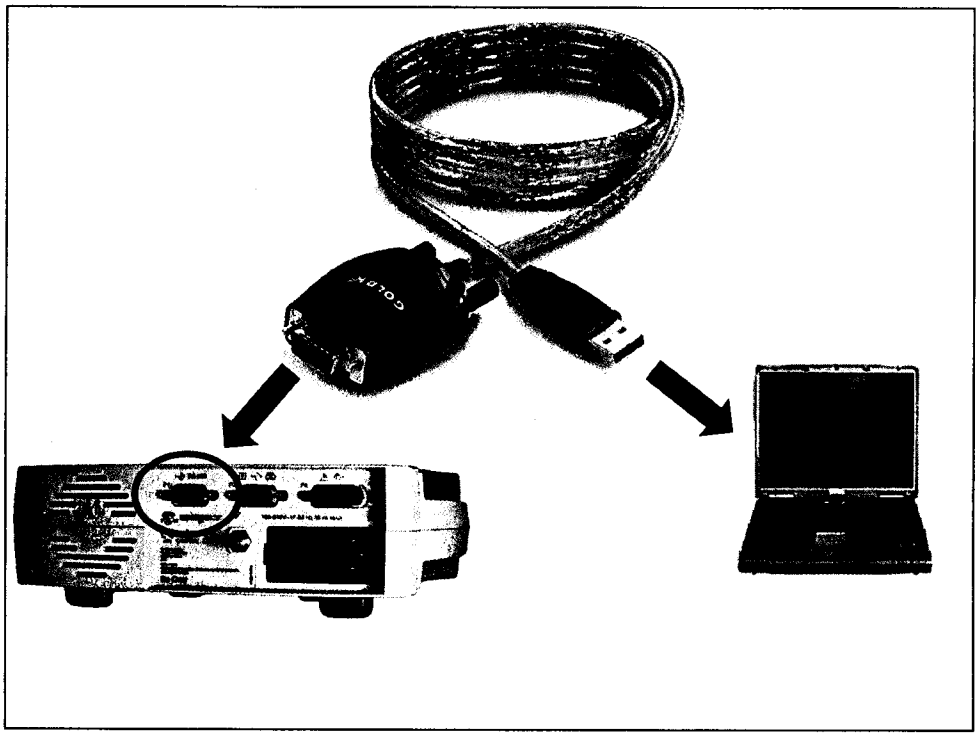
FACILITY NAME				
RETURN SHIP TO ADDRESS				
PHONE NUMBER				
FAX NUMBER				
EMAIL ADDRESS				
PO NUMBER				
CONTACT NAME				
DEPARTMENT				
PRODUCT				
SERIAL/LOT #				
DISCREPANCY				
PRODUCT				
SERIAL/LOT #				
DISCREPANCY				

How to locate the Serial or Lot number

			
Sensors & Cables (On DO NOT DISCARD label on cable)	**Radical™ Handheld (On rear of unit)**	**Radical™ Docking Station (On rear of unit)**	**Rad-9™ (On rear of unit)**

APPENDIX D

SUPPORT DOWN LOAD



Turn Oximeter on.

Select button.

Use arrow key to highlight "Output".

Select button.

Enter the Serial Menu by selecting the button.

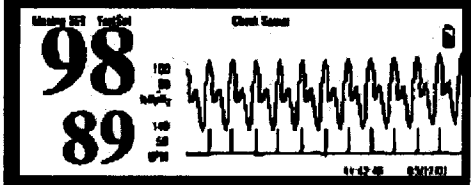
Use arrow key to select "Binary".

Select button.

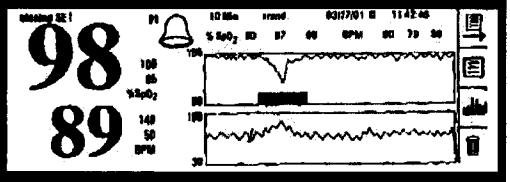
Select button twice.

Quick Reference on Masimo Extraction Utility
Masimo Unit Setup:

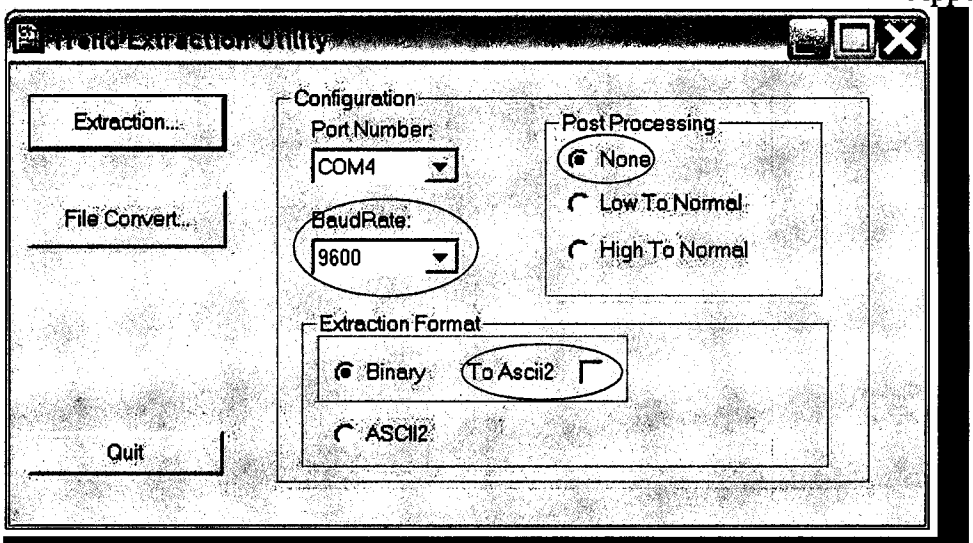
Make sure the Radical is in run mode and not in mode.



YES

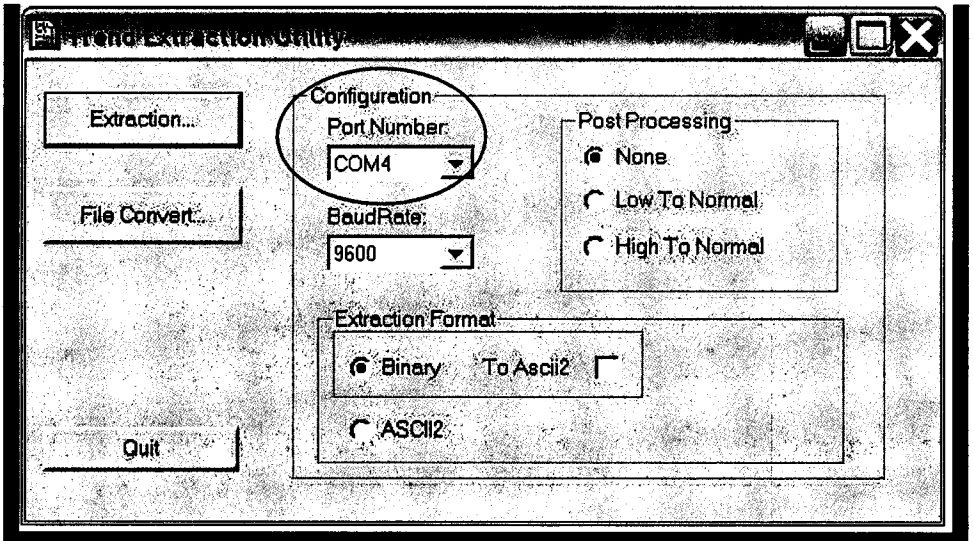


No

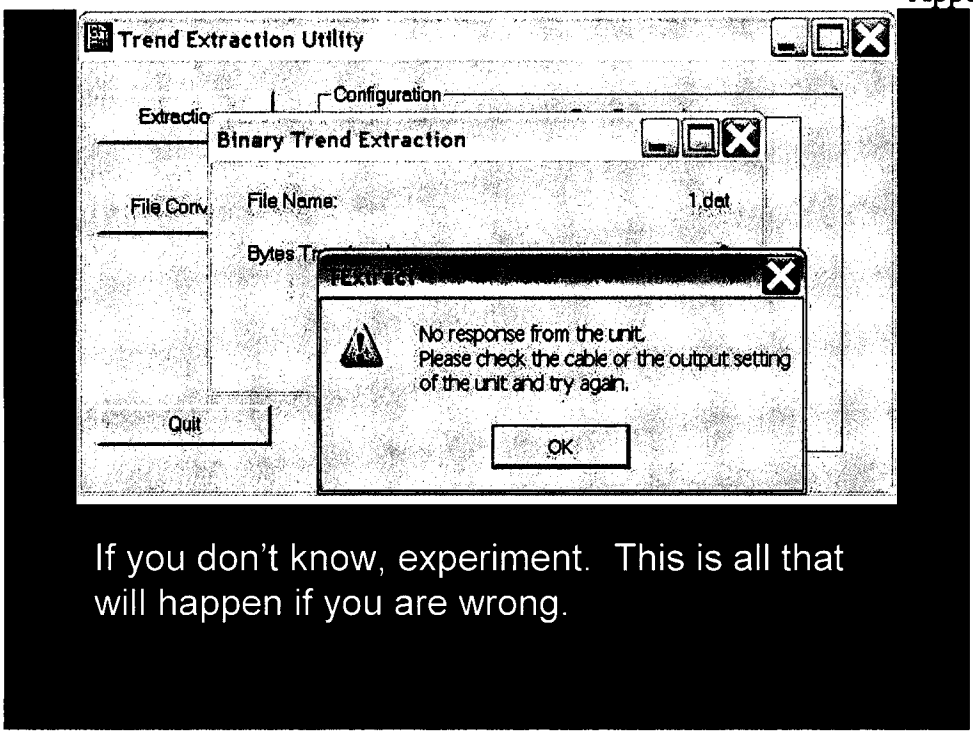


Execute the *TExtract.exe* utility

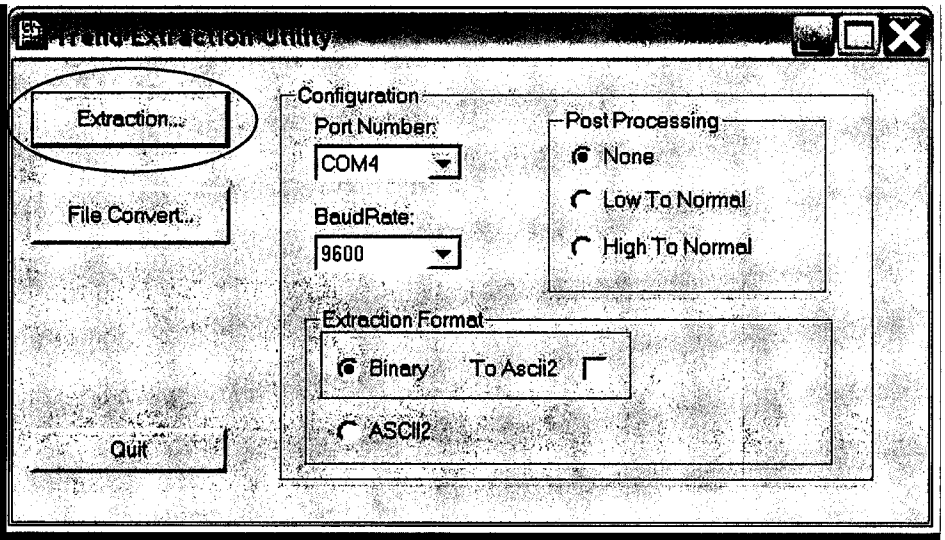
9600 Baud, No Post Processing, No Ascii2



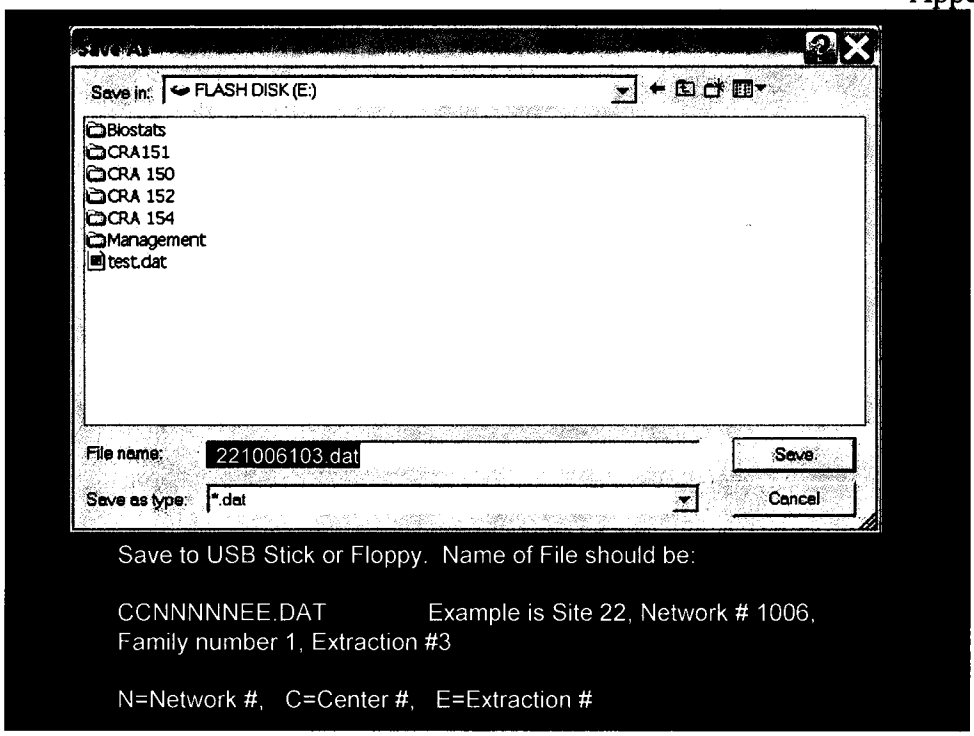
In the "*Configuration*" panel, select the COM port that is currently connected to the Radical unit.



If you don't know, experiment. This is all that will happen if you are wrong.



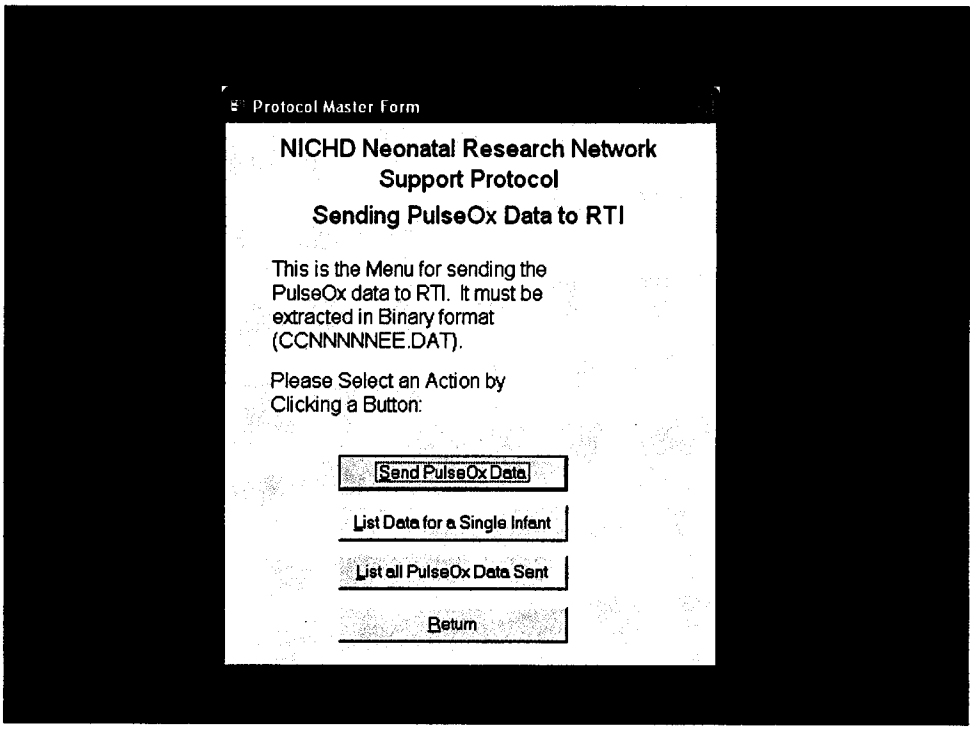
Hit Extraction.

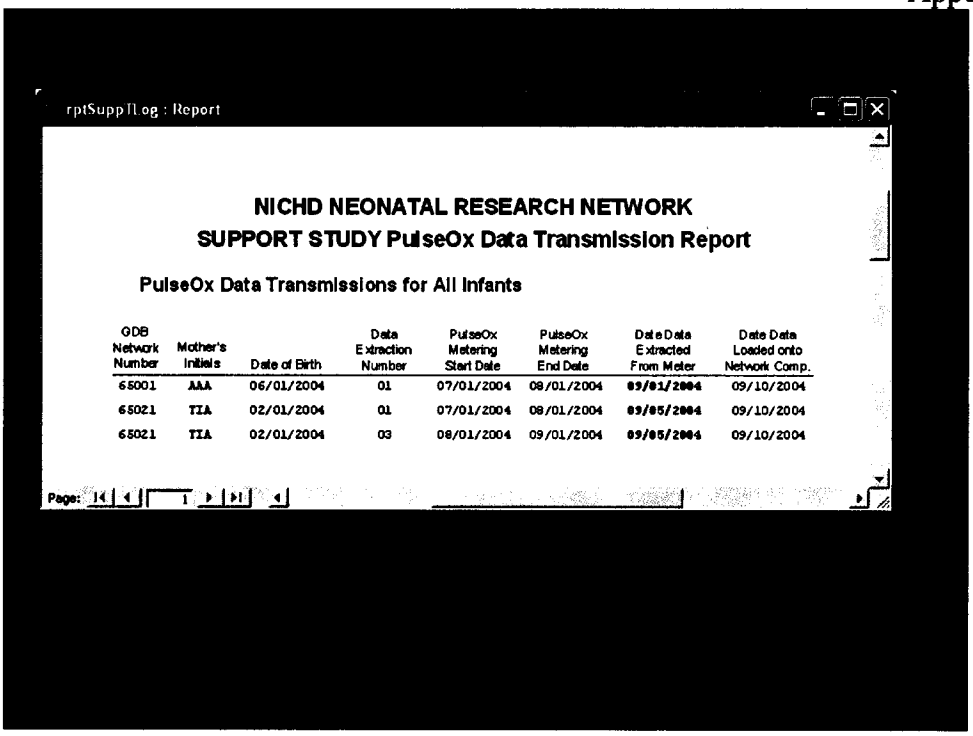


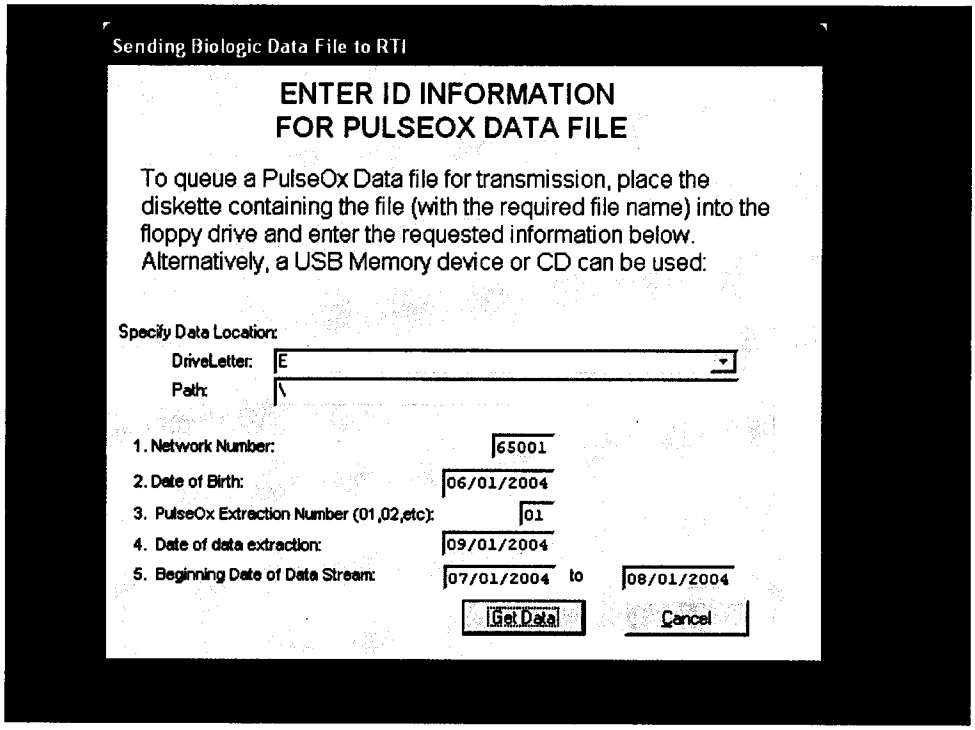
Save to USB Stick or Floppy. Name of File should be:

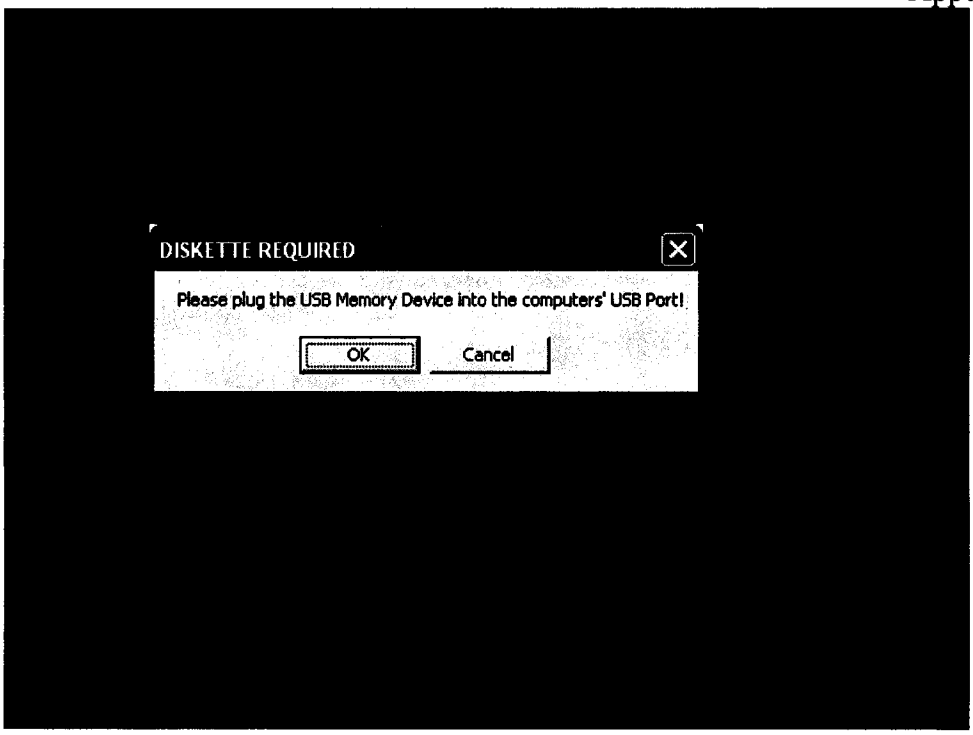
CCNNNNNEE.DAT Example is Site 22, Network # 1006, Family number 1, Extraction #3

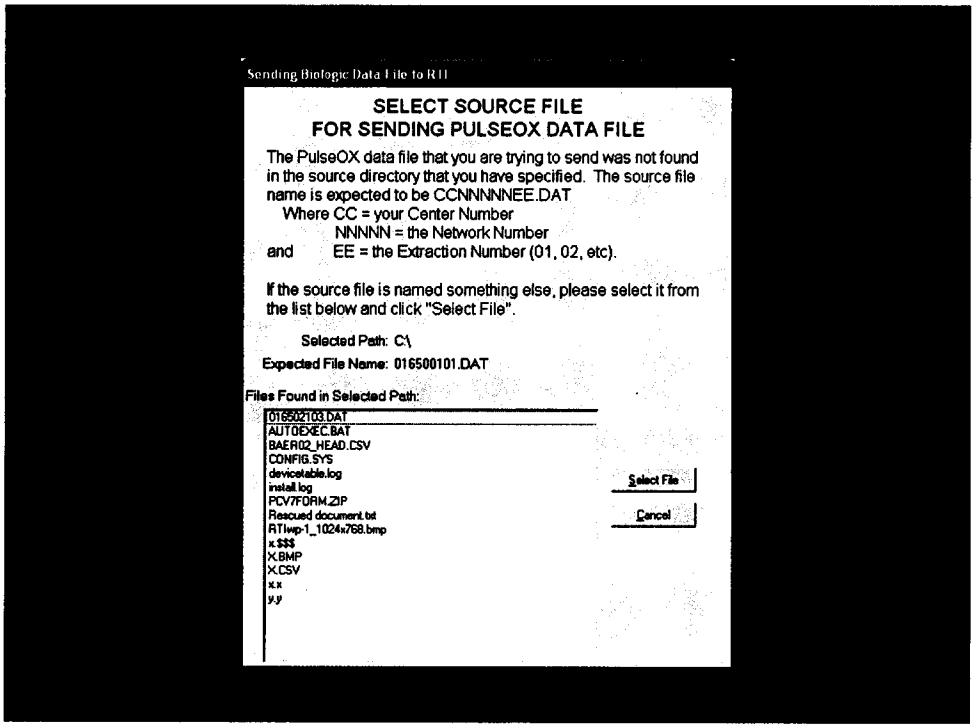
N=Network #, C=Center #, E=Extraction #

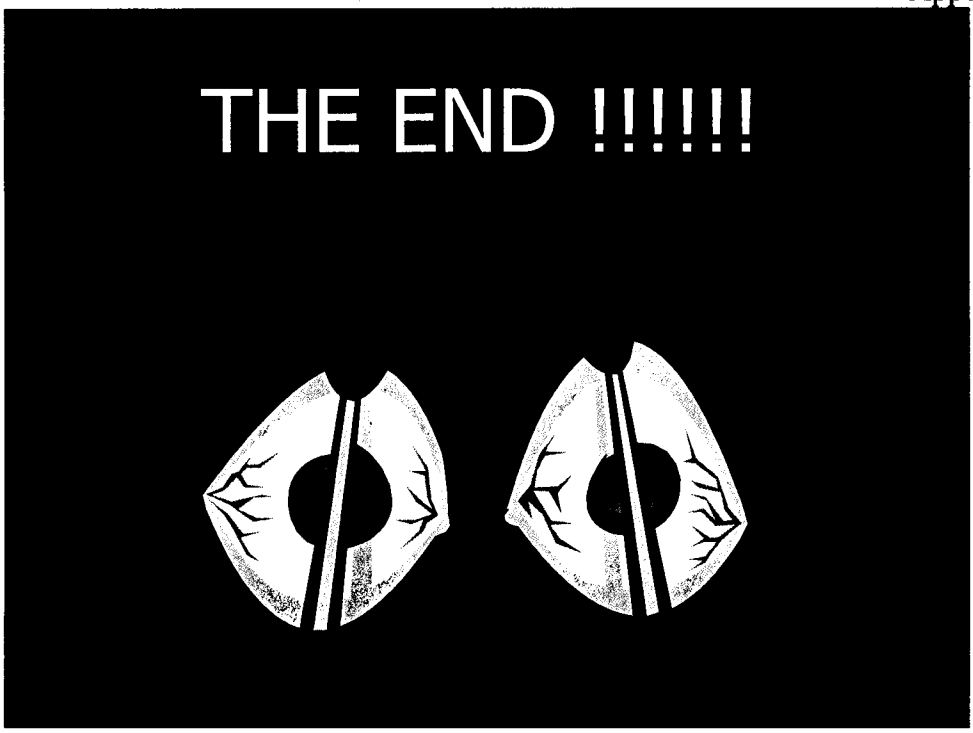



rptSupplLog : Report
NICHD NEONATAL RESEARCH NETWORK
SUPPORT STUDY PulseOx Data Transmission Report
PulseOx Data Transmissions for All Infants
GDB Network Number
Mother's Initials
Date of Birth
Data Extraction Number
PulseOx Metering Start Date
PulseOx Metering End Date
Date Data Extracted From Meter
Date Data Loaded onto Network Comp.
65001 AAA 06/01/2004 01 07/01/2004 08/01/2004 09/01/2004 09/10/2004
65021 TIA 02/01/2004 01 07/01/2004 08/01/2004 09/05/2004 09/10/2004
65021 TIA 02/01/2004 03 08/01/2004 09/01/2004 09/05/2004 09/10/2004
Page:


Sending Biologic Data File to RTI
ENTER ID INFORMATION
FOR PULSEOX DATA FILE
To queue a PulseOx Data file for transmission, place the diskette containing the file (with the required file name) into the floppy drive and enter the requested information below. Alternatively, a USB Memory device or CD can be used:
Specify Data Location:
DriveLetter: E
Path: \
1. Network Number: 65001
2. Date of Birth: 06/01/2004
3. PulseOx Extraction Number (01,02,etc): 01
4. Date of data extraction: 09/01/2004
5. Beginning Date of Data Stream: 07/01/2004 to 08/01/2004
Get Data
Cancel


DISKETTE REQUIRED
Please plug the USB Memory Device into the computers' USB Port!
OK
Cancel


Sending Biologic Data File to RTI
SELECT SOURCE FILE
FOR SENDING PULSEOX DATA FILE
The PulseOX data file that you are trying to send was not found in the source directory that you have specified. The source file name is expected to be CCNNNNNEE.DAT
Where CC = your Center Number
NNNNN = the Network Number
and EE = the Extraction Number (01, 02, etc).
If the source file is named something else, please select it from the list below and click "Select File".
Selected Path: C:\
Expected File Name: 016500101.DAT
Files Found in Selected Path:
016502103.DAT
AUTOEXEC.BAT
BAER02_HEAD.CSV
CONFIG.SYS
devicetable.log
install.log
PCV7FORM.ZIP
Rescued document.txt
RTIwp-1_1024x768.bmp
x.$$$
X.BMP
X.CSV
x.x
y.y
Select File
Cancel


THE END !!!!!!

From:	Wade Rich
To:	Higgins, Rosemary (NIH/NICHD) [E]
Subject:	RE: SUPP11
Date:	Wednesday, June 29, 2005 3:17:44 PM

Rose,

Neil and the group have said it was OK. The only change since I asked them last is the definition of flow rate, which I modified from the
GDB definition of oxygen use, basically saying highest that is not a transient. And Neil approved of this.

Wade

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, June 29, 2005 11:57 AM
To: Hastings, Betty J.; wrich@ucsd.edu
Subject: RE: SUPP11

If Neil is OK with it, I think it is fine.
Thanks
Rose

From: Hastings, Betty J. [mailto:bkh@rti.org]
Sent: Wednesday, June 29, 2005 2:56 PM
To: wrich@ucsd.edu
Cc: Higgins, Rosemary (NIH/NICHD)
Subject: SUPP11

Wade,
Angelita asked if the Subcommittee had seen and approved the revised SUPP11 form and MOP. I am not sure that we have sent this type of revision to the Subcommittee in the past. Could you please check with Neil to see if this is necessary?

What do you think Rose?
Thanks.
Betty

Betty Hastings

RTI International
Statistic Research Division
P.O. Box 12194
Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7740
Fax: (919) 485-7762
bkh@rti.org

From: Hastings, Betty J.
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPP11
Date: Wednesday, June 29, 2005 3:04:11 PM

Thanks. That's what I thought as well.
-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, June 29, 2005 2:57 PM
To: Hastings, Betty J.; wrich@ucsd.edu
Subject: RE: SUPP11

If Neil is OK with it, I think it is fine.
Thanks
Rose

From: Hastings, Betty J. [mailto:bkh@rti.org]
Sent: Wednesday, June 29, 2005 2:56 PM
To: wrich@ucsd.edu
Cc: Higgins, Rosemary (NIH/NICHD)
Subject: SUPP11

Wade,
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What do you think Rose?
Thanks.
Betty

Betty Hastings

RTI International
Statistic Research Division
P.O. Box 12194
Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7740
Fax: (919) 485-7762
bkh@rti.org

From: Shankaran, Seetha
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Athina; Becky; Kennedy, Deborah (DMC)
Subject: pulmonary outcomes study
Date: Tuesday, June 28, 2005 3:32:53 PM

Hi Rose
We discussed this and our preference is that we do the questionnaire
Thanks
Seetha

From: Stevens, Timothy
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: letter of support
Date: Monday, June 27, 2005 5:03:34 PM

Yes, No problem

Thanks again

Tim

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Monday, June 27, 2005 4:53 PM
To: Stevens, Timothy
Subject: RE: letter of support

Great
I will write the letter to Dale, send it tomorrow (is she or someone in the office to sign for it) via FEDEX.
Thanks
Rose

From: Stevens, Timothy [mailto:Timothy_Stevens@URMC.Rochester.edu]
Sent: Monday, June 27, 2005 4:54 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE: letter of support

Thanks Rose,

Here is the info;

1K23HD050646-01	Oxygen, Oxidant Stress and Wheezing in Premature Infants	UNIVERSITY OF ROCHESTER	Pending	06/15/2005

Tim

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Monday, June 27, 2005 4:33 PM
To: Stevens, Timothy
Cc: Phelps, Dale
Subject: RE: letter of support

Tim
One more thing - please send me the title and the grant number.
Rose

From: Stevens, Timothy [mailto:Timothy_Stevens@URMC.Rochester.edu]
Sent: Monday, June 27, 2005 4:21 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: letter of support

Hi Rose,

Can you help me on short notice? I am in the process of resubmitting my K23 for July 1.

I would like to include a letter from the NICHD Network outlining the status of the SUPPORT Pulmonary Outcome Study.

The letter can be very generic, just that the study is approved and funded. I don't think results of the center vote (questionnaires at local center vs. Rochester) and all is necessary.

Thanks

Tim

From: Wade Rich
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Support oxims.
Date: Monday, June 27, 2005 1:55:04 PM

Thanks Rose.
Wade

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Monday, June 27, 2005 10:53 AM
To: wrich@ucsd.edu
Subject: RE: Support oxims.

Wade
it is 10 per site (not 20)

Rose

-----Original Message-----
From: Wade Rich [mailto:wrich@ucsd.edu]
Sent: Monday, June 27, 2005 1:52 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: Support oxims.

Rose,
Please confirm that the number of oxims you have allotted to the 5 "storage" sites is 20.
I want to go ahead and order, as sharp is enrolling like mad.

Thanks,
Wade

Wade Rich, BS,RRT-NPS
Clinical Research Coordinator
Division of Neonatology
UCSD Medical Center
200 W Arbor Dr
San Diego, CA 92103-8774
619-543-5375
pgr 290-5230

From:	Wally Carlo, M.D.
To:	Wally Carlo, M.D.; Higgins, Rosemary (NIH/NICHD) [E]; Wade Rich; Neil Finer; Shahnaz Duara; Ed Donovan; Avroy A. Fanaroff, M.D.; Michele Walsh-Sukys; wrich@ucsd.edu; Higgins, Rosemary (NIH/NICHD) [E]
Subject:	RE: O2 Saturation graphs
Date:	Monday, June 27, 2005 9:49:25 AM

Just to clarify, these data are fake. RTI has not released any data other that what we all saw in their email. wally

---

From: Wally Carlo, M.D.
Sent: Monday, June 27, 2005 8:43 AM
To: Rose Higgins; Wade Rich; Neil Finer; Wally Carlo, M.D.; Shahnaz Duara; Ed Donovan; Avroy A. Fanaroff, M.D.; Michele Walsh-Sukys; wrich@ucsd.edu; Higgins, Rosemary (NIH/NICHD)
Subject: O2 Saturation graphs

To Support Subcommittee:

Enclosed is attachment that addresses SUPPORT O2 saturation monitoring and compliance. We could discuss this during our next conference call. We discussed briefly at the Steering Committee, options to monitor compliance with the O2 saturation arm of the trial. I have put together several options of ways to analyze the data so we can provide feedback to the DSMB, the Subcommittee, and/or the investigators and colleagues. Please look at the various ways to represent data.

Thanks,
Wally

From: Higgins, Rosemary (NIH/NICHD)
To: Wally Carlo, M.D.
Subject: RE: O2 Saturation graphs
Date: Monday, June 27, 2005 9:49:00 AM

OK, Whew, I thought I missed something.
We can discuss on the call
Thanks
Rose

From: Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]
Sent: Monday, June 27, 2005 9:48 AM
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE: O2 Saturation graphs

Rose: Sorry. This is fake data! Wally

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Monday, June 27, 2005 8:47 AM
To: Wally Carlo, M.D.
Subject: RE: O2 Saturation graphs

Wally
As I look at the second figure, if one adds the bars for either of the groups, you get more than 100% of time. Am I reading this correctly (one color bars should add up to 100%, not more)??
Thanks
Rose

From: Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]
Sent: Monday, June 27, 2005 9:43 AM
To: Higgins, Rosemary (NIH/NICHD); Wade Rich; Neil Finer; Wally Carlo, M.D.; Shahnaz Duara; Ed Donovan; Avroy A. Fanaroff, M.D.; Michele Walsh-Sukys; wrich@ucsd.edu; Higgins, Rosemary (NIH/NICHD)
Subject: O2 Saturation graphs

To Support Subcommittee:

Enclosed is attachment that addresses SUPPORT O2 saturation monitoring and compliance. We could discuss this during our next conference call. We discussed briefly at the Steering Committee, options to monitor compliance with the O2 saturation arm of the trial. I have put together several options of ways to analyze the data so we can provide feedback to the DSMB, the Subcommittee, and/or the investigators and colleagues. Please look at the various ways to represent data.

Thanks,
Wally

From: Higgins, Rosemary (NIH/NICHD)
To: "Estelle.Fischer@cchmc.org"
Subject: Re: SUPPORT
Date: Thursday, June 23, 2005 12:03:21 PM

Let me know if you need additional info like affiliations of the members.
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Estelle Fischer <Estelle.Fischer@cchmc.org>
To: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
Sent: Thu Jun 23 11:42:38 2005
Subject: RE: SUPPORT

Thank you

Estelle E. Fischer, MHSA, MBA
Clinical Research Manager
Division of Neonatology
Children's Hospital Medical Center (MLC 7009)
3333 Burnet Avenue
Cincinnati, OH 45229-3039
Phone: 513.558.0005 Fax: 513.558.7770

>>> "Higgins, Rosemary (NIH/NICHD)" <higginsr@mail.nih.gov> 06/23/05 11:08 AM >>>

The membership and disciplines are

Gordon Avery, M.D. – neonatology

Christine Gleason, M.D. – neonatology

Mary D'Alton, M.D. – OB/MFM

Carol Redmond, Ph.D. – statistician

Robert Boyle M.D.– ethics and neonatology

W. Kenneth Poole, Ph.D. – liaison from RTI

Marian Willinger M.D.– NICHD Representative

For the SUPPORT trial, we have ad hoc membership which includes:

Carl Hunt, M.D. - Neonatology and SIDS, NHLBI representative

Merran Thomson, M.D. – Neonatology (specific expertise with CPAP)

Marilee Allen, M.D. – neonatal follow up and long term outcomes

Let me know if you need additional information.

Thanks

Rose

From: Edward Donovan [mailto:Edward.Donovan@cchmc.org]
Sent: Thursday, June 23, 2005 11:00 AM
To: Higgins, Rosemary (NIH/NICHD)
Cc: Estelle Fischer
Subject: SUPPORT

Rose,

Although we will enroll no babies at Children's Hosp., some of our SUPPORT babies will be transferred for surgery, etc.

The Children's IRB has asked for the "composition" of the DSMB. I think disciplines represented would be fine.

Thanks,

Ed

Edward F. Donovan, M.D.
Director
Child Policy Research Center
Children's Hospital Medical Center
3333 Burnet Avenue, ML 7014
Cincinnati, OH 45229-3039
Phone 513-636-0182
Fax 513-636-0171
www.cprc-chmc.uc.edu

From: Higgins, Rosemary (NIH/NICHD)
To: Petrie, Carolyn
Subject: RE: support call
Date: Wednesday, June 22, 2005 3:12:00 PM

Wade is getting me a list of the coordinators who should be on the call – he will send it this PM>
Thanks
Rose

From: Petrie, Carolyn [mailto:petrie@rti.org]
Sent: Wednesday, June 22, 2005 3:06 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: support call

Rose-

Betty and Wade thought it would good to have the coordinators involved with the consent secondary to be on the call. Shall I forward them the information?

Carolyn Petrie

Neonatal Research Network Coordinator
RTI International
6110 Executive Blvd
Suite 902
Rockville, MD 20852
ph. (301) 230-4648
fx. (301) 230-4646

From:	Abbot Laptook
To:	Higgins, Rosemary (NIH/NICHD) [E]
Cc:	Betty Vohr; Angelita Hensman; Lucy Noel; William Oh
Subject:	RE: Pulmonary outcomes secondary study
Date:	Tuesday, June 21, 2005 2:10:34 PM

Rose
I have discussed this issue with Betty and we will do the questionaire from the Brown site. Abbot

---

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Friday, June 17, 2005 10:07 AM
To: Abbot Laptook; Abhik Das; Brenda Poindexter; Carlo Waldemar (E-mail); Charles Rosenfeld; Dale Phelps; Ed Donovan; Ehrenkranz Richard (E-mail); Jobe Alan (E-mail); Lemons Jim (E-mail); Michael O'Shea; Michelle Walsh; Neil Finer; Oh William (E-mail); Poole Kenneth (E-mail); Ronald GOldberg; Shahnaz Duara; Shankaran Seetha (E-mail); Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); Walid Salhab (Walid Salhab); Anna Dusick (adusick@iupui.edu); Betty Vohr ('Betty_Vohr@brown.edu'); Charlie Bauer (cbauer@peds.med.miami.edu); Dee WIlson (drfjcmd@aol.com); Gary Myers (Gary_myers@URMC.Rochester.edu); Ira Adams-Chapman; Jean Steichen (steichjj@email.uc.edu); Myriam Peralta (mperalta@peds.uab.edu); Ricki Goldstein (golds005@mc.duke.edu); Robert Dillard; Roy Heyne; Susan Hintz; Yvette Johnson (yjohnson@med.wayne.edu); Yvonne Vaucher (Yvonne Vaucher)
Cc: Hastings, Betty J.; (kzaterka@rti.org); Petrie, Carolyn
Subject: Pulmonary outcomes secondary study

Hi
Attached are documents and questionnaires associated with the pulmonary outcomes secondary study to the SUPPORT Trial. Please review the documents and send me a preference by June 27 indicating the following:

1. My site will do the Questionnaires
2. Rochester site to do questionnaires on my study subjects

I am checking on the issues regarding how the consents would be phrased in order that information could pass from your site to the Rochester site.

Thanks in advance for all your help!!
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Duara, Shahnaz
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT GROWTH SECONDARY
Date: Tuesday, June 21, 2005 11:18:30 AM

OK

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, June 21, 2005 11:14 AM
To: Duara, Shahnaz
Cc: Navarrete, Cristina
Subject: RE: SUPPORT GROWTH SECONDARY

Shahnaz,
Since this protocol is not yet approved, we are unable to provide a letter of support at this point in time.
Rose

From: Duara, Shahnaz [mailto:SDuara@med.miami.edu]
Sent: Tuesday, June 21, 2005 11:03 AM
To: Higgins, Rosemary (NIH/NICHD)
Cc: Navarrete, Cristina
Subject: FW: SUPPORT GROWTH SECONDARY

Hi Rose,

Would you be willing to give Cristina a letter of support? I am attaching for you a copy of her letter of intent which was sent off by their 5 PM deadline yesterday. Hopefully, ATS will accept a supplemental letter to support her application.

Thanks
Shahnaz
-----Original Message-----
From: Navarrete, Cristina
Sent: Tuesday, June 21, 2005 10:53 AM
To: Duara, Shahnaz
Subject: RE: SUPPORT GROWTH SECONDARY

Good Morning, Dr. Duara! Here it is. Thanks again.

From: Duara, Shahnaz
Sent: Tue 6/21/2005 10:28 AM
To: Navarrete, Cristina
Subject: FW: SUPPORT GROWTH SECONDARY

FYI - do you want me to get a letter of support from Rose for you which you can forward to the ATS? It could be helpful. If you want it, cc me a copy of what you sent ATS - I'll forward it to Rose, get an electronic letter of support for you to forward.
Shahnaz
-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, June 21, 2005 9:25 AM
To: Abbot Laptook (alaptook@WIHRI.org); Abhik Das; Brenda Poindexter; Carlo Waldemar (E-mail); Charles Rosenfeld; Dale Phelps; Ed Donovan; Ehrenkranz Richard (E-mail); Jobe Alan (E-

mail); Lemons Jim (E-mail); Michael O'Shea; Michelle Walsh; Neil Finer; Oh William (E-mail); Poole Kenneth (E-mail); Ronald GOldberg; Duara, Shahnaz; Shankaran Seetha (E-mail); Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); Walid Salhab (Walid Salhab)
Cc: Petrie, Carolyn; Hastings, Betty J.; kzaterka@rti.org
Subject: SUPPORT GROWTH SECONDARY

Hi,
Dr. Cristina Navarrete (University of Miami) is developing a secondary study to the SUPPORT Trial to look at growth. This was presented briefly at the steering committee meeting. The proposal is under revision with the SUPPORT Trial subcommittee. Cristina is in the process of exploring potential options for supplemental/outside funding for this secondary project. Dr. Finer and I have encouraged her to do so; she will apply to the American Thoracic Society.

Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Duara, Shahnaz
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Navarrete, Cristina
Subject: FW: SUPPORT GROWTH SECONDARY
Date: Tuesday, June 21, 2005 11:03:49 AM
Attachments: ATS Unrestricted Research Awards.doc

Hi Rose,

Would you be willing to give Cristina a letter of support? I am attaching for you a copy of her letter of intent which was sent off by their 5 PM deadline yesterday. Hopefully, ATS will accept a supplemental letter to support her application.

Thanks
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Subject: RE: SUPPORT GROWTH SECONDARY

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Sent: Tuesday, June 21, 2005 9:25 AM
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Cc: Petrie, Carolyn; Hastings, Betty J.; kzaterka@rti.org
Subject: SUPPORT GROWTH SECONDARY

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Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine

NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

June 20, 2005

Elisha Malanga
Associate Director, ATS Assembly and Research Programs
61 Broadway 4th FL
New York, NY 10006-2755
Tel: (212) 315-8693
Fax (212) 315-6498
Email: emalanga@thoracic.org

Dear Sir,

I would like to express our intent to apply for the **ATS Unrestricted Research Awards.** Our study is entitled "The Post-natal Growth of a Cohort of Infants Enrolled in the NICHD Neonatal Network Oxygen Saturation (SUPPORT) Study: A Growth Secondary Study".

The main study "SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants (SUPPORT)" is currently an ongoing study of the NICHD Neonatal Research Network, co-funded by NHLBI, in which preterm infants 401-1000 g are randomized to early CPAP or intubation /surfactant with the primary end-point of BPD/death. In a 2x2 factorial design, all infants are also randomized to two levels of oxygen saturation in a blinded manner, with the primary outcome of the oxygen saturation arm being ROP/death. Our center is a member of the Neonatal Research Network and this application is in accordance with Network policy of seeking external funding for specific secondary studies.

Given the great importance of oxygenation upon growth, and the paucity of information in preterm infants, we believe that this is an excellent opportunity to assess the growth impact of different oxygenation strategies. As there is no funding available for measurement of the biochemical growth markers in this secondary proposal, we are requesting the ATS to fund the growth secondary of the SUPPORT trial. This application has not been submitted elsewhere for funding, and if additional support does not become available, the secondary study will not take place.

Thank you very much for this opportunity to further our understanding of the impact of oxygenation on growth in preterm infants. Here's hoping for a favorable response.

Sincerely,

Cristina T. Navarrete, MD
Assistant Professor of Pediatrics
University of Miami
Miller School of Medicine (R-131)
PO Box 016960
Miami, FL 33101
e-mail: cnavarrete@med.miami.edu

A. ATS Unrestricted Research Awards:

Post-natal Growth of a Cohort of Infants Enrolled in the NICHD Neonatal Network Oxygen Saturation (SUPPORT) Study: A Secondary Growth Study

B. Sponsoring Institution:

University of Miami Miller School of Medicine, Miami, FL

C. Principal Investigator:

Cristina Navarrete, MD
Co-investigator: Shahnaz Duara, MD

D. Problem:

The National Institute of Child Health and Development's SURfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants (SUPPORT) will randomize infants to two ranges of SpO2 (low: 85-89% vs. high: 91-95%) in order to test the hypothesis that use of a lower SpO2 range will result in an increase in survival of preterm infants without the occurrence of threshold retinopathy of prematurity and/or the need for surgical intervention (oxygenation arm). With regards to growth, retrospective cohort data from several units in the U.K., with different oxygen supplementation policies, revealed poorer growth patterns in the preterm infants exposed to higher oxygen saturations for the duration of oxygen exposure. Conversely, observational data of infants with established BPD show better growth with home oxygen support, and two recent randomized controlled trials of different target saturations in older oxygen-dependent premature infants showed no difference in short or long-term growth outcomes. **There are no randomized controlled trial data evaluating the short or long-term growth impact of different SpO2 strategies with supplemental oxygen use in a birth cohort of extremely preterm infants. Therefore, this study provides an opportunity for us to obtain critically needed growth information on premature infants who are exposed from birth to different target oxygen saturation strategies**.

Primary Hypothesis:

1. Infants in the low oxygen saturation group (85-89%) will have better in-hospital and better long-term (18-22 months corrected age) growth.
2. Biochemical markers of growth will be better in the low oxygen saturation group.

Secondary Hypothesis:

1. Growth will be greater in infants who spend > 50% of the time with daily median oxygen saturation between 85% -95% while on supplemental oxygen, independent of randomization to low or high oxygen saturation.
2. Infants with BPD will have poorer in-hospital and long-term growth than infants without BPD, independent of randomization to low or high oxygen saturation.
3. Long term growth will be positively related to neuro-developmental outcome, independent of randomization to low or high oxygen saturation

E. Specific Aims:

1. To determine anthropometric measurements (wt, HC, length) in infants randomized to low and high oxygen saturation arms, from birth to hospital discharge and again at 18-22 months corrected age.
2. To determine nutritional intake (parenteral and enteral) during hospital stay.
3. To determine the percentage of infants with growth <10 percentile at 36 weeks PMA or discharge, whichever comes first.
4. To determine the percentage of infants with growth <10 percentile at 18-22 months corrected age.
5. To determine growth in relation to the proportion of time spent with oxygen saturation
   a.<85% and >95%, b. 85-95%

6. To determine growth in relation to the proportion of infants with
   a. median oxygen saturation > 95%, b. median oxygen saturation 75% - 84%, c. median oxygen saturation < 75%
7. To relate incidence of BPD in low and high saturation arms to growth.
8. To determine in-hospital growth velocity in low and high saturation arms.
9. To determine long-term growth velocity, from hospital discharge to follow up at 18-22 months corrected age in low and high saturation arms.
10. To relate neuro-developmental outcome at 18-22 months corrected age to long-term growth in low and high saturation arms.
11. To measure biochemical markers of growth (urinary hydroxyproline, and serum Type I and III procollagen propeptides) in the infants randomized to the two saturation arms.

F. Experimental approach:

Collection of Data

1. Anthropometric Measures – at birth, postnatal days 7(wt), 14(wt), 21(wt), and 28(wt), 32w PMA (wt), 36w PMA or discharge (whichever comes first)
   a. weight (wt), b. length, c. head circumference
2. Clinical Data –
   a. 24 h intake (Parenteral, Enteral) – postnatal days 7, 14, 21, and 28, 32w PMA, 36w PMA or discharge (whichever comes first)
   b. Date of first enteral feed
   c. Date of full enteral feeds (enteral > 120ml/kg/d)
   d. Total number of days on parenteral nutrition
   e. Date when infant regained birth weight
   f. BPD Y/N (Physiological definition)
3. Specimen collection –
   a. urinary hyproxyproline – weekly until 36 weeks
   b. serum type I and III procollagen propeptides – every 4 weeks until 36 weeks
4. Intervention Data –
   a. Duration of time spent in target saturation ranges of interest
   b. Median values for unmasked oxygen saturation while still on supplemental oxygen therapy
   c. Highest daily FiO2
   d. Duration of supplemental oxygen exposure
   e. Documentation of post-discharge oxygen use
5. Follow Up data
   a. Anthropometric measurements at 18-22 months corrected age
   b. Neuro-developmental follow up at 18-22 months corrected age

Primary Outcome:

Growth (in-hospital and at 18-22 months corrected age) of infants in the high and low saturation arms.

Sample size:

Given the importance of using an RCT to establish the impact of different levels of oxygen saturation from birth on short and long term growth, recognizing the wealth of oxygen saturation data that will be available for analysis and the absence of comparable data in the literature, all infants in the SUPPORT Trial should be recruited into this secondary (n=1320)

Statistical Analysis:

Based upon intent-to-treat, differences between treatment arms of continuous data will be assessed by the Student t-test or the Mann-Whitney U-test, depending upon normal or skewed data distribution. Categorical data will be compared by Chi-square. Linear regression will be used to determine the relationship between measures of oxygen saturation and growth. Logistic regression models will be developed to determine whether oxygen saturation independently affects growth after correction for confounding variables that also alter growth.

From: Petrie, Carolyn
To: barbara_stoll@oz.ped.emory.edu
Cc: Higgins, Rosemary (NIH/NICHD) [E]; renee.dunbar-scott@oz.ped.emory.edu
Subject: FW: SUPPORT call
Date: Monday, June 20, 2005 5:01:40 PM

Barbara-

Would you be able to join us for this call? If so, please send availability below.

-----Original Message-----
From: Petrie, Carolyn
Sent: Monday, June 20, 2005 2:23 PM
To: 'Neil Finer'; 'Wade Rich (wrich@ucsd.edu)'; 'Higgins, Rosemary (NIH/NICHD)'
Cc: hsquibb@ucsd.edu; Petrie, Carolyn; Das, Abhik
Subject: SUPPORT call

Hi everyone-

Neil, I know you are away but wanted to start querying the SUPPORT subcommittee for a call to discuss:

- How to fill out screening logs (eligible versus screening)
- Definition of BPD at 36 weeks – three different definitions currently (need Stoll on the call)
- Pulmonary outcomes secondary

Please let me know when we should shoot for a call (July?) and if there are additional items for the agenda.

Thanks,
Carolyn

From:	Petrie, Carolyn
To:	Das, Abhik; Poole, W. Kenneth; Duara, Shahnaz; Edward Donovan; wcarlo@peds.uab.edu; mcw3@po.cwru.edu; Higgins, Rosemary (NIH/NICHD) [E]; wrich@ucsd.edu; reverett@med.miami.edu; Hastings, Betty J.; Zaterka-Baxter, Kristin
Cc:	Neil Finer; hsquibb@ucsd.edu; Petrie, Carolyn
Subject:	SUPPORT conf call
Date:	Monday, June 20, 2005 4:44:49 PM

Please send me your availability for a SUPPORT conference call:

Tues Jul 5
Wed Jul 6
Thur Jul 7
Fri Jul 8

Agenda

- How to fill out screening logs (eligible versus screening)
- Definition of BPD at 36 weeks – three different definitions currently (need Stoll on the call)
- Pulmonary outcomes secondary

thank you!
Carolyn Petrie

Neonatal Research Network Coordinator
RTI International
6110 Executive Blvd
Suite 902
Rockville, MD 20852
ph. (301) 230-4648
fx. (301) 230-4646

From:	Neil Finer
To:	"Petrie, Carolyn"
Cc:	Higgins, Rosemary (NIH/NICHD) [E]; hsquibb@ucsd.edu; fmartinez@ucsd.edu
Subject:	RE: SUPPORT call
Date:	Monday, June 20, 2005 4:32:48 PM

Hi Carolyn

Can we try for the first week in July after the 4th. I am in town, and could do most times except Wednesday morning or afternoon before 4:00PM.
If needed sooner, I can connect from Hi. I will try to work with the group.
Neil

From: Petrie, Carolyn [mailto:petrie@rti.org]
Sent: Monday, June 20, 2005 11:23 AM
To: Neil Finer; wrich@ucsd.edu; Higgins, Rosemary (NIH/NICHD)
Cc: hsquibb@ucsd.edu; Petrie, Carolyn; Das, Abhik
Subject: SUPPORT call

Hi everyone-

Neil, I know you are away but wanted to start querying the SUPPORT subcommittee for a call to discuss:

- How to fill out screening logs (eligible versus screening)
- Definition of BPD at 36 weeks – three different definitions currently (need Stoll on the call)
- Pulmonary outcomes secondary

Please let me know when we should shoot for a call (July?) and if there are additional items for the agenda.

Thanks,
Carolyn

From: Higgins, Rosemary (NIH/NICHD)
To: Burnell, Erica
Subject: RE: Support Trial starting...
Date: Monday, June 20, 2005 2:13:00 PM

Thanks
Rose

-----Original Message-----
From: Burnell, Erica [mailto:Erica_Burnell@URMC.Rochester.edu]
Sent: Friday, June 17, 2005 5:41 PM
To: Higgins, Rosemary (NIH/NICHD)
Cc: Laroia, Nirupama; Reubens, Linda; Phelps, Dale; Jensen, Rosemary
Subject: Support Trial starting...

Hi Dr. Higgins,
I just wanted to make you aware that we recieved our approval for the Support Trial from the IRB today and we have set an estimated start date for our center as of June 27, 2005 to allow us time to prepare and inservice our NICU staff. As you know we sent two of our study oximeters to Case Western for thier use since we did not have approval yet and were not enrolling. With our anticipated start date arriving in a little over a week, we will need to get our oximeters back at some point within the next couple of weeks. I apologize for the inconvenience for Case Western, but hopefully this will give them time to replace ours.
We are excited about our approval and look forward to starting enrollment!
Thanks,
Erica Burnell

Erica Burnell, RN
Golisano's Children's Hospital
601 Elmwood Avenue
Neonatology/Pediatrics
Clinical Research Office 43251
Rochester, NY 14642
(585)275-5427
erica_burnell@urmc.rochester.edu

From: Higgins, Rosemary (NIH/NICHD)
To: Petrie, Carolyn
Subject: RE: support call
Date: Monday, June 20, 2005 2:11:00 PM

Agenda items:
How to fill out screening logs (eligible versus screening)
Definition of BPD at 36 weeks – three different definitions currently (need Stoll on the call)

That's what I have
Thanks
Rose

From: Petrie, Carolyn [mailto:petrie@rti.org]
Sent: Monday, June 20, 2005 2:00 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: support call

I have in my notes that we want a support call to discuss items that include Redefining day on oxygen and the pulmonary outcomes secondary...perhaps other items.

I can refine the agenda with Neil.

Carolyn Petrie

Neonatal Research Network Coordinator
RTI International
6110 Executive Blvd
Suite 902
Rockville, MD 20852
ph. (301) 230-4648
fx. (301) 230-4646

From: Higgins, Rosemary (NIH/NICHD)
To: "dale_phelps@urmc.rochester.edu"; "nfiner@ucsd.edu"
Subject: Re: SUPPORT Start date in Rochester
Date: Friday, June 17, 2005 4:04:54 PM

Terrific!!
I know that linda reubens sent two of your oximeters to case for us. Let us know if you need more!
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Phelps, Dale <Dale_Phelps@URMC.Rochester.edu>
To: 'Neil Finer, MD' <nfiner@ucsd.edu>; Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
Sent: Fri Jun 17 16:02:27 2005
Subject: FW: SUPPORT Start date in Rochester

We will begin enrolling June 27th.

Dale Phelps

From: Jensen, Rosemary
Sent: Friday, June 17, 2005 3:58 PM
To: .... Subject: FW: SUPPORT Start date
Importance: High

Hello all,

We have RSRB approval for SUPPORT trial.

Nursing In-services will begin Monday June 20 and the trial will be officially open in Rochester to enroll patients from Monday June 27, 2005. The COIN Trial will officially close the same day. If patients have consented for the COIN trial and are within the SUPPORT trial gestational age, they will need to be reconsented for SUPPORT.

Fellows: New consent forms will be available on Monday (6/27/05) for Support trial. Inclusion criteria 24 0/7 weeks to 27 6/7 weeks (slightly different from COIN)

Nirupama Laroia, MD

Director, Special Care Nursery, Rochester General Hospital.

Assoc. Professor, Dept of Pediatrics/ Neonatology

Golisano Children's Hospital at Strong, University of Rochester

601 Elmwood Ave, Box 651, Rochester, NY 14642

Phone: 585 275 2972, Fax: 585 461 3614

email: nirupama_laroia@urmc.rochester.edu

From: Wade Rich
To: "Hastings, Betty J."; nfiner@ucsd.edu; Higgins, Rosemary (NIH/NICHD) [E]; "Das, Abhik"
Subject: Support Downloads
Date: Friday, June 17, 2005 10:35:23 AM

All Coordinators:

Until further notice, please download all Support infants every 2 weeks.
Thank you.

Wade

Wade Rich, BS,RRT-NPS
Clinical Research Coordinator
Division of Neonatology
UCSD Medical Center
200 W Arbor Dr
San Diego, CA 92103-8774
619-543-5375
pgr 290-5230

From: Hastings, Betty J.

To: ahensman@wihri.org; mbball@leland.stanford.edu; grisbyca@email.uc.edu; ellen_hale@oz.ped.emory.edu; gaynelle.hensley@utsouthwestern.edu; Georgia E McDavid; auten002@mc.duke.edu; linda_reubens@urmc.rochester.edu; lucmille@iupui.edu; mcollins@peds.uab.edu; monica.konstantino@yale.edu; Nancy.Miller@UTSouthwestern.edu; Nancy Newman; npeters@wfubmc.edu; ae5357@wayne.edu; rbridge@ucsd.edu; risa.demetrio@sharp.com; kathy.arnell@sharp.com; Reverett@med.miami.edu; Theresa Elizabeth Hurlburt; balexanba@hotmail.com; Lenora Jackson; Estelle E. Fischer; Holly Mincey; Jody Shively; Kate Bridges, MD

Cc: wrich@ucsd.edu; nfiner@ucsd.edu; Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik; Zaterka-Baxter, Kristin; Schaefer, Scott E.

Subject: FW: Support Downloads

Date: Friday, June 17, 2005 11:22:01 AM

Importance: High

PLEASE NOTE:

All Coordinators:

Until further notice, please download all Support infants every 2 weeks.

Thank you.

Wade

Wade Rich, BS,RRT-NPS
Clinical Research Coordinator
Division of Neonatology
UCSD Medical Center
200 W Arbor Dr
San Diego, CA 92103-8774
619-543-5375
pgr 290-5230

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]; hubertbp@uab.edu
Cc: "Carlo Waldemar (E-mail)"; "Monica Collins"
Subject: RE: SUPPORT Trial
Date: Tuesday, June 14, 2005 10:17:52 PM

Wally
Bring this up at tomorrows meeting
Neil

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, June 14, 2005 6:30 AM
To: hubertbp@uab.edu
Cc: Carlo Waldemar (E-mail); Monica Collins; Neil Finer
Subject: SUPPORT Trial

HI Bjorn,

Betty Hastings had sent me your request. The NICHD Neonatal Research Network has a steering committee that controls access to the data. Since this is an ongoing trial, unless plans have been put into place (which has happened for certain portions of studies), no data are released. In addition, the data coordinating center at RTI does all of the analyses unless otherwise voted upon by the steering committee. Dr. Carlo and Dr. Finer have developed a pilot study to look at the question you refer to below: how much time are the patients in the given oximetry ranges? IF you have a different question to ask, please speak with Dr. Carlo and consider a secondary submission.

Thanks

Rose

-----Original Message-----
From: Bjorn P Hubert-Wallander [mailto:hubertbp@uab.edu]
Sent: Wednesday, June 08, 2005 11:15 AM
To: Hastings, Betty J.
Subject: SUPPORT Data

Ms. Hastings,
I am a undergraduate student working with Dr. Carlo and Monica Collins in the Department of Neonatology at UAB for the summer. I am helping them with the SUPPORT Trial in gathering data and doing some minor analysis and am given to understand that I could contact you to talk about getting some data on the babies on the pulse oximeters. Specifically, I am interested in how much time (and what percent of the time) the patients at each study center are spending in each oxygen saturation range (84%-87%, 93%-96%, etc.). However, I also would like to know what kind of secondary data you have on these babies that could explain any findings I might come across, as I am not sure exactly what kind of information you collect outside of the oxygen saturation data. If you could let me know how I could get some of this data to analyze, I would be very grateful. Thanks!

Bjorn Hubert-Wallander

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Wally Carlo, M.D.
To: Higgins, Rosemary (NIH/NICHD) [E]; hubertbp@uab.edu
Cc: Monica Collins; nfiner@ucsd.edu
Subject: Re: SUPPORT Trial
Date: Tuesday, June 14, 2005 9:36:07 AM

Neil and Rose. I will talk to you tomorrow. This is about the pilot study to decide how to start monitoring the data so we can provide feedback to the sites. I
Wally
Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
To: hubertbp@uab.edu <hubertbp@uab.edu>
CC: Wally Carlo, M.D. <WCarlo@peds.uab.edu>; Monica Collins <MCollins@peds.uab.edu>; Neil Finer <nfiner@ucsd.edu>
Sent: Tue Jun 14 08:30:26 2005
Subject: SUPPORT Trial

HI Bjorn,

Betty Hastings had sent me your request. The NICHD Neonatal Research Network has a steering committee that controls access to the data. Since this is an ongoing trial, unless plans have been put into place (which has happened for certain portions of studies), no data are released. In addition, the data coordinating center at RTI does all of the analyses unless otherwise voted upon by the steering committee. Dr. Carlo and Dr. Finer have developed a pilot study to look at the question you refer to below: how much time are the patients in the given oximetry ranges? IF you have a different question to ask, please speak with Dr. Carlo and consider a secondary submission.

Thanks

Rose

-----Original Message-----
From: Bjorn P Hubert-Wallander [mailto:hubertbp@uab.edu]
Sent: Wednesday, June 08, 2005 11:15 AM
To: Hastings, Betty J.
Subject: SUPPORT Data

Ms. Hastings,

I am a undergraduate student working with Dr. Carlo and Monica Collins in the Department of Neonatology at UAB for the summer. I am helping them with the SUPPORT Trial in gathering data and doing some minor analysis and am given to understand that I could contact you to talk about getting some data on the babies on the pulse oximeters. Specifically, I am interested in how much time (and what percent of the time) the patients at each study center are spending in each oxygen saturation range (84%-87%, 93%-96%, etc.). However, I also would like to know what kind of secondary data you have on these babies that could explain any findings I might come across, as I am not sure exactly what kind of information you collect outside of the oxygen saturation data. If you could let me know how I could get some of this data to analyze, I would be very grateful. Thanks!

Bjorn Hubert-Wallander

Rosemary D. Higgins, M.D.

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

NICHD, NIH

6100 Executive Blvd., Room 4B03B

MSC 7510

Bethesda, MD 20892

(For overnight delivery, use Rockville, MD 20852)

301-435-7909

301-496-3790 (FAX)

higginsr@mail.nih.gov

From:	Higgins, Rosemary (NIH/NICHD)
To:	Haverkos, Lynne (NIH/NICHD) [E]
Subject:	RE: Clinical trials registration required before publication
Date:	Tuesday, June 14, 2005 9:26:00 AM

Can you resend me a password and the link?
Thanks
Rose

From: Haverkos, Lynne (NIH/NICHD)
Sent: Tuesday, June 14, 2005 9:26 AM
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE: Clinical trials registration required before publication

Rose,
If the follow up study has a new name then you can create a new record for it. If it is just a continuation, then you can add the information in the detailed description section of the parent study.

Lynne

Lynne M. Haverkos, MD, MPH
Program Director,
Behavioral Pediatrics and Health Promotion Research
http://www.nichd.nih.gov/crmc/cdb/p_behave.htm
NICHD/NIH
6100 Executive Blvd. Room 4B05 MSC 7510
Bethesda, MD. 20892-7510
For Fed Ex use: Rockville, MD. 20852
phone: 301-435-6881
fax: 301-480-0230
email: haverkol@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD)
Sent: Monday, June 13, 2005 8:50 AM
To: Haverkos, Lynne (NIH/NICHD)
Subject: RE: Clinical trials registration required before publication

Lynne,
Dr. Neil Finer (nfiner@ucsd.edu) is the trial PI for SUPPORT:

The SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants
The SUPPORT Trial of the NICHD Neonatal Research Network

We are also now going to continue following our hypothermia trial patients through ages 6-7 – do we update the website for this one??

Thanks
Rose

From: Haverkos, Lynne (NIH/NICHD)
Sent: Friday, June 10, 2005 5:00 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE: Clinical trials registration required before publication

Hi Rose,

The Morris phototherapy record is still waiting for Dr. Morris to send a detailed description. If you'd like to create one, then I could release the record. We'd also need to know if she is still recruiting subjects, when she collected the last follow-up date, and the data entry closure date. Here are guidelines for the detailed description section.

Detailed Description

This is a technical description of the protocol for health professionals. NICHD recommends that the Detailed Description be two paragraphs. The first paragraph should briefly address the background, rationale, and purpose of the study. The second paragraph should focus on the methodology of the study, i.e. what will be required of study participants. Include information on number and frequency of study visits, length of study, randomization, interventions, and assessments.

Please give me a little more info on the NRN support trial like who entered the data or the full title. Thanks

Lynne M. Haverkos
Lynne M. Haverkos, MD, MPH
Program Director,
Behavioral Pediatrics and Health Promotion Research
http://www.nichd.nih.gov/crmc/cdb/p_behave.htm
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6100 Executive Blvd. Room 4B05 MSC 7510
Bethesda, MD. 20892-7510
For Fed Ex use: Rockville, MD. 20852
phone: 301-435-6881
fax: 301-480-0230
email: haverkol@mail.nih.gov

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD)
Sent: Friday, June 10, 2005 4:33 PM
To: Haverkos, Lynne (NIH/NICHD)
Subject: RE: Clinical trials registration required before publication

Lynne
Did our NRN phototherapy trial (Brenda Morris UT Houston is the PI) get on clinical trials.gov? Also our NRN SUPPORT Trial?
thanks
Rose

-----Original Message-----
From: Haverkos, Lynne (NIH/NICHD)
Sent: Wednesday, May 25, 2005 1:40 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: Out of Office AutoReply: Clinical trials registration required before publication

I will be out of the office on May 23-31. If you need assistance please call 301-594-1968. I will respond to your email when I return. Thank you and have a great day!

From: Hastings, Betty J.
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: SUPPORT Data
Date: Monday, June 13, 2005 1:14:46 PM

Rose,
I've been meaning to send this message to you. We seem to get getting similar requests about the SUPPORT data. Not sure how we should be handling this.
-----Original Message-----
From: Bjorn P Hubert-Wallander [mailto:hubertbp@uab.edu]
Sent: Wednesday, June 08, 2005 11:15 AM
To: Hastings, Betty J.
Subject: SUPPORT Data

Ms. Hastings,
I am a undergraduate student working with Dr. Carlo and Monica Collins in the Department of Neonatology at UAB for the summer. I am helping them with the SUPPORT Trial in gathering data and doing some minor analysis and am given to understand that I could contact you to talk about getting some data on the babies on the pulse oximeters. Specifically, I am interested in how much time (and what percent of the time) the patients at each study center are spending in each oxygen saturation range (84%-87%, 93%-96%, etc.). However, I also would like to know what kind of secondary data you have on these babies that could explain any findings I might come across, as I am not sure exactly what kind of information you collect outside of the oxygen saturation data. If you could let me know how I could get some of this data to analyze, I would be very grateful. Thanks!

Bjorn Hubert-Wallander

From:	Neil Finer
To:	"Poole, W. Kenneth"
Cc:	"Avroy A. Fanaroff, M.D."; "Betty Hastings"; "Ed Donovan"; Higgins, Rosemary (NIH/NICHD) [E]; "Michele"; "Neil Finer"; "Shahnaz Duara"; "Wade Rich"; "Wally Carlo"
Subject:	RE: Pulse Ox data
Date:	Friday, June 03, 2005 2:27:10 PM

Hi Ken
Can we wait till the Steering Committee meeting? Perhaps you could bring the data with you.
Many thanks
Neil

From: Poole, W. Kenneth [mailto:poo@rti.org]
Sent: Friday, June 03, 2005 10:59 AM
To: nfiner@ucsd.edu
Cc: Das, Abhik; Gantz, Marie
Subject: Pulse Ox data

Neil,

Brown has requested the summary for their pulse ox range data. This would be like the last summary we sent you and Wade (i.e. summarized over babies and treatment groups). What do you think?

From: Higgins, Rosemary (NIH/NICHD)
To: Scholl, Diane (NIH/OD/DEAS)
Subject: FW: ORD Support for Rare Diseases Research Scientific Conferences
Date: Wednesday, June 01, 2005 4:00:00 PM
Attachments: workshopsmemoProgramContactsFY2005Round1.doc
Trans NIH Roster Feb 05.doc
Trans NIH1 Roster.doc
Importance: High

Diane
I need to have ORD in the loop for the oxygen conference. Can you add Dr. Griffin to the list and make sure they get the meeting info?
Thanks
Rose

From: Griffin, Chris (NIH/OD)
Sent: Thursday, February 10, 2005 11:38 AM
To: Bohr, Vilhelm (NIH/NIA/IRP); Purohit, Vishnudutt (NIH/NIAAA); Klion, Amy (NIH/NIAID); Rosa, Patricia (NIH/NIAID); Rogers, Martin J. (NIH/NIAID); Higgs, Elizabeth (NIH/NIAID); Gherardini, Frank (NIH/NIAID); Holland, Steven (NIH/NIAID); Nash, Theodore (NIH/NIAID); Sizemore, Christine (NIH/NIAID); Lymn, Richard (NIH/NIAMS); Hennings, Marsha (NIH/NIAMS); Kaye, Frederic (NIH/NCI); Harris, Curtis (NIH/NCI); Kleinerman, Ruth (NIH/NCI); Moore, Lee (NIH/NCI); O'Brien, Thomas (NIH/NCI); Marks, Cheryl (NIH/NCI); Pavletic, Steven (NIH/NCI); Rabkin, Charles (NIH/NCI); Wei, Jun (NIH/NCI); Reddy, Uma (NIH/NICHD); OsterGranite, MaryLou (NIH/NICHD); Pacak, Karel (NIH/NICHD); Nelson, Lawrence (NIH/NICHD); Raju, Tonse (NIH/NICHD); Higgins, Rosemary (NIH/NICHD); Marini, Joan (NIH/NICHD); Gladwin, Mark (NIH/CC/CCMD); Gorr, Sven (NIH/NIDCR); Payne, Denise (NIH/NIDDK); Doo, Edward (NIH/NIDDK); Rasooly, Rebekah (NIH/NIDDK); Shelby, Michael (NIH/NIEHS); Armstrong, David (NIH/NIEHS); Ikeda, Richard (NIH/NIGMS); Evans, Gregory L (NIH/NHLBI); Schramm, Charlene (NIH/NHLBI); Fakunding, John (NIH/NHLBI); Pearson, Gail (NIH/NHLBI); Green, Eric (NIH/NHGRI); Smith, Ann (NIH/NHGRI); Pearson, Jane L (NIH/NIMH); Finkelstein, Robert (NIH/NINDS); Gwinn-Hardy, Katrina (NIH/NINDS); Ludlow, Christy (NIH/NINDS); Leblanc, Gabrielle (NIH/NINDS); Tagle, Danilo (NIH/NINDS); Oliver, Gene (NIH/NINDS); Hare, Martha (NIH/NINR); Costello, Becky (NIH/OD); Reddy, Uma (NIH/NICHD); Khan, Javed (NIH/NCI)
Cc: Demory, Mary (NIH/OD); Groft, Stephen (NIH/OD)
Subject: ORD Support for Rare Diseases Research Scientific Conferences
Importance: High

DATE: February 10, 2005

TO: IC Program Contacts

FROM: Director, Office of Rare Diseases, OD

SUBJECT: ORD Support for Rare Diseases Research Scientific Conferences

In January we sent a copy of a memorandum from the Office of Rare Diseases of our intent to fund scientific conference(s) in your IC. Transfers of funds for some of the meetings have already occurred or will occur soon. Thank you for cosponsoring a rare disease scientific conference.

I would like to take this opportunity to bring to your attention again the information our office would like to receive from you during the planning of your conference and after your conference has been held.

It is very important that we receive from you the tentative date(s) and the proposed location of your meeting as soon as you know when and where the event will take place. The draft

agenda and list of potential speakers and participants should be submitted to us at least 6 to 8 weeks in advance of the meeting and the final agenda and list of speakers/participants 4 weeks before the meeting takes place.

ORD will publicize on its website the agenda, location and participants as well as a summary of the conference when completed. If you put information about the conference on your website, we will link to it. If you are not planning to put information about the conference on your website, we will post it on our website, unless you are electing to restrict participation at the conference. If you choose not to post the information before the conference, ORD will provide a meeting summary for the public on its website after the conference.

We encourage you to solicit cosponsors and invite representatives from the patient support groups, foundations, or commercial sponsors and also from other ICs or Offices at the NIH that have similar research interests. If you wish, ORD would be pleased to participate in the planning process for your conference.

If you are unable to use the funds we are providing this fiscal year, please let us know as soon as possible and return the funds to us so we can fund other requests for scientific conferences.

Thank you for your request and for your support of research of rare diseases. If you have any questions, please call Mrs. Mary Demory at 301-402-4338 or me at 301-435-6041.

/s/

Stephen C. Groft, Pharm. D.

cc:
Trans-NIH Working Group on Rare Diseases Research

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

National Institutes of Health
Office of Rare Diseases
Bethesda, Maryland 20892

DATE: February 10, 2005

TO: IC Program Contacts

FROM: Director, Office of Rare Diseases, OD

SUBJECT: ORD Support for Rare Diseases Research Scientific Conferences

In January we sent a copy of a memorandum from the Office of Rare Diseases of our intent to fund scientific conference(s) in your IC. Transfers of funds for some of the meetings have already occurred or will occur soon. Thank you for cosponsoring a rare disease scientific conference.

I would like to take this opportunity to bring to your attention again the information our office would like to receive from you during the planning of your conference and after your conference has been held.

It is very important that we receive from you the tentative date(s) and the proposed location of your meeting as soon as you know when and where the event will take place. The draft agenda and list of potential speakers and participants should be submitted to us at least 6 to 8 weeks in advance of the meeting and the final agenda and list of speakers/participants 4 weeks before the meeting takes place.

ORD will publicize on its website the agenda, location and participants as well as a summary of the conference when completed. If you put information about the conference on your website, we will link to it. If you are not planning to put information about the conference on your website, we will post it on our website, unless you are electing to restrict participation at the conference. If you choose not to post the information before the conference, ORD will provide a meeting summary for the public on its website after the conference.

We encourage you to solicit cosponsors and invite representatives from the patient support groups, foundations, or commercial sponsors and also from other ICs or Offices at the NIH that have similar research interests. If you wish, ORD would be pleased to participate in the planning process for your conference.

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National Institute of Environmental Health Sciences (NIEHS)

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and Public Health Activities
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Office of Dietary Supplements (ODS)
OD, NIH

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301-435-2920
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Liaison Representatives

Food and Drug Administration (FDA)

Marlene Haffner, M.D., M.P.H.
Rear Admiral, U.S. Public Health Service
Director, Office of Orphan Products
Development
Parklawn Building
Room 6A55
Rockville MD 20857
301-827-3666
301-827-0017 Fax
mhaffner@oc.fda.gov
http://www.fda.gov/orphan/

From:	Higgins, Rosemary (NIH/NICHD)
To:	Poole, W. Kenneth
Subject:	RE:
Date:	Thursday, May 26, 2005 2:56:00 PM

To allow SUPPORT and this cycled light study to both occur in the Duke NICU.
Thanks
Rose

From: Poole, W. Kenneth [mailto:poo@rti.org]
Sent: Thursday, May 26, 2005 2:52 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE:

What is their plan?

> -----Original Message-----
> **From:** Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
> **Sent:** Thursday, May 26, 2005 12:56 PM
> **To:** Jon E Tyson; Neil Finer; Poole, W. Kenneth; Das, Abhik
> **Subject:** FW:
>
> HI,
> Was a consensus reached regarding this issue?
> Thanks
> Rose

> **From:** Ronald N Goldberg [mailto:goldb008@mc.duke.edu]
> **Sent:** Thursday, May 26, 2005 12:50 PM
> **To:** Higgins, Rosemary (NIH/NICHD)
> **Cc:** Debra Brandon
> **Subject:**
>
> Hi Rose, any word on the issue of Duke's plan for randomization for SUPPORT and the cycled light study?
> ron

From: Higgins, Rosemary (NIH/NICHD)
To: "petrie@rti.org"
Subject: Impotant
Date: Monday, May 23, 2005 7:03:34 AM

Carolyn
For the june steering committee meeting, support should have a 2 hour. Meeting and more time on thurs due to hintz and stevens - I had forgot on friday!
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

From: Petrie, Carolyn
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: do you know
Date: Friday, May 20, 2005 11:29:28 AM

He is applying for a travel grant.
Are they staying at Bolger?
Aug 4-5, how much per night?

> -----Original Message-----
> **From:** Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
> **Sent:** Friday, May 20, 2005 11:27 AM
> **To:** Petrie, Carolyn
> **Subject:** RE: do you know
>
> Yes, the stuff will go out next week.

> **From:** Petrie, Carolyn [mailto:petrie@rti.org]
> **Sent:** Friday, May 20, 2005 11:26 AM
> **To:** Higgins, Rosemary (NIH/NICHD)
> **Subject:** do you know
>
> Anything about an oxygen meeting Aug. ? with neil finer?
>
> Carolyn Petrie
>
> Neonatal Research Network Coordinator
> RTI International
> 6110 Executive Blvd
> Suite 902
> Rockville, MD 20852
> ph. (301) 230-4648
> fx. (301) 230-4646

From: Higgins, Rosemary (NIH/NICHD)
To: "ellen_hale@oz.ped.emory.edu"
Cc: "barbara_stoll@oz.ped.emory.edu"
Subject: Re: SUPPORT
Date: Tuesday, May 17, 2005 9:51:02 AM

Ellen
Thanks for the update. As issues develop, please do not hesitate to contact the Support Subcommittee members or myself.
Thanks for your dedication!
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Ellen Hale <ellen.hale@oz.ped.emory.edu>
To: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
CC: Susie Buchter <susie.buchter@oz.ped.emory.edu>
Sent: Tue May 17 09:47:20 2005
Subject: SUPPORT

Dear Rose,
We have officially started SUPPORT. We have everyting in place and began screening yesterday. We are working with a mom to get consent. I am keeping a log of each trip to a mom's bedside with time spent and reason for visit. Hope this will give us a better idea of time spent in consenting.
Ellen

From: Higgins, Rosemary (NIH/NICHD)
To: Walid Salhab
Subject: RE: MRI SUPPORT secondary
Date: Wednesday, May 11, 2005 3:44:00 PM

Walid
There is a separate protocol. Betty Hastings has posted it on the private website. As far as including the secondary on the consent form, this would be fine - whatever works at the site and local IRB will be fine. We also have a pulmonary outcomes secondary study (also on website), so you may want to do both at once (if this works for your site).
Thanks for your attention to this!
Rose

-----Original Message-----
From: Walid Salhab [mailto:Walid.Salhab@UTSouthwestern.edu]
Sent: Wednesday, May 11, 2005 3:37 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: Re: MRI SUPPORT secondary

Rose,
Charles has replied to you of our participation in Dr Hintz MRI secondary. Should I expect a separate protocol to submit to the IRB with a consent form?
My plan is to submit a modification to the IRB and modify the current consent form to include an MRI at 36 weeks since the HUS will fit in our standard of care.
Let me know if a separate protocol and consent form are being prepared otherwiswe I will proceed with my plan.
Thanks
Walid

>>> "Higgins, Rosemary (NIH/NICHD)" <higginsr@mail.nih.gov> 05/05/05 10:33 AM >>>
Hi Charles and Walid,

Are you planning on participating in the Hintz MRI secondary study to SUPPORT? We are anticipating approximately $1300 per child enrolled. Each infant needs a head US by day 14 of life and an MRI and head US at approximately 36 weeks. Let me know if this will be feasible at Dallas.

Thanks

Rose

Rosemary D. Higgins, M.D.

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

NICHD, NIH

6100 Executive Blvd., Room 4B03B

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higginsr@mail.nih.gov <mailto:higginsr@mail.nih.gov>

Walid A. Salhab, M.D.
Assistant Professor of Pediatrics
Division of Neonatal-Perinatal Medicine
University of Texas, Southwestern Medical School
5323 Harry Hines Blvd
Dallas, TX 75390-9063

Phone: (214) 648-3753
Fax: (214) 648-2481
email: Walid.Salhab@UTsouthwestern.edu

From:	Higgins, Rosemary (NIH/NICHD)
To:	Duara, Shahnaz; wcarlo@peds.uab.edu; edward.donovan@cchmc.org; poo@rti.org; nfiner@ucsd.edu; Michele Walsh
Cc:	Everett, Ruth
Subject:	RE: Enrollment in SUPPORT
Date:	Wednesday, May 11, 2005 10:46:00 AM

Terrific!!
Rose

-----Original Message-----
From: Duara, Shahnaz [mailto:SDuara@med.miami.edu]
Sent: Wednesday, May 11, 2005 10:04 AM
To: wcarlo@peds.uab.edu; edward.donovan@cchmc.org; poo@rti.org; nfiner@ucsd.edu; Higgins, Rosemary (NIH/NICHD); Michele Walsh
Cc: Everett, Ruth
Subject: Enrollment in SUPPORT

Hooray!! Miami admitted the first SUPPORT baby yesterday - Control arm.
So far things look good.

Shahnaz

From:	Wade Rich
To:	ahensman@wihri.org; mbball@leland.stanford.edu; grisbyca@email.uc.edu; ellen_hale@oz.ped.emory.edu; gaynelle.hensley@utsouthwestern.edu; "Mcdavid, Georgia E"; auten002@mc.duke.edu; linda_reubens@urmc.rochester.edu; lucmille@iupui.edu; mcollins@peds.uab.edu; Nancy.Miller@utsouthwestern.edu; "Nancy Newman"; npeters@wfubmc.edu; monica.konstantino@yale.edu; ae5357@wayne.edu; rbridge@ucsd.edu; risa.demetrio@sharp.com; kathy.arnell@sharp.com; Reverett@med.miami.edu; brenda.H.Morris@uth.tmc.edu; cotte010@mc.duke.edu; crosen@mednet.swmed.edu; vanmeurs@leland.stanford.edu; kurt.schibler@cchmc.org; alaptook@wihri.org; Jobea0@chmcc.org; bpoindex@iupui.edu; edward.donovan@chmcc.org; jlemons@iupui.edu; moshea@wfubmc.edu; sshankar@med.wayne.edu; sduara@miami.edu; susie.buchter@oz.ped.emory.edu; wcarlo@peds.uab.edu; mcw3@cwru.edu; Vineet.bhandari@yale.edu; vivek.Narendran@cchmc.org; Walid.Salhab@utsouthwestern.edu; balexanba@hotmail.com; "Lenora Jackson"; "Estelle Fischer"; Mike Danyleiko (Mike Danyleiko); wrich@ucsd.edu; nfiner@ucsd.edu; Higgins, Rosemary (NIH/NICHD) [E]; "Das, Abhik"; "Poole, W. Kenneth"; Schaefer, Scott E.; "Petrie, Carolyn"
Subject:	FW: New SUPPORT Form
Date:	Tuesday, May 10, 2005 5:40:42 PM
Attachments:	SUP02.doc SUPP11 5-5-05 .doc Chapter 16.doc

Fellow coordinator folks,

It was my intent that you guys give some feedback on the best way to do the supplemental data collection form (Supp11)

before it became anything official. Now that Betty has sent you all a copy, please look at it and think about the best way

to gather this data. As I will be away, please forward your comments to Angelita Hensman who will collate them and help

us come up with a best plan for the form.

Thank you.

Wade

Wade Rich, RRT-NPS

Clinical Research Administrator

Division of Neonatology

UCSD Medical Center

200 W Arbor Dr

San Diego, CA 92103-8774

619-543-5375

pgr 290-5230

From: Hastings, Betty J. [mailto:bkh@rti.org]
Sent: Friday, May 06, 2005 6:15 AM
To: ahensman@wihri.org; mbball@leland.stanford.edu; grisbyca@email.uc.edu; ellen_hale@oz.ped.emory.edu; gaynelle.hensley@utsouthwestern.edu; Georgia E McDavid; auten002@mc.duke.edu; linda_reubens@urmc.rochester.edu; lucmille@iupui.edu;

mcollins@peds.uab.edu; Nancy.Miller@utsouthwestern.edu; Nancy Newman; npeters@wfubmc.edu; monica.konstantino@yale.edu; ae5357@wayne.edu; rbridge@ucsd.edu; risa.demetrio@sharp.com; kathy.arnell@sharp.com; Reverett@med.miami.edu; brenda.H.Morris@uth.tmc.edu; cotte010@mc.duke.edu; crosen@mednet.swmed.edu; vanmeurs@leland.stanford.edu; kurt.schibler@cchmc.org; alaptook@wihri.org; Jobea0@chmcc.org; bpoindex@iupui.edu; edward.donovan@chmcc.org; jlemons@iupui.edu; moshea@wfubmc.edu; sshankar@med.wayne.edu; sduara@miami.edu; susie.buchter@oz.ped.emory.edu; wcarlo@peds.uab.edu; mcw3@cwru.edu; Vineet.bhandari@yale.edu; vivek.Narendran@cchmc.org; Walid.Salhab@utsouthwestern.edu; Personal Email Lenora Jackson; Estelle E. Fischer; Holly Mincey; Jody Shively; Kate Bridges, MD
Cc: wrich@ucsd.edu; nfiner@ucsd.edu; higginsr@mail.nih.gov; Das, Abhik; Poole, W. Kenneth; Petrie, Carolyn; Schaefer, Scott E.; Auman, Jeanette O.
Subject: New SUPPORT Form

Attached is a Technical Memo, new SUPPORT study form(SUPP11) and corresponding MOP Chapter 16 for this form. This form is intended to be completed **if an infant is on support after day 14.**

Please let us know if you have questions about this material.
Thanks.
Betty <<SUP02.doc>> <<SUPP11 5-5-05 .doc>> <<Chapter 16.doc>>

Betty Hastings

RTI International
Statistic Research Division
P.O. Box 12194
Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7740
Fax: (919) 485-7762
bkh@rti.org

RTI INTERNATIONAL | Memorandum

May 5, 2005

SUPPORT TECHNICAL MEMO # 2

TO: Network Coordinators
Network PIs

FROM: The Data Coordinating Center
Neil Finer, MD
Wade Rich

SUBJECT: Clarification on discontinuing the study oximeter and a New SUPPORT Form (Supp11)

- The study pulse oximeter should be on the infant until he/she has been **without support** (HFV, CV, CPAP, Nasal Cannula) **for 72 hours**.
- Respiratory Support After 14 Days **(SUPP11 Form).** This form should be completed after the first 14 days. Record the following;
- Date
- Highest FiO2
- Highest Level of Support (Only consider support which the infant was on for at least 4 hours
- Cannula flow rate. **Note: For purposes of this form, a room air nasal cannula should be considered support only if it is > 500cc/min.**

Please let us know if you have questions about this memo.

cc: Rosemary Higgins

NICU Network

The SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants

SUPP11 Rel1.0
May 5, 2005

RESPIRATORY SUPPORT AFTER 14 DAYS

Center: ___ Site No: ___ Network No: ____ Birth No: ___ Mother's Initials: ___

1. Study Day: ___ (This form is only completed if the infant is on support after day 14. Do no fill out if on no support or R/A cannula at <500cc.)

LIST THE HIGHEST LEVEL OF SUPPORT WHICH THE INFANT WAS ON FOR MORE THAN 4 HOURS.

(a) DAY OF SUPPORT	___	___	___	___	___	___
(b) Date	__/__/____ Month Day Year	__/__/____ Month Day Year	__/__/____ Month Day Year	__/__/____ Month Day Year	__/__/____ Month Day Year	__/__/____ Month Day Year
(c). Highest Level of Support	___	___	___	___	___	___
(d) FiO_2 Most Frequent during (c). If two are equal, choose highest.	__.__	__.__	__.__	__.__	__.__	__.__
(e) Flow Rate	____.____ Liters/Min.	____.____ Liters/Min.	____.____ Liters/Min.	____.____ Liters/Min.	____.____ Liters/Min.	____.____ Liters/Min.
(a) DAY OF SUPPORT	___	___	___	___	___	___
(b) Date	__/__/____ Month Day Year	__/__/____ Month Day Year	__/__/____ Month Day Year	__/__/____ Month Day Year	__/__/____ Month Day Year	__/__/____ Month Day Year
(c) Highest Level of Support	___	___	___	___	___	___
(d) FiO_2 Most Frequent during (c) If two are equal, choose highest.	__.__	__.__	__.__	__.__	__.__	__.__
(e) Flow Rate	____.____ Liters/Min.	____.____ Liters/Min.	____.____ Liters/Min.	____.____ Liters/Min.	____.____ Liters/Min.	____.____ Liters/Min.
(a) DAY OF SUPPORT	___	___	___	___	___	___
(b) Date	__/__/____ Month Day Year	__/__/____ Month Day Year	__/__/____ Month Day Year	__/__/____ Month Day Year	__/__/____ Month Day Year	__/__/____ Month Day Year
(c) Highest Level of Support	___	___	___	___	___	___
(d) FiO_2 Most Frequent during (c) If two are equal, choose highest.	__.__	__.__	__.__	__.__	__.__	__.__
(e) Flow Rate	____.____ Liters/Min.	____.____ Liters/Min.	____.____ Liters/Min.	____.____ Liters/Min.	____.____ Liters/Min.	____.____ Liters/Min.

1= HFV 2= CV 3= Nasal SIMV 4= CPAP * 5= NC 6=Hood

*** NOTE: NASAL CANNULA IN ROOM AIR IS ONLY CONSIDERED A LEVEL OF SUPPORT AT FLOW RATES >500cc/min.**

Chapter 16

Respiratory Support after 14 Days

16.1 Introduction

The purpose of this form is to document any respiratory support the infant receives after day 14.

16.1.1 Instructions for completing the Respiratory Support Form after 14 Days (SUPP11)

This form is only to be completed if the infant in on support after day 14. Do not complete this form if the infant is on "No support" or R/A cannula at <500cc. List the highest level of support which the infant was on for **more than 4 days.**

Record the following for each day of support:

- Date
- Highest FiO2,
- Highest Level of Support (Only consider support which the infant was on for at least 4 hours.
- Cannula flow rate **Note:** For purposes of this form, a room air nasal cannula should be considered support only if it is > 500cc/min.

From: Higgins, Rosemary (NIH/NICHD)
To: Charles Rosenfeld
Subject: RE: MRI SUPPORT secondary
Date: Tuesday, May 10, 2005 3:11:00 PM

Charles
Thanks for getting back to me with good news!
Rose

-----Original Message-----
From: Charles Rosenfeld [mailto:Charles.Rosenfeld@UTSouthwestern.edu]
Sent: Tuesday, May 10, 2005 2:41 PM
To: Higgins, Rosemary (NIH/NICHD)
Cc: Walid Salhab
Subject: Re: MRI SUPPORT secondary

Sorry for the prolonged delay. We have checked the cost of the MRI at discharge and it fits into the $1300 per patient. We are happy to be involved and will begin to address this.

Charles

Charles R. Rosenfeld, M.D.
George L. MacGregor Professor of Pediatrics
and Professor of Obstetrics and Gynecology
Director, Division of Neonatal-Perinatal Medicine
UT Southwestern Medical Center at Dallas
5323 Harry Hines Blvd.
Dallas, TX 75390-9063
Telephone: (214) 648-3903
FAX: (214) 648-2481
Email: charles.rosenfeld@utsouthwestern.edu

>>> "Higgins, Rosemary (NIH/NICHD)" <higginsr@mail.nih.gov> 05/05/05 10:33 AM >>>
Hi Charles and Walid,

Are you planning on participating in the Hintz MRI secondary study to SUPPORT? We are anticipating approximately $1300 per child enrolled. Each infant needs a head US by day 14 of life and an MRI and head US at approximately 36 weeks. Let me know if this will be feasible at Dallas.

Thanks

Rose

Rosemary D. Higgins, M.D.

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

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301-435-7909

301-496-3790 (FAX)

higginsr@mail.nih.gov <mailto:higginsr@mail.nih.gov>

From: Tyson, Jon E
To: Debra Brandon
Cc: Ronald N Goldberg; Michael Cotten; Higgins, Rosemary (NIH/NICHD) [E]; Neil Finer
Subject: RE: SUPPORT Trial Concurrent Enrollment with Cycled Light
Date: Tuesday, May 10, 2005 11:05:13 AM

Thanks. I am glad if I was able to be of any help. I'm not in a position to give final approval but will forward to Rose Higgins and Neil Finer to be sure that there isn't anything that would cause a problem for you or others. Good luck.

Jon E. Tyson, MD, MPH
Center for Clinical Research & Evidence-Based Medicine
UT Medical School at Houston
6431 Fannin St., MSB 2.106
Houston, TX 77030
voice 713-500-5651
fax 713-500-0519

From: Debra Brandon [mailto:brand005@mc.duke.edu]
Sent: Monday, May 09, 2005 2:57 PM
To: Tyson, Jon E
Cc: Ronald N Goldberg; Michael Cotten
Subject: SUPPORT Trial Concurrent Enrollment with Cycled Light
Importance: High

Dear Jon,

Sorry it has taken me so long to get back to you regarding the stratification schema, but my statistician was tied up with another deadline. Thanks for your thoughtful suggestions. Ron, Mike and I think the attached schema should be satisfactory for both trials.

Please let me know if we can proceed.

Sincerely,

Debbie Brandon PhD, RN, CCNS
Assistant Professor and Neonatal Specialty Director
Duke University School of Nursing
Neonatal Clinical Nurse Specialist
Duke University Hospital
Box 3322 DUMC
Durham, NC 27710
919-681-3813 voicemail
919-970-6793 pager
919-668-6120 fax

From: Higgins, Rosemary (NIH/NICHD)
To: "moshea@wfubmc.edu"
Subject: Re: MRI SUPPORT Secondary
Date: Monday, May 09, 2005 4:55:54 PM

Thanks
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Michael O'Shea <moshea@wfubmc.edu>
To: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
CC: Nancy Peters <npeters@wfubmc.edu>
Sent: Mon May 09 16:53:24 2005
Subject: RE: MRI SUPPORT Secondary

Rose,
Sorry about the slow response. Yes, we want to participate. See you soon.
Mike

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Monday, May 09, 2005 4:20 PM
To: Michael O'Shea
Subject: MRI SUPPORT Secondary

Hi Mike,

Any word on whether or not Wake can participate in the MRI secondary?
Thanks
rose

Rosemary D. Higgins, M.D.

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

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301-496-3790 (FAX)

higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD)
To: Abbot Laptook; William Oh
Subject: MRI secondary
Date: Monday, May 09, 2005 4:21:00 PM

Hi Abbot and Bill,
Were you able to find out if the Brown site can participate in the MRI secondary study to SUPPORT? Let me know
Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
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301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Neuroimaging secondary
Date: Friday, May 06, 2005 10:55:16 PM

I would send to the sites
Regards
Neil

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Friday, May 06, 2005 9:46 AM
To: Neil Finer
Subject: FW: Neuroimaging secondary

Neil
Do you think the MRI secondary needs another viewing by the subcommittee?
Or are you ok with sending it to the sites?
Thanks
Rose

-----Original Message-----
From: Susan Hintz [mailto:srhintz@stanford.edu]
Sent: Friday, May 06, 2005 12:52 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: Neuroimaging secondary

Hi Rose,

Do you know if RTI is planning on sending the Neuroimaging secondary protocol to sites? I didn't know if the final version I sent our to Neil, Betty, you, etc last Friday needed to be reviewed by the subcommittee before it went out?

Thanks

Susan
--
Susan R. Hintz, M.D.
Assistant Professor of Pediatrics
Division of Neonatal and Developmental Medicine
Stanford University School of Medicine
750 Welch Road, Suite 315
Palo Alto, CA 94304
ph: 650-723-5711
fax: 650-725-8351

From: Charles Rosenfeld
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Walid Salhab
Subject: Re: MRI SUPPORT secondary
Date: Friday, May 06, 2005 4:44:38 PM

---

we are in favor, but need to check the costs at the Children's Hospital before committing.

Charles

Charles R. Rosenfeld, M.D.
George L. MacGregor Professor of Pediatrics
and Professor of Obstetrics and Gynecology
Director, Division of Neonatal-Perinatal Medicine
UT Southwestern Medical Center at Dallas
5323 Harry Hines Blvd.
Dallas, TX 75390-9063
Telephone: (214) 648-3903
FAX: (214) 648-2481
Email: charles.rosenfeld@utsouthwestern.edu

>>> "Higgins, Rosemary (NIH/NICHD)" <higginsr@mail.nih.gov> 05/05/05 10:33 AM >>>
Hi Charles and Walid,

Are you planning on participating in the Hintz MRI secondary study to SUPPORT? We are anticipating approximately $1300 per child enrolled. Each infant needs a head US by day 14 of life and an MRI and head US at approximately 36 weeks. Let me know if this will be feasible at Dallas.

Thanks

Rose

Rosemary D. Higgins, M.D.

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

NICHD, NIH

6100 Executive Blvd., Room 4B03B

MSC 7510

Bethesda, MD 20892

(For overnight delivery, use Rockville, MD 20852)

301-435-7909

301-496-3790 (FAX)

higginsr@mail.nih.gov <mailto:higginsr@mail.nih.gov>

From: Charles Rosenfeld
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: MRI SUPPORT secondary
Date: Thursday, May 05, 2005 6:38:20 PM

I believe it is feasible as the tests are readily available. We will look at the cost and get back.

Charles

Charles R. Rosenfeld, M.D.
George L. MacGregor Professor of Pediatrics
and Professor of Obstetrics and Gynecology
Director, Division of Neonatal-Perinatal Medicine
UT Southwestern Medical Center at Dallas
5323 Harry Hines Blvd.
Dallas, TX 75390-9063
Telephone: (214) 648-3903
FAX: (214) 648-2481
Email: charles.rosenfeld@utsouthwestern.edu

>>> "Higgins, Rosemary (NIH/NICHD)" <higginsr@mail.nih.gov> 05/05/05 10:33 AM >>>
Hi Charles and Walid,

Are you planning on participating in the Hintz MRI secondary study to SUPPORT? We are anticipating approximately $1300 per child enrolled. Each infant needs a head US by day 14 of life and an MRI and head US at approximately 36 weeks. Let me know if this will be feasible at Dallas.

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301-496-3790 (FAX)

higginsr@mail.nih.gov <mailto:higginsr@mail.nih.gov>

From: Higgins, Rosemary (NIH/NICHD)
To: "barbara_stoll@oz.ped.emory.edu"
Subject: Re: SUPPORT MRI Secondary study
Date: Thursday, May 05, 2005 12:54:39 PM

Great!
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Barbara Stoll <barbara.stoll@oz.ped.emory.edu>
To: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
CC: Ellen Hale <ellen.hale@oz.ped.emory.edu>
Sent: Thu May 05 12:50:47 2005
Subject: Re: SUPPORT MRI Secondary study

Oops.....
We WILL be participating in this study-- need to send through the IRB
BJS"Higgins, Rosemary (NIH/NICHD)" <higginsr@mail.nih.gov> on Thursday, May 05, 2005 at 11:37 AM +0000 wrote:
>Hi,
>I have that Emory will NOT participate in the MRI secondary study to
>SUPPORT. Is this correct? For a baby to complete the study, he/she
>needs to have a head US by day 14 then a head US and MRI at approximately
>36 weeks. The capitation is estimated at approximately $1300 per baby.
>Let me know.
>Thanks
>Rose
>
>Rosemary D. Higgins, M.D.
>Program Scientist for the Neonatal Research Network
>Pregnancy and Perinatology Branch
>Center for Developmental Biology and Perinatal Medicine
>NICHD, NIH
>6100 Executive Blvd., Room 4B03B
>MSC 7510
>Bethesda, MD 20892
>(For overnight delivery, use Rockville, MD 20852)
>301-435-7909
>301-496-3790 (FAX)
>[mailto:higginsr@mail.nih.gov]higginsr@mail.nih.gov
>

Barbara J. Stoll, MD
George W. Brumley, Jr., Professor and Chair, Department of Pediatrics
Medical Director, Children's Healthcare of Atlanta at Egleston
Office: 404-727-2456 Fax: 404-727-5737
barbara_stoll@oz.ped.emory.edu

From: Higgins, Rosemary (NIH/NICHD)
To: Duara, Shahnaz
Cc: Everett, Ruth
Subject: RE: SUPPORT secondaries: Hintz and Stevens
Date: Thursday, May 05, 2005 11:34:00 AM

Betty is likely to do this in the next week or two.
Thanks
Rose

-----Original Message-----
From: Duara, Shahnaz [mailto:SDuara@med.miami.edu]
Sent: Thursday, May 05, 2005 11:33 AM
To: Higgins, Rosemary (NIH/NICHD)
Cc: Everett, Ruth
Subject: RE: SUPPORT secondaries: Hintz and Stevens

OK, we'll wait for the update. With our IRB, I'm trying to give them a loo--oong head start, so we can be ready when everyone else is.
Shahnaz

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Thursday, May 05, 2005 11:29 AM
To: Duara, Shahnaz; Hastings, Betty J.
Cc: Petrie, Carolyn
Subject: RE: SUPPORT secondaries: Hintz and Stevens

Shahnaz,
Betty is working on them and will send them to the sites when ready for IRB. Thanks Rose

-----Original Message-----
From: Duara, Shahnaz [mailto:SDuara@med.miami.edu]
Sent: Thursday, May 05, 2005 11:04 AM
To: Hastings, Betty J.
Cc: Higgins, Rosemary (NIH/NICHD); Petrie, Carolyn
Subject: SUPPORT secondaries: Hintz and Stevens

Hi Betty,

Are the SUPPORT secondaries from Hintz and Stevens ready for IRB? Are they going to go up on the web-site soon?

Let me know
Shahnaz

From:	Edward Donovan
To:	Higgins, Rosemary (NIH/NICHD) [E]; "Shahnaz Duara"; M.D." "Avroy A. Fanaroff; "Michele"; "Betty Hastings"; "Ken Poole"; Neil Finer; "Wade Rich"
Subject:	Re: FW: SUPPORT and secondary
Date:	Thursday, April 28, 2005 5:45:44 PM

I don't get what this has to do with the SUPPORT study?
Is there a hypothesis and sample size estimate?

Edward F. Donovan, M.D.
Director
Child Policy Research Center
Children's Hospital Medical Center
3333 Burnet Avenue, ML 7014
Cincinnati, OH 45229-3039
Phone 513-636-0182
Fax 513-636-0171
www.cprc-chmc.uc.edu

From: Higgins, Rosemary (NIH/NICHD)
To: Susan Hintz
Subject: RE: Hi
Date: Wednesday, April 27, 2005 1:04:00 PM

OK
Whatever works, Neil or David can give the MRI SUPPORT update on the 16th if needed.
Thanks
Rose

-----Original Message-----
From: Susan Hintz [mailto:srhintz@stanford.edu]
Sent: Wednesday, April 27, 2005 1:11 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE: Hi

Hi Rose,

I think I may only be able to come for June 15th - the complexities
of the trades are enormous. And weird. I have one last possibility,
however - so I will probably know in the next day or two whether I
can come for just June 15th or both June 15 and 16.

Thanks

Susan
>Yes
>If you want to stay until the 16th, we could put you on the SC agenda very
>early (by 8 AM) and you could then leave.
>
>Let me know
>Thanks
>Rose
>
>-----Original Message-----
>From: Susan Hintz [mailto:srhintz@stanford.edu]
>Sent: Tuesday, April 26, 2005 1:04 PM
>To: Higgins, Rosemary (NIH/NICHD)
>Subject: Hi
>
>Rose,
>
>Would it be possible for me to come to the June meeting, but just for
>June 15th?
>
>Let me know - thanks.
>
>I will be sending Betty Hastings a whole bunch of stuff in the next
>two days pertaining to the MRI secondary. I have mocked up data
>sheets, protocol, consent options, etc. I am sure she will be able to
>give me input -
>
>Susan
>--
>Susan R. Hintz, M.D.

>Assistant Professor of Pediatrics
>Division of Neonatal and Developmental Medicine
>Stanford University School of Medicine
>750 Welch Road, Suite 315
>Palo Alto, CA 94304
>ph: 650-723-5711
>fax: 650-725-8351

From:	Higgins, Rosemary (NIH/NICHD)
To:	Tyson, Jon E
Cc:	Mcdavid, Georgia E
Subject:	RE: oximeters for SUPPORT trial
Date:	Friday, April 22, 2005 3:33:00 PM

We have allotted shipping in the budget. Betty Hastings will send out a technical memo detailing the "sending back and forth processes." Betty will monitor their locations. There will be 4-5 sites with extra oximeters. That's what we have for now!
Thanks
Rose

From: Tyson, Jon E [mailto:Jon.E.Tyson@uth.tmc.edu]
Sent: Friday, April 22, 2005 3:26 PM
To: Higgins, Rosemary (NIH/NICHD)
Cc: Mcdavid, Georgia E
Subject: FW: oximeters for SUPPORT trial

We're happy to do this but as usual, Georgia is way ahead of me in thinking through the details.

Jon E. Tyson, MD, MPH
Center for Clinical Research & Evidence-Based Medicine
UT Medical School at Houston
6431 Fannin St., MSB 2.106
Houston, TX 77030
voice 713-500-5651
fax 713-500-0519

From: Mcdavid, Georgia E
Sent: Friday, April 22, 2005 2:25 PM
To: Tyson, Jon E
Subject: RE: oximeters for SUPPORT trial

Jon,
We do have space in our office for 10 oximeters. I'm assuming we would get 5 orange and 5 blue of the oximeters and 10 bases correct? When we received the oximeters the bases and the oximeters were separate. For our study purposes after charging them they were placed together in a box with the appropriate color sticker (orange/blue) on the outside of the box. The serial number of the oximeter is also on the outside of the box so it can be double checked with our master list. That is how we store them over in the unit. To make this as easy as possible I would have a similar set up with both the oximeter and the base in one box color coded and ready to go. That box could be placed in a larger box that has protective packing and shipped to the site. It would be easiest for us if we could take it to Alice/Ida and they could arrange the shipper (UPS/Fed-Ex) to pick it up. What I would want is pre-printed shipping labels for all the sites we would be shipping to. Would we get extra funds for shipping or since we know the weight of a monitor I suppose we could get them with the postage pre paid? After the site no longer needs the extra monitor will it then be returned to us? If so, we should provide a return address sticker and postage in the box? Would I be responsible for "monitoring" the monitors? When I start running low of "extras" will I be responsible for calling the sites and seeing if they still need the extra monitor? Will there be other sites with "extras"?
So many questions.....

From: Tyson, Jon E
Sent: Friday, April 22, 2005 12:14 PM

To: Mcdavid, Georgia E
Subject: oximeters for SUPPORT trial

Georgia, Rose called to verify that we have space to store 10 more oximeters and that could ship if necessary to other sites (8-5 weekdays only). Is this okay? Are there things we need to discuss with her about the shipping process?

Jon E. Tyson, MD, MPH
Center for Clinical Research & Evidence-Based Medicine
UT Medical School at Houston
6431 Fannin St., MSB 2.106
Houston, TX 77030
voice 713-500-5651
fax 713-500-0519

From: Duara, Shahnaz
To: nfiner@ucsd.edu
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Growth secondary to SUPPORT
Date: Friday, April 22, 2005 10:01:31 AM

Hi Neil,

I haven't received any further feedback on the secondary circulated at the SC mtg. You mentioned that Brenda was going to do a review for you - what should the next step be?

Let me know
Shahnaz

From: Higgins, Rosemary (NIH/NICHD)
To: "petrie@rti.org"
Subject: Re: support
Date: Thursday, April 21, 2005 4:39:06 PM

Thanks

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Petrie, Carolyn <petrie@rti.org>
To: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
Sent: Thu Apr 21 16:32:38 2005
Subject: support

The indirects were incorrect on the previous version. (only corrected for year 2)

Carolyn Petrie

Neonatal Research Network Coordinator

RTI International

6110 Executive Blvd

Suite 902

Rockville, MD 20852

ph. (301) 230-4648

fx. (301) 230-4646

From:	Higgins, Rosemary (NIH/NICHD)
To:	Angelita Hensman; Bara, Rebecca; Bethany Ball; Cathy Grisby (cathy.grisby@uc.edu); Ellen Hale (ehale@emory.edu); Georgia McDavid; Kathy Auten; Linda Reubens; Lucy Miller; Monica Collins; Nancy Miller (buckeyerose7@yahoo.com); Nancy Newman; Nancy Peters; Pat Gettner (pat.gettner@yale.edu); Ruth Everett (reverett@med.miami.edu); Wade RIch
Subject:	FW: SUPPORT Trial
Date:	Thursday, April 21, 2005 2:21:00 PM
Attachments:	SUPPORT Trial_Survey 4-13-05 4.doc

From: Hastings, Betty J. [mailto:bkh@rti.org]
Sent: Thursday, April 14, 2005 11:19 AM
To: ahensman@wihri.org; mbball@leland.stanford.edu; grisbyca@email.uc.edu; ellen_hale@oz.ped.emory.edu; gaynelle.hensley@utsouthwestern.edu; Georgia E McDavid; auten002@mc.duke.edu; linda_reubens@urmc.rochester.edu; lucmille@iupui.edu; mcollins@peds.uab.edu; Nancy.Miller@UTSouthwestern.edu; Nancy Newman; npeters@wfubmc.edu; pat.gettner@yale.edu; ae5357@wayne.edu; rbridge@ucsd.edu; risa.demetrio@sharp.com; kathy.arnell@sharp.com; Reverett@med.miami.edu; monica.konstantino@yale.edu; Personal Email Lenora Jackson; Estelle E. Fischer; Holly Mincey; Jody Shively; Kate Bridges, MD
Cc: wrich@ucsd.edu; nfiner@ucsd.edu; Higgins, Rosemary (NIH/NICHD)
Subject: SUPPORT Trial

Dear All,
We need your help in answering some questions for the SUPPORT Trial. Attached is a brief survey (that you can answer online) regarding common practice of infants 24 0/7 - 27 6/7 at your site.

Pease complete and e-mail to Wade (with a cc to me).
Thanks for your help and SUPPORT.
Wade and Betty

<<SUPPORT Trial_Survey 4-13-05 4.doc>>

Betty Hastings

RTI International
Statistic Research Division
P.O. Box 12194
Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7740
Fax: (919) 485-7762
bkh@rti.org

NICHD Neonatal Research Network
SUPPORT Trial Survey

Date:
Center: **Site:** **Contact Name:**

In order to answer some questions regarding the SUPPORT Trial, we would like for you to describe your practice in infants 24 0/7 to 27 6/7 infants. The specific issues we need answered are as follows:

1. Do you routinely use high flow nasal cannula in these infants? ☐ Yes ☐ No

a. If yes, what is the range of flow rates for these cannulas? . - .

b. If you know the size of cannula used (Premie, Infant, Intermediate, etc) please indicate.

2. Do you routinely place infants on a Room Air nasal cannula? ☐ Yes ☐ No

a. If yes, what is the indication for the R/A NC?

1. Apnea ☐ Yes ☐ No
If yes,
a. Primary mode of treatment? ☐ Yes ☐ No
b. Only after methylxanthines? ☐ Yes ☐ No

2. Weaning from CPAP? ☐ Yes ☐ No

3. Other? (Specify):

3. When do you take an infant off of Room Air nasal cannula?

Thank you for your help in answering these questions. The purpose of these questions is to determine common practice. If you put an infant, 24 0/7 to 27 6/7 weeks gestational age, on room air nasal cannula once per year that is not germane to the study. However, if you do it as a normal procedure in the process of caring for these infants, we need to know this.

You may complete this survey on line and return it by e-mail, to Wade Rich wrich@ucsd.edu with a cc Betty Hastings bkh@rti.org.

From:	Higgins, Rosemary (NIH/NICHD)
To:	Hastings, Betty J.
Subject:	RE: SUPPORT
Date:	Wednesday, April 20, 2005 1:57:00 PM

NO problem, we have plenty of other stuff to do – by the end of the week will be fine.
Thanks
Rose

From: Hastings, Betty J. [mailto:bkh@rti.org]
Sent: Wednesday, April 20, 2005 1:57 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: SUPPORT

Rose,
I don't think that last night's data transmission has been completed. I'll let you know the status of enrollment as soon as they completed it.

Betty

Betty Hastings

RTI International
Statistic Research Division
P.O. Box 12194
Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7740
Fax: (919) 485-7762
bkh@rti.org

From: Higgins, Rosemary (NIH/NICHD)
To: "jobht4@cinbell.blackberry.net"
Subject: Re: MSCIDA Committee for SUPPORT Secondary
Date: Tuesday, April 19, 2005 6:45:04 PM

Is this message from the famous blackberry?

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Dr. Alan Hall Jobe M.D. <jobht4@cinbell.blackberry.net>
To: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
Sent: Tue Apr 19 18:08:19 2005
Subject: Re: MSCIDA Committee for SUPPORT Secondary

OK - AJ
-----Original Message-----
From: "Higgins, Rosemary (NIH/NICHD)" <higginsr@mail.nih.gov>
Date: Tue, 19 Apr 2005 16:08:44
To:Neil Finer <nfiner@ucsd.edu>, "Tyson Jon (E-mail)" <Jon.E.Tyson@uth.tmc.edu>, "Jobe Alan (E-mail)" <Jobea0@chmcc.org>, "Das, Abhik" <adas@rti.org>, "Poole, W. Kenneth" <poo@rti.org>
Cc:David Stevenson <dstevenson@stanford.edu>, "Susan Hintz (srhintz@stanford.edu)" <srhintz@stanford.edu>
Subject: MSCIDA Committee for SUPPORT Secondary

HI,

I would like to request that each of you serve on an MSCIDA committee for Susan Hintzs MRI secondary study. Let me know if this is ok with you.

Thanks

Rose

Rosemary D. Higgins, M.D.

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

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301-435-7909

301-496-3790 (FAX)

higginsr@mail.nih.gov

Sent from my BlackBerry Wireless Handheld from Cincinnati Bell

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: MSCIDA Committee for SUPPORT Secondary
Date: Tuesday, April 19, 2005 5:30:54 PM

Ho Rose
I am delighted to serve on Susan's committee
Neil Finer

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, April 19, 2005 1:09 PM
To: Neil Finer; Tyson Jon (E-mail); Jobe Alan (E-mail); Das, Abhik; Poole, W. Kenneth
Cc: David Stevenson; Susan Hintz (srhintz@stanford.edu)
Subject: MSCIDA Committee for SUPPORT Secondary

HI,
I would like to request that each of you serve on an MSCIDA committee for Susan Hintz's MRI secondary study. Let me know if this is ok with you.
Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
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301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Higgins, Rosemary (NIH/NICHD)
To:	Das, Abhik
Subject:	RE: MSCIDA Committee for SUPPORT Secondary
Date:	Tuesday, April 19, 2005 4:29:00 PM

Mentored Specialized Clinical Investigator Development Award

From: Das, Abhik [mailto:adas@rti.org]
Sent: Tuesday, April 19, 2005 4:18 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE: MSCIDA Committee for SUPPORT Secondary

Fine with me; but what is MSCIDA?!

> -----Original Message-----
> **From:** Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
> **Sent:** Tuesday, April 19, 2005 4:09 PM
> **To:** Neil Finer; Tyson Jon (E-mail); Jobe Alan (E-mail); Das, Abhik; Poole, W. Kenneth
> **Cc:** David Stevenson; Susan Hintz (srhintz@stanford.edu)
> **Subject:** MSCIDA Committee for SUPPORT Secondary
>
> HI,
> I would like to request that each of you serve on an MSCIDA committee for Susan Hintz's MRI secondary study. Let me know if this is ok with you.
> Thanks
> Rose
>
> Rosemary D. Higgins, M.D.
> Program Scientist for the Neonatal Research Network
> Pregnancy and Perinatology Branch
> Center for Developmental Biology and Perinatal Medicine
> NICHD, NIH
> 6100 Executive Blvd., Room 4B03B
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> Bethesda, MD 20892
> (For overnight delivery, use Rockville, MD 20852)
> 301-435-7909
> 301-496-3790 (FAX)
> higginsr@mail.nih.gov

From:	Higgins, Rosemary (NIH/NICHD)
To:	David Stevenson
Cc:	susan.hintz@stanford.edu
Subject:	RE: MSCIDA Committee
Date:	Tuesday, April 19, 2005 3:59:00 PM

I will inform them.
thanks
Rose

From: David Stevenson [mailto:dstevenson@stanford.edu]
Sent: Tuesday, April 19, 2005 3:58 PM
To: Higgins, Rosemary (NIH/NICHD)
Cc: susan.hintz@stanford.edu
Subject: Re: MSCIDA Committee

Rose,

I could not have picked a better group. We would be honored to have all of you join us.
Thanks for your support.
David

At 10:53 AM 4/19/2005, you wrote:

David,
We need to have a committee in place for Susan's MSCIDA Project. I would propose Neil Finer, Jon Tyson, Alan Jobe, Abhik/Ken, and you and myself. Let me know if this is ok.
Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
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301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Wade Rich
To:	Higgins, Rosemary (NIH/NICHD) [E]
Subject:	FW: oximeters
Date:	Tuesday, April 19, 2005 1:53:17 PM

Rose, No problem with Masimo. Will they be ordered at the sites, or as one big order? wade

---

From: Neil Finer [mailto:nfiner@ucsd.edu]
Sent: Tuesday, April 19, 2005 10:17 AM
To: wrich@ucsd.edu
Subject: FW: oximeters

Wade
Can you call?
Neil

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, April 19, 2005 5:51 AM
To: Neil Finer
Cc: Hastings, Betty J.
Subject: oximeters

Neil
We are planning on getting 50 more oximeters – can you check with Masimo to see if they are OK with this (10 at 5 sites- UCSD, CWRU, UAB, Brown, UT Houston).
Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
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301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: oximeters
Date: Tuesday, April 19, 2005 1:17:34 PM

Will do
Thanks
Neil

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, April 19, 2005 5:51 AM
To: Neil Finer
Cc: Hastings, Betty J.
Subject: oximeters

Neil
We are planning on getting 50 more oximeters – can you check with Masimo to see if they are OK with this (10 at 5 sites- UCSD, CWRU, UAB, Brown, UT Houston).
Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
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301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Richard A. Ehrenkranz
To: Neil Finer; pat.gettner@yale.edu
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: FW: oximeters
Date: Friday, April 15, 2005 1:47:03 PM

Neil:
You're welcome. We should be ready to start enrolling patients shortly.
Richard

At 08:08 AM 4/15/2005 -0700, Neil Finer wrote:

>Hi Rich and Pat
>
>I very much appreciate your efforts on behalf of the trial
>
>I hope that at some point we can return the favor and ship you some extra
>oximeters.
>
>Be well
>
>Neil
>
>
>
>
>
>----------
>From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
>Sent: Friday, April 15, 2005 7:54 AM
>To: Ehrenkranz Richard (E-mail); pat.gettner@yale.edu
>Cc: Angelita Hensman; William Oh; Abbot Laptook; Neil Finer; Jobe Alan
>(E-mail)
>Subject: oximeters
>
>
>
>Richard and Pat,
>
>Thanks so much for being helpful with shipping oximeters to the Brown site
>yesterday. It is truly a delight to have a group of individuals committed
>to making SUPPORT work!!!
>Again, thanks!!
>Rose
>
>
>
>Rosemary D. Higgins, M.D.
>
>Program Scientist for the Neonatal Research Network
>
>Pregnancy and Perinatology Branch
>
>Center for Developmental Biology and Perinatal Medicine
>

>NICHD, NIH
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>6100 Executive Blvd., Room 4B03B
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>MSC 7510
>
>Bethesda, MD 20892
>
>(For overnight delivery, use Rockville, MD 20852)
>
>301-435-7909
>
>301-496-3790 (FAX)
>
><mailto:higginsr@mail.nih.gov>higginsr@mail.nih.gov
>
>

Richard A. Ehrenkranz, MD
Department of Pediatrics
Yale University School of Medicine
333 Cedar Street
PO Box 208064
New Haven, CT 06520-8064
tele: 203-688-2320
fax: 203-688-5426

From: Higgins, Rosemary (NIH/NICHD)
To: Poole, W. Kenneth
Subject: RE: ???
Date: Friday, April 15, 2005 11:28:00 AM

Yes
It is apparently outsourced. They did approve the SUPPORT protocol.
Thanks
Rose

From: Poole, W. Kenneth [mailto:poo@rti.org]
Sent: Friday, April 15, 2005 11:27 AM
To: Higgins, Rosemary (NIH/NICHD)
Subject: ???

Is this the group doing Miami's IRB stuff?

Western Institutional Review Board (WIRB)
3535 Seventh Avenue
Olympia, WA 98502-5010
(360) 252-2500 / (800) 562-4789

From:	Neil Finer
To:	Richard Ehrenkranz; pat.gettner@yale.edu
Cc:	Higgins, Rosemary (NIH/NICHD) [E]
Subject:	FW: oximeters
Date:	Friday, April 15, 2005 11:08:32 AM

Hi Rich and Pat
I very much appreciate your efforts on behalf of the trial
I hope that at some point we can return the favor and ship you some extra oximeters.
Be well
Neil

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Friday, April 15, 2005 7:54 AM
To: Ehrenkranz Richard (E-mail); pat.gettner@yale.edu
Cc: Angelita Hensman; William Oh; Abbot Laptook; Neil Finer; Jobe Alan (E-mail)
Subject: oximeters

Richard and Pat,
Thanks so much for being helpful with shipping oximeters to the Brown site yesterday. It is truly a delight to have a group of individuals committed to making SUPPORT work!!!
Again, thanks!!
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD)
To: Morris, Brenda H
Subject: RE: SUPPORT recruiting tool
Date: Thursday, April 14, 2005 4:02:00 PM

Brenda
It is 50-89 cents/bracelet - see Michele's email.
Thanks
Rose

-----Original Message-----
From: Morris, Brenda H [mailto:Brenda.H.Morris@uth.tmc.edu]
Sent: Thursday, April 14, 2005 4:01 PM
To: Higgins, Rosemary (NIH/NICHD); kurt.schibler@cchmc.org; Krisa VanMeurs (VanMeurs, Krisa); cotte010@mc.duke.edu; Laroia, Nirupama; susie.buchter@oz.ped.emory.edu; Vivek.Narendran@cchmc.org; vineet.bhandari@yale.edu; Angelita Hensman; Becky bara; Bethany Ball; Cathy Grisby; Ellen Hale; Mcdavid, Georgia E; Kathy Auten; Linda Reubens; Lucy Miller; Monica Collins; Nancy Miller; Nancy Newman; Nancy Peters; pat.gettner@yale.edu; Ruth Everett; Wade RIch; alaptook@WIHRI.org; Abhik Das; Brenda Poindexter; Carlo Waldemar (E-mail); Charles Rosenfeld; Dale Phelps; Ed Donovan; Ehrenkranz Richard (E-mail); Jobe Alan (E-mail); Lemons Jim (E-mail); Michael O'Shea; Michelle Walsh; Neil Finer; Oh William (E-mail); Poole Kenneth (E-mail); Ronald GOldberg; Shahnaz Duara; Shankaran Seetha (E-mail); Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson, Jon E; Walid Salhab (Walid Salhab)
Subject: RE: SUPPORT recruiting tool

Can we get an idea about what the price would be? We would need about 2,000-3,000 if we allow for moms who do not deliver in the window.
Brenda Morris

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Thursday, April 14, 2005 12:36 PM
To: Kurt Schibler (Kurt Schibler [kurt.schibler@cchmc.org]); Krisa VanMeurs (VanMeurs, Krisa); Morris, Brenda H; Michael Cotten (cotte010@mc.duke.edu); Laroia, Nirupama; susie.buchter@oz.ped.emory.edu; Vivek.Narendran@cchmc.org; vineet.bhandari@yale.edu; Angelita Hensman; Becky bara; Bethany Ball; Cathy Grisby; Ellen Hale; Mcdavid, Georgia E; Kathy Auten; Linda Reubens; Lucy Miller; Monica Collins; Nancy Miller; Nancy Newman; Nancy Peters; Pat Gettner (pat.gettner@yale.edu); Ruth Everett; Wade RIch; Abbot Laptook (alaptook@WIHRI.org); Abhik Das; Brenda Poindexter; Carlo Waldemar (E-mail); Charles Rosenfeld; Dale Phelps; Ed Donovan; Ehrenkranz Richard (E-mail); Jobe Alan (E-mail); Lemons Jim (E-mail); Michael O'Shea; Michelle Walsh; Neil Finer; Oh William (E-mail); Poole Kenneth (E-mail); Ronald GOldberg; Shahnaz Duara; Shankaran Seetha (E-mail); Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson, Jon E; Walid Salhab (Walid Salhab)
Subject: FW: SUPPORT recruiting tool

HI, Please let Michele know if you are interested in getting bracelets for
your SUPPORT subjects.

Thanks
Rose

-----Original Message-----
From: Michele Walsh [mailto:mcw3@case.edu]
Sent: Thursday, April 14, 2005 11:28 AM
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE: SUPPORT recruiting tool

Rose:
We are investigating getting bracelets like the Lance Armstrong one's made
for women enrolled in SUPPORT to wear. We plan on alternating pink and blue
with the word "SUPPORT" stamped on it. We think this might be an added
trigger for identification by personnel when the women are readmitted or
moved back and forth to L&D. We have a supplier identified. The cost is
cheaper with the more that are made. Could you forward this to other
coordinators and PIs and see if they would be interested. Current cost is
50 cents-89 cents/ each depending on volume. Regards, Michele

From: Higgins, Rosemary (NIH/NICHD)
To: Hastings, Betty J.
Subject: RE: Oximeter_ Transfers - SUPPORT.doc
Date: Thursday, April 14, 2005 3:57:00 PM

That's fine
Thanks
Rose

From: Hastings, Betty J. [mailto:bkh@rti.org]
Sent: Thursday, April 14, 2005 3:56 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE: Oximeter_ Transfers - SUPPORT.doc

Well, I was thinking that I could keep it as a record but they would need to notify me about any transfer. That way all they would have to do is send an e-mail.

> -----Original Message-----
> **From:** Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
> **Sent:** Thursday, April 14, 2005 3:48 PM
> **To:** Hastings, Betty J.
> **Subject:** RE: Oximeter_ Transfers - SUPPORT.doc
>
> This would be fine – should we show it to a few of the coordinators and ask them if it is user friendly?
> Thanks
> Rose

> **From:** Hastings, Betty J. [mailto:bkh@rti.org]
> **Sent:** Thursday, April 14, 2005 3:47 PM
> **To:** Higgins, Rosemary (NIH/NICHD)
> **Subject:** Oximeter_ Transfers - SUPPORT.doc
>
> I probably could do something as simple as this to keep up with any oximeter transfers from one site to the other. I would just need to know when it happens.
>
> <<Oximeter_ Transfers - SUPPORT.doc>>

From: Higgins, Rosemary (NIH/NICHD)
To: Maynard Rasmussen (Maynard.Rasmussen@sharp.com)
Subject: FW: SUPPORT recruiting tool
Date: Thursday, April 14, 2005 2:15:00 PM
Attachments: Michele Walsh.vcf

Maynard
Let Michele know if you are interested.
Thanks
Rose
-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD)
Sent: Thursday, April 14, 2005 1:36 PM
To: Kurt Schibler (Kurt Schibler [kurt.schibler@cchmc.org]); Krisa VanMeurs (VanMeurs, Krisa); Brenda Morris (Brenda.H.Morris@uth.tmc.edu); Michael Cotten (cotte010@mc.duke.edu); 'Laroia, Nirupama'; 'susie.buchter@oz.ped.emory.edu'; 'Vivek.Narendran@cchmc.org'; 'vineet.bhandari@yale.edu'; Angelita Hensman; Becky bara; Bethany Ball; Cathy Grisby; Ellen Hale; Georgia McDavid; Kathy Auten; Linda Reubens; Lucy Miller; Monica Collins; Nancy Miller; Nancy Newman; Nancy Peters; Pat Gettner (pat.gettner@yale.edu); Ruth Everett; Wade RIch; Abbot Laptook (alaptook@WIHRI.org); 'Abhik Das'; 'Brenda Poindexter'; 'Carlo Waldemar (E-mail)'; 'Charles Rosenfeld'; 'Dale Phelps'; 'Ed Donovan'; 'Ehrenkranz Richard (E-mail)'; 'Jobe Alan (E-mail)'; 'Lemons Jim (E-mail)'; 'Michael O'Shea'; 'Michelle Walsh'; 'Neil Finer'; 'Oh William (E-mail)'; 'Poole Kenneth (E-mail)'; 'Ronald GOldberg'; 'Shahnaz Duara'; 'Shankaran Seetha (E-mail)'; 'Stevenson David (E-mail)'; 'Stoll Barbara (E-mail)'; 'Tyson Jon (E-mail)'; Walid Salhab (Walid Salhab)
Subject: FW: SUPPORT recruiting tool

HI, Please let Michele know if you are interested in getting bracelets for your SUPPORT subjects.

Thanks
Rose
-----Original Message-----
From: Michele Walsh [mailto:mcw3@case.edu]
Sent: Thursday, April 14, 2005 11:28 AM
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE: SUPPORT recruiting tool

Rose:
We are investigating getting bracelets like the Lance Armstrong one's made for women enrolled in SUPPORT to wear. We plan on alternating pink and blue with the word "SUPPORT" stamped on it. We think this might be an added trigger for identification by personnel when the women are readmitted or moved back and forth to L&D. We have a supplier identified. The cost is cheaper with the more that are made. Could you forward this to other coordinators and PIs and see if they would be interested. Current cost is 50 cents-89 cents/ each depending on volume. Regards, Michele

specific written consent of the person to whom it pertains, or as otherwise permitted by law.

From: Brenda Poindexter
To: Higgins, Rosemary (NIH/NICHD) [E]; mcw3@case.edu
Subject: Re: SUPPORT recruiting tool
Date: Thursday, April 14, 2005 2:08:08 PM

Michele,
I think this is a great idea!
Brenda

>
> HI, Please let Michele know if you are interested in getting bracelets for
> your SUPPORT subjects.
>
> Thanks
> Rose
> -----Original Message-----
> From: Michele Walsh [mailto:mcw3@case.edu]
> Sent: Thursday, April 14, 2005 11:28 AM
> To: Higgins, Rosemary (NIH/NICHD)
> Subject: RE: SUPPORT recruiting tool
>
> Rose:
> We are investigating getting bracelets like the Lance Armstrong one's made
> for women enrolled in SUPPORT to wear. We plan on alternating pink and blue
> with the word "SUPPORT" stamped on it. We think this might be an added
> trigger for identification by personnel when the women are readmitted or
> moved back and forth to L&D. We have a supplier identified. The cost is
> cheaper with the more that are made. Could you forward this to other
> coordinators and PIs and see if they would be interested. Current cost is
> 50 cents-89 cents/ each depending on volume. Regards, Michele
>
>

From: Petrie, Carolyn
To: nfiner@ucsd.edu; wrich@ucsd.edu; Higgins, Rosemary (NIH/NICHD) [E]
Cc: hsquibb@ucsd.edu
Subject: SUPPORT call
Date: Thursday, April 14, 2005 12:13:08 PM

Neil-

Did you want to set up a SUPPORT conference call to discuss the nasal cannula issue, etc?

If so, please send me your availability until May 16th.

Carolyn Petrie

Neonatal Research Network Coordinator
RTI International
6110 Executive Blvd
Suite 902
Rockville, MD 20852
ph. (301) 230-4648
fx. (301) 230-4646

From:	Hastings, Betty J.
To:	ahensman@wihri.org; mbball@leland.stanford.edu; grisbyca@email.uc.edu; ellen_hale@oz.ped.emory.edu; gaynelle.hensley@utsouthwestern.edu; Georgia E McDavid; auten002@mc.duke.edu; linda_reubens@urmc.rochester.edu; lucmille@iupui.edu; mcollins@peds.uab.edu; Nancy.Miller@UTSouthwestern.edu; Nancy Newman; npeters@wfubmc.edu; pat.gettner@yale.edu; ae5357@wayne.edu; rbridge@ucsd.edu; risa.demetrio@sharp.com; kathy.arnell@sharp.com; Reverett@med.miami.edu; monica.konstantino@yale.edu; balexanba@hotmail.com; Lenora Jackson; Estelle E. Fischer; Holly Mincey; Jody Shively; Kate Bridges, MD
Cc:	wrich@ucsd.edu; nfiner@ucsd.edu; Higgins, Rosemary (NIH/NICHD) [E]
Subject:	SUPPORT Trial
Date:	Thursday, April 14, 2005 11:19:03 AM
Attachments:	SUPPORT Trial_Survey 4-13-05 4.doc

Dear All,
We need your help in answering some questions for the SUPPORT Trial. Attached is a brief survey (that you can answer online) regarding common practice of infants 24 0/7 - 27 6/7 at your site.

Pease complete and e-mail to Wade (with a cc to me).
Thanks for your help and SUPPORT.
Wade and Betty

<<SUPPORT Trial_Survey 4-13-05 4.doc>>

Betty Hastings

RTI International
Statistic Research Division
P.O. Box 12194
Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7740
Fax: (919) 485-7762
bkh@rti.org

NICHD Neonatal Research Network
SUPPORT Trial Survey

Date:
Center: **Site:** **Contact Name:**

In order to answer some questions regarding the SUPPORT Trial, we would like for you to describe your practice in infants 24 0/7 to 27 6/7 infants. The specific issues we need answered are as follows:

1. Do you routinely use high flow nasal cannula in these infants? ☐ Yes ☐ No

a. If yes, what is the range of flow rates for these cannulas? . - .

b. If you know the size of cannula used (Premie, Infant, Intermediate, etc) please indicate.

2. Do you routinely place infants on a Room Air nasal cannula? ☐ Yes ☐ No

a. If yes, what is the indication for the R/A NC?

1. Apnea ☐ Yes ☐ No
If yes,
a. Primary mode of treatment? ☐ Yes ☐ No
b. Only after methylxanthines? ☐ Yes ☐ No

2. Weaning from CPAP? ☐ Yes ☐ No

3. Other? (Specify):

3. When do you take an infant off of Room Air nasal cannula?

Thank you for your help in answering these questions. The purpose of these questions is to determine common practice. If you put an infant, 24 0/7 to 27 6/7 weeks gestational age, on room air nasal cannula once per year that is not germane to the study. However, if you do it as a normal procedure in the process of caring for these infants, we need to know this.

You may complete this survey on line and return it by e-mail, to Wade Rich wrich@ucsd.edu with a cc Betty Hastings bkh@rti.org.

From:	Angelita Hensman
To:	Higgins, Rosemary (NIH/NICHD) [E]
Cc:	William Oh; Abbot Laptook
Subject:	Pulse oximeters
Date:	Thursday, April 14, 2005 10:35:53 AM

Hi Rose,
We have not heard back from our fiscal department as yet. Either way it will probably take till next week to get this sorted out and ordered. I spoke to Monica at Yale this morning and she will Fedex 2 orange coded p.o's to us today. This way we will be covered for the weekend and next week.
Thanks for your help with this.
Angelita

From: William Oh
To: Higgins, Rosemary (NIH/NICHD) [E]; Angelita Hensman
Cc: Poe, Grace (NIH/NICHD) [E]
Subject: RE: oximeters
Date: Wednesday, April 13, 2005 4:57:53 PM

Will do

William Oh,MD
Professor of Pediatrics
Brown Medical School
Attending Neonatologist
Women and Infants' Hospital
101 Dudley St., Providence,RI, 02905
Phone (w) 401 274 1122 ext.1432
Fax 401 453 7571
cell 401 714 1199

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, April 13, 2005 4:38 PM
To: Angelita Hensman; William Oh
Cc: Poe, Grace (NIH/NICHD)
Subject: oximeters

Angelita and Bill -
In order to purchase additional oximeters in advance of the anticipated capitation award for the SUPPORT study for this year, can your grants office approved a pre-award advance for you to purchase 10 additional oximeters? If not, a request to use previously awarded or carryover funds signed by Dr. Oh and the grants office is needed and you may fax it to us.
Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Higgins, Rosemary (NIH/NICHD)
To:	nfiner@ucsd.edu
Cc:	"Avroy A. Fanaroff, M.D."; "Betty Hastings"; "Ed Donovan"; "Ken Poole"; "Michele"; "Neil Finer"; "Shahnaz Duara"; "Wade Rich"
Subject:	RE: SUPPORT Agenda
Date:	Friday, April 08, 2005 1:13:00 PM

Thanks
We will have extra copies on hand.
Rose

From: Neil Finer [mailto:nfiner@ucsd.edu]
Sent: Friday, April 08, 2005 1:12 PM
To: Higgins, Rosemary (NIH/NICHD)
Cc: 'Avroy A. Fanaroff, M.D.'; 'Betty Hastings'; 'Ed Donovan'; 'Ken Poole'; 'Michele'; 'Neil Finer'; 'Shahnaz Duara'; 'Wade Rich'
Subject: RE: SUPPORT Agenda

Hi Rose
Here is an agenda
See you Monday.
Neil

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Friday, April 08, 2005 6:35 AM
To: nfiner@ucsd.edu; Wade Rich
Cc: Petrie, Carolyn
Subject: SUPPORT Agenda

Hi
Do you have an agenda for the SUPPORT Subcommittee meeting?

Please send it this am so we can make copies.

We also have the DSMC document.
Also, Mary Anne Berberich from NHLBI will attend the subcommittee meeting.
Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
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301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Neil Finer
To:	Higgins, Rosemary (NIH/NICHD) [E]
Cc:	"Avroy A. Fanaroff, M.D."; "Betty Hastings"; "Ed Donovan"; "Ken Poole"; "Michele"; "Neil Finer"; "Shahnaz Duara"; "Wade Rich"
Subject:	RE: SUPPORT Agenda
Date:	Friday, April 08, 2005 1:12:39 PM
Attachments:	Support Subcommittee Agenda.doc

Hi Rose
Here is an agenda
See you Monday.
Neil

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Friday, April 08, 2005 6:35 AM
To: nfiner@ucsd.edu; Wade Rich
Cc: Petrie, Carolyn
Subject: SUPPORT Agenda

Hi
Do you have an agenda for the SUPPORT Subcommittee meeting?

Please send it this am so we can make copies.

We also have the DSMC document.
Also, Mary Anne Berberich from NHLBI will attend the subcommittee meeting.
Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
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Support Subcommittee Agenda - April 11, 2005

I Introduction and Review of Enrollment to Date – Neil Finer

II DSMC/Stopping Rules – Neil Finer, Rose Higgins

III Site Issues – Wade Rich, Betty Hastings
- A. Enrollment Log
- B. Adverse Events
- C. NSIMV, use of nasal cannula
- D. Oximeters – Rose Higgins
- E. Other site issues

IV Review of Delivery Room Decisions – Neil Finer

From:	Higgins, Rosemary (NIH/NICHD)
To:	Berberich, Mary Anne (NIH/NHLBI)
Subject:	RE: April 11-12 meeting
Date:	Monday, April 04, 2005 4:20:00 PM

Apr 11 will be fine – I will fill you in on the events of April 12.
Thanks
Rose

From: Berberich, Mary Anne (NIH/NHLBI)
Sent: Monday, April 04, 2005 4:20 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE: April 11-12 meeting

Hope to be able to attend the Mon Apr 11 session. Tues AM presents a conflict, but perhaps you could fill me in later.

> -----Original Message-----
> **From:** Higgins, Rosemary (NIH/NICHD)
> **Sent:** Monday, April 04, 2005 3:28 PM
> **To:** Berberich, Mary Anne (NIH/NHLBI)
> **Cc:** petrie@rti.org
> **Subject:** April 11-12 meeting
>
> Hi Mary Anne
> The NICHD Neonatal Research Network Steering Committee will meet on 4/11-4/12. The agenda is attached as are directions to the Bolger Center in Potomac Maryland. The SUPPORT Subcommittee will meet from 3-4 PM on 4/11 and Dr. Finer will present an update at 8:00 AM on Tuesday April 12. Please let me know if you plan to attend either or both sessions.
> Thanks
> Rose
>
> Rosemary D. Higgins, M.D.
> Program Scientist for the Neonatal Research Network
> Pregnancy and Perinatology Branch
> Center for Developmental Biology and Perinatal Medicine
> NICHD, NIH
> 6100 Executive Blvd., Room 4B03B
> MSC 7510
> Bethesda, MD 20892
> (For overnight delivery, use Rockville, MD 20852)
> 301-435-7909
> 301-496-3790 (FAX)
> higginsr@mail.nih.gov

From:	Higgins, Rosemary (NIH/NICHD)
To:	Berberich, Mary Anne (NIH/NHLBI)
Cc:	petrie@rti.org
Subject:	April 11-12 meeting
Date:	Monday, April 04, 2005 3:27:00 PM
Attachments:	April 11_12 SC Agenda 3_29_05 (2).doc Bolger center Driving Directions (2).doc

Hi Mary Anne
The NICHD Neonatal Research Network Steering Committee will meet on 4/11-4/12. The agenda is attached as are directions to the Bolger Center in Potomac Maryland. The SUPPORT Subcommittee will meet from 3-4 PM on 4/11 and Dr. Finer will present an update at 8:00 AM on Tuesday April 12. Please let me know if you plan to attend either or both sessions.
Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
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higginsr@mail.nih.gov

NICHD Neonatal Research Network Steering Committee

April 11, 2005 Bolger Center, Potomac, MD

6-8:30am	**Breakfast served in the Bolger cafeteria)**
Conf Rm 134 7:00-8:00am (1hr)→	**Hypothermia/aEEG** (Shankaran, Laptook, Ehrenkranz, Walsh, Tyson, Laptook, Donovan, Cotten, O'Shea, Higgins, Das, Hastings, Petrie, Bara, all coordinators welcome)
Conf Rm 134 8:00-9:00am (1hr)---→	**HOPE-GDB Subcommittee** (Stoll, Walsh, Duara, Goldberg, Oh, Laptook, Higgins, Das, Hastings, Petrie, Hale, Newman, all coordinators welcome)
Conf Rm 126 8:00-9:00am (1hr)---→	**Protocol Review** (Ehrenkranz, Finer, O'Shea, Phelps, Shankaran, Tyson, Higgins, Das)
Conf Rm 134 9:00-10:00am (1hr)-→	**Phototherapy Subcommittee** (Morris, Tyson, Oh, O'Shea, Phelps, Stevenson, Das, Higgins, Hastings, Petrie, Grisby, McDavid, coordinators)
Conf Rm 126 9:00-10:00am (1hr)-→	**Genomics Subcommittee** (Duara, Donovan, Poindexter, Stoll, Ehrenkranz, Cotton, Higgins, Das, Hastings, Petrie)
Conf Rm 134 10:00-11:00am (1hr)-→	**NEC** (Blakely, Tyson, Stevenson, Stoll, Jobe, Higgins, Das)
Conf Rm 126 10:00-11:00am (1hr)-→	**Probiotics Group** (Oh, Stoll, Laptook, Goldberg, Carlo, Higgins, Das)
Conf Rm 134 11:00-12:00pm (1hr)-→	**Publications** (Donovan, Carlo, Cotten, Stevenson, Shankaran, Higgins, Das)
Conf Rm 126 11:00-12:00pm (1hr)-→	**Seizure Working Group** (Guillet, Phelps, Laptook, O'Shea, Higgins, Das, Hastings, Petrie, all coordinators welcome)
12:00 – 1:00pm (subject to change)	**Lunch provided in Bolger cafeteria**
Conf Rm 134 1:00-2:00pm (1hr)-→	**Cytokines** (Carlo, Shankaran, Cotten, Phelps, Ehrenkranz, Tyson, Stoll, Higgins, Das, Hastings, Petrie
Conf Rm 126 1:00-2:00pm (1hr)-→	**Coordinator's Meeting** (all Coordinators)
Conf Rm 126 2:00-3:00pm (1hr)--→	**Inositol** (Phelps, Ehrenkranz, Cotten, Poindexter, Oh, O'Shea, Higgins, Das, Hastings, Petrie, Ball, Gettner, Auten, L Miller, Hensman, Peters)
Conf Rm 134 2:00-3:00pm (1hr)--→	**PGE1 Working Group** (Sood, Shankaran, Poindexter, Carlo, Finer, Duara, Higgins, Das)
Conf Rm 126 3:00-4:00pm (1hr)----→	**SUPPORT** (Finer, Duara, Donovan, Carlo, Walsh, Higgins, Das, Hastings, Petrie, Rich, all coordinators welcome)
Conf Rm 126 4:00-5:00pm (1hr)----→	**Candida** (Benjamin, Stoll, Walsh, Cotten, Phelps, Shankaran, Duara, Das, Higgins, Hastings, Petrie, Auten, N Miller, all coordinators welcome)
Conf Rm 134 4:00-5:00pm (1hr)----→	**PiNO** (Van Meurs, Stevenson, Poindexter, Ehrenkranz, Das, Higgins, Hastings, Petrie)
Conf Rm 126 5:00-6:00pm (1hr)----→	**PCV7** (D'Angio, Phelps, Stoll, Stevenson, Carlo, O'Shea, Duara, Shankaran, Das, Higgins, Hastings, Petrie, Peters, McDavid, N Miller, Everett, Bara, Hale, Collins, Auten, Rich, Murray, Ang)
Conf Rm 134 6:00-7:00pm (1hr)----→	**Benchmarking Intervention sites** (Walsh, Finer, Laptook, Poindexter, Shankaran, Stevenson, Stoll, Higgins, Das, Hastings, Petrie, Newman, Rich, N Miller, Bara, Hale)
Dinner at the Bolger Center is served 5-8pm	

NICHD Neonatal Research Network Steering Committee

April 12, 2005 Bolger Center, Potomac, MD

Conference Room 134

7:00 AM	Welcome	Dr. Jobe
7:05 AM	PCV7	Drs. D'Angio/Ang/Murray
7:30 AM	HOPE-GDB	Dr. Stoll
7:45 AM	Na Restriction	Dr. Oh
8:00 AM	SUPPORT	Dr. Finer
8:15 AM	NEC	Dr. Blakely
8:30 AM	Benchmarking	Dr. Walsh
9:00 AM	Phototherapy	Dr. Morris
9:15 AM	Publications	Dr. Donovan
9:30 AM	Protocol Review	Dr. Ehrenkranz
9:45 AM	Genomics	Dr. Duara
10:00 AM	Retrospective Repository	Dr. Cotton
10:15 AM	Seizures	Dr. Guillet
10:30 AM	Coordinator Update	Ms. Gettner
10:45 AM	Inositol	Dr. Phelps
11:00 AM	Candida	Dr. Benjamin
11:15 AM	MFMU	Dr. Harper
11:30 AM	Cytokines	Dr. Carlo
11:45 PM	International Networks	Ms. McClure
12:00 PM	Lunch	
1:15 PM	Hypothermia FU/aEEG	Dr. Shankaran
1:30 PM	Follow-up Study	Dr. Vohr
1:45 PM	Preemie iNO	Dr. Van Meurs
2:00 PM	TIN	Dr. Stevenson
2:15 PM	IPGE1	Dr. Sood
2:30 PM	RTI Report	Dr. Das
2:45 PM	New business	Drs. Jobe, Higgins
3:00 PM	Adjourn	

☑ Items requiring a vote

WILLIAM F. Bolger Center
FOR LEADERSHIP DEVELOPMENT
A Training and Conference Center

Driving Directions to the William F. Bolger Center for Leadership Development

Directions from Dulles Airport
- Take Dulles access road from airport toward Washington D.C.
- From Dulles access road take 495 North. (Frederick/Baltimore, MD.)
- From 495 take exit 39, River road. (Route 190 West)
- Continue on River until you reach Falls Road, make a right onto Falls Road
- Continue on Falls Road ¼ mile, at the next light make a right onto Democracy Blvd.
- Follow Democracy for 1.5 miles then make a right into the William F. Bolger Center for Leadership Development.

Directions from National Airport
- As you come out of the airport you are on the George Washington Pkwy. In Virginia.
- Toward the end of the Pkwy you will see signs for 495, bear right (North) on 495.
- From 495 take exit 39, River Road, (Route 190 West).
- Continue on River Road until you reach Falls Road, make a right onto Falls Road
- Continue on Falls Road ¼ mile, at the next light make a right onto Democracy Blvd.
- Follow Democracy 1.5 miles and then make a right into the William F. Bolger Center for Leadership Development.

Directions from BWI airport
- Take route I-95 South toward Washington D.C.
- From route I-95 exit onto 495 going West.
- From 495 take exit 39, River Road, (Route 190 West).
- Continue on River Road until you reach Falls Road, make a right onto Falls Road
- Continue on Falls Road ¼ mile, at the next light make a right onto Democracy Blvd.
- Follow Democracy 1.5 miles and make a right into the William F. Bolger Center for Leadership Development.

Directions from Union Station
- Take Massachusetts Ave. West toward 495.
- Near the end of Mass. Ave. you will see signs for 495, bear right (North) on 495.
- From 495 take exit 39, River Road, (Route 190 West).
- Continue on River Road until you reach Falls Road, make a right onto Falls Road
- Continue on Falls Road ¼ mile, at the next light make a right onto Democracy Blvd.
- Follow Democracy 1.5 miles and make a right into the William F. Bolger Center for Leadership Development.

Directions from Bethesda Metro
- Follow signs to Old Georgetown Road (Route 187) going North.
- Take a left onto Democracy Blvd.
- Continue 4 miles on Democracy Blvd., make a make a left into the William F. Bolger Center for Leadership Development.

Directions from L'Enfant Plaza
- Take 395 South (14th street bridge), to George Washington Pkwy. (West), toward 495
- Toward the end of the Pkwy you will see signs for 495, bear right (North) on 495.
- From 495 take exit 39, River Road, (Route 190 West).
- Continue on River Road until you reach Falls Road, make a right onto Falls Road
- Continue on Falls Road ¼ mile, at the next light make a right onto Democracy Blvd.
- Follow Democracy for 1.5 miles then make a make a right into the William F. Bolger Center for Leadership Development.

**** From Main Entrance follow signs to the Reception Building.

From:	Neil Finer
To:	Higgins, Rosemary (NIH/NICHD) [E]
Subject:	RE: DSMC Monitoring--SUPPORT Trial
Date:	Monday, April 04, 2005 2:44:02 PM

Thanks Rose

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Monday, April 04, 2005 10:02 AM
To: Neil Finer
Cc: Hastings, Betty J.
Subject: FW: DSMC Monitoring--SUPPORT Trial

Hi Neil,
I will make copies of these two items to have at the steering committee meeting if the PIs want to see what was sent to the DSMC
Thanks
Rose

From: Hastings, Betty J. [mailto:bkh@rti.org]
Sent: Monday, April 04, 2005 12:58 PM
To: ckr3+@pitt.edu; cgleason@u.washington.edu; Personal Email md511@columbia.edu; rjb6j@hscmail.mcc.virginia.edu; Hunt, Carl (NIH/NHLBI); mcallen@jhmi.edu; merran.thomson@ic.ac.uk
Cc: Higgins, Rosemary (NIH/NICHD); Willinger, Marian (NIH/NICHD); Berberich, Mary Anne (NIH/NHLBI); Jobea0@chmcc.org; edward.donovan@chmcc.org; nfiner@ucsd.edu; sduara@miami.edu; wcarlo@peds.uab.edu; mcw3@cwru.edu; Das, Abhik; Poole, W. Kenneth; Gantz, Marie
Subject: DSMC Monitoring--SUPPORT Trial

Attached are the following two documents relating to the Support Trial:

- A memo to the SUPPORT Data and Safety Monitoring Committee
- A document containing suggested guidelines to aid the DSMC in monitoring the SUPPORT Trial.

Please let us know if you have any comment or questions about this material.

<<DSMC Monitoring Memo 4-4-05 2.doc>> <<3.2. 05 DSMC Monitoring adrev1.doc>>

Thanks
Betty

Betty Hastings

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Statistic Research Division
P.O. Box 12194
Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7740
Fax: (919) 485-7762
bkh@rti.org

From:	Hastings, Betty J.
To:	ahensman@wihri.org; mbball@leland.stanford.edu; grisbyca@email.uc.edu; ellen_hale@oz.ped.emory.edu; gaynelle.hensley@utsouthwestern.edu; Georgia E McDavid; auten002@mc.duke.edu; linda_reubens@urmc.rochester.edu; lucmille@iupui.edu; mcollins@peds.uab.edu; Nancy.Miller@UTSouthwestern.edu; Nancy Newman; npeters@wfubmc.edu; pat.gettner@yale.edu; ae5357@wayne.edu; rbridge@ucsd.edu; risa.demetrio@sharp.com; kathy.arnell@sharp.com; Reverett@med.miami.edu; brenda.H.Morris@Uth.tmc.edu; cotte010@mc.duke.edu; crosen@mednet.swmed.edu; vanmeurs@leland.stanford.edu; kurt.schibler@cchmc.org; alaptook@wihri.org; Jobea0@chmcc.org; bpoindex@iupui.edu; edward.donovan@chmcc.org; jlemons@iupui.edu; moshea@wfubmc.edu; sshankar@med.wayne.edu; sduara@miami.edu; susie.buchter@oz.ped.emory.edu; wcarlo@peds.uab.edu; mcw3@cwru.edu; Vineet.bhandari@yale.edu; vivek.Narendran@cchmc.org; Walid.Salhab@UTSouthwestern.edu; balexanba@hotmail.com; Lenora Jackson; Estelle E. Fischer; Holly Mincey; Jody Shively; Kate Bridges, MD
Cc:	wrich@ucsd.edu; nfiner@ucsd.edu; Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik; Poole, W. Kenneth
Subject:	SUPPORT
Date:	Monday, April 04, 2005 1:13:08 PM

From Wade Rich:

Dear Fellow Coordinators and Principal Investigators,

I was asked a question today I thought was worth answering to the group, as it is critical for our oximeter numbers. If a subject is off of oxygen for 72 hours his/her study oximeter should be removed, downloaded, and cleared. This will make it available for another infant. If the infant needs to go back

on an oximeter, one of the same "color" should be put back on. At this time, this does not include transient oxygen for feeding.

Thanks.

Wade

Wade Rich, RRT-NPS
Clinical Research Administrator
Division of Neonatology
UCSD Medical Center
200 W Arbor Dr
San Diego, CA 92103-8774
619-543-5375
pgr 290-5230

Betty Hastings

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Statistic Research Division
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Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7740
Fax: (919) 485-7762
bkh@rti.org

From:	Higgins, Rosemary (NIH/NICHD)
To:	Neil Finer
Cc:	Hastings, Betty J.
Subject:	FW: DSMC Monitoring--SUPPORT Trial
Date:	Monday, April 04, 2005 1:01:00 PM
Attachments:	DSMC Monitoring Memo 4-4-05 2.doc 3.2. 05 DSMC Monitoring adrev1.doc

Hi Neil,
I will make copies of these two items to have at the steering committee meeting if the PIs want to see what was sent to the DSMC
Thanks
Rose

From: Hastings, Betty J. [mailto:bkh@rti.org]
Sent: Monday, April 04, 2005 12:58 PM
To: ckr3+@pitt.edu; cgleason@u.washington.edu; Personal Email md511@columbia.edu; rjb6j@hscmail.mcc.virginia.edu; Hunt, Carl (NIH/NHLBI); mcallen@jhmi.edu; merran.thomson@ic.ac.uk
Cc: Higgins, Rosemary (NIH/NICHD); Willinger, Marian (NIH/NICHD); Berberich, Mary Anne (NIH/NHLBI); Jobea0@chmcc.org; edward.donovan@chmcc.org; nfiner@ucsd.edu; sduara@miami.edu; wcarlo@peds.uab.edu; mcw3@cwru.edu; Das, Abhik; Poole, W. Kenneth; Gantz, Marie
Subject: DSMC Monitoring--SUPPORT Trial

Attached are the following two documents relating to the Support Trial:

- A memo to the SUPPORT Data and Safety Monitoring Committee
- A document containing suggested guidelines to aid the DSMC in monitoring the SUPPORT Trial.

Please let us know if you have any comment or questions about this material.

<<DSMC Monitoring Memo 4-4-05 2.doc>> <<3.2. 05 DSMC Monitoring adrev1.doc>>

Thanks
Betty

Betty Hastings

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RTI INTERNATIONAL

Memorandum

April 4, 2005

TO: SUPPORT Trial Data Safety and Monitoring Committee

FROM: The Data Coordinating Center
Dr. Rosemary Higgins, NICHD
Support Trial Subcommittee

SUBJECT: Data and Safety and Monitoring Plans for the SUPPORT Trial

Attached is a document containing suggested guidelines to aid the DSMC in monitoring the SUPPORT Trial. This document, prepared by the SUPPORT Trial Subcommittee, contains rates and ranges of various common neonatal complications seen in this population of infants at neonatal research network sites. This information is provided to the DSMC as a guide for relative rates of complications in the population currently being enrolled for the SUPPORT Trial.

Please send any comment/concerns you may have to Dr. Neil Finer (Chair, SUPPORT Subcommittee) nfiner@ucsd.edu or Dr. Rosemary Higgins (Program Scientist, NICHD) higginsr@mail.nih.gov.

April 4, 2005

The SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants

The SUPPORT Trial

DATA AND SAFETY MONITORING PLANS

Adverse Events

Data on the following potential adverse events that may be related to the study maneuver will be recorded and evaluated as part of continuous safety monitoring during the trial by RTI:

1. Air leak on admission to the NICU, or during the initial 14 days of life
2. The need for chest compressions, and/or epinephrine in the delivery room or NICU
3. The occurrence of severe IVH (Grades 3-4, Papile)
4. Death

As background information to help the DSMC monitor this trial, we are providing the following observational data from the network's generic database from January 1, 2002 - December 31, 2004. The proportions listed give the overall rate of an adverse event in the network population for each of the gestational age subgroups. The range of proportions for each adverse event across centers is presented to provide an idea about the variation seen over the sites for these outcomes. It is hoped that this information will provide detailed background statistics regarding the population for study in this trial.

It is suggested by the SUPPORT Subcommittee that consideration for a recommendation to stop the trial based on a safety concern would need to involve a statistically significant difference in an adverse event between the treatment groups, and that the occurrence of the adverse event is outside of the limits of plausibility for that specific event according to the most recent Neonatal Research Network data presented below.

Table 1: Overall proportion, variability and ranges across network centers for infants with gestational age 24-27 weeks at birth

Variable	N	Proportion	SD	Range of proportion across centers
IVH grade (3 or 4)	3753	0.237	0.43	0.108-0.371
DR Chest compressions	4050	0.108	0. 31	0.035-0.258
Pneumothorax	3861	0.087	0..29	0.023-0.195
Death within first 14 days	4055	0.159	0.37	0.092-0.325

Table 2: Overall proportion, variability and ranges across network centers for infants with gestational age 24-25 weeks at birth

Variable	N	Proportion	SD	Range of proportion across centers
IVH grade (3 or 4)	1599	0.327	0.47	0.153-0.520
DR Chest compressions	1805	0.133	0. 34	0.029-0.340
Pneumothorax	1667	0.116	0. 32	0.026-0.239
Death within first 14 days	1808	0.249	0.44	0.124-0.485

Table 3: Overall proportion, variability and ranges across network centers for infants with gestational age 26-27 weeks at birth

Variable	N	Proportion	SD	Range of proportion across centers
IVH grade (3 or 4)	2154	0.170	0.38	0.022-0.263
DR Chest compressions	2245	0.088	0.29	0.034-0.200
Pneumothorax	2194	0.066	0.25	0.022-0.155
Death within first 14 days	2247	0.086	0.28	0.039-0.160

Note: The sample includes infants that were born on or after January 1, 2002 that have reached status. SD denotes standard deviation.

Data Safety Monitoring Committee

The Data Safety Monitoring Committee will review the progress of the study with respect to efficacy and adverse events in a sequential fashion by using interim monitoring boundaries. O'Brien-Fleming[i] boundaries will be used for efficacy monitoring and will be constructed for four looks at the data at 25%, 50%, 75%, and 100% of outcome assessment. Pocock boundaries will be used for adverse event monitoring and will be viewed after every 30 infants have been enrolled. A special adverse event form will collect the information so that it may be entered into the data base in a timely fashion.

From: Higgins, Rosemary (NIH/NICHD)
To: Hastings, Betty J.
Subject: RE: SUPPORT DSMC document
Date: Friday, April 01, 2005 9:12:00 AM

Fine
Rose

From: Hastings, Betty J. [mailto:bkh@rti.org]
Sent: Friday, April 01, 2005 9:05 AM
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE: SUPPORT DSMC document

I will. If it's okay with you, I'll have Ken look it over again on Monday.

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Friday, April 01, 2005 9:01 AM
To: Hastings, Betty J.
Subject: RE: SUPPORT DSMC document

> Yes,
> I don't think they were aware – this was brought up in Dec or Jan after the DSMC met.
> It would be great if you could do a little memo.
> Thanks
> Rose
>
> ---
>
> **From:** Hastings, Betty J. [mailto:bkh@rti.org]
> **Sent:** Friday, April 01, 2005 9:00 AM
> **To:** Higgins, Rosemary (NIH/NICHD)
> **Subject:** RE: SUPPORT DSMC document
>
> Sure. They are not aware of this are they? I was wondering if we should write some type of cover memo. Shall I draft something and send back to you?
> Thanks.
> Betty
>
> > -----Original Message-----
> > **From:** Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
> > **Sent:** Friday, April 01, 2005 8:55 AM
> > **To:** Hastings, Betty J.
> > **Cc:** Poole, W. Kenneth; Das, Abhik
> > **Subject:** SUPPORT DSMC document
> >
> > Hi Betty
> > Can you distribute this document to the DSMC for assistance in monitoring the SUPPORT Trial? I think it is the final version.
> > Thanks
> > Rose
> >
> > Rosemary D. Higgins, M.D.
> > Program Scientist for the Neonatal Research Network
> > Pregnancy and Perinatology Branch
> > Center for Developmental Biology and Perinatal Medicine
> > NICHD, NIH

6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Duara, Shahnaz
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT
Date: Monday, March 28, 2005 11:55:58 AM

I received a phone message that they were going to look at the protocol last Friday. No feed-back as of yet. Will let you know as soon as I hear anything.
Thanks
Shahnaz

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Monday, March 28, 2005 11:47 AM
To: Duara, Shahnaz
Subject: SUPPORT

Hi Shahnaz,
Have you heard about the SUPPORT trial from your IRB?
Let me know
Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Hastings, Betty J.
To:	brenda.H.Morris@Uth.tmc.edu; cotte010@mc.duke.edu; crosen@mednet.swmed.edu; vanmeurs@leland.stanford.edu; kurt.schibler@cchmc.org; alaptook@wihri.org; edward.donovan@chmcc.org; jlemons@iupui.edu; moshea@wfubmc.edu; nfiner@ucsd.edu; sshankar@med.wayne.edu; sduara@miami.edu; susie.buchter@oz.ped.emory.edu; wcarlo@peds.uab.edu; mcw3@cwru.edu; Vineet.bhandari@yale.edu; vivek.Narendran@cchmc.org; Walid.Salhab@UTSouthwestern.edu; Reverett@med.miami.edu; ahensman@wihri.org; mbbali@leland.stanford.edu; ellen_hale@oz.ped.emory.edu; gaynelle.hensley@utsouthwestern.edu; Georgia F McDavid; auten002@mc.duke.edu; linda_reubens@urmc.rochester.edu; lucmille@iupui.edu; mcollins@peds.uab.edu; Nancy.Miller@UTSouthwestern.edu; Nancy Newman; npeters@wfubmc.edu; pat.gettner@yale.edu; kathy.arnell@sharp.com; Wade Rich; grisbyca@email.uc.edu; Rebecca Bara; Risa Demetrio; Personal Email; Lenora Jackson; Estelle E. Fischer; Holly Mincey; Jody Shively; Kate Bridges, MD
Cc:	Das, Abhik; Petrie, Carolyn; Poole, W. Kenneth; Gantz, Marie; Schaefer, Scott E.; Higgins, Rosemary (NIH/NICHD) [E]
Subject:	SUPPORT Trial
Date:	Thursday, March 24, 2005 12:24:53 PM
Attachments:	SUP01.doc

Attached is SUP01, a Technical Memo which outlines the changes that have been made to the Manual and Study Forms since the January 4, 2005 version was placed on the Web site. The majority of the changes are minor and were based on the questions that have been received from the sites using the current versions.

I will not be sending these revised documents but will have them placed on the Web site. They should be added to the Web this afternoon or

or tomorrow. If you would like to receive an electronic version of any of this material, please let me know and I'll be glad to send it to you.

Please send any questions you may have, about these revisions, to Wade Rich or to me.
Thanks. <<SUP01.doc>>
Betty
Betty Hastings

RTI International
Statistic Research Division
P.O. Box 12194
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Telephone: (919) 485-7740
Fax: (919) 485-7762
bkh@rti.org

RTI INTERNATIONAL | Memorandum

March 24, 2005

SUPPORT TECHNICAL MEMO # 1

TO: Network Coordinators
Network PIs

FROM: The Data Coordinating Center
Neil Finer, MD
Wade Rich

SUBJECT: Changes to the SUPPORT Forms and Manual of Operations

Please note that the following changes to the SUPPORT Study Forms and Manual of Operations reflect changes that have been made since the January 4, 2005 version was posted on the Web site.

Clarifications/Changes to the SUPPORT Study Forms

SUPPO1 (Screening Log) -- No changes since the January 4, 2005 version.

SUPP02 (Eligibility Form) --No changes since the January 4, 2005 version.

SUPP03 (Delivery Form) -- Question A.6, added code 4= As required by randomization assignment. **Current version dated March 10, 2005, Rel 2.0.**

SUPP04 (NICU Admission and Procedures Form) -- No changes since the January 4, 2005 version.

SUPP05 (Safety Monitoring Form)--Current version dated March 10, 2005, Rel 2.0

- Revised the heading. Note: Study Day 1 is day of randomization and is based on the **calendar day (00:00 - 23:59).**
- Changed the Instructions for Completing Section A to "Complete Section A if the infant is Intubated/CPAP for > 8 hours on this Day".
- Changed a.3 Scheduled time from 24:00 to 23:59.
- (h) Mode of Support- Add Codes 5=NC and 6=Hood
- Changed the Instructions for Completing Section B to "Complete Section B if the infant is on Cannula/Hood for > 8 hours on this Day".
- Section C Intubated/Extubation Information-- Added (For NICU Only) If more than one Intubation/Extubation occurs in one day, complete the SUPP05A Froms
- Added new Question 1.a, If Yes, Record the time of intubation.
- Added new Question 2.a, If Yes, Record the time of extubation.

New SUPPO5A (Supplemental Safety Monitoring Form) This form should be used if more than one intubation/extubation occurs on the same day. The SUPPO5A form contains the same information as Section C on the SUPP05 Form. **This form is dated March 10, 2004 Rel 1.0.**

SUPP08 (Adverse Event Form) Current version dated March 10, 2005, Rel 2.0. Removed the Date of Onset from Question 5.

SUPP09 (Outcome Status Form) -- No changes since the January 4, 2005 Version.

SUPP10 (ROP Outcomes and Tracking Summary) Changed Retinal Detachment to Post-surgical Retinal Detachment.
^Surgery: Revised Code 3= Both/laser/cryo. Added Codes 4=Scleral buckle, 5=Vitrectomey and 6= Other. **Current version dated March 10, 2005, Rel 2.0.**

Clarifications/Changes to the Manual of Operations

Chapter 4
Section 4.1.1 Randomization and Masking, Storing and Assigning Oximeters. 3rd and 5th paragraphs have been revised.

Chapter 5
Section 5.1.4 NICU Management
Questions 1 **Intubation, second bullet removed "An arterial"** and changed to read A $PaCO_2$ > 65 torr (arterial or capillary samples, if venous PvCO2 > 70 torr) documented on a single blood gas.
Questions 4 **Re-Intubation Criteria, second bullet removed "An arterial"** and changed to read A $PaCO_2$ > 65 torr (arterial or capillary samples, if venous PvCO2 > 70 torr) documented on a single blood gas.

Section 5.4 Protocol Violations
Questions 1-5-- To clarify, changed Treatment infants to Early Extubation and CPAP infants and Control infants to Prophylactic/Early Surfactant and Ventilation infants.

Section 5.5 Adverse Events
Added: 4. Pulmonary hemorrhage and 5. Nasal breakdown requiring discontinuation of nasal prongs.

Chapter 6

Revised instructions on page 6.2 (for completing the Date of Birth, Enrolled in Study and Network Number) to read **"The Following Information Will Be Filled Out On Those Patients Who Have Given Consent When The Infant Is Born Within The Eligible Window".**

Chapter 7

Section 7.3 Form D. Randomization
Question 1.a Date of Randomization- Changed the instruction to: "Enter the date on which the randomization envelope was opened to enroll the infant into the study. All dates for this study are recorded using the M/DD/YYYY format".
Question 1.b Time of Randomization Changed the instruction to: "Enter the local time at which the envelope was opened to randomize the infant.
Question 1.d-Treatment Assignment: Changed (for clarification) 1= Early CPAP to **Early Extubation and CPAP.** Changed 2= Early Surfactant to **Early Surfactant and Ventilation**.

Chapter 8

Section 8.2 Form Section A. Delivery Room Information
Question 6. Indication for intubation. Added Code 4 = As required by randomization assignment. Code 4 will be used to indicate that the infant was intubated because of the protocol assignment to Early Surfactant.

Chapter 9

Section 9.3 NICU Procedures
Question 3.a Changed Date to "Record the date the infant received the first dose of surfactant in the NICU and for the first 14 days. Day begins at 00:00, ends at 23:59".
Questions 3.b Changed Time to "Record the time the infant received the first dose of surfactant in the NICU".

Chapter 10

Section 10.2.1 Section A. Blood Gas Information
Revised instructions to "Complete Section A If infant Intubated/CPAP for > 8 hours on this day".
All questions in this section pertain to the results of blood gas analyses done at 3 daily time points closest to 08:00, 16:00, and 23:59. Record the blood gas **results closest to the scheduled time if available.** In no blood gases were measured, record the FiO_2 and the Mode of Support.
Changes scheduled times from 24:00 to 23:59 for all occurrences.
b. Time Measured
Revised instructions to "Record the time that the blood samples were collected based on a 24-hour clock. This time should be closest to 08:00, 16:00 or 23:59. If one blood gas qualifies as closest to two scheduled times (e.g. 23:59 and 8:00am the next day) enter the blood gas on the earlier of the selected times and enter ** : ** for the later one".

Record the results of the blood draw: If **No** blood gases were measured, record the time of the FiO_2 and the mode of support, leave questions c, d, e and g blank.
h. Mode of Support
Added additional codes 5= NC, 6= Hood, 7= No Support.

Section 10.2.2 Section B. Supplemental Oxygen Information
Revised instructions to "Complete Section B If the infant is on Cannula/Hood for >8 hours on this day. The FiO_2 should be recorded once a day closest to Noon".

Section 10.2.3 Section C. Intubation/Extubation Information
Revised instructions to "(For NICU ONLY) If more than one intubation/extubation occurs in one day, complete the SUPP05A Form".
Question 1 "Was the infant intubated on this day?" Added 1.a If yes, record the time of intubation.
Question 2 "Was the infant extubated on this day?" Added 2.a If yes, record the time of extubation.

Chapter 14

Section 14.1.3Section B - Neurologic

Question 1.a Date of Ultrasound Added "If more than one head ultrasound is done between 4 - 21 days of age, record the date of the most severe".

Chapter 15

Section 15.1.1 Instructions for completing the ROP Outcomes and tracking Summary (SUPP10)

Question 9. Changed Retinal Detachment to "Post-surgical Retinal Detachment after surgery".

From:	Kathy J Auten
To:	Nancy Peters
Cc:	ahensman@wihri.org; ae5357@wayne.edu; mbball@leland.stanford.edu; grisbyca@email.uc.edu; ellen_hale@oz.ped.emory.edu; Georgia.E.McDavid@uth.tmc.edu; lucmille@iupui.edu; mcollins@peds.uab.edu; Nancy.Miller@UTSouthwestern.edu; nxs5@cwru.edu; pat.gettner@yale.edu; auten002@mc.duke.edu; linda_reubens@urmc.rochester.edu; reverett@med.miami.edu; wrich@ucsd.edu; bss5@cwru.edu; Jackie.Hickman@Childrens.com; "Vivien Phillips " (E-mail); Kathy.Arnell@sharp.com; Risa Demetrio; Higgins, Rosemary (NIH/NICHD) [E]; nfiner@ucsd.edu
Subject:	Re: SUPPORT & oximeter sensors
Date:	Saturday, March 19, 2005 1:04:10 PM

Thanks for the information, Nancy.

The Masimo sensor with velcro wrap (not adhesive) is the Neo Soft Touch for neonates <1kg (part # 1651). They come in boxes of 20 and retail for $400.00/bx. I asked to have a sample sent to me. Dr. Sayre of Masimo will set a research price if we are interested in the product. Since our skin care team won't allow us to use the adhesive sensors, the velcro sensor would have to be pretty poor for me not to want to stock it. I'll let you know what price they quote the Network. In the meantime, I suggest you email Vicki Bishop of Masimo if you'd like to look at the velcro sensor. Her email address is "Vicki Bishop <VBishop@masimo.com> ".

Kathy A

"Nancy Peters" <npeters@wfubmc.edu>
03/18/2005 15:25

To: <ahensman@wihri.org>, <ae5357@wayne.edu>, <mbball@leland.stanford.edu>, <grisbyca@email.uc.edu>, <ellen_hale@oz.ped.emory.edu>, <Georgia.E.McDavid@uth.tmc.edu>, <lucmille@iupui.edu>, <mcollins@peds.uab.edu>, <Nancy.Miller@UTSouthwestern.edu>, <nxs5@cwru.edu>, <pat.gettner@yale.edu>, <auten002@mc.duke.edu>, <linda_reubens@urmc.rochester.edu>, <reverett@med.miami.edu>, <wrich@ucsd.edu>, <bss5@cwru.edu>, <Jackie.Hickman@Childrens.com>, "'Vivien Phillips ' (E-mail)" <VPhillips@peds.uab.edu>, <Kathy.Arnell@sharp.com>, "Risa Demetrio" <risa.demetrio@sharp.com>

cc: "Higgins, Rosemary (NIH/NICHD)" <higginsr@mail.nih.gov>, <nfiner@ucsd.edu>

bcc:

Subject: SUPPORT & oximeter sensors

Hi,

We were discussing SUPPORT at one of our sites this morning and I had mentioned the conversation regarding skin care and the pulse ox sensors and the infant's <1000 grams. For their infants they are placing tegaderm (or a similar product) on the adhesive portion of the pulse ox sensor that goes against the body so that it does not adhere to the skin of the most fragile infants. The staff has found that this works quite well --- just be sure to leave enough of the adhesive area free to seal the sensor once it is in place. Although they have been pleased with this adaption of the sensor, they expressed interest in the product mentioned during our call yesterday --- something specifically designed for this population for whom skin integrity can be an issue. I will have to admit that I did not make a note of the specifics of this product, therefore I would appreciate hearing from the coordinator who has knowledge of an acceptable sensor that could be used for this study and for the smaller infants that we

enroll. In addition, I wanted to share with you a method that one nursery found worked for them.

Thanks. I hope you all have a great weekend.

Nancy (Peters)

From: Hastings, Betty J.
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT_IRB-Oximeter Status. doc.doc
Date: Wednesday, March 16, 2005 9:10:58 AM
Attachments: SUPPORT_IRB-Oximeter Status. doc.doc

SUPPORT TRIAL
IRB/Oximeter Status-

March 16, 2005

Center	IRB Status	Oximeters Ordered	Oximeters Received
Case	Waiting for IRB Approval	**Yes**	**Yes**
UT-Dallas	Waiting for IRB Approval	**Yes**	**Yes**
Wayne State	?	**No**	
Miami	?	**No**	
Emory	Received IRB Approval	**No**	
Cincinnati	Received IRB Approval	**Yes**	**Yes**
Indiana	Provisional Approval	**Yes**	**Yes**
Yale	Received IRB Approval	**Yes**	**Yes**
Brown	Received IRB Approval	**Yes**	**Yes**
Stanford	Received IRB Approval	**Yes**	
UAB	Received IRB Approval	**Yes**	**No**
UT-Houston	Received IRB Approval	**Yes**	**Yes**
Duke	Pending IRB Approval	**Yes**	
Wake Forest	Received IRB Approval	**Yes**	**Yes**
Rochester	Received IRB Approval	**Yes**	**Yes**
UCSD	Received IRB Approval	**Yes**	**Yes**

From: Higgins, Rosemary (NIH/NICHD)
To: Hastings, Betty J.
Subject: FW: SUPPORT_IRB-Oximeter Status. doc.doc
Date: Wednesday, March 16, 2005 9:05:00 AM
Attachments: SUPPORT_IRB-Oximeter Status. doc.doc

Here it is.

From: Hastings, Betty J. [mailto:bkh@rti.org]
Sent: Monday, February 28, 2005 10:19 AM
To: Higgins, Rosemary (NIH/NICHD)
Subject: SUPPORT_IRB-Oximeter Status. doc.doc

Rose,
I think this is pretty up-to-date.

<<SUPPORT_IRB-Oximeter Status. doc.doc>>

SUPPORT TRIAL
IRB/Oximeter Status-

January 6, 2005

Center	IRB Status	Oximeters Ordered	Oximeters Received
Case	Waiting for IRB Approval	**Yes**	**Yes**
UT-Dallas	Waiting for IRB Approval	**Yes**	**Yes**
Wayne State	?	**No**	
Miami	?	**No**	
Emory	Approval at one site	**No**	
Cincinnati	Approved at one site	**Yes**	**Yes**
Indiana	Provisional Approval	**Yes**	**Yes**
Yale	Received IRB Approval	**Yes**	**Yes**
Brown	Received IRB Approval	**Yes**	**Yes**
Stanford	Waiting for IRB Approval	**No**	
UAB	Received IRB Approval	**Yes**	**No**
UT-Houston	Received IRB Approval	**Yes**	**Yes**
Duke	Pending IRB Approval	**Yes**	
Wake Forest	Pending IRB Approval	**Yes**	**Yes**
Rochester	Received IRB Approval	**Yes**	**Yes**
UCSD	Received IRB Approval	**Yes**	**Yes**

From: Hastings, Betty J.
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT_IRB-Oximeter Status. doc.doc
Date: Wednesday, March 16, 2005 9:07:12 AM

Thanks.

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, March 16, 2005 9:05 AM
To: Hastings, Betty J.
Subject: FW: SUPPORT_IRB-Oximeter Status. doc.doc

Here it is.

From: Hastings, Betty J. [mailto:bkh@rti.org]
Sent: Monday, February 28, 2005 10:19 AM
To: Higgins, Rosemary (NIH/NICHD)
Subject: SUPPORT_IRB-Oximeter Status. doc.doc

Rose,
I think this is pretty up-to-date.

<<SUPPORT_IRB-Oximeter Status. doc.doc>>

From: Hastings, Betty J.
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT--IRBs
Date: Wednesday, March 16, 2005 9:03:23 AM

Rose,
Could you please send me the table I sent you on the 28th? I can't seem to find this in my files. Thanks a lot.
Betty

Betty Hastings

RTI International
Statistic Research Division
P.O. Box 12194
Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7740
Fax: (919) 485-7762
bkh@rti.org

From: Barbara Stoll
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT DSMC
Date: Sunday, March 13, 2005 9:10:56 PM

Rose

I reviewed the SUPPORT DSMC doc and think it looks good

BJS

From: Laroia, Nirupama
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT Protocol
Date: Friday, March 11, 2005 12:42:35 PM

Thank you.

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Friday, March 11, 2005 12:06 PM
To: Phelps, Dale; 'Carolyn Petrie'
Cc: Laroia, Nirupama; Reubens, Linda
Subject: RE: SUPPORT Protocol

Dale, We will do this.
Thanks
Rose

From: Phelps, Dale [mailto:Dale_Phelps@URMC.Rochester.edu]
Sent: Friday, March 11, 2005 12:03 PM
To: 'Carolyn Petrie'; Higgins, Rosemary (NIH/NICHD)
Cc: Laroia, Nirupama; Reubens, Linda
Subject: FW: SUPPORT Protocol

I would like to request that Nirupama Laroia, MD be added to the 'distribution list' for the SUPPORT study.
She is the local PI in Rochester and has a need to know.

Dale Phelps

-----Original Message-----
From: Laroia, Nirupama
Sent: Tuesday, March 08, 2005 5:38 PM
To: Phelps, Dale
Subject: RE: SUPPORT Protocol

Thanks Dale. Could I be added to the mailing list. That will prevent duplication and hit or miss with forwarded mail. Thanks.

-----Original Message-----
From: Phelps, Dale
Sent: Tuesday, March 08, 2005 3:36 PM
To: Laroia, Nirupama; Reubens, Linda
Subject: FW: SUPPORT Protocol

Didn't see you on the list on my first skim, so here if fwd

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, March 08, 2005 3:33 PM
To: Guillet, Ronnie; Michael Cotten (cotte010@mc.duke.edu); Maynard Rasmussen (maynard.rasmussen@sharp.com); Kurt Schibler (Kurt Schibler [kurt.schibler@cchmc.org]); Krisa VanMeurs (VanMeurs, Krisa); D'Angio, Carl; Brenda Morris (Brenda.H.Morris@uth.tmc.edu); Av Fanaroff (aaf2@po.cwru.edu); Abbot Laptook (alaptook@WIHRI.org); Abhik Das; Brenda Poindexter; Carlo Waldemar (E-mail); Charles Rosenfeld; Phelps, Dale; Ed Donovan; Ehrenkranz Richard (E-mail); Jobe Alan (E-mail); Lemons Jim (E-mail); Michael O'Shea; Michelle Walsh; Neil Finer; Oh William (E-

mail); Poole Kenneth (E-mail); Ronald GOldberg; Shahnaz Duara; Shankaran Seetha (E-mail); Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); Walid Salhab (Walid Salhab); Anna Dusick (adusick@iupui.edu); Betty Vohr ('Betty_Vohr@brown.edu'); Charlie Bauer (cbauer@peds.med.miami.edu); Dee WIlson [redacted] Myers, Gary; Ira Adams-Chapman; Jean Steichen (steichjj@email.uc.edu); Myriam Peralta (mperalta@peds.uab.edu); Ricki Goldstein (golds005@mc.duke.edu); Robert Dillard; Roy Heyne; Yvette Johnson (yjohnson@med.wayne.edu); Yvonne Vaucher (Yvonne Vaucher); Angelita Hensman; Becky bara; Bethany Ball; Cathy Grisby; Ellen Hale; Georgia McDavid; Kathy Auten; Reubens, Linda; Lucy Miller; Monica Collins; Nancy Miller; Nancy Newman; Nancy Peters; Pat Gettner (pat.gettner@yale.edu); Ruth Everett; Wade RIch
Cc: Petrie, Carolyn; bkh@rti.org
Subject: SUPPORT Protocol

Hi,
To clarify in the SUPPORT Trial -
For the control group - these infants are supposed to receive surfactant in the first 60 minutes of life. For delivery room management, one should follow the **general guidelines of neonatal resuscitation**. Once stabilized, they can be intubated (if not part of their resuscitation) and given surfactant by 60 minutes of age.

Let me know if there are questions

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Neil Finer
To:	Higgins, Rosemary (NIH/NICHD) [E]
Subject:	RE: SUPPORT oximetry ranges
Date:	Tuesday, March 08, 2005 3:17:40 PM

Thanks Rose
Neil

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, March 08, 2005 11:38 AM
To: poo@rti.org; adas@rti.org
Cc: 'Neil Finer '
Subject: SUPPORT oximetry ranges

Ken and Abhik
For compliance for the SUPPORT Trial we will need percent of time 88-92% and percent of time 85% to 95% for compliance monitoring. How do you suggest we do this for each site and over the network? The oximeters are to be downloaded on a monthly basis.
Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
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MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Poole, W. Kenneth
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT oximetry ranges
Date: Tuesday, March 08, 2005 3:12:01 PM

We can do this by site and overall.

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, March 08, 2005 2:38 PM
To: Poole, W. Kenneth; Das, Abhik
Cc: 'Neil Finer '
Subject: SUPPORT oximetry ranges

Ken and Abhik
For compliance for the SUPPORT Trial we will need percent of time 88-92% and percent of time 85% to 95% for compliance monitoring. How do you suggest we do this for each site and over the network? The oximeters are to be downloaded on a monthly basis.
Thanks
Rose

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Program Scientist for the Neonatal Research Network
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Center for Developmental Biology and Perinatal Medicine
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MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Richard A. Ehrenkranz
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT DOCUMENT FOR DSMC
Date: Saturday, March 05, 2005 1:31:48 PM

Rose:
I think that the information provided by this document is very reasonable.
Richard

At 04:33 PM 3/3/2005 -0500, you wrote:

>HI,
>
>The SUPPORT Subcommittee has finalized a document for assistance with
>potential trial complications for use by the DSMC. Your comments are
>welcome. Note that ranges of complications are included for reference or
>guidance for the NICHD NRN population. Please comment by March 14.
>
>Thanks
>
>Rose
>
>
>
>Rosemary D. Higgins, M.D.
>
>Program Scientist for the Neonatal Research Network
>
>Pregnancy and Perinatology Branch
>
>Center for Developmental Biology and Perinatal Medicine
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>
>301-435-7909
>
>301-496-3790 (FAX)
>
><mailto:higginsr@mail.nih.gov>higginsr@mail.nih.gov
>
>

Richard A. Ehrenkranz, MD
Department of Pediatrics

Yale University School of Medicine
333 Cedar Street
PO Box 208064
New Haven, CT 06520-8064
tele: 203-688-2320
fax: 203-688-5426

From: David Stevenson
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT DOCUMENT FOR DSMC
Date: Thursday, March 03, 2005 5:29:59 PM

Rose,

Looks reasonable to me.
Thanks,
David

At 01:33 PM 3/3/2005, you wrote:

> HI,
> The SUPPORT Subcommittee has finalized a document for assistance with potential trial complications for use by the DSMC. Your comments are welcome. Note that ranges of complications are included for reference or guidance for the NICHD NRN population. Please comment by March 14.
> Thanks
> Rose
>
> Rosemary D. Higgins, M.D.
> Program Scientist for the Neonatal Research Network
> Pregnancy and Perinatology Branch
> Center for Developmental Biology and Perinatal Medicine
> NICHD, NIH
> 6100 Executive Blvd., Room 4B03B
> MSC 7510
> Bethesda, MD 20892
> (For overnight delivery, use Rockville, MD 20852)
> 301-435-7909
> 301-496-3790 (FAX)
> higginsr@mail.nih.gov

From:	Duara, Shahnaz
To:	Higgins, Rosemary (NIH/NICHD) [E]; Wally Carlo, M.D.; wrich@ucsd.edu; Neil Finer; Everett, Ruth; edward.donovan@chmcc.org; Duara, Shahnaz; Michele Walsh; Poole, W. Kenneth; Das, Abhik; Jobe Alan (E-mail)
Cc:	Petrie, Carolyn; bkh@rti.org
Subject:	RE: SUPPORT DSMC monitoring
Date:	Wednesday, March 02, 2005 6:32:29 PM

Hi Rose,
Looks fine
Shahnaz

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, March 02, 2005 12:52 PM
To: Wally Carlo, M.D.; wrich@ucsd.edu; Neil Finer; Everett, Ruth; edward.donovan@chmcc.org; Duara, Shahnaz; Michele Walsh; Poole, W. Kenneth; Das, Abhik; Jobe Alan (E-mail)
Cc: Petrie, Carolyn; bkh@rti.org
Subject: SUPPORT DSMC monitoring

Hi,
Attached is a revised document for DSMC monitoring for SUPPORT. We have deleted the 2X SD and 2X SE but have maintained the SD in the table (would include 67% of the population). Please send me final comments by tomorrow afternoon (March 3), so that I can send it to the steering committee on Friday for input and suggestions.
Thanks for all of the thought and effort that has gone into this!!
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
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6100 Executive Blvd., Room 4B03B
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Bethesda, MD 20892
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301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Edward Donovan
To:	mcw3@case.edu; ALAN JOBE; Higgins, Rosemary (NIH/NICHD) [E]; REverett@med.miami.edu; sduara@miami.edu; WCarlo@peds.uab.edu; adas@rti.org; poo@rti.org; nfiner@ucsd.edu; wrich@ucsd.edu
Cc:	bkh@rti.org; petrie@rti.org
Subject:	Re: SUPPORT DSMC monitoring
Date:	Wednesday, March 02, 2005 4:37:16 PM

this looks fine to me

Edward F. Donovan, M.D.
Director
Child Policy Research Center
Children's Hospital Medical Center
3333 Burnet Avenue, ML 7014
Cincinnati, OH 45229-3039
Phone 513-636-0182
Fax 513-636-0171
www.cprc-chmc.uc.edu

>>> "Higgins, Rosemary (NIH/NICHD)" <higginsr@mail.nih.gov> 03/02/2005 12:52:03 PM >>>
Hi,
Attached is a revised document for DSMC monitoring for SUPPORT. We have deleted the 2X SD and 2X SE but have maintained the SD in the table (would include 67% of the population). Please send me final comments by tomorrow afternoon (March 3), so that I can send it to the steering committee on Friday for input and suggestions.
Thanks for all of the thought and effort that has gone into this!!
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
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301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Neil Finer
To:	"Krisa Van Meurs"
Cc:	"Avroy A. Fanaroff, M.D."; "Betty Hastings"; "Ed Donovan"; Higgins, Rosemary (NIH/NICHD) [E]; "Ken Poole"; "Michele"; "Neil Finer"; "Shahnaz Duara"; "Wade Rich"
Subject:	RE: SUPPORT
Date:	Wednesday, March 02, 2005 3:24:14 PM

Hi Krisa
How are you?
We have indicated that the target CPAP should be 5 cm H2O plus minus your usual variation.
CPAP with a rate can be used for infants who have been extubated - that is - it cannot be used for the initial management of a CPAP baby who was never intubated. Once extubated, nasal breaths are allowed for any child in any arm.
Be well
Neil

-----Original Message-----
From: Krisa Van Meurs [mailto:vanmeurs@stanford.edu]
Sent: Wednesday, March 02, 2005 11:16 AM
To: nfiner@ucsd.edu
Cc: mbball@stanford.edu Personal Email
Subject: SUPPORT

Neil,

A few (only 2) questions regarding SUPPORT:

In the CPAP arm can we choose the CPAP pressure or is there a top/bottom limit?

Can CPAP with a rate be used at any point?

We should be starting up soon. A few more in-services to complete.

Thanks,

Krisa

From: Higgins, Rosemary (NIH/NICHD)
To: "nfiner@ucsd.edu"
Subject: Fw: SUPPORT_IRB-Oximeter Status. doc.doc
Date: Monday, February 28, 2005 1:01:06 PM
Attachments: SUPPORT_IRB-Oximeter Status. doc.doc

Irb approvals
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Hastings, Betty J. <bkh@rti.org>
To: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
Sent: Mon Feb 28 10:19:07 2005
Subject: SUPPORT_IRB-Oximeter Status. doc.doc

Rose,
I think this is pretty up-to-date.

<<SUPPORT_IRB-Oximeter Status. doc.doc>>

SUPPORT TRIAL
IRB/Oximeter Status-

January 6, 2005

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Duke	Pending IRB Approval	**Yes**	
Wake Forest	Pending IRB Approval	**Yes**	**Yes**
Rochester	Received IRB Approval	**Yes**	**Yes**
UCSD	Received IRB Approval	**Yes**	**Yes**

From: Hastings, Betty J.
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT_IRB-Oximeter Status. doc.doc
Date: Monday, February 28, 2005 10:19:10 AM
Attachments: SUPPORT_IRB-Oximeter Status. doc.doc

Rose,
I think this is pretty up-to-date.

<<SUPPORT_IRB-Oximeter Status. doc.doc>>

SUPPORT TRIAL
IRB/Oximeter Status-

January 6, 2005

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Indiana	Provisional Approval	Yes	Yes
Yale	Received IRB Approval	Yes	Yes
Brown	Received IRB Approval	Yes	Yes
Stanford	Waiting for IRB Approval	No	
UAB	Received IRB Approval	Yes	No
UT-Houston	Received IRB Approval	Yes	Yes
Duke	Pending IRB Approval	Yes	
Wake Forest	Pending IRB Approval	Yes	Yes
Rochester	Received IRB Approval	Yes	Yes
UCSD	Received IRB Approval	Yes	Yes

From: Wade Rich
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT protocol
Date: Tuesday, February 15, 2005 3:53:20 PM

To my knowledge no. I will check with Joe Kiani, pres.
Wade

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, February 15, 2005 12:46 PM
To: Neil Finer (nfiner@ucsd.edu); Wade RIch
Cc: Everett, Ruth; Shahnaz Duara (sduara@miami.edu)
Subject: FW: SUPPORT protocol

Hi Wade and Neil,
Did Massimo get any documentation (email, letter) from FDA regarding the use of the approved oximeter for use in research so we can assist on the IRB issue.
Thanks
Rose

-----Original Message-----
From: Everett, Ruth [mailto:REverett@med.miami.edu]
Sent: Tuesday, February 15, 2005 3:42 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: FW: SUPPORT protocol

This is the second letter, after I sent the letter form Masimo to her.

From: Cindy Gates [mailto:Cgates@wirb.com]
Sent: Fri 2/11/2005 4:27 PM
To: Everett, Ruth
Cc: sduara@peds.med.maimi.edu; Wayne Roice; Greg Lim
Subject: RE: SUPPORT protocol

Dear Ms. Everett:

Thank you for this information. The FDA has specific requirements that must be met before devices can be cleared for marketing. The information you submitted stated that the FDA number for this model is K992340. However, the approval information in the FDA files seems to be for the unaltered model rather than for the model that will be used in this study. Is there any information that the sponsor can provide indicating that this altered device is cleared by the FDA for use in this research?

Thanks,
Cindy
-----Original Message-----
From: Everett, Ruth [mailto:REverett@med.miami.edu]
Sent: Friday, February 11, 2005 9:10 AM

To: Cindy Gates
Cc: sduara@peds.med.maimi.edu
Subject: SUPPORT protocol

Attach is the letter from the Masimo company regarding the changes made to the equipment, the modifications does not increase the risk of the infants since all of the monitoring will be done in the ranges currently used for premature infants 85%-95%. As stated in the study if the baby goes out of this range the monitors will respond as usual to alert the staff to make decisions as part of the standard protocols used in many intensive care units throughout the United States and Europe. The objective of this study is to make the current usuage range 85% to 95% much tighter, so the currently used range will be limited to a 5% difference rather than a 10% difference from the low level range to the high level range.

From: Higgins, Rosemary (NIH/NICHD)
To: Neil Finer
Cc: wrich@ucsd.edu
Subject: pulse oximeters
Date: Friday, February 25, 2005 3:47:00 PM

Hi Neil
As we discussed, I received a call from Dr. Owen Reese, Western IRB, and reviewer of the University of Miami protocol for the NICHD Neonatal Research Network's SUPPORT Trial. He would like a letter of exemption from the FDA for the altered pulse oximeters prior to study approval for the Miami site. The Masimo pulse oximeters are FDA approved. The study oximeters have a software modification between 85-95% saturation range. The alarms are set to sound for high (> 95%) and low (<85%) saturations. These are custom devices specifically for the study. The referenced FDA section is: Title 21 – Food and Drugs, Chapter 1, FDA, DHHS, Subchapter H – Medical Devices, Part 812 - Investigational Device Exemptions (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.2).

It appears that the oximeters for the study are "custom devices" with a modification of the software in the desired ranges as dictated by the protocol which appear to fall under a category of exemption. Please contact Masimo so they can contact the appropriate FDA individual(s) in order to obtain the needed exemption for the University of Miami site.

Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT NEJM forms received
Date: Wednesday, February 17, 2010 1:33:24 PM
Attachments: SUPPORT NEJM forms received.xls

Here the list of what I have so far.

NEJM Forms received

	Copyright Transfer	ICMJE Disclosure	
The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets in Extremely Premature Infants (09-11781)			
Abbot R. Laptook, MD	X	X	
Abhik Das, PhD			
Anthony J. Piazza, MD	X	X	
Beena G. Sood, MD MS			
Bradley A. Yoder, MD		X	Copyright sent, but not signed
Brenda B. Poindexter, MD MS			
Brenda H. Morris, MD			
C. Michael Cotten, MD MHS	X	X	
Dale L. Phelps, MD	X	X	
Edward F. Bell, MD	X	X	
Ivan D. Frantz III, MD			
Krisa P. Van Meurs, MD	X		
Kristi L. Watterberg, MD		X	
Kurt Schibler, MD	X	X	
Marie Gantz, PhD			
Michele C. Walsh, MD MS			
Nancy S. Newman, RN	X	X	
Neil N. Finer, MD		X	
Nirupama Laroia, MD			
Pablo J. Sánchez, MD	X	X	
Richard A. Ehrenkranz, MD	X	X	
Roger G. Faix, MD	X	X	
Rosemary D. Higgins, MD			
Shahnaz Duara, MD	X	X	
T. Michael O'Shea, MD, MPH			
Vivek Narendran, MD MRCP	X	X	
W. Kenneth Poole, PhD			
Wade Rich, RRT			
Waldemar A. Carlo, MD	X	X	
Early CPAP versus Surfactant in Very Preterm Infants: The SUPPORT Trial (09-11783)			
Abbot R. Laptook, MD	X	X	
Abhik Das, PhD			
Beena Sood. MD, MS			
Bradley A. Yoder, MD		X	Copyright sent, but not signed
Brenda B. Poindexter, MD MS			
Brenda H. Morris, MD			
C. Michael Cotten, MD MHS	X	X	
Edward Donovan			
Edward F. Bell, MD	X	X	
Ivan D. Frantz III, MD			
Krisa P, Van Meurs, MD	X		

Kristi L. Watterberg, MD		X
Kurt Schibler		
Marie Gantz, PhD		
Michele C. Walsh, MD MS		
Namasivayam Ambalavanan, MD		X
Nancy Newman, RN	X	X
Neil N. Finer, MD		X
Nirupama Laroia, MD		
Pablo J. Sánchez, MD	X	X
Roger G. Faix, MD	X	X
Rosemary D. Higgins, MD		
Shahnaz Duara, MD	X	X
Susie Buchter, MD	X	X
T. Michael O'Shea, MD, MPH		
Vineet Bhandari, MD, DM	X	X
W. Kenneth Poole, PhD		
Wade Rich, RRT, CCRC		
Waldemar A. Carlo, MD	X	X

From: Higgins, Rosemary (NIH/NICHD)
To: wrich@ucsd.edu
Subject: RE: SUPPORT protocol
Date: Tuesday, February 15, 2005 3:54:00 PM

We are testing oximetry ranges, not the oximeter per se.
Thanks
Rose

-----Original Message-----
From: Wade Rich [mailto:wrich@ucsd.edu]
Sent: Tuesday, February 15, 2005 3:53 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE: SUPPORT protocol

To my knowledge no. I will check with Joe Kiani, pres.
Wade

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, February 15, 2005 12:46 PM
To: Neil Finer (nfiner@ucsd.edu); Wade RIch
Cc: Everett, Ruth; Shahnaz Duara (sduara@miami.edu)
Subject: FW: SUPPORT protocol

Hi Wade and Neil,
Did Massimo get any documentation (email, letter) from FDA regarding the use of the approved oximeter for use in research so we can assist on the IRB issue.
Thanks
Rose

-----Original Message-----
From: Everett, Ruth [mailto:REverett@med.miami.edu]
Sent: Tuesday, February 15, 2005 3:42 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: FW: SUPPORT protocol

This is the second letter, after I sent the letter form Masimo to her.

From: Cindy Gates [mailto:Cgates@wirb.com]
Sent: Fri 2/11/2005 4:27 PM
To: Everett, Ruth
Cc: sduara@peds.med.maimi.edu; Wayne Roice; Greg Lim
Subject: RE: SUPPORT protocol

Dear Ms. Everett:

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the approval information in the FDA files seems to be for the unaltered model rather than for the model that will be used in this study. Is there any information that the sponsor can provide indicating that this altered device is cleared by the FDA for use in this research?

Thanks,
Cindy
-----Original Message-----
From: Everett, Ruth [mailto:REverett@med.miami.edu]
Sent: Friday, February 11, 2005 9:10 AM
To: Cindy Gates
Cc: sduara@peds.med.maimi.edu
Subject: SUPPORT protocol

Attach is the letter from the Masimo company regarding the changes made to the equipment, the modifications does not increase the risk of the infants since all of the monitoring will be done in the ranges currently used for premature infants 85%-95%. As stated in the study if the baby goes out of this range the monitors will respond as usual to alert the staff to make decisions as part of the standard protocols used in many intensive care units throughout the United States and Europe. The objective of this study is to make the current usuage range 85% to 95% much tighter, so the currently used range will be limited to a 5% difference rather than a 10% difference from the low level range to the high level range.

From: Higgins, Rosemary (NIH/NICHD)
To: Everett, Ruth
Cc: nfiner@ucsd.edu; Wade RIch
Subject: RE: FDA/SUPPORT/WIRB
Date: Tuesday, February 15, 2005 3:29:00 PM
Attachments: Safety Letter Masimo7_01.pdf

Hi Ruth,
I am attaching a letter - is this the one you already provided?
Thanks
Rose

-----Original Message-----
From: Everett, Ruth [mailto:REverett@med.miami.edu]
Sent: Tuesday, February 15, 2005 3:26 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: FDA/SUPPORT/WIRB

Hello Dr. Higgins,

Currently , the University of Miami has decided to handle the very large volume of clinical protocols by contracting with an external IRB, called WIRB (Western IRB) for all new protocols. Therefore, the SUPPORT protocol was transferred to this new IRB, and currently it is being reviewed by their staff to make sure all of the necessary paper work is there before it goes to committee. As part of the protocol application process, we had to state who our sponsoring entity was, and give a contact name and number - hence, we have provided them with your information, and you may hear from them directly from time to time.

As part of the initial review process for SUPPORT, one of the internal reviewers noted that we plan to use a medical device that had been FDA approved but altered after approval, and she wanted a letter from the FDA stating that this device has been exempt from further review . I forwarded her the letter we received from Masimo through Wade to submit with our pilot protocol but she still insists on an FDA letter. I am aware of the effort the Network has gone through regarding this part of the study, and I know that if this was our internal IRB reviewing the protocol this would not be a problem. In an effort to clarify the matter I have already contacted Dr Sayer from Masimo regarding this issue and she stated that this device alteration was not submitted to the FDA again for an exempt review because they do not plan to market the device, and it was only altered for this research at the request of the P.I. (Neil Finer) and NICHD. Therefore, I am requesting your advice at this time to see what steps we should take next , and if you could possibly give us a cover letter stating that the agency is satisfied with the minor changes made by Masimo after its monitor was FDA approved, since safety issues are satisfied by the fact that the real values will be used for critical alarms, triggered by values below 85% and above 95% oxygen saturation. I will forward you the e-mail that I received from the WIRB and I will attach the letter we received from Wade (the letter was scanned so it will take a few minutes to appear on your screen).

Thanks

Ruth

(for Dr. Duara)

MASIMO®
40 Parker
Irvine, CA 92618
Tel: 949-297-7000
Fax: 949-297-7001

June 30, 2004

To Whom It May Concern:

This letter is to inform the reader about the modifications performed on the Masimo SET Radical Pulse Oximeter to be used in an NICHD Neonatal Network trial entitled " The Surfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants (SUPPORT) Trial". This study, lead by Dr. Neil Finer (UCSD) will evaluate two oxygenation ranges on infants immediately after birth and during their hospital stay. In order to mask the oxygenation ranges from the clinicians in the study, these researchers have asked Masimo Corporation to slightly alter the reading displayed on the Masimo Radical pulse oximeter between the 84% to 96% range. One group of pulse oximeters will read approximately 3% higher than the actual number while the other group of pulse oximeters will read approximately 3% low in this range. The researchers have required that the actual number be displayed below 85% and above 95%. The alarm will sound at 84% and 96%.

Masimo has performed validation tests on this software and found it works per the researchers' request. In addition, all alarms and error messages are still intact and active.

Masimo was willing to mask the pulse oximeters per the researchers' instructions since the intended ranges used in the study are in common use in Neonatal Intensive Care Units (NICUs) across the country. This study is aimed at refining the guidelines as to the best oxygen management range for neonates.

Respectfully,

Michael T. Petterson
Sr. Director, Clinical Research
Masimo Corporation

James Cronin
Vice President, Regulatory Affairs
Masimo Corporation
Irvine, CA

From: Higgins, Rosemary (NIH/NICHD)
To: Petrie, Carolyn
Cc: Wade RIch
Subject: RE: FDA Part 15 Hearing on Reporting Adverse Events to IRBs
Date: Monday, February 14, 2005 9:29:00 AM

This pertains to trials with an IND (investigational new drug) or IDE (investigational new device). Neither is the case in the SUPPORT Trial. We will continue on as planned. I don't think we need to send this out.
Thanks
Rose

From: Petrie, Carolyn [mailto:petrie@rti.org]
Sent: Monday, February 14, 2005 9:23 AM
To: Higgins, Rosemary (NIH/NICHD)
Subject: FW: FDA Part 15 Hearing on Reporting Adverse Events to IRBs

Do you foresee any problems with me forwarding this info?

-----Original Message-----
From: Wade Rich [mailto:wrich@ucsd.edu]
Sent: Thursday, February 10, 2005 10:24 AM
To: Petrie, Carolyn
Subject: FW: FDA Part 15 Hearing on Reporting Adverse Events to IRBs

Carolyn,
Is it appropriate to pass this on to the coordinators and investigators? It is certainly something that effects the network
on a daily basis.
Wade

From: Office for Human Research Protections (OHRP) [mailto:OHRP-L@LIST.NIH.GOV] **On Behalf Of** El-Hinnawy, Patricia
Sent: Thursday, February 10, 2005 6:46 AM
To: OHRP-L@LIST.NIH.GOV
Subject: FDA Part 15 Hearing on Reporting Adverse Events to IRBs

> On March 21, 2005, the Food and Drug Administration will hold a Part 15 public hearing on reporting of adverse events to institutional review boards. For more information regarding this hearing, including instructions for participating in the hearing and submitting comments to the FDA, please see the Federal Register notice posted at http://www.fda.gov/OHRMS/DOCKETS/98fr/05-2300.pdf.

From: Higgins, Rosemary (NIH/NICHD)
To: Das, Abhik
Subject: RE: DSMC stuff
Date: Wednesday, February 09, 2005 4:05:00 PM

Great!!

From: Das, Abhik [mailto:adas@rti.org]
Sent: Wednesday, February 09, 2005 3:58 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: DSMC stuff

Rose:

I did verify that the babies we included in this analysis for SUPPORT were those born on or after Jan 1, 2002 who have reached status (which triggers an NG03) as of 1/20/05.

Thanks
Abhik

Abhik Das, Ph.D.
Research Statistician

RTI International
6110 Executive Blvd., Suite 420
Rockville, MD 20852-3903
e-mail: adas@rti.org
Phone: 301-770-8214
Fax: 301-230-4646

From:	Higgins, Rosemary (NIH/NICHD)
To:	Pearson, Gail (NIH/NHLBI) [E]
Subject:	forms etc
Date:	Wednesday, February 09, 2005 1:37:00 PM
Attachments:	Support protocol.pdf SUPP06.pdf SUPP08.pdf PHT07.pdf PN08.pdf

---

Hi Gail,
Good to talk with you. I have attached the SUPPORT protocol and a few forms you may find helpful – violations/deviations and adverse events. Please let me know if you need more help/forms/etc.

Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

Protocol for the NICHD Neonatal Research Network

The SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants

The SUPPORT Trial

Final

August 28, 2004
Revised September 16, 2004

1.1 Statement of Problem

At the present time, there is no recommendation or standard teaching regarding the early use of CPAP/PEEP during resuscitation and continuing after NICU admission for the extremely low birth weight (ELBW) infant. However, a number of studies, mostly retrospective in nature, have suggested that the use of early CPAP may be associated with improved outcomes, including a decreased need for mechanical ventilation, a decreased need for surfactant therapy, and a decrease in oxygen supplementation and/or death at 28 days after birth and at 36 weeks post menstrual age. There has not been a prospective study which has randomized ELBW infants to CPAP/PEEP beginning in the delivery room, and continuing in the NICU and a permissive ventilation strategy if intubation is required and compared their outcomes to infants treated with prophylactic or early natural surfactant, interventions with known efficacy in reducing mortality, severity of disease and the incidence of chronic lung disease (CLD).

Retinopathy of prematurity (ROP) remains a significant cause of morbidity among ELBW infants and its occurrence is inversely proportional to gestational age and duration of oxygen exposure. It is known that ROP is increased by the prolonged use of supplemental oxygen from observations published in the 1950s, and but early trials were unable to pinpoint the actual level of arterial PaO_2 which was the threshold for triggering the pathophysiology of this disorder.[1] However, there have been a very few prospective studies evaluating the benefit of higher versus lower levels of oxygenation in infants, especially for ELBW infants, none of which were performed during the acute illness. While retrospective cohort studies have suggested that the use of lower SpO2 ranges and adherence to strict nursery policies may result in a lower incidence of severe ROP, there is no current agreement on the accepted SpO2 ranges for managing the ELBW infant from birth.

1.2 Background

Positive End Expiratory Pressure (PEEP) has been shown to be of benefit in maintaining functional residual capacity (FRC). Although no formal recommendation has been made to date about maintaining PEEP in the delivery room setting, continuous positive airway pressure appears beneficial during cardiopulmonary resuscitation[2]. Gregory et al in 1971 first demonstrated that the use of CPAP started at approximately 5.9hours ($\pm$12.4hrs) for their infants < 1500 gm at birth, improved oxygenation[3] in newborn infants with respiratory distress; these observations were followed by prospective studies that demonstrated improved survival in premature infants treated with early CPAP[4]. Premature infants who do not achieve a FRC are more likely to develop hyaline membrane disease (HMD) requiring mechanical ventilation[5]. CPAP may prevent the excessive consumption of surfactant in newborn infants with limited surfactant production.[6] A review of prospective studies evaluating early (not delivery room) CPAP in the pre-surfactant, pre-antenatal steroid era suggested that early CPAP may improve survival in infants greater than 1500 gm.[7]

Similarly, there is no definite recommendation or standard teaching regarding the level of oxygenation that should be maintained in ELBW infants. Oxygen supplementation has to be used liberally as ELBW infants frequently have desaturation episodes and thus wide saturation ranges are tolerated clinically. However, oxygen toxicity can result in increased risk for CLD, retinopathy of prematurity (ROP) and other disorders. Alternatively, oxygen restriction may impair neurodevelopment. The pulse oximeter is a newer technology that can be used to improve the control of oxygenation levels. There is great potential benefit to determining the oxygenation levels that prevents ROP and CLD but does not result in neurodevelopmental impairment with a randomized controlled trial of levels of oxygen saturations on the high and low side of the currently utilized levels.

While prevention of hyperoxia may decrease the risk for ROP and CLD, efforts to maintain lower oxygenation levels may result in an increase in periods of hypoxemia because of the marked variability in oxygen in ELBW infants. Thus, it is necessary to determine if lower oxygenation levels that may prevent ROP and CLD are deleterious for brain development and result in impaired neurologic outcome.

1.3 Animal Studies

Nilsson et al demonstrated that the use of 5 cm H_2O PEEP in the initial ventilation of premature rabbit pups resulted in increased lung-thorax compliance, and reduced the extent of bronchiolar epithelial lesions seen with mechanical ventilation[8]. The use of early PEEP starting at delivery, improves the response to surfactant, improves lung mechanics increases surfactant pools, and reduces lung injury.[9,10]

More recently studies by Jobe et al have demonstrated that premature lambs treated with CPAP alone at birth had significantly decreased neutrophils and hydrogen peroxide in their alveolar wash when compared with animals who were ventilated from birth.[11]

1.4 Human Experience: Ventilatory Support

CPAP was introduced by Gregory et al in 1970 and was shown to improve gas exchange and outcomes in preterm infants with respiratory distress.[12] A subsequent review of CPAP for respiratory distress concluded that "In preterm infants with RDS the application of CDP either as CPAP or CNP is associated with benefits in terms of reduced respiratory failure and reduced mortality. CDP is associated with an increased rate of pneumothorax. The applicability of these results to current practice is difficult to assess, given the intensive care setting of the 1970s when four out of five of these trials were done."[13]

There is now a body of information from Europe that provides further evidence that early CPAP can reduce the need for intubation in a significant number of VLBW infants. Jonsson et al treated VLBW infants from 1988 to 1993 that required > 30% oxygen with nasal CPAP usually within 30 minutes of delivery[14]. From 1991 onward, infants with severe distress or apnea were intubated for a $PaCO_2$ greater than 60 mmHg, and were given surfactant. Twenty-five percent of all infants required only supplemental oxygen and 24% of all infants were ventilated from birth. Fifty-one percent were treated with nasal CPAP, with one-third of these subsequently requiring ventilation. Almost all infants < 24 weeks required ventilation suggesting that this group may require a different approach. Gittermann et al reported that the use of early CPAP for infants < 1500gm (VLBW) significantly reduced the frequency of intubation, reduced mortality ($p=0.038$), and shortened the duration of intubation and length of stay[15]. In this study the CPAP was applied as soon a signs of respiratory distress occurred (usually within 15 minutes of birth). Poets et al[16] in a report of 2001 VLBW infants (500 to 1499 g) born from 1992 to 1994 reported that there was an increase in the proportion of patients not intubated and mechanically ventilated from 7% to 14% in infants <1000 g and from 28% to 44% in those $\geq$1000 g ($P < 0.02$ and <0.01, respectively). The decrease in intubation was not associated with a significant increase in adverse outcome such as death, intraventricular hemorrhage, periventricular leukomalacia, or BPD. The proportion of infants <1000 g that survived without BPD increased from 38% in 1992 to 48% in 1994; $p < .05$, and the proportion of infants ≥1000 g in whom BPD developed decreased from 14% to 9%; $p < .05$. None of these observations was from a prospective controlled trial, and in none was there a contemporaneous control group who did not receive early CPAP.

The first prospective trial comparing prophylactic CPAP, started at birth, with conventional management was that of Han et al. They compared the use of nasal CPAP given by nasopharyngeal tube with conventional management in 82 infants, 32 weeks gestational age at birth, and in this study it would appear that CPAP was begun in the DR, but may have been delayed for up to 2 hours.[17] No infants in this trial received surfactant, and no mothers were treated with antenatal steroid. There was no advantage observed with the use of early CPAP, and oxygenation was worse in the early CPAP treated infants. The reviewers of the use of prophylactic CPAP in the Cochrane library concluded that "A multicenter randomized controlled trial comparing prophylactic nasal CPAP with "standard" methods of treatment is needed to clarify its clinical role."[18]

In the post surfactant era, Verder et al conducted the first prospective evaluation of early CPAP (not necessarily delivery room CPAP) and short-term intubation for surfactant administration in a multicenter collaborative trial conducted from September 1991 to October 1992.[19] The primary hypothesis was that the use of early CPAP and brief intubation for surfactant in infants meeting pre-established criteria would reduce the percentage of infants requiring mechanical ventilation from 80% to 40%. Infants randomized to surfactant [Curosurf®] received 200 mg/kg, (2.5 ml/kg) following intubation, with manual ventilation for 2-5 minutes and were then extubated if stable. This study was stopped after an interim analysis demonstrated a significant benefit for the surfactant treated infants. Thirty-three of the 35 infants randomized to early surfactant were extubated after such treatment, and 13 required reintubation at a median of nine hours after surfactant treatment, compared with 28 of 33 control infants who were intubated a median of three hours after randomization, (p=0.003). The overall duration of ventilation in both groups was 2.5 days; there were no other differences between the groups. Verder et al performed a second multicenter prospective trial from April 1995 to January 1997 and enrolled infants <30 weeks with similar criteria to the previous trial, apart from an entry a/A ratio of .35 to .22, which decreased over 30 minutes, which was less stringent, allowing infants to be treated at lesser degrees of oxygen requirement, than their first study. These infants were initially all treated with CPAP and were enrolled up to 72 hours of age (median 4.1 hours, range 0.3 to 40.1hrs).This trial was also stopped after an interim analysis demonstrated a statistically significant reduction in the need for ventilation or death within seven days from 63% in the late-treated infants to 21% in early-treated infants. The median duration of ventilation in both trials was 2.5 days[20]. This study was not a prospective evaluation of early CPAP because CPAP was initiated in all infants at variable ages, and they did not evaluate infants of less than 25 weeks gestation.

Lindner et al recently reviewed their experience using a continuous prolonged (15 seconds duration) pressure controlled (20 to 25 cm H_2O) inflation of the lungs followed by continuous positive airway pressure (CPAP) of 4 to 6 cm H_2O for all ELBW infants immediately after delivery to establish a functional residual capacity (FRC) and to avoid intubation and ventilation[21]. The criteria for subsequent intubation were a $PaCO_2$ > 70 mmHg, an FiO_2 >.6 and respiratory distress with severe recurrent apnea. The rate of early intubation and mechanical ventilation in the delivery room decreased from 84% in 1994 to 40% in 1996. In 1996, 25% of the ELBW infants were never intubated (compared with 7% in 1994). There was no difference in mortality and overall there was less IVH > Grade 2 and BPD for the later cohort. No infant had an air leak upon admission to the NICU, suggesting that use of a prolonged inflation was well tolerated. Only 1 of 11 infants of 24 weeks gestation was able to avoid intubation in this study. Once again, there was no contemporaneous control group who did not receive delivery room CPAP. All of the above studies required high levels of $PaCO_2$ before initiating ventilation for this indication.

There is retrospective evidence suggesting a benefit for early CPAP in experiences from the USA. A survey of eight neonatology units in the USA in 1987 demonstrated that one unit, Columbia, had the lowest rate of CLD[22]. A more recent comparison of practices and outcomes between two neonatology units in Boston and the Babies and Children's Hospital unit (Columbia) evaluated VLBW infants born in 1991 to 1993.[23] This study revealed that 75% of infants at the Boston centers were initially treated with mechanical ventilation compared with 29% at Columbia, whereas initial CPAP was used in 63% of infants at Columbia vs. 11% at the Boston centers. Columbia also used less surfactant, 10% versus 45%, (all $p<0.001$). In addition the rates of CLD were significantly lower at Columbia compared to the other two centers (4% vs. 22%).

de Klerk and de Klerk recently published a five-year retrospective review of the outcome of 1 to 1.5 kg infants (n-116) treated with early CPAP vs. usual care (delayed CPAP)[24]. During 1996 -1998 infants were placed on CPAP within 10 minutes of admission (they did not describe the use of delivery room CPAP). Early CPAP beginning following admission to the neonatal unit decreased endotracheal intubation from 65 to 14%, $p<0.001$ and surfactant use (40 to 12%, $p<0.001$). Ventilator days were reduced from a median of 6 to 2 days ($p<0.01$) and oxygen supplementation or death at 28 days from 16 to 3%, $p<0.05$. Oxygen supplementation or death at 36 weeks did not significantly decrease (11 to 3% $p=0.25$). Ventilation and surfactant use were very high during the delayed CPAP (control period) so it is unclear whether other improvements in care may have coincided with the change to early CPAP.

Sandri et al[25] have recently published preliminary data from a multicenter randomized controlled trial of 155 infants 28 to 31 weeks gestation randomized to CPAP within 30 minutes of birth or to CPAP if the FiO_2 requirement exceeded 40%. Use of surfactant (22 to 21%, NS) and ventilator support (10 to 9%, NS) was not reduced with early CPAP. However, this trial included relatively bigger infants and the control group received CPAP at relatively low FiO_2, minimizing the difference between the experimental and control groups. This study did not evaluate the use of delivery room CPAP.

More recently Thomson et al presented the results of a multicenter trial of 237 infants from 27 to 29 weeks gestation[26], who were randomized to prophylactic surfactant followed by nasal CPAP using the Infant Flow DriverTM, early nasal CPAP followed by rescue surfactant, early IPPV with prophylactic surfactant, and conventional management. They reported that CPAP was initiated by 6 hours of age in 76% and 79% of the first 2 treatment groups, and those infants in the CPAP and rescue surfactant and prophylactic surfactant followed by CPAP groups required the lowest duration of ventilation. There were no differences in the incidence of CLD or other neonatal complications. Neither of these studies instituted the use of CPAP in the delivery room.

In a preliminary feasibility trial we have evaluated the ability of 5 sites of the NICHD Network to initiate CPAP during resuscitation, and continue its use in the NICU. In that study 103 infants were randomized to receive resuscitation with either CPAP/PEEP or no CPAP/PEEP. All infants were treated with CPAP following NICU admission. During delivery room resuscitation, 46 infants were intubated, 27 of 55 CPAP infants and 19 of 48 control infants ($p=0.33$). All 23 week gestation infants were intubated in the delivery room, irrespective of treatment group, whereas only 3 of 22 (13%) infants of 27 weeks required such intubation. When evaluated by birth weight, all 3 infants of less than 500 gm birth weight and 6 of 11 infants between 500-600 gm birth weights were intubated in the delivery room. All remaining infants were admitted to the NICU and had CPAP initiated. For infants not intubated in the DR, 36 infants were subsequently intubated in the NICU by day 7, 16 CPAP infants and 20 Control infants, ($p=0.21$). Infants in the CPAP group developed criteria for intubation sooner than the Control infants, with means and medians of 10.5 and 1.8 hours versus 20.7 and 3.3 hours,

p=0.41. These infants met criteria established for this trial which included an FiO2 > .3 to maintain an SpO2 > 90% or a PaO2 > 45 torr, an arterial PaCO2 > 55-60 with a pH < 7.25. or apnea requiring bag and mask ventilation. CPAP infants were intubated at an average FiO2 = 0.5 compared to 0.4 for control infants.

The literature thus suggests that early CPAP may be of substantial benefit, although none of this information has been obtained from prospective randomized trials of CPAP randomly applied in the delivery room to a population of VLBW or ELBW infants, with an appropriate control group. The terms early CPAP in the above studies (apart from that of Lindner et al[15]) involved the application of CPAP shortly following birth, not immediately after delivery. It is not surprising, therefore, that the recent revised NRP guidelines do not mention the use of CPAP/PEEP for neonatal resuscitation.[27] There is also some evidence that the level of CPAP needed may vary depending on the actual device utilized. Pandit et al and Courtney et al have demonstrated that variable flow CPAP was associated with a lower work of breathing and increased compliance at all levels of CPAP whereas constant flow nasal CPAP increased compliance only at 8 cm H2O.[28] In addition, variable flow CPAP devices were effective at recruiting lung volume at all tested CPAP levels.[29] A more recent trial compared the use of variable flow CPAP to conventional CPAP at extubation for 162 ELBW infants and reported no significant differences with either form of CPAP.[30] This study noted that 40% of ELBW infants failed extubation primarily because of apnea.

There are no studies in the surfactant and antenatal steroid era which have prospectively compared delivery room, CPAP with a more conventional approach, such as the use of prophylactic surfactant and conventional ventilation. The current available evidence demonstrates that prophylactic natural surfactant treatment significantly decreases mortality, air leak, and BPD in preterm infants.[31] Early surfactant, defined as surfactant at less than 2 hours of life is also of benefit and reduces air leaks, and mortality.[32] These reviewers noted that "early surfactant administration significantly reduces the risk of key clinical outcomes including pneumothorax, PIE, chronic lung disease, and neonatal mortality. Given the efficacy of prophylactic surfactant therapy (Soll 1999), this meta-analysis suggests that early selective surfactant administration to intubated infants with early signs of RDS may be part of a clinical spectrum of improved outcomes with earlier treatment". The most recent experience regarding early surfactant was presented by Horbar et al at the SPR in May, 2003. Their study which involved a cluster randomization in 57 NICUs of a practice to administer surfactant earlier compared with 57 control NICUs. They noted that infants at the intervention sites received their surfactant more often in the DR (54.7 vs 18.2%, p < 0.001) and earlier than the control sites (21 vs 78 minutes, p <0.001). There were no differences in mortality and pneumothoraces, the intervention centers had a lower rate of overall and severe IVH (28% vs 33%, p < 0.04, 10% vs 14%, p < 0.001) which were secondary outcomes of this trial.[33]

The most recent published study by Tooley and Dyke evaluated the use of prophylactic surfactant and early extubation to CPAP versus prophylactic surfactant and continuing management.[34] In this study 42 infants of 25 to 28(+6) wk of gestation were intubated at birth and given one dose of surfactant. They were then randomized within one hour of birth to either continue with conventional ventilation or to be extubated to nCPAP. They reported that 8 out of 21 (38%) babies randomized to nCPAP did not require subsequent re-ventilation. (Ventilation rates of 62% vs 100%, p = 0.0034). The smallest baby successfully extubated weighed 745 g. There were also significantly fewer infants intubated in the nCPAP group at 72 h of age (47% vs 81%, p = 0.025). There was no significant difference between the two groups in the number of babies that died, developed chronic lung disease or severe intraventricular hemorrhage. This study demonstrates that a significant number of very preterm babies with RDS can be extubated

to nCPAP after receiving one dose of surfactant. The current SUPPORT study will address this population, extended to 24 weeks, using a similar methodology for the infants of 24 to 27 6/7ths weeks who fail initial CPAP, with adequate power to determine if this approach is associated with significant benefits in terms of important short and longer term clinical outcomes.

Oxygen Saturation:

There is now an emerging body of information that suggests that many of the morbid conditions associated with extreme immaturity are potentiated by an excess of free-radicals occurring in infants who are intrinsically deficient in antioxidants such as superoxide dismutase, catalase, and glutathione peroxidase. During hypoxia, metabolic alterations prime hypoxic cells to produce free oxygen radicals when subsequently exposed to oxygen. Such reperfusion injury, in addition to increasing the production of free oxygen radicals, is associated with other metabolic changes which may produce long lasting harmful effects. Silvers et al reported that a low plasma antioxidant activity at birth in premature infants was an independent risk factor for mortality.[35] Pulmonary oxygen toxicity, through the generation of reactive oxygen/nitrogen species in excess-of antioxidant defenses, is believed to be a major contributor to the development of BPD.[363738] For example the preterm macrophage showed a significant increase in cytokine mRNA and protein after overnight incubation in 95% oxygen compared with cells from term animals. Only macrophages from premature animals had a significant increase in intracellular oxygen radical content, measured by 2', 7'-dichlorofluorescin analysis, after incubation in 95% oxygen. This enhanced inflammatory cytokine response to oxygen has been postulated to be a mechanism involved in the early development of chronic lung disease in premature infants.[39] Varsila et al noted that immaturity is the most important factor explaining free radical-mediated pulmonary protein oxidation in premature newborn infants and that oxidation of proteins is related to the development of chronic lung disease.[40]

There are a number of prospective randomized trials that have compared the use of room air with 100% oxygen for neonatal resuscitation, and these have reported Infants resuscitated with room air resumed spontaneous breathing faster and required less positive pressure ventilation than infants resuscitated with oxygen.[41 42] Vento et al also demonstrated that that infants resuscitated with oxygen demonstrated long lasting evidence of oxidative stress and activities of superoxide dismutase and catalase in erythrocytes that were 69% and 78% higher, respectively compared with control infants resuscitated with room air at 28 days of postnatal life.[43] A recent meta-analysis of room air vs 100% oxygen resuscitation comprising of 1,693 infants in five trials revealed decreased neonatal resuscitation in infants resuscitated with room air (6 vs 11%, $p<0.005$ or 0.57 (95% CI 0.40 – 0.81))[44]. While these studies described results of mostly term infants, some infants were premature and the premature infant is known to have decreased antioxidants which would increase their susceptibility to oxygen toxicity. In the only randomized prospective trial to evaluate room air compared with oxygen in preterm infants, Lundstrom et al resuscitated infants of less than 33 weeks gestation who were randomized to receive either 80% oxygen or room air and noted that 2 hours following delivery, the room air infants had a higher cerebral blood flow compared with oxygen resuscitated infants. (median (interquartile range)): 15.9 (13.6-21.9) v 12.2 (10.7-13.8) ml/100 g/minute).[45] They did not find any significant differences in short or long-term outcomes but did note that SpO2 was lower in the room air infants with values at 5 and 7 minutes of 75% and 80% compared with 92% and 94% in the 80% oxygen group ($p<0.001$). Current monitoring with pulse oximetry using limits of 95 to 96% will result in significant periods wherein the infants actual PaO2 may increase to very high levels, as there are rapid increases in PaO2 with very small increments in SpO2 at this plateau portion of the hemoglobin dissociation curve.

Tin et al retrospectively reviewed outcomes for infants admitted to various neonatal intensive care units in northern England from 1990 to 1994 and managed with lower (70-90%) or higher SpO2 ranges (88%-98%).[46] They reported that infants who were managed for at least the first 8 weeks of life with SpO2s from 88-98% developed retinopathy of prematurity severe enough to be treated with cryotherapy four times as often as infants managed with the lower SpO2 ranges. Infants managed with the lower SpO2 ranges did not have increased risk of mortality or neurodevelopmental impairment. Bancalari et al using transcutaneous oxygen monitoring were able to show that infants who received continuous monitoring had a similar incidence of ROP to infants who were monitored by intermittent sampling had similar incidences of ROP, however for subgroup of infants $\geq$ 1100gm, there was a decrease in the incidence of ROP.[47] The STOP-ROP trial randomized infants with already established pre-threshold retinopathy and an SpO2 less than 94% to two ranges of SpO2 (89% to 94% versus 96% to 99%), for at least 2 weeks and until both eyes were at study endpoints. The higher range of SpO2 was associated with a non-significant decrease in the progression of ROP, but was associated with a greater need for oxygen and more exacerbations of BPD.[48]

Chow et al reported their observations following the institution in 1993 of a detailed oxygen management policy that included strict guidelines in the practices of increasing and weaning of fraction of inspired oxygen (FIO2) and the monitoring of oxygen saturation parameters in the delivery room, during in-house transport of infants to the NICU, and throughout hospitalization.[49] The main objectives were to avoid hyperoxia and repeated episodes of hypoxia-hyperoxia in very low birth weight infants. Their approach was initiated at birth, and included the avoidance of repeated increases and decreases of the FIO2, and a change in previously used alarm limits. They reported that following the implementation of these new management strategies that the incidence of ROP Grades 3 to 4 decreased consistently in a 5-year period from 12.5% in 1997 to 2.5% in 2001 and that the need for ROP laser treatment decreased from 4.5% in 1997 to 0% in the last 3 years. They adopted an SpO2 range of 85% to 95% for infants > 32 weeks gestation at birth, and a range of 85% to 93% for infants < 32 weeks. In addition some of their faculty used a range of 83% to 93%. This study did not provide any prospective values of the actual SpO2 ranges that were actually achieved in their infants, and thus it is uncertain whether their observed reductions in ROP were related to the altered SpO2 changes, or to overall changes in management over the period of the study. While these observations are encouraging, the authors did not report the complete neurodevelopmental outcomes for the infants cared for during the period of the new oxygen guidelines, and in the absence of contemporaneous controls, these results cannot be considered as proof that the SpO2 ranges used by this group are beneficial in terms of significant longer -term neurodevelopmental outcomes.

The most recent trial conducted in Australia compared SpO2 ranges of 91% - 94% versus 95% - 98% in 358 infants of less than 30 weeks who remained oxygen dependent at 32 weeks. The primary outcomes were growth and neurodevelopmental measures at a corrected age of 12 months. The high-saturation group received oxygen for a longer period after randomization (median, 40 days vs. 18 days; P<0.001) and had a significantly higher rate of dependence on supplemental oxygen at 36 weeks of postmenstrual age and a significantly higher frequency of home-based oxygen therapy. but resulted in an increased duration of oxygen supplementation.[50] They reported that additional oxygen supplementation did not improve survival, growth, or the occurrence of cerebral palsy at 18 to 24 months. Anderson et al have recently reported the results of a survey of pulse oximetry practices in 142 NICUs in the USA and noted a wide range of monitoring limits from 82% to 100%. They reported a lowered rate of ablative eye surgery in units that used lower maximal SpO2 limits, with the lowest range seen in units that had a maximum SpO2 of < 92%.[51]

In a recent review of oxygen toxicity in the premature infant Weinberger et al recommended that a strategy of limiting oxygen supplementation should be explored to reduce significant morbidities in the premature infant.[52] No studies to date have prospectively randomized ELBW infants to differing oxygenation ranges from birth onwards to determine if there is a benefit of lower versus higher saturation ranges.

1.5 Recent Relevant Studies

We have recently evaluated an FDA approved device specifically designed to facilitate neonatal resuscitation (Neopuff Infant Resuscitator, Fisher and Paykel, Auckland, New Zealand). This device has a t-piece that attaches to a mask and to a simple pressure generator. The inspiratory pressure can be set to a determined level, and a twist valve at the top of the t-piece determines the end-expiratory pressure. Most operators, with the exception of experienced respiratory therapists cannot routinely deliver a predetermined level of positive inspiratory pressures and PEEP[53] using an anesthesia-type manual bag and a neonatal manikin. In contrast, all operators could deliver the predetermined pressures with little intra-individual variation using the Neopuff®. The device operates identically using either a mask or endotracheal tube connection with or without PEEP/CPAP and the operator can adjust the positive inspiratory pressure (PIP) manually during resuscitation. At a flow of 10 liter per minute (lpm) or less, the maximum inadvertent CPAP/PEEP is 0.5 cm H_2O; which does not increase up to rates of 80 breaths per minute, the highest tested rate. The wave form is square, and is more similar to ventilator wave forms than to wave forms obtained using an anesthesia device. It should be noted, that the standard anesthesia devices used in delivery rooms may not deliver the desired CPAP/PEEP, depending on the operator's experience and skill, and may result in overshooting the desired PIP, even when the device is used by experienced operators. The Neopuff® device is now used as the standard resuscitation device in a number of hospitals in the USA, including at least two units in the NICHD Network.

There has been a recent trial evaluating earlier criteria for retinal laser ablative surgery for ROP, the ETROP study.[54] This study has demonstrated that using such criteria the visual outcomes are improved and reported that grating acuity results showed a reduction in unfavorable visual acuity outcomes with earlier treatment, from 19.5% to 14.5% (P=.01)and that unfavorable structural outcomes were reduced from 15.6% to 9.1% (P<.001) at 9 months. They recommend retinal ablative therapy for eyes with type I ROP, defined as zone I, any stage ROP with plus disease (a degree of dilation and tortuosity of the posterior retinal blood vessels meeting or exceeding that of a standard photograph); zone I, stage 3 ROP without plus disease; or zone II, stage 2 or 3 ROP with plus disease. While these results are likely to be integrated into Network practice, there is currently no baseline data regarding the number of infants who would meet these criteria, and thus we will utilize the presence of Stage 3 or greater ROP and/or the receipt of retinal surgery to power our current trial.

2.1 Study Design

This will be a prospective, randomized, factorial 2X2 design multi-center trial conducted by the NICHD Neonatal Research Network. The individual factors to be tested will be:

1) A prospective comparison of CPAP and a permissive ventilatory strategy begun in the delivery room and continuing in the NICU with early ($\leq$ 1 hour) surfactant and mechanical ventilation.

2) A prospective comparison of a lower SpO2 range (85% to 89%) with a higher more conventional SpO2 range (91% to 95%) until the infant is no longer requiring ventilatory support

or oxygen.

The oxygen saturation monitoring portion of our study will be designed to parallel the planned POST-ROP trial, a multicenter, multinational prospective trial to evaluate different SpO2 levels from birth.[55] The methodology described under oxygen monitoring (**Section 4.1B**) was developed for the current protocol to allow a blinded comparison of 2 different SpO2 levels using specially designed pulse oximeters. These devices have been developed by the Masimo Corporation (Irvine Ca) and tested prior to initiation of this trial, and the POST-ROP study group has agreed to use the ranges described in this protocol, and the methodology that will allow the oximeters to provide actual SpO2 values when the SpO2 is < 85% and > 95%(Personal communication, Cynthia Cole 2004). This methodology will provide the clinicians and caretakers with the infants' actual SpO2 values during hypoxia and hyperoxia, within the current parameters of clinically accepted practice.

Please see **Section 8.2** for further Tables describing details regarding the projected outcomes relative to the study interventions

Randomized Intervention	**Low SpO2 85% to 89%**	**High SpO2 91 to 95%**
Treatment **Early CPAP**	Early CPAP + Low SpO2	Early CPAP + High SpO2
Control **Prophylactic/Early Surfactant**	Control + Low SpO2	Control + High SpO2

2.2 Primary Hypotheses

1). We hypothesize that relative to infants managed with prophylactic/early surfactant and conventional ventilation that the use of early CPAP and a permissive ventilatory strategy in infants of less than 28 weeks gestation with continuing CPAP in the NICU will result in an increased survival without BPD at 36 weeks.

2). We hypothesize that that relative to infants managed with a higher SpO2 range that the use of a lower SpO2 range (85% to 89%) will result in an increase in survival without the occurrence of threshold ROP and/or the need for surgical intervention.

2.3 Secondary Hypotheses

We hypothesize that the use of continuous positive airway pressure (CPAP) with a permissive ventilator strategy and/or a lower SpO2 range starting at birth in the delivery room will result in the following:

- A decreased Mortality/NDI at 18-22 months corrected age.

- A decreased frequency of endotracheal intubation before 10 minutes of age
- A decrease of the total duration of mechanical ventilation during the entire NICU stay
- A decreased incidence of surfactant treatment
- A decreased incidence of air leaks on admission and overall
- A decreased duration of intubation
- A decreased duration of mechanical ventilation
- A decreased duration of oxygen supplementation
- A decreased duration of the percentage of pulse oximetry values > 90%
- A decreased incidence of blindness of at least one eye at 18-22 month follow-up
- A decrease in the percentage of infants who receive postnatal steroids to prevent or treat BPD
- A decreased incidence of BPD at 36 weeks using the physiologic definition of BPD
- A decreased incidence of ROP or Stage 3 ROP
- A decreased incidence of necrotizing enterocolitis (NEC)
- A decreased incidence of IVH and severe IVH
- A decreased incidence of periventricular leukomalacia
- A decreased incidence of neurodevelopmental impairment at 18-22 month follow-up
- A decreased incidence of cerebral palsy at 18-22 month follow-up

3.1 Study Population

Study subjects are infants of 24 0/7ths to 27 6/7th weeks at birth for which a decision has been made to provide full resuscitation as required. Infants 27 weeks or less gestation (completed weeks by best obstetric estimate) will be enrolled because over 80% of such infants in the Network are intubated, usually early in their neonatal course. It is important to note that previous studies have included few, if any infants less than 25 weeks gestation and such infants are not included in the current COIN trial or the proposed Vermont Oxford Trial. Such infants will be enrolled in this trial because they are the group of infants with the highest mortality and morbidity. The feasibility trial demonstrated that the 5 NICHD centers involved could reduce intubation in the delivery room to less than 50% of such infants if they are not intubated for surfactant. We will exclude infants of 23 weeks or less in view of their extremely high mortality and morbidity, and their almost universal need for delivery room intubation for resuscitation. We have included Tables at the end of the protocol utilizing infants from 23 to 28 weeks to demonstrate that our sample size estimates will not be adversely affected if we should choose to include infants of 23 and/or 28 weeks.

Strata: There will be 2 randomization strata, infants of 24 0/7ths to 25 6/7ths weeks, and infants of 26 0/7ths-27 6/7ths weeks by best obstetrical estimate. The purpose of stratification is to assure an appropriate distribution of risk among the four study arms. The study will not be powered to detect outcome differences between strata.

3.2 Inclusion Criteria

- Infants with a minimal gestational age of 24 weeks 0 days to 27 completed weeks (up to 27 6/7ths) by best obstetrical estimate
- Infants who will receive full resuscitation as necessary, i.e., no parental request or physician decision to forego resuscitation
- Infants whose parents/legal guardians have provided consent for enrollment, or
- Infants without known major congenital malformations

3.3 Exclusion Criteria

- Any infant transported to the center after delivery
- Infants whose parents/legal guardians refuse consent
- Infants born during a time when the research apparatus/study personnel are not available
- Infants < 24 weeks 0 days or ≥ 28 weeks 0 days, completed weeks of gestation

3.4 Sampling Recruitment and Screening Procedures

Infants will be recruited for this study by approaching one or both parents at the time of admission to the hospital where there is deemed to be a risk of premature delivery at 27 6/7ths weeks or less.

3.5 Screening Procedures

All admissions for threatened premature delivery will be screened on a daily basis to ensure that eligible patients can be enrolled. We will inform our obstetrical colleagues at each involved institution of the nature of this study, and encourage them to discuss this study with their patients at risk of premature delivery. The study coordinator at each site will maintain a screening log of potentially eligible patients. In addition the usual practice of neonatal consultation for all such at risk deliveries will provide a second opportunity to approach mothers with fetuses at risk of preterm delivery

3.6 Other Procedures

A T-piece resuscitator, a neonatal ventilator, or an equivalent CPAP methodology will be used at all sites for the delivery room administration of CPAP. A training video to explain the proper use of the Neopuff® will be provided to any site which wishes to use it and is not familiar with the device.

3.7 Randomization

Randomization will be stratified by gestational age group, will occur prior to delivery for consented deliveries, and will be performed by utilizing specially prepared double-sealed envelopes. Deliveries will be randomized as a unit, thus multiples, twins, triplets etc will be randomized to the same arm of the trial. We believe that this methodology will improve the percentage of consents, since in previous trials parents of multiple infants have expressed concern that their infants were being randomized to different treatment arms. We have made an appropriate sample size adjustment to account for this clustering effect.

Each randomization will indicate either Treatment Group (CPAP and permissive ventilation management) or Control Group (Prophylactic/Early surfactant and conventional ventilator management) and either the Low (85%-89%) or High (91% - 95%) SpO2 group. Parents will be approached for consent before delivery, but the randomization envelope will only be opened when delivery is imminent for a consented family.

The Pulse Oximeters (PO) will have unique identifying labels and the oximeter specified in the randomization will be identified by a unique number which will match the number of the study Pulse Oximeter assigned for that infant. All caretakers including the coordinators will be blinded to the Pulse Oximeter range, and an identification code for each site will be maintained by the PI/Site Coordinator should identification be required for patient safety. RTI will work with Masimo to ensure that the POs are labeled with unique identifiers, whose code will identify the

actual range of the individual PO. These would be affixed prior to shipping to the sites, and a copy of the labels sent to the site would be provided to RTI.

This methodology should reduce the work load to the sites at the time of randomization, providing the care team with the information needed for the infants' randomization, and will allow the study center to be notified within 24 hours of any randomization.

3.8 Informed Consent:

Parents will be approached prior to delivery for informed consent, and their infants enrolled at delivery. As previously noted we will randomize by family, thus all offspring will be randomized to the same trial arms, provided adequate equipment and personnel are available at the time of delivery.

3.9 Management and Retention of Study Population

All enrolled infants will be seen at follow-up-up at 18 to 22 months corrected age. We do not anticipate a significant loss other than death (13% in the first 12 hours , approximately 32% before discharge, based on year 2000 registry data), and will plan for a further 15% attrition.

4.1 A: Study Intervention: Mode of Ventilatory Support

The intervention will begin after birth when the infant is given to the resuscitation team. The conduct of the resuscitation will follow usual guidelines, and once stabilized, all Control infants in both strata will receive prophylactic/early surfactant (within 1 hour of age) whereas all Treatment infants will be placed on CPAP/PEEP following stabilization, and be intubated only for resuscitation indications.

The assignment to either a high or low SpO2 by study oximeter assignment will be performed immediately following NICU admission, with a maximum allowable delay of 2 hours following NICU admission.

TREATMENT: CPAP Group : Early Extubation and CPAP

Delivery Room Management

FiO2:

Standard of care.

CPAP:

CPAP or ventilation with PEEP will be utilized if the infant requires positive pressure during resuscitation. CPAP will be continued until admission to the NICU using the Neopuff or equivalent device and a face mask or nasal prongs. Initial PPV will be at a PIP of 15-25 cm H_2O and a PEEP/CPAP of 5 cm cmH_2O.

Intubation:

Infants may not be intubated for surfactant only in the DR. Infants who require intubation for resuscitation will receive surfactant within 60 minutes of birth.
Intubation will be performed only for the standard NRP indications including failure to respond to PPV with evidence of continuing cyanosis or bradycardia, the need for chest compressions, the need to administer intratracheal medications, or other situations in which the resuscitation team determines that surfactant is urgently required.

Intubation may be performed at any time for the occurrence of repetitive apnea requiring bag and mask ventilation, clinical shock, sepsis, and/or the need for surgery

The other aspects of the resuscitation will be managed according to the NRP guidelines and follow current center practice.

NICU Management

These infants will be managed on nasal CPAP, and intubation is never required by protocol. They *MAY* be intubated if they meet ***ANY*** *of* the criteria listed below. If intubated within the first 48 hours of life they should receive surfactant

Intubation:

- An FiO_2 >.50 required to maintain an indicated SpO2 $\geq$ 88% (using the altered Pulse Oximeters) for one hour
- An arterial $PaCO_2$ > 65 torr (arterial or capillary samples, if venous PvCO2 > 70 torr) documented on a single blood gas within 1 hour of intubation
- Hemodynamic instability defined as a low blood pressure for gestational age and/or poor perfusion, requiring volume and/or pressor support for a period of 4 hours or more. (Note that clinically defined shock is an accepted indication for intubation.)

Intubation may be performed at any time for the occurrence of repetitive apnea requiring bag and mask ventilation, clinical shock, sepsis, and/or the need for surgery

These criteria will continue in effect for a minimum of 14 days of life.

Intubation performed without meeting any of the above criteria will be considered a study protocol violation unless extenuating circumstances are noted.
(e.g. - Upper airway obstruction (choanal atresia, micrognathia/glossoptosis)).

Extubation:

An intubated CPAP-Treatment infant ***MUST*** *have extubation attempted within 24 hours if* **ALL** *of the following criteria are met and documented on a single blood gas*

- $PaCO_2$ < 65 torr with a pH > 7.20 (arterial or capillary samples)
- An indicated SpO2 $\geq$ 88% with an FiO2 $\leq$ 50%
- A mean airway pressure (MAP) < 10 cm H_2O, ventilator rate $\leq$ 20 bpm, an amplitude < 2X MAP if on high frequency ventilation (HFV)
- Hemodynamically stable (Defined as an infant with clinically acceptable blood pressure and perfusion in the opinion of the clinical team – such an infant may be receiving ionotropic/vasopressor agents, but should not require ongoing volume infusions to stabilize the circulation and the doses of any continuously infused medications for circulatory stabilization should not have increased within 1 hour of any planned extubation).
- Absence of clinically significant PDA

These criteria will continue in effect for the first 14 days of life.

Failure to extubate an infant meeting all of the above criteria will be recorded as a study protocol violation unless extenuating circumstances are noted. (e.g. - PIE, airleak)

Reintubation

If a Treatment infant is extubated as per Protocol Criteria, and requires re-intubation for any indication, any further attempt at extubation may be delayed for 24 – 48 hrs based on the clinician's decision.

Re-intubation criteria are the same as those for Intubation for the CPAP infants. Thus, intubation is not required, but these infants **MAY** be reintubated if they meet **ANY** of the following:

Re-Intubation Criteria:

- An FiO_2 >.50 required to maintain an indicated SpO2 $\geq$ 88% (using the altered Pulse Oximeters) for one hour
- An arterial $PaCO_2$ > 65 torr (arterial or capillary samples, if venous PvCO2 > 70 torr) for 2 successive blood gases at least 15 minutes apart.
- Hemodynamic instability defined as a low blood pressure for gestational age and/or poor perfusion, requiring volume and/or pressor support for a period of 4 hours or more. (Note that clinically defined shock is an accepted indication for intubation as noted above on page 13)

Intubation may be performed at any time for the occurrence of repetitive apnea requiring bag and mask ventilation, clinical shock, sepsis, and/or the need for surgery.

Re-intubation performed without meeting any of the above criteria will be considered a study protocol violation unless extenuating circumstances are noted.

D/C CPAP

Treated infants who remain in Room Air for at least 1 hour may have their CPAP discontinued. CPAP may be discontinued earlier and follow unit Standard of Care. CPAP may be restarted at any time in such infants.

CPAP infants who require intubation three times, for any criteria, will have all subsequent treatment including subsequent extubations and any further re-intubations performed using unit Standard of Care. This addition is to prevent such infants from being exposed to further protocol driven intubations and extubations.

Surfactant

Infants intubated in the first 48 hours for respiratory distress should be given a minimum of one dose of surfactant

Up to 4 surfactant administrations may be given if the FiO2 is greater than 50% following manufacturers' recommendations for dose and dosing interval.

Explanation:

The purpose of the above criteria is to minimize the duration of intubation of Treatment infants. The Criteria for extubation are more severe than those of the Control Group infants, and extubation must be attempted for any infant who fulfills the stated criteria.

The criteria for re-intubation recognize that intubation is traumatic, and is designed to avoid frequent attempts at extubation for infants who fail.

CONTROL- Prophylactic/Early Surfactant and Ventilation

Delivery Room Management:

Infants will be intubated in the delivery room and given surfactant or receive surfactant

within 60 min minutes of birth. The other aspects of the resuscitation will be managed according to the NRP guidelines and follow current center practice.

NICU Management:

:

***Extubation*:**

An intubated Surfactant-Control infant will continue to receive mechanical ventilation until extubation criteria are satisfied, but **MUST** have Extubation attempted within 24 hours of fulfilling ***ALL*** of the following criteria documented on a single blood gas.

- $PaCO_2$ < 50 torr and pH > 7.30 (arterial or capillary samples)
- An FiO2 ≤ 35 with a SpO2 ≥ 88% using the study pulse oximeters with
- A mean airway pressure (MAP) < 8 cm H_2O, ventilator rate ≤ 20 bpm, an amplitude < 2X MAP if on high frequency ventilation (HFO)
- Hemodynamically stable (Defined as an infant with clinically acceptable blood pressure and perfusion in the opinion of the clinical team – such an infant may be receiving ionotropic / vasopressor agents, but should not require ongoing volume infusions to stabilize the circulation and the doses of any continuously infused medications for circulatory stabilization should not have increased within 1 hour of any planned extubation).
- Absence of clinically significant PDA (Defined as bounding pulses, audible murmur and Echo confirmation of L-R shunting with increased LA/Ao size

These criteria will continue in effect for a minimum of 14 days for all infants.

Failure to attempt to extubate an infant meeting all of the above criteria, or extubation prior to reaching criteria, will be recorded as a study protocol violation unless extenuating circumstances are noted.

Weaning

This protocol will not define strict weaning criteria for the Control infants, but it is to be understood that reasonable attempts should be made to extubate these infants. While it is understood that some centers may be using somewhat more severe FiO2 and PaCO2 criteria than those listed here as current practice, these Criteria are thought to reflect current Network practice and practice at 2 of the 3 Best practice centers.

Reintubation:

- Control Infants may be reintubated using Standard of Care.

Explanation:

Control infants are to be treated using an approach considered similar to current standards of care. Apparatus for resuscitation for Control Infants at each center will represent their usual equipment for the resuscitation of an ELBW infant. The Neopuff may be utilized for such infants as above, but this is not mandatory. It is anticipated that the majority of these infants will be intubated and receive surfactant in the delivery room.

4.1 B: Study Intervention: Low versus High SpO2 Range:

There will be 2 ranges of SpO2 utilized during this trial. The Low target range will be 85% to 89% and the High target range will be 91% to 95%. The altered Pulse Oximeters (PO) are described below, and will display a range of 88% to 92% when the SpO2 ranges are in the Target ranges indicated above. Thus a Low range PO will read 88% when the actual SpO2 is

approximately 86%, and 92% when the actual SpO2 is 89%. Similarly the High range PO will display 88% when the actual SpO2 is 91% and indicate 92% when the actual SpO2 is approximately 95%. See below for further explanation. This deviation is similar to the BOOST trial which used a continuous 3% offset.[42] As an added safety feature, the POs used in this trial will revert to the actual SpO2 values and allow the caretakers to be aware of actual SpO2 values < 85% and > 95%.

Low Range Infants:

These infants will be monitored with a target SpO2 range of 85% -89% with suggested indicated alarm limits of 85% and 95%, representing approximately a 10% span for alarms as long as the infants are receiving any ventilatory support, CPAP, and/or supplemental oxygen. **The study pulse oximeters will be applied to the infant within two hours following NICU admission.** The assigned PO will remain on the infant and will be removed once the infant has been in room air and off ventilatory support or CPAP for 72 hours, and if oxygen is subsequently required a similar altered pulse oximeter providing the same SpO2 range will be used until 36 weeks PCA.

High Range Infants:

These infants will be monitored with a target SpO2 range of 91% -95% with suggested indicated alarm limits of 85% to 95% representing approximately 10% span for alarms as long as they are receiving any ventilatory support, CPAP and/or supplemental oxygen. The study pulse oximeters will be removed once the infant has been in room air for 72 hours, and if oxygen is subsequently required a similar altered pulse oximeter providing the same SpO2 range will be used until 36 weeks PCA.

These interventions will be delivered using specially developed pulse oximeters whose displays (the actual readings seen by caretakers) will be adjusted so that the randomized range of SpO2 (either 85%-89%, or 91%-95%) will be indicated by a range of 88%-92%. This is done by progressively altering the offset as the alarm limits are approached, and Masimo has confirmed that this technology is workable. The target oxygen saturation (88-92%) of the display will be the same in both groups as indicated in Table1 below.

These POs will be able to display trend plots of the SpO2 display for a preceding interval to allow the caretakers to receive feedback regarding the actual SpO2 ranges of their baby.

The suggested alarms limits will be 84% and 96% for both groups.

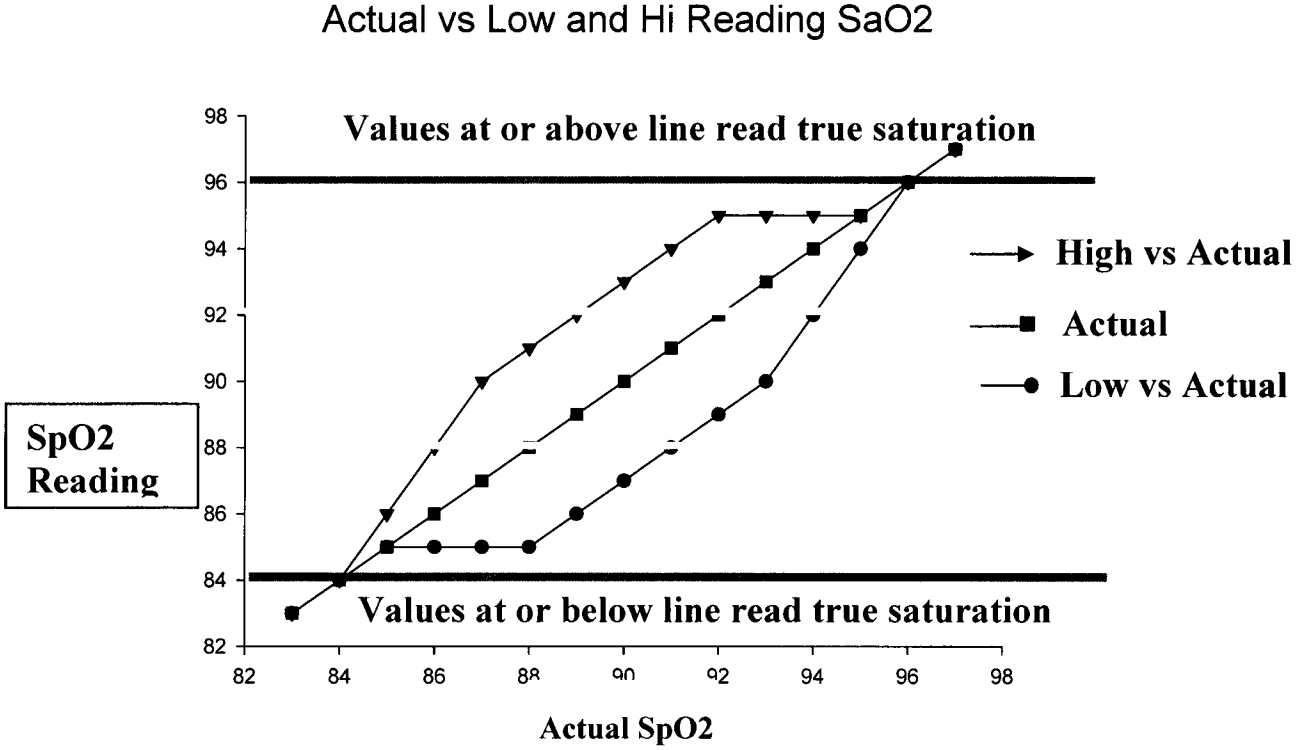
Table 1. Output and Actual SpO2 Targets and Alarms

SpO2 Group	Displayed Target	Actual Target	Alarm Values
Low SpO2	88-92%	85-89%	<85 and >95%
High SpO2	88-92%	91-95%	<85 and >95%

The pulse oximeters will display the actual reading when then the SpO2 is below 85% and above 95%. This will provide for an overall set of limits on actual SpO2 of 84% to 96% which we believe will avoid unacceptable levels of hypoxia, (< 85%) and hyperoxia (> 95%) **All data below 85% and above 95% will be unaltered on all oximeters**. An averaging time of 16 seconds will be applied in keeping with the settings used by POST-ROP. The preset alarm

delay will be 10 seconds. The fail-safe alarm will alarm whenever the reading is 5% below the low alarm limit, in the study this will be at 80%. Some network centers use an averaging interval of 30 seconds, others use very short averaging times. This setting will allow for appropriate response times without unmasking the caretakers.

We believe that this methodology will provide an acceptable ethical design for this trial. The diagram below demonstrates how the pulse oximeter readings are altered between values of 85% to 95%. Readings below or above these levels will not be altered, and will represent actual SpO2 as determined by the pulse oximeter. Note that the entire range of actual SpO2 is altered to either a lower (Low SpO2 Group) value or higher value (High SpO2 Group) till the ends of the alarm ranges of 85% and 95% which will ensure that the infants SpO2 will be separated throughout this range.



Every 30 days until 36 weeks PCA or until the infant is no longer receiving ventilatory support or oxygen, the stored actual SpO2 values (one value per 10 seconds of monitoring) will be downloaded and transmitted to RTI for subsequent analyses. (This interval of sampling may change to a less frequent interval for the convenience of the study personnel, without losing significant data). These data points will be used to confirm that the infants were managed at the target ranges and provide objective confirmation of the SpO2 Group assignments. The technology for downloading and interpreting this data was used in the DR CPAP Pilot trial, but recent technology utilizing a software program (Profox, Profox Inc, Escondido, Ca) which has been written to facilitate this process, will dramatically simplify this procedure.

Non-study pulse oximeters cannot be used on enrolled patients. If a second oximeter is

required for such a patient, the site coordinator will provide an identical oximeter for the patient.

All ventilatory care after 14 days of age will follow the standard of care for each unit. Each unit will provide guidelines for their approach to continuing mechanical ventilation.

4.2 Delivery of Interventions

CPAP/PEEP in the DR

CPAP and positive pressure ventilation (PPV) in the delivery room for Treatment infants will be administered via a T-piece resuscitator, a neonatal ventilator or an equivalent device that is currently used by the site for the delivery of CPAP. (See **3.6**).

Use of Nasal SIMV;

This approach is currently used by some Network units and has been previously established as being superior to CPAP following extubation in three prospective trials.[56,57,58] For uniformity nasal SIMV may be used in place of CPAP ***only following extubation for both Treatment and Control infants.***

Use of Caffeine:

Caffeine may be administered 2 hours prior to planned extubation, and for any clinically significant apnea.[59]

Surfactant Type:

All centers are asked to follow current unit practice in determining the type of surfactant utilized, and manufacturers' recommendations for redosing intervals.

The protocol requires that at least one dose of surfactant be administered to any infant intubated within 48 hours of birth, with evidence of respiratory distress, who has not previously received surfactant.:

Postnatal Steroids

Postnatal steroids for the purpose of preventing or treating BPD/CLD will be prohibited for any infant in this trial in the first 21 days of life. Hydrocortisone for hypotension may be used as noted below.

If postnatal steroid use is considered after 21 days of life for any infant for the prevention/treatment of established lung disease the following guidelines should be followed:

1. The AAP statement and recommendations regarding Post-natal steroids should be adhered to.[60]
2. The lowest dose of dexamethasone considered effective should be used and if ineffective after 24 – 48 hours they should be stopped.
3. Consider using hydrocortisone as a first therapy at a dose of 1 -2 mg/kg/day before using dexamethasone.
4. For hypotension, hydrocortisone in a dose of 1 mg/kg/dose should be given after fluid administration and standard doses of ionotropes/pressors have failed to correct the low blood pressure.

Head Ultrasound

If a Head ultrasound is done between days 4 and 21 the results will be recorded for this study. If one is not done for standard of care, the study requires that at least one HUS be completed during this window

4.3 Protocol Violations:

The occurrence of any one of the following criteria will determine whether an individual infant will be considered a protocol violation:

1. Intubation of a treatment group infant in the DR for the exclusive purpose of giving surfactant, in the absence of bradycardia (HR< 100 bpm) and/or poor color or an SpO2< 85-90% in an infant with adequate spontaneous respirations or receiving adequate ventilation
2. Failure to continue CPAP on admission to the NICU for a treatment infant requiring supplemental oxygen
3. Intubation and surfactant administration of a treatment infant without meeting stated protocol criteria.
4. Failure to extubate a Treatment infant who fulfills all the extubation criteria.
5. Extubation of a Control infant who does not meet any of the Extubation criteria.

All protocol violations will be reviewed by the center PI who will discuss each protocol violation with the involved clinicians and provide a written summary including steps taken to avoid future violations.

4.4 Adverse Events

Serious and unanticipated adverse events may be anticipated in this vulnerable population. Data on the following potential adverse events that may be related to the study maneuver will be recorded and evaluated as part of continuous safety monitoring during the trial by RTI:

1. Air leak on admission to the NICU, or during the initial 14 days of life
2. The need for chest compressions, and/or epinephrine in the delivery room or NICU
3. The occurrence of severe IVH (Grades 3-4, Papile)
4. Death

These outcomes will be evaluated on a monthly basis by RTI, and if the incidence of any of these outcomes is determined to be 5% - 10% greater in any arm of the study, this information will be provided to the Study PI and committee and the DSMC for immediate consideration, and evaluated for consideration of termination of the study or treatment arm.

4.5 Data Safety Monitoring Committee

The Data Safety Monitoring Committee will review the progress of the study with respect to efficacy and adverse events in a sequential fashion by using interim monitoring boundaries. Obrien-Fleming [61] boundaries will be used for efficacy monitoring and will be constructed for four looks at the data at 25%, 50%, 75%, and 100% of outcome assessment. Pocock [62] boundaries will be used for adverse event monitoring and will be viewed after every 30 infants have been enrolled. A special adverse event form will collect the information so that it may be entered into the data base in a timely fashion.

5.1 Measurement Methods:

The PO stored data will be retrieved using a routine provided to all site coordinators, and the resultant data file will be sent electronically to RTI to be included as part of the study data collection.

5.2 Schedule of Data Collection: (See Data tables in Appendix A)

5.3 Primary and Secondary Outcome Measures

5.3.1 Primary Outcome Measure

The primary outcome will be the percentage of infants surviving without BPD (using the Physiologic Definition) or severe ROP (threshold disease or the need for surgery).

5.3.2 Secondary Outcome Measures

- The five minute Apgar score
- The percentage of infants with death or neurodevelopmental impairment at 18 months
- The total duration of mechanical ventilation during the entire NICU stay
- The percent of infants alive and off ventilation by day 7
- The proportion of infants receiving surfactant treatment
- The incidence of air leaks on admission and overall
- The incidence of BPD at 36 weeks using the physiologic definition of BPD
- The incidence of death
- The proportion of infants with severe IVH
- The proportion of infants with PVL
- The proportion of infants with threshold ROP and requiring surgery for ROP
- The proportion of infants requiring endotracheal intubation before 10 minutes of age
- The proportion of infants with of air leaks on admission and overall
- The duration of oxygen supplementation
- The percentage of pulse oximetry values > 90%
- A decreased incidence of blindness of at least one eye at 18-22 month follow-up
- The proportion of infants who receive postnatal steroids to prevent or treat BPD
- The proportion of infants with who develop necrotizing enterocolitis (NEC)
- The proportion of infants with cerebral palsy at 18-22 month follow-up

6.1 Training Study Personnel

6.1.1 Job Descriptions of Study Personnel

The NICHD coordinators will assist the respiratory therapists in each unit regarding the set up the equipment for the delivery of CPAP in the delivery room, and in the NICU.

6.1.2 Training of Personnel

There will be a training session held in Cincinnati about the delivery of CPAP in the delivery room and in the NICU, and a review of available devices that may be used for this intervention.

7.1 Data Collection and Management

We will develop the required CRFs as per Network procedures. It will be our aim to minimize these to ensure that data is collected regarding the intervention, the adherence to the protocol for intubation, surfactant administration, and extubation, and the occurrence of the primary and secondary end-points. All remaining information will be extracted for the current data forms.

8.1 Statistical Analysis

8.1.1 Analysis Plan

The primary analyses of this factorial trial will be a logistic regression analysis of the percent of each Group (Treatment vs Control, High vs Low SpO2) who developed their respective outcome measure (survival without BPD or ROP at 36 weeks respectively). An important analysis of a secondary outcome will determine if there is an effect of the interventions on the percent infants who survive without neurodevelopmental sequelae at 2 years For all secondary outcomes, univariate analysis for continuous variables will be performed using parametric (e.g., Student t tests, ANOVA), and non-parametric (e.g., Mann-Whitney U) tests where appropriate; categorical variables including the primary outcome, feasibility, will be examined by Chi square analysis. Analysis of covariance and multiple regression models will be used to examine the interaction between, and the independent effects of, various factors, (e.g., birth weight, gestational age, gender, treatment group, center, etc.) upon secondary outcomes (i.e., time to improvement in oxygen saturation, duration of positive pressure ventilation, five minute Apgar score, duration of mechanical ventilation, surfactant requirement, incidence of air leaks, and incidence of BPD).

8.2 Sample Size

As discussed above, there are two main outcomes for the factorial design: mortality or BPD; mortality or ROP. Mortality or NDI is a secondary outcome. For the cohort of infants born in 2000, 401-1000g birth weight, we have the following prevalence of outcomes for four subgroups of that cohort: Please note that we used population groupings to include or exclude infants of 23 and 28 weeks. These additional groups do not change the sample size estimates as the outcomes are essentially similar.

Subgroup	Death/BPD	Death/> Stage III ROP	Death/NDI
23-27 GA	70.6	53.1	65.7
24-28 GA	64.8	44.5	59.3
24-27 GA	66.6	46.8	60.7
23-28 GA	68.6	50.4	64.0

If the study is powered for the two outcomes, Death/BPD and Death/>Stage III ROP, then the sample size is driven by the prevalence nearest 50% for a given absolute percentage detectable change in the outcome. In this case it's the Death/>Stage III ROP outcome with a range of 44.5% to 53.1% across the subgroups. Furthermore, the sample size depends on the outcome rate only through the standard deviation of the rate and this turns out to be essentially

50% for all subgroups (i.e. ranges from 49.7% to 50.0%). Hence one sample size table suffices for all.

Hence, for any of the four groups the table below gives the total sample sizes required for a range of absolute percent changes, a two-tailed alpha level test of 5% and for powers of 80% and 90%. The N1 column powers the 2 x 2 factorial for the two primary outcomes and the N2 column assures comparable power for the Death/NDI outcome.

With regard to the power for detecting the interaction between the two factors in the factorial, a fourfold increase in the stated sample size would be required to detect an interaction effect as large or larger as that stated in the table (i.e. the Detectable Difference), assuming the same alpha level and power. The interaction effect referred to is the classical one where the difference in outcome for one of the treatments in the factorial differs according to the level of the other treatment (i.e. the treatment effects are not additive).

If the study is powered for the two primary outcomes and mortality/NDI is considered as a secondary outcome then the table below gives the total sample size required for a 5% overall level test at 80% and 90% power. These represent the total numbers enrolled. To correct for two outcomes, we chose a conservative 2% level of significance and a conservative outcome rate of 50% in making the calculations. These sample sizes are given in the N1 column and would also allow a 10% difference in NDI/death to be detected with a power of 73%. If an 80% power is desired for the NDI/mortality outcome this would result in sample sizes in the N2 column.

TOTAL SAMPLE SIZES REQUIRED

	80% Power		90% Power	
Detectable Difference (absolute %)	Total N1*	Total N2**	Total N1*	Total N2**
8%	1792	2096	2284	2676
9%	1388	1624	1792	2096
10% (multiples to same arm)	1120	1312	1456	1704
11%	940	1104	1208	1416
12%	784	920	1032	1208
13%	672	788	860	1008
14%	584	680	756	880
15%	504	588	652	768

* sample sizes to insure the appropriate power for the two primary outcomes (BPD/Death, ROP/Death)

** sample sizes to insure the appropriate power for the secondary outcome (NDI/Death)

We have increased the sample size by a factor of 1.12 to allow for multiples to be randomized to the same treatment as this introduces a clustering effect into the design. The analysis of the GDB data base resulted in the 1.12 estimate. We also inflated the sample sizes by 17% to adjust for attrition after discharge and before follow-up. This figure was also determined from the GDB data base. Thus the actual sample size for this trial would be 1310 for 80% power for detecting an absolute difference of 10% in the two primary outcomes and the NDI secondary outcome. This sample size is not sufficient to permit detection of interactive effects between the two treatments with reasonable power.

HYPOTHESIZED TREATMENT EFFECTS FOR SUPPORT

When sample sizes were estimated for the SUPPORT trial the following base rates for the three outcomes (rounded) were calculated from the GDB:

--BPD/Mortality—67%
--ROP $\geq$ Grade III/Mortality—47%
--NDI/Mortality—61%.

Sample sizes were calculated for a range of absolute treatment effects and 10% seemed to be the smallest plausible effect for the study. Rounding the above rates to 65, 45, and 60 percent the following tables show what the data would look like under the assumption of a 10% reduction in outcome and control rates of 65, 45, and 60 percent for the DRCPAP (No)/ SpO2 (High) group. Interactive effects are assumed to be zero. Tables are presented which show treatment effects when both treatments affect the BPD and the ROP outcomes and when only one of the treatments affects outcome. The NDI table is only for the case where both treatments affect outcome.

Table IA

Treatment Effects for SpO2 (High, Low) and CPAP (Yes, No) on BPD/Mortality **Assuming a 10% Main Effect for Each Factor**—Table Entries are Outcome Rates (%)

SpO2

CPAP	Low	High	Overall
Yes	45	55	50
No	55	65	60
Overall	50	60	55

Table IB

Treatment Effects for SpO2 (High, Low) and CPAP (Yes, No) on BPD/Mortality **Assuming a 10% Main Effect for CPAP Only**—Table Entries are Outcome Rates (%)

SpO2

CPAP	Low	High	Overall
Yes	55	55	55
No	65	65	65
Overall	60	60	60

Table IIA

Treatment Effects for SpO2 (High, Low) and DRCPAP (Yes, No) on ROP≥ Grade III/Mortality **Assuming a 10% Main Effect for Each Factor**—Table Entries are Outcome Rates (%)

SpO2

SpO2

CPAP	Low	High	Overall
Yes	25	35	30
No	35	45	40
Overall	30	40	35

Table IIB

Treatment Effects for SpO2 (High, Low) and CPAP (Yes, No) on ROP≥ Grade III/Mortality **Assuming a 10% Main Effect for SpO2 Only**—Table Entries are Outcome Rates (%)

		SpO2		
		Low	High	Overall
CPAP	Yes	35	45	40
	No	35	45	40
	Overall	35	45	40

Table III

Treatment Effects for SpO2 (High, Low) and CPAP (Yes, No) on NDI/Mortality **Assuming a 10% Main Effect for Each Factor**—Table Entries are Outcome Rates (%)

		SpO2		
		Low	High	Overall
CPAP	Yes	40	50	45
	No	50	60	55
	Overall	45	55	50

9.1 Quality Control

The selection of personnel will be left to the site PI's. No specific job descriptions are required for this protocol. The actual duties of the individual who will perform the randomization will be detailed in the manual for the study. Protocol violations will be reviewed, and if frequent, may require a site visit and consideration for termination of a collaborating site.

10.1 Risks and Benefits

Potential risks to the use of CPAP and/or PEEP include pneumothoraces; however this is unlikely to be increased over the risk of PPV alone. The level of CPAP/PEEP will be set at 5-6 cmH_2O, a level that is not thought to increase the incidence of pneumothorax. Recent data from Dr Morley suggest that this level is probably the lowest effective level especially when the infant's mouth is open, and is well tolerated. Objections to use of PEEP or CPAP could be countered by the argument that the majority of neonatologists use PEEP in resuscitation, thus the standard of care at most centers probably include the administration of CPAP and/or PEEP. Another potential risk is the administration of CPAP in the DR to infants without respiratory distress, which could conceivably cause vagal stimulation and resultant bradycardia and gastric distension.

Perhaps the major risk of this trial is that the known benefit of early surfactant with a reduction of death and disease severity, and a reduction of BPD with natural surfactant may not be offset by the early use of CPAP. However, the increasing trend in the use of early CPAP without such evidence represents an even greater risk.

Appendix A

Study Tables

Table 1. Patient Description

	Treatment	Control	P Value
Birth weight (grams) (M + SD)			
Gestation (weeks) (M + SD)			
Apgar 1 min < 3 Assigned			
Apgar 5 min < 3 Assigned			
Received PPV (Number, %)			
Surfactant in DR (Number, %)			
Received Chest Compression (N%)			
Received Epinephrine (N, %)			

Table 2. Other Outcomes

	Treatment	Control	P Value
Total Duration of Mechanical Vent (M +SD)			
Duration of Oxygen (Total days)			
Duration of CPAP			
Duration of nSIMV			
% alive off MV by Day 7 (+SD)			
Pneumothoraces (N, %)			
Other air leaks (N, %)			
BPD at 36 weeks (O_2 dependence)			
BPD by Physiologic Definition (N%+SD)			
Survived to discharge (N,% +SD)			
Number Never Intubated (N, %)			
Number receiving PNS for BPD (N, % %)			
Alive without neurdevelopmental impairment at (18-22 months) years (N, %, +/-SD)			

Appendix B

Study Tables

Table 1. Patient Description

	Low Saturation	High Saturation	RR	CI	p value
Birth weight (grams) (M + SD)					
Gestation (weeks) (M + SD)					
Race (W, B, H, other) %					
Antenatal steroids (%)					
Apgars ≤3 at 5 min					

Table 2. Primary Outcomes

	Low Saturation	High Saturation	RR	CI	p value
Threshold ROP/Surgery or death by 36 weeks (%)					
Death by 36 weeks (%)					
Threshold ROP in alive infants at 36 weeks (%)					
BPD or Death by 36 weeks (%) ±					

Table 3. Secondary Outcomes

	Low Saturation	High Saturation	RR	CI	p value
Death by discharge status (%)					
BPD in alive infants at 36 weeks (%)					
IVH 3 or 4/PVL or death by 36 weeks (%)					
IVH 3 or 4 in alive infants at 36 weeks (%)†					
Cystic PVL in alive infants at 36 weeks (%)†					
Neurodevelopmental impairment or death by 18-22 months (%)					
Death by 18-22 months (%)					
Neurodevelopmental impairment at 18-22 months (%)†					
Cerebral palsy at 18-22 months (%)†					
MDI < 70 (%)					
PDI < 70 (%)					
Any blindness at 18-22 months (%)†					
Unilateral blindness at 18-22 months (%)†					
Deafness at 18-22 months†					

†Analyzed for survivors

Table 4. Other Outcomes

	Low Saturation	High Saturation	RR CI	P Value
Total Duration of Ventilation (M+SD)				
On ventilator or death by day 7 (%)				
Pneumothorax (%)				
Any air leak (%)				
Postnatal steroids for BPD (%)				
Necrotizing enterocolitis ≥2 (%)				
PDA requiring surgery				

	Early CPAP/Early Extubation	Prophylactic Surfactant
Delivery Room Management	Resuscitate using CPAP. If necessary, initial PPV settings PIP 15-25, PEEP 5. Transport on CPAP If intubated for resuscitation, give surfactant within 1 hour of age. Do not intubate unless indicated by NRP guidelines	Intubate and give surfactant within 1 hour of age Transport with PPV according to SOC
Upon NICU Admission	Randomize within 2 hours to Pulse Oximeter	Randomize within 2 hours to Pulse Oximeter
Intubation Criteria	**Not Required. May intubate for ANY of these criteria** • FiO_2 >.50 required to maintain indicated SpO2 $\geq$ 88% (using the altered Pulse Oximeters) for one hour • $PaCO_2$ > 65 torr (art. or cap. samples, if venous $PaCO_2$ > 70 torr) documented on a single blood gas • Hemodynamic instability defined as a low blood pressure for gestational age and/or poor perfusion, requiring volume and/or pressor support for a period of 4 hours or more. **If intubated, give surfactant within the first 48 hrs if in respiratory distress**	**Reintubation Criteria** **Standard of Care**
Extubation Criteria	**Attempt extubation within 24 hours of fulfilling all of the following criteria:** • $PaCO_2$ < 65 torr with a pH > 7.20 (arterial or capillary samples) • An indicated SpO2 $\geq$ 88% with an FiO2 $\leq$ 50% • Mean airway pressure (MAP) < 10 cm H_2O, vent rate $\leq$ 20 bpm, amplitude < 2X MAP if on HFV • Absence of clinically significant PDA • Hemodynamically stable	**Keep intubated and ventilated until criteria met. Attempt extubation within 24 hours of fulfilling all of the following criteria** • $PaCO_2$ < 50 torr and pH > 7.30 (arterial or capillary samples) • FiO2 $\leq$ 35 with SpO2 > 88% • Mean airway pressure (MAP) < 8 cm H_2O, vent. rate $\leq$ 20 bpm, amplitude < 2X MAP on HFV • Absence of clinically significant PDA • Hemodynamically stable
Repeated Surf Doses	Subsequent doses may be given at the manufacturer's recommended dose up to a total of 4 doses.	
Intubation	Intubation may be performed at any time for the occurrence of repetitive apnea requiring bag and mask ventilation, clinical shock, sepsis, and/or the need for surgery	
CPAP D/C	In room air for at least 1 hour	
CPAP Resumption	At any time	
Duration of Intervention	14 days	14 days

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NICU Network	The SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants *DRAFT* PROTOCOL DEVIATION FORM	SUPP06 Rel 1.0 January 4, 2005

Center: __ __ Site No: ___ Network No. __ __ __ __ Birth No: ___ Mother's Initials: __ __ __ Report No: __

This form should be completed for all randomized patients whenever a protocol deviation is encountered by study personnel. This form will be keyed at the sites.

1. Date of Protocol Deviation: __ __/__ __/__ __ __ __ (Month / Day / Year)

2. Type of protocol deviation:
   1. Infant intubated without meeting study criteria.
   2. CPAP not initiated if required by protocol.
   3. Surfactant not given in the first hour.
   4. Mechanical ventilation initiated for other than study criteria.
   5. NSIMV initiated in infant not previously intubated.
   6. Extubation (exclude unplanned extubation) for other than study criteria?
   7. Failure to extubate CPAP infant if all criteria met.
   8. Infant received incorrect treatment assignment.

      If protocol deviation =8, indicate treatment arm ___

1= Ventilator Strategy	2= Oximetry Strategy	3= Both

   9. Oximeter not started within 2 hours.
   10. Other? *(Specify)*_____

3. Circumstances of the Protocol Deviation:

   _____

   _____

   _____

4. Additional Comments:

   _____

   _____

   _____

5. Name of Person who reported the protocol deviation on this form:

   _____

6. Date Protocol Deviation Form is completed: __ __/__ __/__ __ __ __ (Month / Day / Year)

   Initials of person completing this form: __ __ __

NICU Network

The SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants
Adverse Event Form

SUPP08 Rel 1.0
January 4, 2005

Center: __ __ Site No: ___ Network No: __ __ __ __ Birth No: ___ Mother's Initials: __ __ __ Report No. __ __

Complete this form for any randomized infant who experienced one or more of the following adverse events during the initial 14 days of life or prior to study status. This form will be keyed at the sites.

1. Did the infant have any adverse events during the first 14 days of life? Y N

If Yes,

ADVERSE EVENT	DATE Of ONSET (mm/dd/yyyy)	ATTRIBUTABLE TO SUPPORT STUDY 0 = No 1 = Not likely 2 = Possibly 3 = Probably	COMMENTS
1. Air leak in the first 14 days	__/__/__ __ __ __	___	
2. Need for chest compressions and/or epinephrine in the delivery room	__/__/__ __ __ __	___	
3. The occurrence of severe IVH (grades III-IV)	__/__/__ __ __ __	___	
4. Pulmonary Hemorrhage	__/__/__ __ __ __	___	
5. Nasal breakdown requiring discontinuation of nasal prongs	Date of Death __/__/__ __ __ __	___	
6. Death	Date of Death __/__/__ __ __ __	___	
7. Other (Specify) _____ _____ _____	__/__/__ __ __ __	___	

Initials of Person Completing this Form: ___ ___ ___

MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

For VOLUNTARY reporting by health professionals of adverse events and product problems

Page ___ of ___

Form Approved: OMB No. 0910-0291 Expires: 11/30/99
See OMB statement on reverse

FDA Use Only
Triage unit sequence #

PLEASE TYPE OR USE BLACK INK

A. Patient information

1. Patient identifier — In confidence
2. Age at time of event: or Date of birth:
3. Sex: ☐ female ☐ male
4. Weight: ____ lbs or ____ kgs

B. Adverse event or product problem

1. ☐ Adverse event and/or ☐ Product problem (e.g., defects/malfunctions)
2. Outcomes attributed to adverse event (check all that apply)
   - ☐ death ____ (mo/day/yr)
   - ☐ life-threatening
   - ☐ hospitalization – initial or prolonged
   - ☐ disability
   - ☐ congenital anomaly
   - ☐ required intervention to prevent permanent impairment/damage
   - ☐ other: ____
3. Date of event (mo/day/yr)
4. Date of this report (mo/day/yr)
5. Describe event or problem
6. Relevant tests/laboratory data, including dates
7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
   #1 ____
   #2 ____
2. Dose, frequency & route used
   #1 ____
   #2 ____
3. Therapy dates (if unknown, give duration) from/to (or best estimate)
   #1 ____
   #2 ____
4. Diagnosis for use (indication)
   #1 ____
   #2 ____
5. Event abated after use stopped or dose reduced
   #1 ☐ yes ☐ no ☐ doesn't apply
   #2 ☐ yes ☐ no ☐ doesn't apply
6. Lot # (if known)
   #1 ____
   #2 ____
7. Exp. date (if known)
   #1 ____
   #2 ____
8. Event reappeared after reintroduction
   #1 ☐ yes ☐ no ☐ doesn't apply
   #2 ☐ yes ☐ no ☐ doesn't apply
9. NDC # (for product problems only)
   – –
10. Concomitant medical products and therapy dates (exclude treatment of event)

D. Suspect medical device

1. Brand name
2. Type of device
3. Manufacturer name & address
4. Operator of device
   - ☐ health professional
   - ☐ lay user/patient
   - ☐ other: ____
5. Expiration date (mo/day/yr)
6. model # ____
   catalog # ____
   serial # ____
   lot # ____
   other # ____
7. If implanted, give date (mo/day/yr)
8. If explanted, give date (mo/day/yr)
9. Device available for evaluation? (Do not send to FDA)
   ☐ yes ☐ no ☐ returned to manufacturer on ____ (mo/day/yr)
10. Concomitant medical products and therapy dates (exclude treatment of event)

E. Reporter (see confidentiality section on back)

1. Name & address
   phone #
2. Health professional? ☐ yes ☐ no
3. Occupation
4. Also reported to
   - ☐ manufacturer
   - ☐ user facility
   - ☐ distributor
5. If you do NOT want your identity disclosed to the manufacturer, place an " X " in this box. ☐

FDA

Mail to: MEDWATCH, 5600 Fishers Lane, Rockville, MD 20852-9787 or FAX to: 1-800-FDA-0178

FDA Form 3500

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

A separate form should be completed whenever a protocol deviation/violation is encountered. Fax the report to Betty Hastings at RTI (919) 485-7762 by the end of the next working day.

1. Date of protocol deviation/violation: __ __/__ __/__ __ __ __ (Month Day Year)

2. Nature of the protocol deviation/violation: ___

   1= Unmasking

   2= Wrong study gas administered

   3= Study gas never started

   4= Study gas given > 336 hours

   5= After 240 hours study gas, > 1 ppm given

   6= Provision of open-label NO

   7= Other deviation/violation (please describe):

   _____

   _____

   8= Unable to complete study gas dose response due to clinical instability

   9= Administration of study gas via HFFI outside of parameters in Appendix I.

3. Circumstances of the protocol deviation/violation:

   _____

   _____

   _____

   _____

   _____

   _____

   _____

   _____

   _____

   _____

   _____

4. Additional information:

   _____

   _____

   _____

   _____

   _____

   _____

   _____

   _____

5. Name of the person reporting the protocol deviation/violation:

   _____

   Initials of person completing this form: ___ ___ ___

From:	Archer, Stephanie (NIH/NICHD) [E]
To:	Wally Carlo (wcarlo@peds.uab.edu); Neil Finer (nfiner@ucsd.edu)
Cc:	Higgins, Rosemary (NIH/NICHD) [E]; "Pablo Sanchez (Pablo.Sanchez@UTSouthwestern.edu)"; Archer, Stephanie (NIH/NICHD) [E]
Subject:	Boilerplate | SUPPORT
Date:	Tuesday, February 02, 2010 2:42:46 PM

Hi Wally and Neil,

Pablo would like to add "Diana M Vasil, RNC, NIC" to the list of people in the acknowledgements for UT Southwestern.

When you get the galleys back, I can review the boilerplate information for you.

Thanks,

Stephanie

Stephanie Wilson Archer
The Eunice Kennedy Shriver
National Institute of Child Health and Human Development
Pregnancy & Perinatology Branch
6100 Executive Boulevard, Room 4B03
Rockville, MD 20852

Tel. 301-496-0430
Fax 301-496-3790
archerst@mail.nih.gov

From:	Rowe, Mona (NIH/NICHD) [E]
To:	Higgins, Rosemary (NIH/NICHD) [E]; McGrath, John (NIH/NICHD) [E]; Fowler-Lee, Triesta (NIH/NICHD) [E]
Cc:	Spong, Catherine (NIH/NICHD) [E]; Archer, Stephanie (NIH/NICHD) [E]
Subject:	RE: Antenatal_Consent_Paper_Network_Revision for Submission Feb 1
Date:	Tuesday, February 02, 2010 11:28:21 AM

HI rosemary – we will look at and get back to you asap

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Tuesday, February 02, 2010 11:18 AM
To: Rowe, Mona (NIH/NICHD) [E]; McGrath, John (NIH/NICHD) [E]
Cc: Spong, Catherine (NIH/NICHD) [E]; Archer, Stephanie (NIH/NICHD) [E]
Subject: Antenatal_Consent_Paper_Network_Revision for Submission Feb 1

Hi,
Attached is a paper which has already gone through NICHD clearance; there are no NICHD authors on the paper. The SUPPORT study was co-funded by us and NHLBI. The reviewers asked for a cost estimate for the antenatal consent process and the authors have inserted two paragraphs - one in the results and one in the discussion which I have highlighted. Will these be acceptable? Let me know by the end of this week if this is a problem as the authors want to get the paper back to Pediatrics.

Thanks
Rose

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT | NEJM forms received
Date: Monday, February 01, 2010 11:09:14 AM

I gathered the NEJM forms from the fax machine, your chair, and the pile next to your printer. Any other places I should look for these?

Here's what I have so far (yellow highlight is where someone faxed only one of the required forms):

NEJM Forms received

	Copyright Transfer	ICMJE Disclosure
The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets in Extremely Premature Infants (09-11781)		
Abbot R. Laptook, MD	X	X
Abhik Das, PhD		
Anthony J. Piazza, MD		
Beena G. Sood, MD MS		
Bradley A. Yoder, MD		
Brenda B. Poindexter, MD MS		
Brenda H. Morris, MD		
C. Michael Cotten, MD MHS	X	X
Dale L. Phelps, MD		
Edward F. Bell, MD		
Ivan D. Frantz III, MD		
Krisa P. Van Meurs, MD	X	
Kristi L. Watterberg, MD		X
Kurt Schibler, MD	X	X
Marie Gantz, PhD		
Michele C. Walsh, MD MS		
Nancy S. Newman, RN	X	X
Neil N. Finer, MD		
Nirupama Laroia, MD		
Pablo J. Sánchez, MD		
Richard A. Ehrenkranz, MD	X	X
Roger G. Faix, MD		
Rosemary D. Higgins, MD		
Shahnaz Duara, MD	X	X
T. Michael O'Shea, MD, MPH		
Vivek Narendran, MD MRCP	X	X
W. Kenneth Poole, PhD		
Wade Rich, RRT		
Waldemar A. Carlo, MD	X	X
Early CPAP versus Surfactant in Very Preterm Infants: The SUPPORT Trial (09-11783)		
Abbot R. Laptook, MD	X	X

Abhik Das, PhD		
Beena Sood. MD, MS		
Bradley A. Yoder, MD		
Brenda B. Poindexter, MD MS		
Brenda H. Morris, MD		
C. Michael Cotten, MD MHS	X	X
Edward Donovan		
Edward F. Bell, MD		
Ivan D. Frantz III, MD		
Krisa P, Van Meurs, MD	X	
Kristi L. Watterberg, MD		X
Kurt Schibler		
Marie Gantz, PhD		
Michele C. Walsh, MD MS		
Namasivayam Ambalavanan, MD		X
Nancy Newman, RN	X	X
Neil N. Finer, MD		
Nirupama Laroia, MD		
Pablo J. Sánchez, MD		
Roger G. Faix, MD		
Rosemary D. Higgins, MD		
Shahnaz Duara, MD	X	X
Susie Buchter, MD	X	X
T. Michael O'Shea, MD, MPH		
Vineet Bhandari, MD, DM	X	X
W. Kenneth Poole, PhD		
Wade Rich, RRT, CCRC		
Waldemar A. Carlo, MD	X	X

From:	Higgins, Rosemary (NIH/NICHD)
To:	Everett, Ruth
Cc:	Poe, Grace (NIH/NICHD) [E]; sduara@miami.edu
Subject:	RE: SUPPORT
Date:	Tuesday, February 01, 2005 10:50:00 AM

Hi Ruth,
For the SUPPORT Study, you will need Radical Blue Screen pulse Oximeters with the LNOP NEO disposable probes and the Neopuff Resuscitator device with the single use circuit and gas supply lines which were budgeted in last year's award. Please let us know if you need additional information.
Thanks
Rose

From: Everett, Ruth [mailto:REverett@med.miami.edu]
Sent: Tuesday, February 01, 2005 10:25 AM
To: Higgins, Rosemary (NIH/NICHD)
Subject: SUPPORT

Hello Dr. Higgins, could you please e-mail to me a statement regarding the need for the following equipment Radical Blue Screen pulse Oximeter with the LNOP NEO disposable probes and the Neopuff Resuscitator device with the single use circuit and gas supply lines, in order to process my paper work here at the university as the equipment is needed for SUPPORT study. Thanks, the person who handles this paper work states that it will go through the process much faster than giving them a copy of the original protocol.

Ruth Everett-Thomas, RN, MSN
Nurse Specialist II
Coordinator
NICHD Neonatal Network
reverett@med.miami.edu
Office: (305) 585-8433
Fax: (305) 545-6581

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]; dale_phelps@urmc.rochester.edu; Stevens, Timothy
Subject: Re: SUPPORT SECONDARY STUDY
Date: Monday, January 31, 2005 10:07:32 PM

Congratulations Tim and Dale
I am delighted to see this very important study move ahead.
Be well
Neil

----- Original Message -----
From: Higgins, Rosemary (NIH/NICHD)
To: Dale Phelps (dale_phelps@urmc.rochester.edu) ; Stevens, Timothy
Cc: Neil Finer (nfiner@ucsd.edu)
Sent: Monday, January 31, 2005 12:43 PM
Subject: SUPPORT SECONDARY STUDY

Hi Tim and Dale,
The votes are in for the support secondary study 12 – yes and 0 no – therefore this is considered approved by the Steering Committee. I will get a letter up to you ASAP that you can send to the Scientific Review Administrator for your K award. We will send this for advisory board/outside review input.
Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From:	Higgins, Rosemary (NIH/NICHD)
To:	Phelps, Dale
Subject:	RE: SUPPORT SECONDARY STUDY
Date:	Monday, January 31, 2005 4:13:00 PM

It comes to you as the network PI – it will say it is from us – Have fun!!
Thanks
Rose

From: Phelps, Dale [mailto:Dale_Phelps@URMC.Rochester.edu]
Sent: Monday, January 31, 2005 4:18 PM
To: Higgins, Rosemary (NIH/NICHD)
Subject: RE: SUPPORT SECONDARY STUDY

Wonderful!

Is it coming to Tim, or to me?

I am out of town Tues-Sat. and if it is coming to me, he'll have to open my mail, with my permission.

Dale

> -----Original Message-----
> **From:** Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
> **Sent:** Monday, January 31, 2005 4:09 PM
> **To:** Phelps, Dale
> **Subject:** RE: SUPPORT SECONDARY STUDY
>
> Dale
> I spoke to Tim - the letter of support is in the FED EX mailing tonight - you should get it tomorrow!
> Thanks for your patience!
> Rose

> **From:** Phelps, Dale [mailto:Dale_Phelps@URMC.Rochester.edu]
> **Sent:** Monday, January 31, 2005 4:10 PM
> **To:** Higgins, Rosemary (NIH/NICHD)
> **Subject:** RE: SUPPORT SECONDARY STUDY
>
> Thank you very much Rose !
> Dale
>
> > -----Original Message-----
> > **From:** Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
> > **Sent:** Monday, January 31, 2005 3:43 PM
> > **To:** Phelps, Dale; Stevens, Timothy
> > **Cc:** Neil Finer (nfiner@ucsd.edu)
> > **Subject:** SUPPORT SECONDARY STUDY
> >
> > Hi Tim and Dale,
> > The votes are in for the support secondary study 12 - yes and 0 no - therefore this is considered approved by the Steering Committee. I will get a letter up to you ASAP that you can send to the Scientific Review Administrator for your K award. We will send this for advisory board/outside review input.
> > Thanks
> > Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD)
To: "nfiner@ucsd.edu"
Subject: Re: POST ROP Meeting at NICHD
Date: Friday, January 28, 2005 6:59:23 PM

Neil
I need to check to see if Dr. Askie was included on the original vote for release of the SUPPORT protocol. I think that the australian group was but need to re-check. I will be in touch with you on Monday.
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Neil Finer <nfiner@ucsd.edu>
To: Lisa Askie <laskie@cochrane.co.uk>
CC: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
Sent: Fri Jan 28 18:57:03 2005
Subject: Re: POST ROP Meeting at NICHD

Hi Lisa
Because we are going to hopefully collaborate in the prospective meta analysis, I am going to email, you the current version of the protocol. I will need to delay till Monday for 2 reasons. I want to send you the current version which I do not have as I am not in the office, and I want Rose Higgins to be aware and SUPPORT this request. I have answered your questions below.
Be well
Neil Finer
----- Original Message -----
From: "Lisa Askie" <laskie@cochrane.co.uk>
To: "'Neil Finer'" <nfiner@ucsd.edu>
Sent: Friday, January 28, 2005 9:20 AM
Subject: RE: POST ROP Meeting at NICHD

> Dear
> Neil,
> I am just following up a couple of matters in relation to the prospective
> meta-analysis (PMA) of planned oxygen trials as I have heard that NICHD
> has
> given support for SUPPORT to consider contributing data to the planned
> PMA.
>
> Have you been able to obtain permission for me to see a copy of the
> SUPPORT
> trial protocol? If not, are you able to answer the following few simple
> questions:
> - what is the planned sample size?1310
> - what is the projected timeline for recruitment, 2- 2.5 yrs follow-up
> 18-22 months and publication as soon as we can
> of results?
> - what are the intervention comparisons being tested (factorial design?)?
> CPAP and a permissive vent stratgegy vs Intubation + Surfactant within 1

> hour and conventional ventilation and SPO2 target 85%-89% vs 91% to 95%
> from 2 hours of age
>
> It would be good to have this information for a few reasons. Firstly I am
> drafting a very preliminary version of the PMA protocol and one of the
> appendices is a list of potentially eligible trials which includes planned
> sample size and timelines for completion (so we can planned when data will
> be available for merging). I would like to send you a copy so it would be
> good to have the correct information included re SUPPORT. Also, the New
> Zealand group need to answer a query form their funding application peer
> review regarding how the inclusion of SUPPORT to the planned PMA would
> improve its power. I have attached a sheet containing the rough sample
> size
> calculations which I would like to send onto Brian Darlow and, again, it
> would be good to include the correct SUPPORT figures.
>
> If you are able to address these issues I would be very grateful indeed.
>
> Regards,
> Lisa
>
> ◇◇◇◇◇◇◇◇◇◇◇◇◇◇◇◇◇◇◇◇
> Lisa Askie PhD MPH
> NHMRC Sidney Sax Postdoctoral Fellow
> PARIS Collaboration Coordinator
>
> UK Cochrane Centre
> Summertown Pavilion
> Middle Way
> Oxford. OX2 7LG. UK.
>
> Phone: + 44 (0)1865 516 300
> Direct: + 44 (0)1865 517 621
> Fax: + 44 (0)1865 516 311
> Mobile: + 44 (0)7879 658 326
> Email: laskie@cochrane.co.uk
> ◇◇◇◇◇◇◇◇◇◇◇◇◇◇◇◇◇◇◇◇
>
>
>
> -----Original Message-----
> From: Neil Finer [mailto:nfiner@ucsd.edu]
> Sent: Tuesday, November 02, 2004 3:36 AM
> To: ccole@bidmc.harvard.edu
> Cc: williamtm@med.usyd.edu.au; laskie@cochrane.co.uk
> Subject: Re: POST ROP Meeting at NICHD
>
> Cindy
> I will try to call you tomorrow.Lisa
> I haven't forgotten - I am awaiting approval to send you Cindy and William
> an electronic protocol.
> Be well
> Neil
> ----- Original Message -----
> From: <ccole@bidmc.harvard.edu>
> To: <williamtm@med.usyd.edu.au>; <nfiner@ucsd.edu>
> Cc: <laskie@cochrane.co.uk>

> Sent: Monday, November 01, 2004 10:58 AM
> Subject: RE: POST ROP Meeting at NICHD
>
>
>> Dear William, Neil, and Lisa,
>> I look forward to hearing good news from Australia next week.
>> At this time the NICHD POST ROP budget has not been finalized. The
> realistic
>> (estimated)budget presented on Oct 27th to Tonse will need to be reduced.
>> We discussed, but did not resolve, if the PMA will be included in the
>> POST
>> ROP proposal and budget, or if the PMA would be submitted as a separate
>> proposal.
>> The decision will be influenced by the budget for POST ROP and the budget
>> for PMA.
>> Could you, Lisa, et al provide guidance rgarding your thoughts on a
>> budget
>> for PMA? I will send you mine. Ideally, I want to propose as much as
>> possible to the NICHD to help support the PMA, including support for
>> Lisa.
>> After I propose a budget for POST ROP and PMA, then Tonse will be able to
>> advise us on strategy for funding each.
>>
>> I hope Australian elections go well. Who knows what November 2 will bring
>> for the USA!
>>
>> Dear William and Neil -
>> We did discuss the importance of research on 'desaturations continuously
>> recorded and neuro-developmental/ cognitive outcomes'. Tonse, Rose, Anne,
>> and Neal were VERY KEEN on this. We obviously did not go into tremendous
>> detail. I view the oxygenation variability and neuro-outcomes as a
> separate
>> proposal to NINDS. Correct? So, Neil, you have my full vote for us to
> move
>> forward on this. We should discuss this in more detail with Tonse and
> Rose.
>>
>>
>> -----Original Message-----
>> From: williamtm@med.usyd.edu.au [mailto:williamtm@med.usyd.edu.au]
>> Sent: Monday, November 01, 2004 11:45 AM
>> To: ccole@bidmc.harvard.edu
>> Subject: Re: POST ROP Meeting at NICHD
>>
>>
>> Dear Cindy
>>
>> Thank you and congratulations on this encouraging outcome of your meeting
> at
>> NICHD and on your phenomenal energy and stamina. I am writing to you
>> individually, but please copy your reply to all as appropriate.
>>
>> We have been notified that we will hear the result of the BOOST II NHMRC
>> application next week - somewhat delayed because of the Australian
> election.
>>
>> Please clarify two points.

>>
>> Was there support for inclusion in the RO1 application of the expenses/
> part
>> time salary and infrastructural costs for a specific individual, such as
>> Lisa Askie, in establishing and co-ordinating a formal PMA of all POST
>> ROP/BOOST II trials (assuming BOOST II is funded in Australia)?
>>
>> Please let Neil Finer know how you would like to proceed on the
> possibility
>> of a research question on desaturations continuously recorded and
>> neuro-developmental/ cognitive outcomes that would be of interest to
> NINDS.
>> He is eminently placed to develop this angle, and to be a co-investigator
>> and would respond rapidly and thoroughly.
>>
>> Congratulations again !
>>
>>
>> William
>>
>>
>>
>> Quoting ccole@bidmc.harvard.edu:
>>
>> > Dear Neil, William, and MIchael (and all who are copied),
>> >
>> > Anne Lindblad, Neal Oden, and I had an excellent meeting on Wednesday,
>> > Oct 27 with Tonse Raju and Rosemary Higgins. We discussed
>> > justification and strategy of POST ROP submission to NICHD. The
>> > following is a brief summary of the meeting's highlights. This email
>> > will not go into extensive detail of the discussions and decisions. I
>> > apologize for the delay in getting this response to each of you. These
>> > have been 18-20 hr days, I have been on-service in the NICU and
>> > working again all last night. I will submit an overview of POST ROP
>> > status and proposed plan to the USA Planning Group this week for their
>> > review and response.
>> >
>> > Please consider this email 'confidential' as we do not know who will
>> > be on our study section (domestic or foreign) to review our NICHD
>> > proposal.
>> >
>> > 1. Justification of NICHD supporting POST ROP (in light of SUPPORT
>> > trial funded by NICHD via Neonatal Network): Tonse and Rosemary feel
>> > that POST ROP is absolutely justified even with SUPPORT. In fact,
>> > Tonse and Rosemary strongly advised us to not draw attention to the
>> > NICHD SUPPORT trial in our submission. Tonse
>> > (appropriately) indicated that the Study Section's sole responsibility
>> > was to review POST ROP based on its own merit and that the Study
>> > Section should NOT score the proposal based on other trials supported
>> > by NICHD Neonatal Network.
>> >
>> > 2. R01 vs. R34 planning grant: Tonse and Rosemary strongly advised us
>> > to go for the R01 submission Feb 1, 2005. They feel that we are in
>> > excellent position for an R01 submission and that a pilot study is not
>> > necessary for the R01 Submission. Tonse and Rosemary believe that we
>> > (investigators and
>> > EMMES) have a strong background in STOP ROP, BOOST I, AViOx to document

>> > experience in trials involving pulse oximetry and pulse oximetry
> analysis.
>> > 'The 'pros' of going for an R01 outweighed the 'pros' of R34 planning
>> grant.
>> > The negative impact of delaying the onset of the trial if we went the
> 'R34
>> > planning grant' route was viewed as a greater liability.
>> >
>> > 3. To Do for R01: This is not a complete list. Obviously much must
>> > be/will be accomplished by Feb 1st. a. Submit new POST ROP Summary and
>> > budget to Tonse ASAP so that he can begin to do his work alerting
>> > NICHD that a proposal will be submitted that will exceed $500,000
>> > budget and begin to discuss with other NIH institutes if they are
>> > interested in co-funding. b. Actively recruit centers now. We have to
>> > justify the ability of each center's participation. Letters from each
>> > site's PI (regarding their agreement to participate in the POST ROP
>> > trial) must accompany the R01 submission.
>> > c. Make POST ROP proposal as pragmatic as possible (i.e. make it as
>> similar
>> > as BOOST II). This includes minimizing the data collection.
>> > d. Issues that still need resolution:
>> > i. neurodevelopmental outcomes and assessment tool(s): These need
>> > to
>> be
>> > feasible (to maximize compliance and to minimize missing data) and
>> conducted
>> > by all centers for the Prospective Meta-Analysis (PMA). We will discuss
> if
>> a
>> > subset of centers will do Bayleys in addition to the "common
>> > neurodevelopmental" assessment.
>> > ii. ophthalmology outcomes at 2 yrs and specific assessments
> necessary
>> > for such.
>> > a. We need at least one pragmatic vision outcome for all
>> > centers
>> for
>> > the PMA analysis that will maximal assessment (and minimize missing
> data)
>> of
>> > whether the child has severe visual impairment.
>> > b. For the USA centers, Dr. Repka supports an eye exam at 2
> years
>> > age. Advice by neos is welcomed, but it is critical to have the POST
> ROP
>> > ophthalmology group discuss and advise us on these outcomes and
>> assessments.
>> >
>> > c. Resolution of 'Standardization and certification'.
>> > Web-based proposal is still supported by many, especially for global
>> > ophthalmic purposes. Develop and maintain web-site for this.
>> > d. Develop and maintain website for public inquiry and
>> > updates; password-secure access for Planning Group and collaborators.
>> > e. Education program: Our POST ROP Research Nurse (Brenda
>> > MacKinnon) is now employed at BIDMC (welcome Brenda!). We want to work
>> > with William et al to make substantial progress in this program for
>> > nursing, parents, (and physicians).

>> >
>> > This is all for now. Anne and Neil, if I have omitted a major point,
>> > please respond to all.
>> >
>> > ----Original Message-----
>> > From: Neil Finer [mailto:nfiner@ucsd.edu]
>> > Sent: Saturday, October 30, 2004 9:24 PM
>> > To: William Tarnow-Mordi
>> > Cc: ccole@bidmc.harvard.edu
>> > Subject: Re: Proposal for discussion with Raju Tonse at NICHD: re
>> > NINDS,
>> > intermittent hypoxia and neurodevelopmental outcome
>> >
>> >
>> >
>> > William
>> > I am happy to work with Cindy. Her last email indicated that she was
>> > meeting with Tonse Raju. I will wait till I hear from her regarding
>> > that meeting. Have you received any notification regarding the funding
>> > of your trial? Regards Neil
>> >
>> > ----- Original Message -----
>> > From: William Tarnow-Mordi <mailto:williamt@westgate.wh.usyd.edu.au>
>> > To: nfiner@ucsd.edu <mailto:nfiner@ucsd.edu> ; Cole,
>> > <mailto:CCole@tufts-nemc.org> Cynthia
>> > Sent: Wednesday, October 27, 2004 8:12 PM
>> > Subject: Re: Proposal for discussion with Raju Tonse at NICHD: re
>> > NINDS,
>> > intermittent hypoxia and neurodevelopmental outcome
>> >
>> > Neil
>> >
>> > Can you draft a research question on intermittent hypoxia/
>> > bradycardia/ cardio respiratory events and neurological outcome for
>> > the POST ROP/ BOOST II/ SUPPORT prospective meta analysis proposal as
>> > confirmed by Cindy?
>> >
>> > William
>> >
>> > Neil Finer wrote:
>> >
>> >
>> > I am willing to help/participate in any way.
>> >
>> > Neil
>> >
>> >
>> >
>> > -----Original Message-----
>> >
>> > From: williamtm@med.usyd.edu.au <mailto:williamtm@med.usyd.edu.au>
>> > [mailto:williamtm@med.usyd.edu.au <mailto:williamtm@med.usyd.edu.au>]
>> >
>> > Sent: Tuesday, October 26, 2004 2:57 PM
>> >
>> > To: nfiner@ucsd.edu <mailto:nfiner@ucsd.edu>
>> >

>> > Cc: 'William Tarnow-Mordi'; ccole@bidmc.harvard.edu
>> > <mailto:ccole@bidmc.harvard.edu>
>> >
>> > Subject: Proposal for discussion with Raju Tonse at NICHD: re NINDS,
>> >
>> > intermittent hypoxia and neurodevelopmental outcome
>> >
>> >
>> >
>> > Dear Cindy and Neil
>> >
>> >
>> >
>> > Cindy - when is your meeting with Tonse Raju? If it has not already
>> >
>> > occurred,
>> >
>> > please consider the following.
>> >
>> >
>> >
>> > The current J Peds has an article and editorial by Carl E. Hunt, MD,
>> >
>> > Director,
>> >
>> > National Center on Sleep Disorders Research, National Heart, Lung, and
>> > Blood
>> >
>> > Institute, 6705 Rockledge Dr, Ste 6022, Bethesda, MD 20892-7993 which
>> > I have
>> >
>> > attached, with a related pdf article re effect of intermittent hypoxia
>> > in
>> >
>> > young
>> >
>> > rats on later learning ability. Hunt's group reports "Having 5+
>> >
>> > cardiorespiratory events (during home monitoring in term and preterm
>> > infants
>> >
>> > at
>> >
>> > risk for SIDS) is associated with lower adjusted mean differences in
>> >
>> > MDI in term and preterm infants." In his editorial, Hunt states "
>> > These
>> >
>> > provocative findings need to be confirmed in other cohorts and their
>> >
>> > longer-term significance established, but they do suggest substantial
>> > gaps
>> >
>> > in
>> >
>> > our knowledge."
>> >

>> >
>> >
>> > Can Neil propose a draft research question attractive to NINDS for
>> > Cindy to
>> >
>> > discuss with Tonse Raju expanding point(4) in our previous
>> > correspondence
>> >
>> > below?
>> >
>> >
>> >
>> > We could use the same definitions of cardiorespiratory events as in
>> > the
>> >
>> > CHIME
>> >
>> > study - apnea >/=20 seconds or heart rate <60 to 80 bpm or <50 to 60
>> > bpm,
>> >
>> > for
>> >
>> >
>> >
>> > /=5 to 15 seconds, depending on age.
>> >
>> >
>> >
>> >
>> >
>> > We could point out that prospective meta analysis of SUPPORT/ POST
>> > ROP/
>> >
>> > BOOST
>> >
>> > II would provide greatly enhanced power to investigate the hypothesis
>> > that
>> >
>> > cardiorespiratory events in extremely preterm infants are CAUSALLY
>> > related
>> >
>> > to
>> >
>> > later neurodevelopmental and cognitive deficit NDI CI, by determining
>> > if low
>> >
>> > or
>> >
>> > high targeted SaO2 increases CR events and rate of NDI CI, because
>> > these are
>> >
>> > RCTs, not observational studies.
>> >
>> >
>> >
>> > Other potential advantages are likley considerably higher rates of
>> >

>> > ascertainment and follow up than in the CHIME study (as most of the
>> >
>> > monitoring
>> >
>> > will be done in hospital before discharge)
>> >
>> >
>> >
>> > Is it worth discussing with Tonse whether to contact Carl Hunt for
>> > input?
>> >
>> > Who
>> >
>> > would be the right persons at NINDS to talk to?
>> >
>> >
>> >
>> > Good luck.
>> >
>> >
>> >
>> >
>> >
>> > William
>> >
>> >
>> >
>> >
>> >
>> > Quoting Neil Finer <mailto:nfiner@ucsd.edu> <nfiner@ucsd.edu>:
>> >
>> >
>> >
>> >
>> >
>> > Hi William and Cynthia
>> >
>> >
>> >
>> > I have made some changes below. I remain firmly in support - I am
>> > going to
>> >
>> > mention prospective meta analysis in another editorial that I have
>> > been
>> >
>> > asked to write regarding an upcoming publication. It seemed like an
>> >
>> > opportunity to further support this approach. Are there any more
>> > recent
>> >
>> > references about prospective meta analysis - have any other such
>> > studies
>> >
>> > been completed? Is the Simes trial (Simes et al Eur Heart J,
>> >
>> >
>> >

>> > 2002;23:207)
>> >
>> >
>> >
>> > the only completed prospective meta analysis?
>> >
>> >
>> >
>> > The rest below sounds great.
>> >
>> >
>> >
>> > I made a few suggestions to your editorial. This looks fine. Feel free
>> > to
>> >
>> > ignore any and all such changes.
>> >
>> >
>> >
>> > Be well
>> >
>> >
>> >
>> > Neil
>> >
>> >
>> >
>> >
>> >
>> >
>> >
>> >
>> > _____
>> >
>> >
>> >
>> > From: William Tarnow-Mordi [mailto:williamt@westgate.wh.usyd.edu.au
>> > <mailto:williamt@westgate.wh.usyd.edu.au>]
>> >
>> > Sent: Sunday, October 17, 2004 9:53 PM
>> >
>> > To: ccole@bidmc.harvard.edu <mailto:ccole@bidmc.harvard.edu> ;
>> > nfiner@ucsd.edu <mailto:nfiner@ucsd.edu>
>> >
>> > Subject: Outcomes of meeting with Neil Finer in San Diego and one
>> > further
>> >
>> > point from Tonse Raju
>> >
>> >
>> >
>> >
>> >
>> >
>> >
>> > Dear Cindy and Neil (please both of you comment on anything that needs
>> >
>> > correction, development or adding)

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>> >
>> >
>> > I am writing to report my discussions with Neil in San Diego and one
>> >
>> >
>> >
>> > further
>> >
>> >
>> >
>> > point discussed with Tonse Raju. Both meetings were fruitful. Neil is
>> > a
>> >
>> > staunch ally in the move towards a prospective meta-analysis (PMA) of
>> >
>> > neonatal oxygen trials and a supporter of large, simple neonatal
>> > trials.
>> >
>> > Tonse also supports both concepts, but points out that the higher the
>> >
>> >
>> >
>> > score
>> >
>> >
>> >
>> > the POST ROP application attracts, the more scope there is for its
>> > support
>> >
>> > and development. Please both respond to each of the 10 points below,
>> >
>> >
>> >
>> > point
>> >
>> >
>> >
>> > by point.
>> >
>> >
>> >
>> > (1) Neil had valuable suggestions about the need for overall
>> > collaborative
>> >
>> > group authorship for multicentre studies, including the possible
>> > oxygen
>> >
>> >
>> >
>> > PMA,
>> >
>> >
>> >
>> > with the contribution of every participating centre acknowledged at
>> > the
>> >

>> >
>> >
>> > end
>> >
>> >
>> >
>> > (or beginning) of the paper. He felt it was important to address this
>> > and
>> >
>> > other aspects of recognition and rewards for those who participate.
>> >
>> >
>> >
>> > (2) Neil requested clarification of the fact that, provided none of
>> > the
>> >
>> > results of comparisons from the individual trials had been published
>> > or
>> >
>> > revealed in any form, new trials and new hypotheses could be added to
>> > the
>> >
>> > PMA.
>> >
>> >
>> >
>> > (3) Neil responded favourably to my invitation to him to join you and
>> > me
>> >
>> >
>> >
>> > as
>> >
>> >
>> >
>> > co-authors on the Special Article which Jerry Lucey asked me to write
>> > for
>> >
>> > Pediatrics on "Large scale randomised evidence in neonatology: Why do
>> > we
>> >
>> > need it and how can it be achieved?" and on the article on Prospective
>> >
>> >
>> >
>> > Meta
>> >
>> >
>> >
>> > Analysis which we also plan to write (see 5 below).
>> >
>> >
>> >
>> > (4) Neil proposed that we consider including as a major secondary
>> > research
>> >
>> > question, or co-primary research question, in the SUPPORT Trial and

>> > POST
>> >
>> >
>> >
>> > ROP
>> >
>> >
>> >
>> > and BOOST II and the oxygen PMA the relationship between measures of
>> >
>> > continuously recorded oxygen saturation during the first few weeks
>> > after
>> >
>> > birth in very preterm infants and later cognitive and
>> > neuro-developmental
>> >
>> > outcome in early childhood . The trials will be in a unique position
>> > to
>> >
>> > address this issue in unprecedented detail, because of the capacity of
>> > the
>> >
>> > Masimo oximeters to gather the data every 16 (This can be user
>> > defined -
>> >
>> > SUPPORT will use 1 sample every 10 seconds which should produce
>> > reasonable
>> >
>> > resolution) seconds, store and download it, with very little or no
>> > extra
>> >
>> > work for frontline clinical staff. The data co-ordinating centre (RTI)
>> > for
>> >
>> > the SUPPORT trial already works closely with NICHD and could be
>> > approached
>> >
>> > to store and analyse these data from SUPPORT and POST ROP and BOOST II
>> > or
>> >
>> > other trials as appropriate. This research question is likely to be
>> >
>> > attractive to the National Institute of Neurological Disorders and
>> > Stroke
>> >
>> > (NINDS), who might agree to consider and co-fund an application for
>> > POST
>> >
>> > ROP, along with NEI and NICHD. I would like to recommend that we
>> > take
>> >
>> >
>> >
>> > up
>> >
>> >
>> >

>> > this suggestion and invite Neil to be a chief investigator working
>> > with
>> >
>> >
>> >
>> > you
>> >
>> >
>> >
>> > to develop it further.
>> >
>> >
>> >
>> > (5) Neil would like to develop the proposals for a neonatal PMA of
>> > oxygen
>> >
>> > trials to a point where a formal presentation can be made to the NICHD
>> >
>> > Neonatal Intensive Care Unit Network, to request their approval that
>> > the
>> >
>> > SUPPORT Trial be registered as a contributing study. This would need
>> > to
>> >
>> >
>> >
>> > be
>> >
>> >
>> >
>> > developed over the next few months. I believe that we will invite
>> >
>> >
>> >
>> > Cynthia
>> >
>> >
>> >
>> > to the January Network Meeting - I have discussed with Rose Higgins
>> >
>> >
>> >
>> > (6) I have been asked by Alan Jobe to contribute a 400 word commentary
>> > for
>> >
>> > the March 2005 issue of Journal of Pediatrics on the 50th anniversary
>> > of
>> >
>> >
>> >
>> > an
>> >
>> >
>> >
>> > editorial on Control of oxygen therapy to prevent retrolental
>> > fibroplasia,
>> >

>> > which was published in Journal in 1955. I attach my draft and would
>> >
>> > appreciate any comments from you and from Neil. The deadline is
>> > almost
>> >
>> > immediately.
>> >
>> >
>> >
>> > (7) In my last phone conversation with Tonse Raju, he said (if I
>> > recall
>> >
>> > correctly) that he would like to organise a seminar to discuss the
>> > need
>> >
>> >
>> >
>> > for
>> >
>> >
>> >
>> > oxygen trials and prospective meta analysis. Please would you follow
>> > this
>> >
>> >
>> >
>> > up
>> >
>> >
>> >
>> > with him when you meet him in Washington at the end of this month,
>> > Cindy.
>> >
>> >
>> >
>> > (8) As things stand, I think that the best strategy for POST ROP is
>> > not
>> >
>> >
>> >
>> > to
>> >
>> >
>> >
>> > go for a full application immediately but to apply for a planning
>> > grant
>> >
>> > whose score is likely to be considerably strengthened by the following
>> >
>> >
>> >
>> > * Need for large scale randomized evidence to exclude a small but
>> >
>> > clinically important increase in Neurodevelopmental Impairment of 5%
>> > or
>> >
>> > less, which no single trial will have the power to detect.

>> >
>> > * Commitment to develop a prospective meta analysis of neonatal oxygen
>> >
>> > trials in c. 5,000 infants.
>> >
>> > * Successful funding for BOOST II (outcome available in next month)
>> >
>> > * Invitation to submit applications to UK MRC and Canadian IHR.
>> >
>> > * Proposal to NINDS to co-fund collaborative research into the longer
>> >
>> > term neurologic effects of continuously monitored oxygen saturation
>> > and
>> >
>> > desaturation during the first weeks after birth.
>> >
>> > * Commitment by NEI to co-fund a simpler version of POST ROP.
>> >
>> >
>> >
>> >
>> >
>> > (9) One disadvantage of the currently projected Planning Grant process
>> > for
>> >
>> > POST ROP is that even a one year period to develop a Manual of
>> > Operations
>> >
>> > would delay the start of a full POST ROP study (if successful) to
>> > early
>> >
>> > 2008. Is there any possibility of having the MOP completed in 6
>> > months of
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>> > the Planning Grant instead of one year? Could that bring us on track
>> > to
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>> > start recruitment into a full POST ROP study in 2007?
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>> > (10) I would like to come to the States in early December, around the
>> > time
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>> > of my trip to the UK for the annual steering group meeting of the INIS
>> >
>> > trial, to visit Alan Jobe's department in Cincinatti, if possible, to
>> >
>> > present some of these ideas and discuss them with him. Does that
>> > sound a
>> >
>> > sensible plan?
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>> >
>> > kindest regards
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>> > William
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>> >
>> > William Tarnow-Mordi
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>> > Professor of Neonatal Medicine
>> >
>> > University of Sydney
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>> > Westmead Hospital and The Children's Hospital at Westmead
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>> > Head of Neonatology
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>> > Ph (0)2 9845 8911 or (0)2 9845 5555 and pager 08352
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From: Higgins, Rosemary (NIH/NICHD)
To: "alan.jobe@chmcc.org"
Subject: Re: Ball
Date: Friday, January 21, 2005 10:23:46 AM

John can be reached through the main number at 301-496-5575.
I will let John know. John said he would give you a call later this am
I will call you later today about support as we are trying to develop some details to stopping recommendations.
I was not invited to any of the presidential gatherings, so did not need a new dress!!

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: CHMCC Groupwise <alan.jobe@chmcc.org>
To: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
Sent: Fri Jan 21 09:13:05 2005
Subject: Ball

Hope you got a new dress for the Presidents Ball. Sorry that I missed it.

Hope all is well - see you on Monday - if the weather holds.

Do you have a tele # for Ilikis (sp?) - I want to talk to him about this
neonatal genomics thing on the schedule for Monday.

Thanks
Alan H. Jobe, MD, PhD
Professor of Pediatrics
Division of Pulmonary Biology/Neonatology
Cincinnati Children's Hospital Medical Center
3333 Burnet Avenue, ML#7029
Cincinnati, Ohio 45229
ph: 513-636-8563
fax: 513-636-8691
E-mail: alan.jobe@cchmc.org

From: Higgins, Rosemary (NIH/NICHD)
To: Spong, Catherine (NIH/NICHD) [E]
Subject: FW: SUPPORT Protocol
Date: Thursday, January 13, 2005 9:58:00 AM
Attachments: Support protocol.pdf

Cathy
Here is the prior email about the SUPPORT Trial overlap – do you know if the MFMU concurrent research committee had a chance to weigh in?
Thanks
Rose

From: Higgins, Rosemary (NIH/NICHD)
Sent: Thursday, October 21, 2004 1:22 PM
To: Spong, Catherine (NIH/NICHD)
Subject: SUPPORT Protocol

Cathy
here is the protocol

I will let our PI's know that it is going to the MFMU concurrent research committee. It is randomized and if there is felt to be overlap, our concurrent research subcommittee (Jon Tyson, chair) may want to also weigh in. I believe the DR CPAP pilot was presented on several occasions at the MFMU meeting. I know I presented it once and did say we were developing a larger trial

Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(for Fed X use Rockville, MD 20852)
301-435-7909

301-496-3790 (FAX)

Protocol for the NICHD Neonatal Research Network

The SUrfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants

The SUPPORT Trial

Final

August 28, 2004
Revised September 16, 2004

1.1 Statement of Problem

At the present time, there is no recommendation or standard teaching regarding the early use of CPAP/PEEP during resuscitation and continuing after NICU admission for the extremely low birth weight (ELBW) infant. However, a number of studies, mostly retrospective in nature, have suggested that the use of early CPAP may be associated with improved outcomes, including a decreased need for mechanical ventilation, a decreased need for surfactant therapy, and a decrease in oxygen supplementation and/or death at 28 days after birth and at 36 weeks post menstrual age. There has not been a prospective study which has randomized ELBW infants to CPAP/PEEP beginning in the delivery room, and continuing in the NICU and a permissive ventilation strategy if intubation is required and compared their outcomes to infants treated with prophylactic or early natural surfactant, interventions with known efficacy in reducing mortality, severity of disease and the incidence of chronic lung disease (CLD).

Retinopathy of prematurity (ROP) remains a significant cause of morbidity among ELBW infants and its occurrence is inversely proportional to gestational age and duration of oxygen exposure. It is known that ROP is increased by the prolonged use of supplemental oxygen from observations published in the 1950s, and but early trials were unable to pinpoint the actual level of arterial PaO_2 which was the threshold for triggering the pathophysiology of this disorder.[1] However, there have been a very few prospective studies evaluating the benefit of higher versus lower levels of oxygenation in infants, especially for ELBW infants, none of which were performed during the acute illness. While retrospective cohort studies have suggested that the use of lower SpO2 ranges and adherence to strict nursery policies may result in a lower incidence of severe ROP, there is no current agreement on the accepted SpO2 ranges for managing the ELBW infant from birth.

1.2 Background

Positive End Expiratory Pressure (PEEP) has been shown to be of benefit in maintaining functional residual capacity (FRC). Although no formal recommendation has been made to date about maintaining PEEP in the delivery room setting, continuous positive airway pressure appears beneficial during cardiopulmonary resuscitation[2]. Gregory et al in 1971 first demonstrated that the use of CPAP started at approximately 5.9hours ($\pm$12.4hrs) for their infants < 1500 gm at birth, improved oxygenation[3] in newborn infants with respiratory distress; these observations were followed by prospective studies that demonstrated improved survival in premature infants treated with early CPAP[4]. Premature infants who do not achieve a FRC are more likely to develop hyaline membrane disease (HMD) requiring mechanical ventilation[5]. CPAP may prevent the excessive consumption of surfactant in newborn infants with limited surfactant production.[6] A review of prospective studies evaluating early (not delivery room) CPAP in the pre-surfactant, pre-antenatal steroid era suggested that early CPAP may improve survival in infants greater than 1500 gm.[7]

Similarly, there is no definite recommendation or standard teaching regarding the level of oxygenation that should be maintained in ELBW infants. Oxygen supplementation has to be used liberally as ELBW infants frequently have desaturation episodes and thus wide saturation ranges are tolerated clinically. However, oxygen toxicity can result in increased risk for CLD, retinopathy of prematurity (ROP) and other disorders. Alternatively, oxygen restriction may impair neurodevelopment. The pulse oximeter is a newer technology that can be used to improve the control of oxygenation levels. There is great potential benefit to determining the oxygenation levels that prevents ROP and CLD but does not result in neurodevelopmental impairment with a randomized controlled trial of levels of oxygen saturations on the high and low side of the currently utilized levels.

While prevention of hyperoxia may decrease the risk for ROP and CLD, efforts to maintain lower oxygenation levels may result in an increase in periods of hypoxemia because of the marked variability in oxygen in ELBW infants. Thus, it is necessary to determine if lower oxygenation levels that may prevent ROP and CLD are deleterious for brain development and result in impaired neurologic outcome.

1.3 Animal Studies

Nilsson et al demonstrated that the use of 5 cm H_2O PEEP in the initial ventilation of premature rabbit pups resulted in increased lung-thorax compliance, and reduced the extent of bronchiolar epithelial lesions seen with mechanical ventilation [8]. The use of early PEEP starting at delivery, improves the response to surfactant, improves lung mechanics increases surfactant pools, and reduces lung injury. [9,10]

More recently studies by Jobe et al have demonstrated that premature lambs treated with CPAP alone at birth had significantly decreased neutrophils and hydrogen peroxide in their alveolar wash when compared with animals who were ventilated from birth. [11]

1.4 Human Experience: Ventilatory Support

CPAP was introduced by Gregory et al in 1970 and was shown to improve gas exchange and outcomes in preterm infants with respiratory distress.[12] A subsequent review of CPAP for respiratory distress concluded that "In preterm infants with RDS the application of CDP either as CPAP or CNP is associated with benefits in terms of reduced respiratory failure and reduced mortality. CDP is associated with an increased rate of pneumothorax. The applicability of these results to current practice is difficult to assess, given the intensive care setting of the 1970s when four out of five of these trials were done." [13]

There is now a body of information from Europe that provides further evidence that early CPAP can reduce the need for intubation in a significant number of VLBW infants. Jonsson et al treated VLBW infants from 1988 to 1993 that required > 30% oxygen with nasal CPAP usually within 30 minutes of delivery[14]. From 1991 onward, infants with severe distress or apnea were intubated for a $PaCO_2$ greater than 60 mmHg, and were given surfactant. Twenty-five percent of all infants required only supplemental oxygen and 24% of all infants were ventilated from birth. Fifty-one percent were treated with nasal CPAP, with one-third of these subsequently requiring ventilation. Almost all infants < 24 weeks required ventilation suggesting that this group may require a different approach. Gittermann et al reported that the use of early CPAP for infants < 1500gm (VLBW) significantly reduced the frequency of intubation, reduced mortality ($p=0.038$), and shortened the duration of intubation and length of stay[15]. In this study the CPAP was applied as soon a signs of respiratory distress occurred (usually within 15 minutes of birth). Poets et al[16] in a report of 2001 VLBW infants (500 to 1499 g) born from 1992 to 1994 reported that there was an increase in the proportion of patients not intubated and mechanically ventilated from 7% to 14% in infants <1000 g and from 28% to 44% in those $\geq$1000 g ($P < 0.02$ and <0.01, respectively). The decrease in intubation was not associated with a significant increase in adverse outcome such as death, intraventricular hemorrhage, periventricular leukomalacia, or BPD. The proportion of infants <1000 g that survived without BPD increased from 38% in 1992 to 48% in 1994; $p < .05$, and the proportion of infants =1000 g in whom BPD developed decreased from 14% to 9%; $p < .05$. None of these observations was from a prospective controlled trial, and in none was there a contemporaneous control group who did not receive early CPAP.

The first prospective trial comparing prophylactic CPAP, started at birth, with conventional management was that of Han et al. They compared the use of nasal CPAP given by nasopharyngeal tube with conventional management in 82 infants, 32 weeks gestational age at birth, and in this study it would appear that CPAP was begun in the DR, but may have been delayed for up to 2 hours.[17] No infants in this trial received surfactant, and no mothers were treated with antenatal steroid. There was no advantage observed with the use of early CPAP, and oxygenation was worse in the early CPAP treated infants. The reviewers of the use of prophylactic CPAP in the Cochrane library concluded that "A multicenter randomized controlled trial comparing prophylactic nasal CPAP with "standard" methods of treatment is needed to clarify its clinical role."[18]

In the post surfactant era, Verder et al conducted the first prospective evaluation of early CPAP (not necessarily delivery room CPAP) and short-term intubation for surfactant administration in a multicenter collaborative trial conducted from September 1991 to October 1992.[19] The primary hypothesis was that the use of early CPAP and brief intubation for surfactant in infants meeting pre-established criteria would reduce the percentage of infants requiring mechanical ventilation from 80% to 40%. Infants randomized to surfactant [Curosurf®] received 200 mg/kg, (2.5 ml/kg) following intubation, with manual ventilation for 2-5 minutes and were then extubated if stable. This study was stopped after an interim analysis demonstrated a significant benefit for the surfactant treated infants. Thirty-three of the 35 infants randomized to early surfactant were extubated after such treatment, and 13 required reintubation at a median of nine hours after surfactant treatment, compared with 28 of 33 control infants who were intubated a median of three hours after randomization, (p=0.003). The overall duration of ventilation in both groups was 2.5 days; there were no other differences between the groups. Verder et al performed a second multicenter prospective trial from April 1995 to January 1997 and enrolled infants <30 weeks with similar criteria to the previous trial, apart from an entry a/A ratio of .35 to .22, which decreased over 30 minutes, which was less stringent, allowing infants to be treated at lesser degrees of oxygen requirement, than their first study. These infants were initially all treated with CPAP and were enrolled up to 72 hours of age (median 4.1 hours, range 0.3 to 40.1hrs).This trial was also stopped after an interim analysis demonstrated a statistically significant reduction in the need for ventilation or death within seven days from 63% in the late-treated infants to 21% in early-treated infants. The median duration of ventilation in both trials was 2.5 days[20]. This study was not a prospective evaluation of early CPAP because CPAP was initiated in all infants at variable ages, and they did not evaluate infants of less than 25 weeks gestation.

Lindner et al recently reviewed their experience using a continuous prolonged (15 seconds duration) pressure controlled (20 to 25 cm H_2O) inflation of the lungs followed by continuous positive airway pressure (CPAP) of 4 to 6 cm H_2O for all ELBW infants immediately after delivery to establish a functional residual capacity (FRC) and to avoid intubation and ventilation[21]. The criteria for subsequent intubation were a $PaCO_2$ > 70 mmHg, an FiO_2 >.6 and respiratory distress with severe recurrent apnea. The rate of early intubation and mechanical ventilation in the delivery room decreased from 84% in 1994 to 40% in 1996. In 1996, 25% of the ELBW infants were never intubated (compared with 7% in 1994). There was no difference in mortality and overall there was less IVH > Grade 2 and BPD for the later cohort. No infant had an air leak upon admission to the NICU, suggesting that use of a prolonged inflation was well tolerated. Only 1 of 11 infants of 24 weeks gestation was able to avoid intubation in this study. Once again, there was no contemporaneous control group who did not receive delivery room CPAP. All of the above studies required high levels of $PaCO_2$ before initiating ventilation for this indication.

There is retrospective evidence suggesting a benefit for early CPAP in experiences from the USA. A survey of eight neonatology units in the USA in 1987 demonstrated that one unit, Columbia, had the lowest rate of CLD[22]. A more recent comparison of practices and outcomes between two neonatology units in Boston and the Babies and Children's Hospital unit (Columbia) evaluated VLBW infants born in 1991 to 1993.[23] This study revealed that 75% of infants at the Boston centers were initially treated with mechanical ventilation compared with 29% at Columbia, whereas initial CPAP was used in 63% of infants at Columbia vs. 11% at the Boston centers. Columbia also used less surfactant, 10% versus 45%, (all $p<0.001$). In addition the rates of CLD were significantly lower at Columbia compared to the other two centers (4% vs. 22%).

de Klerk and de Klerk recently published a five-year retrospective review of the outcome of 1 to 1.5 kg infants (n-116) treated with early CPAP vs. usual care (delayed CPAP)[24]. During 1996 -1998 infants were placed on CPAP within 10 minutes of admission (they did not describe the use of delivery room CPAP). Early CPAP beginning following admission to the neonatal unit decreased endotracheal intubation from 65 to 14%, $p<0.001$ and surfactant use (40 to 12%, $p<0.001$). Ventilator days were reduced from a median of 6 to 2 days ($p<0.01$) and oxygen supplementation or death at 28 days from 16 to 3%, $p<0.05$. Oxygen supplementation or death at 36 weeks did not significantly decrease (11 to 3% $p=0.25$). Ventilation and surfactant use were very high during the delayed CPAP (control period) so it is unclear whether other improvements in care may have coincided with the change to early CPAP.

Sandri et al[25] have recently published preliminary data from a multicenter randomized controlled trial of 155 infants 28 to 31 weeks gestation randomized to CPAP within 30 minutes of birth or to CPAP if the FiO_2 requirement exceeded 40%. Use of surfactant (22 to 21%, NS) and ventilator support (10 to 9%, NS) was not reduced with early CPAP. However, this trial included relatively bigger infants and the control group received CPAP at relatively low FiO_2, minimizing the difference between the experimental and control groups. This study did not evaluate the use of delivery room CPAP.

More recently Thomson et al presented the results of a multicenter trial of 237 infants from 27 to 29 weeks gestation[26], who were randomized to prophylactic surfactant followed by nasal CPAP using the Infant Flow DriverTM, early nasal CPAP followed by rescue surfactant, early IPPV with prophylactic surfactant, and conventional management. They reported that CPAP was initiated by 6 hours of age in 76% and 79% of the first 2 treatment groups, and those infants in the CPAP and rescue surfactant and prophylactic surfactant followed by CPAP groups required the lowest duration of ventilation. There were no differences in the incidence of CLD or other neonatal complications. Neither of these studies instituted the use of CPAP in the delivery room.

In a preliminary feasibility trial we have evaluated the ability of 5 sites of the NICHD Network to initiate CPAP during resuscitation, and continue its use in the NICU. In that study 103 infants were randomized to receive resuscitation with either CPAP/PEEP or no CPAP/PEEP. All infants were treated with CPAP following NICU admission. During delivery room resuscitation, 46 infants were intubated, 27 of 55 CPAP infants and 19 of 48 control infants ($p=0.33$). All 23 week gestation infants were intubated in the delivery room, irrespective of treatment group, whereas only 3 of 22 (13%) infants of 27 weeks required such intubation. When evaluated by birth weight, all 3 infants of less than 500 gm birth weight and 6 of 11 infants between 500-600 gm birth weights were intubated in the delivery room. All remaining infants were admitted to the NICU and had CPAP initiated. For infants not intubated in the DR, 36 infants were subsequently intubated in the NICU by day 7, 16 CPAP infants and 20 Control infants, ($p=0.21$). Infants in the CPAP group developed criteria for intubation sooner than the Control infants, with means and medians of 10.5 and 1.8 hours versus 20.7 and 3.3 hours,

p=0.41. These infants met criteria established for this trial which included an FiO2 > .3 to maintain an SpO2 > 90% or a PaO2 > 45 torr, an arterial PaCO2 > 55-60 with a pH < 7.25. or apnea requiring bag and mask ventilation. CPAP infants were intubated at an average FiO2 = 0.5 compared to 0.4 for control infants.

The literature thus suggests that early CPAP may be of substantial benefit, although none of this information has been obtained from prospective randomized trials of CPAP randomly applied in the delivery room to a population of VLBW or ELBW infants, with an appropriate control group. The terms early CPAP in the above studies (apart from that of Lindner et al[15]) involved the application of CPAP shortly following birth, not immediately after delivery. It is not surprising, therefore, that the recent revised NRP guidelines do not mention the use of CPAP/PEEP for neonatal resuscitation.[27] There is also some evidence that the level of CPAP needed may vary depending on the actual device utilized. Pandit et al and Courtney et al have demonstrated that variable flow CPAP was associated with a lower work of breathing and increased compliance at all levels of CPAP whereas constant flow nasal CPAP increased compliance only at 8 cm H2O.[28] In addition, variable flow CPAP devices were effective at recruiting lung volume at all tested CPAP levels.[29] A more recent trial compared the use of variable flow CPAP to conventional CPAP at extubation for 162 ELBW infants and reported no significant differences with either form of CPAP.[30] This study noted that 40% of ELBW infants failed extubation primarily because of apnea.

There are no studies in the surfactant and antenatal steroid era which have prospectively compared delivery room, CPAP with a more conventional approach, such as the use of prophylactic surfactant and conventional ventilation. The current available evidence demonstrates that prophylactic natural surfactant treatment significantly decreases mortality, air leak, and BPD in preterm infants.[31] Early surfactant, defined as surfactant at less than 2 hours of life is also of benefit and reduces air leaks, and mortality.[32] These reviewers noted that "early surfactant administration significantly reduces the risk of key clinical outcomes including pneumothorax, PIE, chronic lung disease, and neonatal mortality. Given the efficacy of prophylactic surfactant therapy (Soll 1999), this meta-analysis suggests that early selective surfactant administration to intubated infants with early signs of RDS may be part of a clinical spectrum of improved outcomes with earlier treatment". The most recent experience regarding early surfactant was presented by Horbar et al at the SPR in May, 2003. Their study which involved a cluster randomization in 57 NICUs of a practice to administer surfactant earlier compared with 57 control NICUs. They noted that infants at the intervention sites received their surfactant more often in the DR (54.7 vs 18.2%, p < 0.001) and earlier than the control sites (21 vs 78 minutes, p <0.001). There were no differences in mortality and pneumothoraces, the intervention centers had a lower rate of overall and severe IVH (28% vs 33%, p < 0.04, 10% vs 14%, p < 0.001) which were secondary outcomes of this trial.[33]

The most recent published study by Tooley and Dyke evaluated the use of prophylactic surfactant and early extubation to CPAP versus prophylactic surfactant and continuing management.[34] In this study 42 infants of 25 to 28(+6) wk of gestation were intubated at birth and given one dose of surfactant. They were then randomized within one hour of birth to either continue with conventional ventilation or to be extubated to nCPAP. They reported that 8 out of 21 (38%) babies randomized to nCPAP did not require subsequent re-ventilation. (Ventilation rates of 62% vs 100%, p = 0.0034). The smallest baby successfully extubated weighed 745 g. There were also significantly fewer infants intubated in the nCPAP group at 72 h of age (47% vs 81%, p = 0.025). There was no significant difference between the two groups in the number of babies that died, developed chronic lung disease or severe intraventricular hemorrhage. This study demonstrates that a significant number of very preterm babies with RDS can be extubated

to nCPAP after receiving one dose of surfactant. The current SUPPORT study will address this population, extended to 24 weeks, using a similar methodology for the infants of 24 to 27 6/7ths weeks who fail initial CPAP, with adequate power to determine if this approach is associated with significant benefits in terms of important short and longer term clinical outcomes.

Oxygen Saturation:

There is now an emerging body of information that suggests that many of the morbid conditions associated with extreme immaturity are potentiated by an excess of free-radicals occurring in infants who are intrinsically deficient in antioxidants such as superoxide dismutase, catalase, and glutathione peroxidase. During hypoxia, metabolic alterations prime hypoxic cells to produce free oxygen radicals when subsequently exposed to oxygen. Such reperfusion injury, in addition to increasing the production of free oxygen radicals, is associated with other metabolic changes which may produce long lasting harmful effects. Silvers et al reported that a low plasma antioxidant activity at birth in premature infants was an independent risk factor for mortality.[35] Pulmonary oxygen toxicity, through the generation of reactive oxygen/nitrogen species in excess-of antioxidant defenses, is believed to be a major contributor to the development of BPD.[363738] For example the preterm macrophage showed a significant increase in cytokine mRNA and protein after overnight incubation in 95% oxygen compared with cells from term animals. Only macrophages from premature animals had a significant increase in intracellular oxygen radical content, measured by 2', 7'-dichlorofluorescin analysis, after incubation in 95% oxygen. This enhanced inflammatory cytokine response to oxygen has been postulated to be a mechanism involved in the early development of chronic lung disease in premature infants.[39] Varsila et al noted that immaturity is the most important factor explaining free radical-mediated pulmonary protein oxidation in premature newborn infants and that oxidation of proteins is related to the development of chronic lung disease.[40]

There are a number of prospective randomized trials that have compared the use of room air with 100% oxygen for neonatal resuscitation, and these have reported Infants resuscitated with room air resumed spontaneous breathing faster and required less positive pressure ventilation than infants resuscitated with oxygen.[41 42] Vento et al also demonstrated that that infants resuscitated with oxygen demonstrated long lasting evidence of oxidative stress and activities of superoxide dismutase and catalase in erythrocytes that were 69% and 78% higher, respectively compared with control infants resuscitated with room air at 28 days of postnatal life.[43] A recent meta-analysis of room air vs 100% oxygen resuscitation comprising of 1,693 infants in five trials revealed decreased neonatal resuscitation in infants resuscitated with room air (6 vs 11%, $p<0.005$ or 0.57 (95% CI 0.40 – 0.81))[44]. While these studies described results of mostly term infants, some infants were premature and the premature infant is known to have decreased antioxidants which would increase their susceptibility to oxygen toxicity. In the only randomized prospective trial to evaluate room air compared with oxygen in preterm infants, Lundstrom et al resuscitated infants of less than 33 weeks gestation who were randomized to receive either 80% oxygen or room air and noted that 2 hours following delivery, the room air infants had a higher cerebral blood flow compared with oxygen resuscitated infants. (median (interquartile range)): 15.9 (13.6-21.9) v 12.2 (10.7-13.8) ml/100 g/minute).[45] They did not find any significant differences in short or long-term outcomes but did note that SpO2 was lower in the room air infants with values at 5 and 7 minutes of 75% and 80% compared with 92% and 94% in the 80% oxygen group ($p<0.001$). Current monitoring with pulse oximetry using limits of 95 to 96% will result in significant periods wherein the infants actual PaO2 may increase to very high levels, as there are rapid increases in PaO2 with very small increments in SpO2 at this plateau portion of the hemoglobin dissociation curve.

Tin et al retrospectively reviewed outcomes for infants admitted to various neonatal intensive care units in northern England from 1990 to 1994 and managed with lower (70-90%) or higher SpO2 ranges (88%-98%).[46] They reported that infants who were managed for at least the first 8 weeks of life with SpO2s from 88-98% developed retinopathy of prematurity severe enough to be treated with cryotherapy four times as often as infants managed with the lower SpO2 ranges. Infants managed with the lower SpO2 ranges did not have increased risk of mortality or neurodevelopmental impairment. Bancalari et al using transcutaneous oxygen monitoring were able to show that infants who received continuous monitoring had a similar incidence of ROP to infants who were monitored by intermittent sampling had similar incidences of ROP, however for subgroup of infants $\geq$ 1100gm, there was a decrease in the incidence of ROP.[47] The STOP-ROP trial randomized infants with already established pre-threshold retinopathy and an SpO2 less than 94% to two ranges of SpO2 (89% to 94% versus 96% to 99%), for at least 2 weeks and until both eyes were at study endpoints. The higher range of SpO2 was associated with a non-significant decrease in the progression of ROP, but was associated with a greater need for oxygen and more exacerbations of BPD.[48]

Chow et al reported their observations following the institution in 1993 of a detailed oxygen management policy that included strict guidelines in the practices of increasing and weaning of fraction of inspired oxygen (FIO2) and the monitoring of oxygen saturation parameters in the delivery room, during in-house transport of infants to the NICU, and throughout hospitalization.[49] The main objectives were to avoid hyperoxia and repeated episodes of hypoxia-hyperoxia in very low birth weight infants. Their approach was initiated at birth, and included the avoidance of repeated increases and decreases of the FIO2, and a change in previously used alarm limits. They reported that following the implementation of these new management strategies that the incidence of ROP Grades 3 to 4 decreased consistently in a 5-year period from 12.5% in 1997 to 2.5% in 2001 and that the need for ROP laser treatment decreased from 4.5% in 1997 to 0% in the last 3 years. They adopted an SpO2 range of 85% to 95% for infants > 32 weeks gestation at birth, and a range of 85% to 93% for infants < 32 weeks. In addition some of their faculty used a range of 83% to 93%. This study did not provide any prospective values of the actual SpO2 ranges that were actually achieved in their infants, and thus it is uncertain whether their observed reductions in ROP were related to the altered SpO2 changes, or to overall changes in management over the period of the study. While these observations are encouraging, the authors did not report the complete neurodevelopmental outcomes for the infants cared for during the period of the new oxygen guidelines, and in the absence of contemporaneous controls, these results cannot be considered as proof that the SpO2 ranges used by this group are beneficial in terms of significant longer -term neurodevelopmental outcomes.

The most recent trial conducted in Australia compared SpO2 ranges of 91% - 94% versus 95% - 98% in 358 infants of less than 30 weeks who remained oxygen dependent at 32 weeks. The primary outcomes were growth and neurodevelopmental measures at a corrected age of 12 months. The high-saturation group received oxygen for a longer period after randomization (median, 40 days vs. 18 days; P<0.001) and had a significantly higher rate of dependence on supplemental oxygen at 36 weeks of postmenstrual age and a significantly higher frequency of home-based oxygen therapy. but resulted in an increased duration of oxygen supplementation.[50] They reported that additional oxygen supplementation did not improve survival, growth, or the occurrence of cerebral palsy at 18 to 24 months. Anderson et al have recently reported the results of a survey of pulse oximetry practices in 142 NICUs in the USA and noted a wide range of monitoring limits from 82% to 100%. They reported a lowered rate of ablative eye surgery in units that used lower maximal SpO2 limits, with the lowest range seen in units that had a maximum SpO2 of < 92%.[51]

In a recent review of oxygen toxicity in the premature infant Weinberger et al recommended that a strategy of limiting oxygen supplementation should be explored to reduce significant morbidities in the premature infant.[52] No studies to date have prospectively randomized ELBW infants to differing oxygenation ranges from birth onwards to determine if there is a benefit of lower versus higher saturation ranges.

1.5 Recent Relevant Studies

We have recently evaluated an FDA approved device specifically designed to facilitate neonatal resuscitation (Neopuff Infant Resuscitator, Fisher and Paykel, Auckland, New Zealand). This device has a t-piece that attaches to a mask and to a simple pressure generator. The inspiratory pressure can be set to a determined level, and a twist valve at the top of the t-piece determines the end-expiratory pressure. Most operators, with the exception of experienced respiratory therapists cannot routinely deliver a predetermined level of positive inspiratory pressures and PEEP[53] using an anesthesia-type manual bag and a neonatal manikin. In contrast, all operators could deliver the predetermined pressures with little intra-individual variation using the Neopuff®. The device operates identically using either a mask or endotracheal tube connection with or without PEEP/CPAP and the operator can adjust the positive inspiratory pressure (PIP) manually during resuscitation. At a flow of 10 liter per minute (lpm) or less, the maximum inadvertent CPAP/PEEP is 0.5 cm H_2O; which does not increase up to rates of 80 breaths per minute, the highest tested rate. The wave form is square, and is more similar to ventilator wave forms than to wave forms obtained using an anesthesia device. It should be noted, that the standard anesthesia devices used in delivery rooms may not deliver the desired CPAP/PEEP, depending on the operator's experience and skill, and may result in overshooting the desired PIP, even when the device is used by experienced operators. The Neopuff® device is now used as the standard resuscitation device in a number of hospitals in the USA, including at least two units in the NICHD Network.

There has been a recent trial evaluating earlier criteria for retinal laser ablative surgery for ROP, the ETROP study.[54] This study has demonstrated that using such criteria the visual outcomes are improved and reported that grating acuity results showed a reduction in unfavorable visual acuity outcomes with earlier treatment, from 19.5% to 14.5% (P=.01)and that unfavorable structural outcomes were reduced from 15.6% to 9.1% (P<.001) at 9 months. They recommend retinal ablative therapy for eyes with type I ROP, defined as zone I, any stage ROP with plus disease (a degree of dilation and tortuosity of the posterior retinal blood vessels meeting or exceeding that of a standard photograph); zone I, stage 3 ROP without plus disease; or zone II, stage 2 or 3 ROP with plus disease. While these results are likely to be integrated into Network practice, there is currently no baseline data regarding the number of infants who would meet these criteria, and thus we will utilize the presence of Stage 3 or greater ROP and/or the receipt of retinal surgery to power our current trial.

2.1 Study Design

This will be a prospective, randomized, factorial 2X2 design multi-center trial conducted by the NICHD Neonatal Research Network. The individual factors to be tested will be:

1) A prospective comparison of CPAP and a permissive ventilatory strategy begun in the delivery room and continuing in the NICU with early ($\leq$ 1 hour) surfactant and mechanical ventilation.

2) A prospective comparison of a lower SpO2 range (85% to 89%) with a higher more conventional SpO2 range (91% to 95%) until the infant is no longer requiring ventilatory support

or oxygen.

The oxygen saturation monitoring portion of our study will be designed to parallel the planned POST-ROP trial, a multicenter, multinational prospective trial to evaluate different SpO2 levels from birth.[55] The methodology described under oxygen monitoring (**Section 4.1B**) was developed for the current protocol to allow a blinded comparison of 2 different SpO2 levels using specially designed pulse oximeters. These devices have been developed by the Masimo Corporation (Irvine Ca) and tested prior to initiation of this trial, and the POST-ROP study group has agreed to use the ranges described in this protocol, and the methodology that will allow the oximeters to provide actual SpO2 values when the SpO2 is < 85% and > 95%(Personal communication, Cynthia Cole 2004). This methodology will provide the clinicians and caretakers with the infants' actual SpO2 values during hypoxia and hyperoxia, within the current parameters of clinically accepted practice.

Please see **Section 8.2** for further Tables describing details regarding the projected outcomes relative to the study interventions

Randomized Intervention	**Low SpO2 85% to 89%**	**High SpO2 91 to 95%**
Treatment **Early CPAP**	Early CPAP + Low SpO2	Early CPAP + High SpO2
Control **Prophylactic/Early Surfactant**	Control + Low SpO2	Control + High SpO2

2.2 Primary Hypotheses

1). We hypothesize that relative to infants managed with prophylactic/early surfactant and conventional ventilation that the use of early CPAP and a permissive ventilatory strategy in infants of less than 28 weeks gestation with continuing CPAP in the NICU will result in an increased survival without BPD at 36 weeks.

2). We hypothesize that that relative to infants managed with a higher SpO2 range that the use of a lower SpO2 range (85% to 89%) will result in an increase in survival without the occurrence of threshold ROP and/or the need for surgical intervention.

2.3 Secondary Hypotheses

We hypothesize that the use of continuous positive airway pressure (CPAP) with a permissive ventilator strategy and/or a lower SpO2 range starting at birth in the delivery room will result in the following:

- A decreased Mortality/NDI at 18-22 months corrected age.

- A decreased frequency of endotracheal intubation before 10 minutes of age
- A decrease of the total duration of mechanical ventilation during the entire NICU stay
- A decreased incidence of surfactant treatment
- A decreased incidence of air leaks on admission and overall
- A decreased duration of intubation
- A decreased duration of mechanical ventilation
- A decreased duration of oxygen supplementation
- A decreased duration of the percentage of pulse oximetry values > 90%
- A decreased incidence of blindness of at least one eye at 18-22 month follow-up
- A decrease in the percentage of infants who receive postnatal steroids to prevent or treat BPD
- A decreased incidence of BPD at 36 weeks using the physiologic definition of BPD
- A decreased incidence of ROP or Stage 3 ROP
- A decreased incidence of necrotizing enterocolitis (NEC)
- A decreased incidence of IVH and severe IVH
- A decreased incidence of periventricular leukomalacia
- A decreased incidence of neurodevelopmental impairment at 18-22 month follow-up
- A decreased incidence of cerebral palsy at 18-22 month follow-up

3.1 Study Population

Study subjects are infants of 24 0/7ths to 27 6/7th weeks at birth for which a decision has been made to provide full resuscitation as required. Infants 27 weeks or less gestation (completed weeks by best obstetric estimate) will be enrolled because over 80% of such infants in the Network are intubated, usually early in their neonatal course. It is important to note that previous studies have included few, if any infants less than 25 weeks gestation and such infants are not included in the current COIN trial or the proposed Vermont Oxford Trial. Such infants will be enrolled in this trial because they are the group of infants with the highest mortality and morbidity. The feasibility trial demonstrated that the 5 NICHD centers involved could reduce intubation in the delivery room to less than 50% of such infants if they are not intubated for surfactant. We will exclude infants of 23 weeks or less in view of their extremely high mortality and morbidity, and their almost universal need for delivery room intubation for resuscitation. We have included Tables at the end of the protocol utilizing infants from 23 to 28 weeks to demonstrate that our sample size estimates will not be adversely affected if we should choose to include infants of 23 and/or 28 weeks.

Strata: There will be 2 randomization strata, infants of 24 0/7ths to 25 6/7ths weeks, and infants of 26 0/7ths-27 6/7ths weeks by best obstetrical estimate. The purpose of stratification is to assure an appropriate distribution of risk among the four study arms. The study will not be powered to detect outcome differences between strata.

3.2 Inclusion Criteria

- Infants with a minimal gestational age of 24 weeks 0 days to 27 completed weeks (up to 27 6/7ths) by best obstetrical estimate
- Infants who will receive full resuscitation as necessary, i.e., no parental request or physician decision to forego resuscitation
- Infants whose parents/legal guardians have provided consent for enrollment, or
- Infants without known major congenital malformations

3.3 Exclusion Criteria

- Any infant transported to the center after delivery
- Infants whose parents/legal guardians refuse consent
- Infants born during a time when the research apparatus/study personnel are not available
- Infants < 24 weeks 0 days or ≥ 28 weeks 0 days, completed weeks of gestation

3.4 Sampling Recruitment and Screening Procedures

Infants will be recruited for this study by approaching one or both parents at the time of admission to the hospital where there is deemed to be a risk of premature delivery at 27 6/7ths weeks or less.

3.5 Screening Procedures

All admissions for threatened premature delivery will be screened on a daily basis to ensure that eligible patients can be enrolled. We will inform our obstetrical colleagues at each involved institution of the nature of this study, and encourage them to discuss this study with their patients at risk of premature delivery. The study coordinator at each site will maintain a screening log of potentially eligible patients. In addition the usual practice of neonatal consultation for all such at risk deliveries will provide a second opportunity to approach mothers with fetuses at risk of preterm delivery

3.6 Other Procedures

A T-piece resuscitator, a neonatal ventilator, or an equivalent CPAP methodology will be used at all sites for the delivery room administration of CPAP. A training video to explain the proper use of the Neopuff® will be provided to any site which wishes to use it and is not familiar with the device.

3.7 Randomization

Randomization will be stratified by gestational age group, will occur prior to delivery for consented deliveries, and will be performed by utilizing specially prepared double-sealed envelopes. Deliveries will be randomized as a unit, thus multiples, twins, triplets etc will be randomized to the same arm of the trial. We believe that this methodology will improve the percentage of consents, since in previous trials parents of multiple infants have expressed concern that their infants were being randomized to different treatment arms. We have made an appropriate sample size adjustment to account for this clustering effect.

Each randomization will indicate either Treatment Group (CPAP and permissive ventilation management) or Control Group (Prophylactic/Early surfactant and conventional ventilator management) and either the Low (85%-89%) or High (91% - 95%) SpO2 group. Parents will be approached for consent before delivery, but the randomization envelope will only be opened when delivery is imminent for a consented family.

The Pulse Oximeters (PO) will have unique identifying labels and the oximeter specified in the randomization will be identified by a unique number which will match the number of the study Pulse Oximeter assigned for that infant. All caretakers including the coordinators will be blinded to the Pulse Oximeter range, and an identification code for each site will be maintained by the PI/Site Coordinator should identification be required for patient safety. RTI will work with Masimo to ensure that the POs are labeled with unique identifiers, whose code will identify the

actual range of the individual PO. These would be affixed prior to shipping to the sites, and a copy of the labels sent to the site would be provided to RTI.

This methodology should reduce the work load to the sites at the time of randomization, providing the care team with the information needed for the infants' randomization, and will allow the study center to be notified within 24 hours of any randomization.

3.8 Informed Consent:

Parents will be approached prior to delivery for informed consent, and their infants enrolled at delivery. As previously noted we will randomize by family, thus all offspring will be randomized to the same trial arms, provided adequate equipment and personnel are available at the time of delivery.

3.9 Management and Retention of Study Population

All enrolled infants will be seen at follow-up-up at 18 to 22 months corrected age. We do not anticipate a significant loss other than death (13% in the first 12 hours , approximately 32% before discharge, based on year 2000 registry data), and will plan for a further 15% attrition.

4.1 A: Study Intervention: Mode of Ventilatory Support

The intervention will begin after birth when the infant is given to the resuscitation team. The conduct of the resuscitation will follow usual guidelines, and once stabilized, all Control infants in both strata will receive prophylactic/early surfactant (within 1 hour of age) whereas all Treatment infants will be placed on CPAP/PEEP following stabilization, and be intubated only for resuscitation indications.

The assignment to either a high or low SpO2 by study oximeter assignment will be performed immediately following NICU admission, with a maximum allowable delay of 2 hours following NICU admission.

TREATMENT: CPAP Group : Early Extubation and CPAP

Delivery Room Management

FiO2:

Standard of care.

CPAP:

CPAP or ventilation with PEEP will be utilized if the infant requires positive pressure during resuscitation. CPAP will be continued until admission to the NICU using the Neopuff or equivalent device and a face mask or nasal prongs. Initial PPV will be at a PIP of 15-25 cm H_2O and a PEEP/CPAP of 5 cm cmH_2O.

Intubation:

Infants may not be intubated for surfactant only in the DR. Infants who require intubation for resuscitation will receive surfactant within 60 minutes of birth.

Intubation will be performed only for the standard NRP indications including failure to respond to PPV with evidence of continuing cyanosis or bradycardia, the need for chest compressions, the need to administer intratracheal medications, or other situations in which the resuscitation team determines that surfactant is urgently required.

Intubation may be performed at any time for the occurrence of repetitive apnea requiring bag and mask ventilation, clinical shock, sepsis, and/or the need for surgery

The other aspects of the resuscitation will be managed according to the NRP guidelines and follow current center practice.

NICU Management

These infants will be managed on nasal CPAP, and intubation is never required by protocol. They *MAY* be intubated if they meet ***ANY*** *of* the criteria listed below. If intubated within the first 48 hours of life they should receive surfactant

Intubation:

- An FiO_2 >.50 required to maintain an indicated SpO2 $\geq$ 88% (using the altered Pulse Oximeters) for one hour
- An arterial $PaCO_2$ > 65 torr (arterial or capillary samples, if venous PvCO2 > 70 torr) documented on a single blood gas within 1 hour of intubation
- Hemodynamic instability defined as a low blood pressure for gestational age and/or poor perfusion, requiring volume and/or pressor support for a period of 4 hours or more. (Note that clinically defined shock is an accepted indication for intubation.)

Intubation may be performed at any time for the occurrence of repetitive apnea requiring bag and mask ventilation, clinical shock, sepsis, and/or the need for surgery

These criteria will continue in effect for a minimum of 14 days of life.

Intubation performed without meeting any of the above criteria will be considered a study protocol violation unless extenuating circumstances are noted.
(e.g. - Upper airway obstruction (choanal atresia, micrognathia/glossoptosis)).

Extubation:

An intubated CPAP-Treatment infant ***MUST*** *have extubation attempted within 24 hours if* **ALL** *of the following criteria are met and documented on a single blood gas*

- $PaCO_2$ < 65 torr with a pH > 7.20 (arterial or capillary samples)
- An indicated SpO2 $\geq$ 88% with an FiO2 $\leq$ 50%
- A mean airway pressure (MAP) < 10 cm H_2O, ventilator rate $\leq$ 20 bpm, an amplitude < 2X MAP if on high frequency ventilation (HFV)
- Hemodynamically stable (Defined as an infant with clinically acceptable blood pressure and perfusion in the opinion of the clinical team – such an infant may be receiving ionotropic/vasopressor agents, but should not require ongoing volume infusions to stabilize the circulation and the doses of any continuously infused medications for circulatory stabilization should not have increased within 1 hour of any planned extubation).
- Absence of clinically significant PDA

These criteria will continue in effect for the first 14 days of life.

Failure to extubate an infant meeting all of the above criteria will be recorded as a study protocol violation unless extenuating circumstances are noted. (e.g. - PIE, airleak)

Reintubation

If a Treatment infant is extubated as per Protocol Criteria, and requires re-intubation for any indication, any further attempt at extubation may be delayed for 24 – 48 hrs based on the clinician's decision.
Re-intubation criteria are the same as those for Intubation for the CPAP infants. Thus, intubation is not required, but these infants **MAY** be reintubated if they meet **ANY** of the following:

Re-Intubation Criteria:

- An FiO_2 >.50 required to maintain an indicated SpO2 $\geq$ 88% (using the altered Pulse Oximeters) for one hour
- An arterial $PaCO_2$ > 65 torr (arterial or capillary samples, if venous PvCO2 > 70 torr) for 2 successive blood gases at least 15 minutes apart.
- Hemodynamic instability defined as a low blood pressure for gestational age and/or poor perfusion, requiring volume and/or pressor support for a period of 4 hours or more. (Note that clinically defined shock is an accepted indication for intubation as noted above on page 13)

Intubation may be performed at any time for the occurrence of repetitive apnea requiring bag and mask ventilation, clinical shock, sepsis, and/or the need for surgery.

Re-intubation performed without meeting any of the above criteria will be considered a study protocol violation unless extenuating circumstances are noted.

D/C CPAP

Treated infants who remain in Room Air for at least 1 hour may have their CPAP discontinued. CPAP may be discontinued earlier and follow unit Standard of Care. CPAP may be restarted at any time in such infants.

CPAP infants who require intubation three times, for any criteria, will have all subsequent treatment including subsequent extubations and any further re-intubations performed using unit Standard of Care. This addition is to prevent such infants from being exposed to further protocol driven intubations and extubations.

Surfactant

Infants intubated in the first 48 hours for respiratory distress should be given a minimum of one dose of surfactant
Up to 4 surfactant administrations may be given if the FiO2 is greater than 50% following manufacturers' recommendations for dose and dosing interval.

Explanation:

The purpose of the above criteria is to minimize the duration of intubation of Treatment infants. The Criteria for extubation are more severe than those of the Control Group infants, and extubation must be attempted for any infant who fulfills the stated criteria.

The criteria for re-intubation recognize that intubation is traumatic, and is designed to avoid frequent attempts at extubation for infants who fail.

CONTROL- Prophylactic/Early Surfactant and Ventilation

Delivery Room Management:

Infants will be intubated in the delivery room and given surfactant or receive surfactant

within 60 min minutes of birth. The other aspects of the resuscitation will be managed according to the NRP guidelines and follow current center practice.

NICU Management:

Extubation:

An intubated Surfactant-Control infant will continue to receive mechanical ventilation until extubation criteria are satisfied, but **MUST** have Extubation attempted within 24 hours of fulfilling ***ALL*** of the following criteria documented on a single blood gas.

- $PaCO_2$ < 50 torr and pH > 7.30 (arterial or capillary samples)
- An FiO2 = 35 with a SpO2 > 88% using the study pulse oximeters with
- A mean airway pressure (MAP) < 8 cm H_2O, ventilator rate ≤ 20 bpm, an amplitude < 2X MAP if on high frequency ventilation (HFO)
- Hemodynamically stable (Defined as an infant with clinically acceptable blood pressure and perfusion in the opinion of the clinical team – such an infant may be receiving ionotropic / vasopressor agents, but should not require ongoing volume infusions to stabilize the circulation and the doses of any continuously infused medications for circulatory stabilization should not have increased within 1 hour of any planned extubation).
- Absence of clinically significant PDA (Defined as bounding pulses, audible murmur and Echo confirmation of L-R shunting with increased LA/Ao size

These criteria will continue in effect for a minimum of 14 days for all infants.

Failure to attempt to extubate an infant meeting all of the above criteria, or extubation prior to reaching criteria, will be recorded as a study protocol violation unless extenuating circumstances are noted.

Weaning

This protocol will not define strict weaning criteria for the Control infants, but it is to be understood that reasonable attempts should be made to extubate these infants. While it is understood that some centers may be using somewhat more severe FiO2 and PaCO2 criteria than those listed here as current practice, these Criteria are thought to reflect current Network practice and practice at 2 of the 3 Best practice centers.

Reintubation:

- Control Infants may be reintubated using Standard of Care.

Explanation:

Control infants are to be treated using an approach considered similar to current standards of care. Apparatus for resuscitation for Control Infants at each center will represent their usual equipment for the resuscitation of an ELBW infant. The Neopuff may be utilized for such infants as above, but this is not mandatory. It is anticipated that the majority of these infants will be intubated and receive surfactant in the delivery room.

4.1 B: Study Intervention: Low versus High SpO2 Range:

There will be 2 ranges of SpO2 utilized during this trial. The Low target range will be 85% to 89% and the High target range will be 91% to 95%. The altered Pulse Oximeters (PO) are described below, and will display a range of 88% to 92% when the SpO2 ranges are in the Target ranges indicated above. Thus a Low range PO will read 88% when the actual SpO2 is

approximately 86%, and 92% when the actual SpO2 is 89%. Similarly the High range PO will display 88% when the actual SpO2 is 91% and indicate 92% when the actual SpO2 is approximately 95%. See below for further explanation. This deviation is similar to the BOOST trial which used a continuous 3% offset.[42] As an added safety feature, the POs used in this trial will revert to the actual SpO2 values and allow the caretakers to be aware of actual SpO2 values < 85% and > 95%.

Low Range Infants:

These infants will be monitored with a target SpO2 range of 85% -89% with suggested indicated alarm limits of 85% and 95%, representing approximately a 10% span for alarms as long as the infants are receiving any ventilatory support, CPAP, and/or supplemental oxygen. **The study pulse oximeters will be applied to the infant within two hours following NICU admission.** The assigned PO will remain on the infant and will be removed once the infant has been in room air and off ventilatory support or CPAP for 72 hours, and if oxygen is subsequently required a similar altered pulse oximeter providing the same SpO2 range will be used until 36 weeks PCA.

High Range Infants:

These infants will be monitored with a target SpO2 range of 91% -95% with suggested indicated alarm limits of 85% to 95% representing approximately 10% span for alarms as long as they are receiving any ventilatory support, CPAP and/or supplemental oxygen. The study pulse oximeters will be removed once the infant has been in room air for 72 hours, and if oxygen is subsequently required a similar altered pulse oximeter providing the same SpO2 range will be used until 36 weeks PCA.

These interventions will be delivered using specially developed pulse oximeters whose displays (the actual readings seen by caretakers) will be adjusted so that the randomized range of SpO2 (either 85%-89%, or 91%-95%) will be indicated by a range of 88%-92%. This is done by progressively altering the offset as the alarm limits are approached, and Masimo has confirmed that this technology is workable. The target oxygen saturation (88-92%) of the display will be the same in both groups as indicated in Table1 below.

These POs will be able to display trend plots of the SpO2 display for a preceding interval to allow the caretakers to receive feedback regarding the actual SpO2 ranges of their baby.

The suggested alarms limits will be 84% and 96% for both groups.

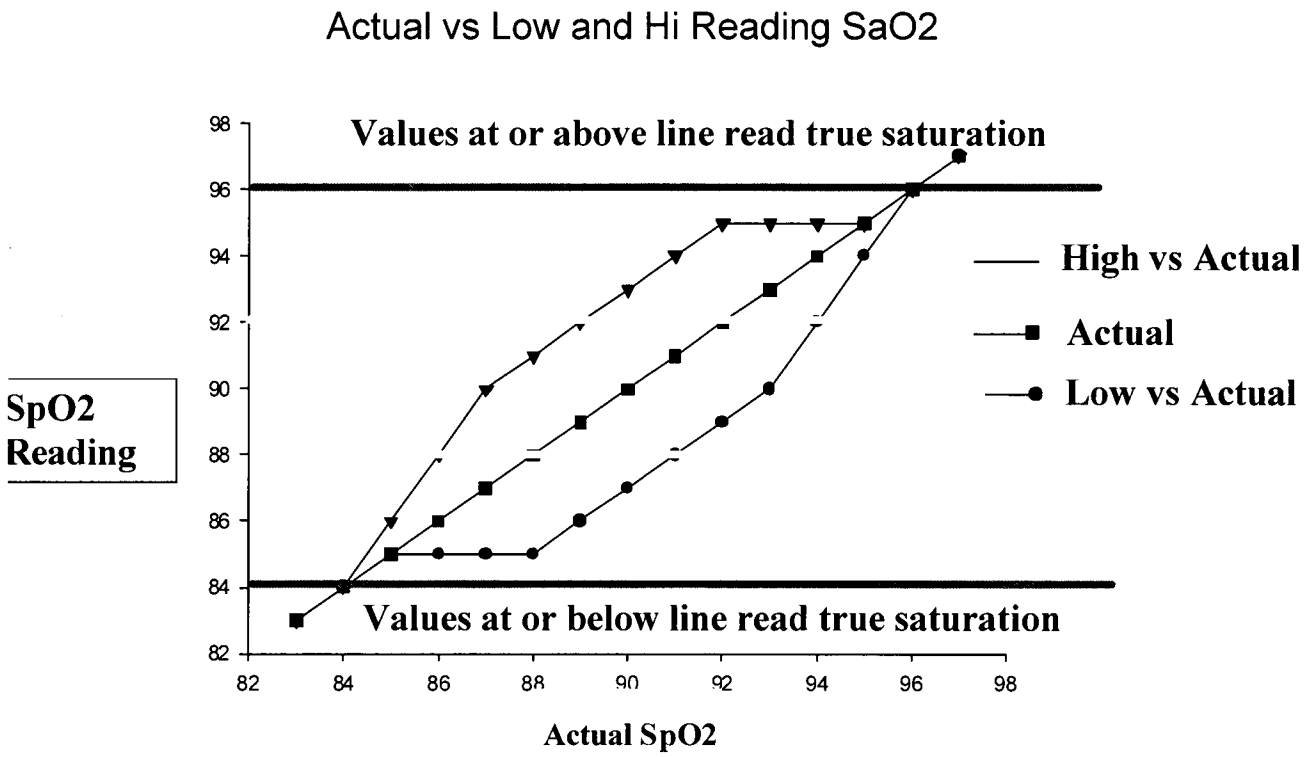
Table 1. Output and Actual SpO2 Targets and Alarms

SpO2 Group	Displayed Target	Actual Target	Alarm Values
Low SpO2	88-92%	85-89%	<85 and >95%
High SpO2	88-92%	91-95%	<85 and >95%

The pulse oximeters will display the actual reading when then the SpO2 is below 85% and above 95%. This will provide for an overall set of limits on actual SpO2 of 84% to 96% which we believe will avoid unacceptable levels of hypoxia, (< 85%) and hyperoxia (> 95%) **All data below 85% and above 95% will be unaltered on all oximeters**. An averaging time of 16 seconds will be applied in keeping with the settings used by POST-ROP. The preset alarm

delay will be 10 seconds. The fail-safe alarm will alarm whenever the reading is 5% below the low alarm limit, in the study this will be at 80%. Some network centers use an averaging interval of 30 seconds, others use very short averaging times. This setting will allow for appropriate response times without unmasking the caretakers.

We believe that this methodology will provide an acceptable ethical design for this trial. The diagram below demonstrates how the pulse oximeter readings are altered between values of 85% to 95%. Readings below or above these levels will not be altered, and will represent actual SpO2 as determined by the pulse oximeter. Note that the entire range of actual SpO2 is altered to either a lower (Low SpO2 Group) value or higher value (High SpO2 Group) till the ends of the alarm ranges of 85% and 95% which will ensure that the infants SpO2 will be separated throughout this range.



Every 30 days until 36 weeks PCA or until the infant is no longer receiving ventilatory support or oxygen, the stored actual SpO2 values (one value per 10 seconds of monitoring) will be downloaded and transmitted to RTI for subsequent analyses. (This interval of sampling may change to a less frequent interval for the convenience of the study personnel, without losing significant data). These data points will be used to confirm that the infants were managed at the target ranges and provide objective confirmation of the SpO2 Group assignments. The technology for downloading and interpreting this data was used in the DR CPAP Pilot trial, but recent technology utilizing a software program (Profox, Profox Inc, Escondido, Ca) which has been written to facilitate this process, will dramatically simplify this procedure.

Non-study pulse oximeters cannot be used on enrolled patients. If a second oximeter is

required for such a patient, the site coordinator will provide an identical oximeter for the patient.

All ventilatory care after 14 days of age will follow the standard of care for each unit. Each unit will provide guidelines for their approach to continuing mechanical ventilation.

4.2 Delivery of Interventions

CPAP/PEEP in the DR

CPAP and positive pressure ventilation (PPV) in the delivery room for Treatment infants will be administered via a T-piece resuscitator, a neonatal ventilator or an equivalent device that is currently used by the site for the delivery of CPAP. (See **3.6**).

Use of Nasal SIMV;

This approach is currently used by some Network units and has been previously established as being superior to CPAP following extubation in three prospective trials.[56,57,58] For uniformity nasal SIMV may be used in place of CPAP ***only following extubation for both Treatment and Control infants.***

Use of Caffeine:

Caffeine may be administered 2 hours prior to planned extubation, and for any clinically significant apnea.[59]

Surfactant Type:

All centers are asked to follow current unit practice in determining the type of surfactant utilized, and manufacturers' recommendations for redosing intervals.

The protocol requires that at least one dose of surfactant be administered to any infant intubated within 48 hours of birth, with evidence of respiratory distress, who has not previously received surfactant.:

Postnatal Steroids

Postnatal steroids for the purpose of preventing or treating BPD/CLD will be prohibited for any infant in this trial in the first 21 days of life. Hydrocortisone for hypotension may be used as noted below.

If postnatal steroid use is considered after 21 days of life for any infant for the prevention/treatment of established lung disease the following guidelines should be followed:

1. The AAP statement and recommendations regarding Post-natal steroids should be adhered to.[60]
2. The lowest dose of dexamethasone considered effective should be used and if ineffective after 24 – 48 hours they should be stopped.
3. Consider using hydrocortisone as a first therapy at a dose of 1 -2 mg/kg/day before using dexamethasone.
4. For hypotension, hydrocortisone in a dose of 1 mg/kg/dose should be given after fluid administration and standard doses of ionotropes/pressors have failed to correct the low blood pressure.

Head Ultrasound

If a Head ultrasound is done between days 4 and 21 the results will be recorded for this study. If one is not done for standard of care, the study requires that at least one HUS be completed during this window

4.3 Protocol Violations:

The occurrence of any one of the following criteria will determine whether an individual infant will be considered a protocol violation:

1. Intubation of a treatment group infant in the DR for the exclusive purpose of giving surfactant, in the absence of bradycardia (HR< 100 bpm) and/or poor color or an SpO2< 85-90% in an infant with adequate spontaneous respirations or receiving adequate ventilation
2. Failure to continue CPAP on admission to the NICU for a treatment infant requiring supplemental oxygen
3. Intubation and surfactant administration of a treatment infant without meeting stated protocol criteria.
4. Failure to extubate a Treatment infant who fulfills all the extubation criteria.
5. Extubation of a Control infant who does not meet any of the Extubation criteria.

All protocol violations will be reviewed by the center PI who will discuss each protocol violation with the involved clinicians and provide a written summary including steps taken to avoid future violations.

4.4 Adverse Events

Serious and unanticipated adverse events may be anticipated in this vulnerable population. Data on the following potential adverse events that may be related to the study maneuver will be recorded and evaluated as part of continuous safety monitoring during the trial by RTI:

1. Air leak on admission to the NICU, or during the initial 14 days of life
2. The need for chest compressions, and/or epinephrine in the delivery room or NICU
3. The occurrence of severe IVH (Grades 3-4, Papile)
4. Death

These outcomes will be evaluated on a monthly basis by RTI, and if the incidence of any of these outcomes is determined to be 5% - 10% greater in any arm of the study, this information will be provided to the Study PI and committee and the DSMC for immediate consideration, and evaluated for consideration of termination of the study or treatment arm.

4.5 Data Safety Monitoring Committee

The Data Safety Monitoring Committee will review the progress of the study with respect to efficacy and adverse events in a sequential fashion by using interim monitoring boundaries. Obrien-Fleming [61] boundaries will be used for efficacy monitoring and will be constructed for four looks at the data at 25%, 50%, 75%, and 100% of outcome assessment. Pocock [62] boundaries will be used for adverse event monitoring and will be viewed after every 30 infants have been enrolled. A special adverse event form will collect the information so that it may be entered into the data base in a timely fashion.

5.1 Measurement Methods:

The PO stored data will be retrieved using a routine provided to all site coordinators, and the resultant data file will be sent electronically to RTI to be included as part of the study data collection.

5.2 Schedule of Data Collection: (See Data tables in Appendix A)

5.3 Primary and Secondary Outcome Measures

5.3.1 Primary Outcome Measure

The primary outcome will be the percentage of infants surviving without BPD (using the Physiologic Definition) or severe ROP (threshold disease or the need for surgery).

5.3.2 Secondary Outcome Measures

- The five minute Apgar score
- The percentage of infants with death or neurodevelopmental impairment at 18 months
- The total duration of mechanical ventilation during the entire NICU stay
- The percent of infants alive and off ventilation by day 7
- The proportion of infants receiving surfactant treatment
- The incidence of air leaks on admission and overall
- The incidence of BPD at 36 weeks using the physiologic definition of BPD
- The incidence of death
- The proportion of infants with severe IVH
- The proportion of infants with PVL
- The proportion of infants with threshold ROP and requiring surgery for ROP
- The proportion of infants requiring endotracheal intubation before 10 minutes of age
- The proportion of infants with of air leaks on admission and overall
- The duration of oxygen supplementation
- The percentage of pulse oximetry values > 90%
- A decreased incidence of blindness of at least one eye at 18-22 month follow-up
- The proportion of infants who receive postnatal steroids to prevent or treat BPD
- The proportion of infants with who develop necrotizing enterocolitis (NEC)
- The proportion of infants with cerebral palsy at 18-22 month follow-up

6.1 Training Study Personnel

6.1.1 Job Descriptions of Study Personnel

The NICHD coordinators will assist the respiratory therapists in each unit regarding the set up the equipment for the delivery of CPAP in the delivery room, and in the NICU.

6.1.2 Training of Personnel

There will be a training session held in Cincinnati about the delivery of CPAP in the delivery room and in the NICU, and a review of available devices that may be used for this intervention.

7.1 Data Collection and Management

We will develop the required CRFs as per Network procedures. It will be our aim to minimize these to ensure that data is collected regarding the intervention, the adherence to the protocol for intubation, surfactant administration, and extubation, and the occurrence of the primary and secondary end-points. All remaining information will be extracted for the current data forms.

8.1 Statistical Analysis

8.1.1 Analysis Plan

The primary analyses of this factorial trial will be a logistic regression analysis of the percent of each Group (Treatment vs Control, High vs Low SpO2) who developed their respective outcome measure (survival without BPD or ROP at 36 weeks respectively). An important analysis of a secondary outcome will determine if there is an effect of the interventions on the percent infants who survive without neurodevelopmental sequelae at 2 years For all secondary outcomes, univariate analysis for continuous variables will be performed using parametric (e.g., Student t tests, ANOVA), and non-parametric (e.g., Mann-Whitney U) tests where appropriate; categorical variables including the primary outcome, feasibility, will be examined by Chi square analysis. Analysis of covariance and multiple regression models will be used to examine the interaction between, and the independent effects of, various factors, (e.g., birth weight, gestational age, gender, treatment group, center, etc.) upon secondary outcomes (i.e., time to improvement in oxygen saturation, duration of positive pressure ventilation, five minute Apgar score, duration of mechanical ventilation, surfactant requirement, incidence of air leaks, and incidence of BPD).

8.2 Sample Size

As discussed above, there are two main outcomes for the factorial design: mortality or BPD; mortality or ROP. Mortality or NDI is a secondary outcome. For the cohort of infants born in 2000, 401-1000g birth weight, we have the following prevalence of outcomes for four subgroups of that cohort: Please note that we used population groupings to include or exclude infants of 23 and 28 weeks. These additional groups do not change the sample size estimates as the outcomes are essentially similar.

Subgroup	Death/BPD	Death/> Stage III ROP	Death/NDI
23-27 GA	70.6	53.1	65.7
24-28 GA	64.8	44.5	59.3
24-27 GA	66.6	46.8	60.7
23-28 GA	68.6	50.4	64.0

If the study is powered for the two outcomes, Death/BPD and Death/>Stage III ROP, then the sample size is driven by the prevalence nearest 50% for a given absolute percentage detectable change in the outcome. In this case it's the Death/>Stage III ROP outcome with a range of 44.5% to 53.1% across the subgroups. Furthermore, the sample size depends on the outcome rate only through the standard deviation of the rate and this turns out to be essentially

50% for all subgroups (i.e. ranges from 49.7% to 50.0%). Hence one sample size table suffices for all.

Hence, for any of the four groups the table below gives the total sample sizes required for a range of absolute percent changes, a two-tailed alpha level test of 5% and for powers of 80% and 90%. The N1 column powers the 2 x 2 factorial for the two primary outcomes and the N2 column assures comparable power for the Death/NDI outcome.

With regard to the power for detecting the interaction between the two factors in the factorial, a fourfold increase in the stated sample size would be required to detect an interaction effect as large or larger as that stated in the table (i.e. the Detectable Difference), assuming the same alpha level and power. The interaction effect referred to is the classical one where the difference in outcome for one of the treatments in the factorial differs according to the level of the other treatment (i.e. the treatment effects are not additive).

If the study is powered for the two primary outcomes and mortality/NDI is considered as a secondary outcome then the table below gives the total sample size required for a 5% overall level test at 80% and 90% power. These represent the total numbers enrolled. To correct for two outcomes, we chose a conservative 2% level of significance and a conservative outcome rate of 50% in making the calculations. These sample sizes are given in the N1 column and would also allow a 10% difference in NDI/death to be detected with a power of 73%. If an 80% power is desired for the NDI/mortality outcome this would result in sample sizes in the N2 column.

TOTAL SAMPLE SIZES REQUIRED

	80% Power		90% Power	
Detectable Difference (absolute %)	Total N1*	Total N2**	Total N1*	Total N2**
8%	1792	2096	2284	2676
9%	1388	1624	1792	2096
10% (multiples to same arm)	1120	1312	1456	1704
11%	940	1104	1208	1416
12%	784	920	1032	1208
13%	672	788	860	1008
14%	584	680	756	880
15%	504	588	652	768

* sample sizes to insure the appropriate power for the two primary outcomes (BPD/Death, ROP/Death)

** sample sizes to insure the appropriate power for the secondary outcome (NDI/Death)

We have increased the sample size by a factor of 1.12 to allow for multiples to be randomized to the same treatment as this introduces a clustering effect into the design. The analysis of the GDB data base resulted in the 1.12 estimate. We also inflated the sample sizes by 17% to adjust for attrition after discharge and before follow-up. This figure was also determined from the GDB data base. Thus the actual sample size for this trial would be 1310 for 80% power for detecting an absolute difference of 10% in the two primary outcomes and the NDI secondary outcome. This sample size is not sufficient to permit detection of interactive effects between the two treatments with reasonable power.

HYPOTHESIZED TREATMENT EFFECTS FOR SUPPORT

When sample sizes were estimated for the SUPPORT trial the following base rates for the three outcomes (rounded) were calculated from the GDB:

--BPD/Mortality—67%
--ROP $\geq$ Grade III/Mortality—47%
--NDI/Mortality—61%.

Sample sizes were calculated for a range of absolute treatment effects and 10% seemed to be the smallest plausible effect for the study. Rounding the above rates to 65, 45, and 60 percent the following tables show what the data would look like under the assumption of a 10% reduction in outcome and control rates of 65, 45, and 60 percent for the DRCPAP (No)/ SpO2 (High) group. Interactive effects are assumed to be zero. Tables are presented which show treatment effects when both treatments affect the BPD and the ROP outcomes and when only one of the treatments affects outcome. The NDI table is only for the case where both treatments affect outcome.

Table IA

Treatment Effects for SpO2 (High, Low) and CPAP (Yes, No) on BPD/Mortality **Assuming a 10% Main Effect for Each Factor**—Table Entries are Outcome Rates (%)

SpO2

CPAP	Low	High	Overall
Yes	45	55	50
No	55	65	60
Overall	50	60	55

Table IB

Treatment Effects for SpO2 (High, Low) and CPAP (Yes, No) on BPD/Mortality **Assuming a 10% Main Effect for CPAP Only**—Table Entries are Outcome Rates (%)

SpO2

CPAP	Low	High	Overall
Yes	55	55	55
No	65	65	65
Overall	60	60	60

Table IIA

Treatment Effects for SpO2 (High, Low) and DRCPAP (Yes, No) on ROP≥ Grade III/Mortality **Assuming a 10% Main Effect for Each Factor**—Table Entries are Outcome Rates (%)

SpO2

SpO2

CPAP	Low	High	Overall
Yes	25	35	30
No	35	45	40
Overall	30	40	35

Table IIB

Treatment Effects for SpO2 (High, Low) and CPAP (Yes, No) on ROP≥ Grade III/Mortality **Assuming a 10% Main Effect for SpO2 Only**—Table Entries are Outcome Rates (%)

		SpO2		
		Low	High	Overall
CPAP	Yes	35	45	40
	No	35	45	40
	Overall	35	45	40

Table III

Treatment Effects for SpO2 (High, Low) and CPAP (Yes, No) on NDI/Mortality **Assuming a 10% Main Effect for Each Factor**—Table Entries are Outcome Rates (%)

		SpO2		
		Low	High	Overall
CPAP	Yes	40	50	45
	No	50	60	55
	Overall	45	55	50

9.1 Quality Control

The selection of personnel will be left to the site PI's. No specific job descriptions are required for this protocol. The actual duties of the individual who will perform the randomization will be detailed in the manual for the study. Protocol violations will be reviewed, and if frequent, may require a site visit and consideration for termination of a collaborating site.

10.1 Risks and Benefits

Potential risks to the use of CPAP and/or PEEP include pneumothoraces; however this is unlikely to be increased over the risk of PPV alone. The level of CPAP/PEEP will be set at 5-6 cmH_2O, a level that is not thought to increase the incidence of pneumothorax. Recent data from Dr Morley suggest that this level is probably the lowest effective level especially when the infant's mouth is open, and is well tolerated. Objections to use of PEEP or CPAP could be countered by the argument that the majority of neonatologists use PEEP in resuscitation, thus the standard of care at most centers probably include the administration of CPAP and/or PEEP. Another potential risk is the administration of CPAP in the DR to infants without respiratory distress, which could conceivably cause vagal stimulation and resultant bradycardia and gastric distension.

Perhaps the major risk of this trial is that the known benefit of early surfactant with a reduction of death and disease severity, and a reduction of BPD with natural surfactant may not be offset by the early use of CPAP. However, the increasing trend in the use of early CPAP without such evidence represents an even greater risk.

Appendix A

Study Tables

Table 1. Patient Description

	Treatment	Control	P Value
Birth weight (grams) (M + SD)			
Gestation (weeks) (M + SD)			
Apgar 1 min < 3 Assigned			
Apgar 5 min < 3 Assigned			
Received PPV (Number, %)			
Surfactant in DR (Number, %)			
Received Chest Compression (N%)			
Received Epinephrine (N, %)			

Table 2. Other Outcomes

	Treatment	Control	P Value
Total Duration of Mechanical Vent (M +SD)			
Duration of Oxygen (Total days)			
Duration of CPAP			
Duration of nSIMV			
% alive off MV by Day 7 (+SD)			
Pneumothoraces (N, %)			
Other air leaks (N, %)			
BPD at 36 weeks (O_2 dependence)			
BPD by Physiologic Definition (N%+SD)			
Survived to discharge (N,% +SD)			
Number Never Intubated (N, %)			
Number receiving PNS for BPD (N, % %)			
Alive without neurdevelopmental impairment at (18-22 months) years (N, %, +/-SD)			

Appendix B

Study Tables

Table 1. Patient Description

	Low Saturation	High Saturation	RR	CI	p value
Birth weight (grams) (M + SD)					
Gestation (weeks) (M + SD)					
Race (W, B, H, other) %					
Antenatal steroids (%)					
Apgars ≤3 at 5 min					

Table 2. Primary Outcomes

	Low Saturation	High Saturation	RR	CI	p value
Threshold ROP/Surgery or death by 36 weeks (%)					
Death by 36 weeks (%)					
Threshold ROP in alive infants at 36 weeks (%)					
BPD or Death by 36 weeks (%) ±					

Table 3. Secondary Outcomes

	Low Saturation	High Saturation	RR	CI	p value
Death by discharge status (%)					
BPD in alive infants at 36 weeks (%)					
IVH 3 or 4/PVL or death by 36 weeks (%)					
IVH 3 or 4 in alive infants at 36 weeks (%)†					
Cystic PVL in alive infants at 36 weeks (%)†					
Neurodevelopmental impairment or death by 18-22 months (%)					
Death by 18-22 months (%)					
Neurodevelopmental impairment at 18-22 months (%)†					
Cerebral palsy at 18-22 months (%)†					
MDI < 70 (%)					
PDI < 70 (%)					
Any blindness at 18-22 months (%)†					
Unilateral blindness at 18-22 months (%)†					
Deafness at 18-22 months†					

†Analyzed for survivors

Table 4. Other Outcomes

	Low Saturation	High Saturation	RR CI	P Value
Total Duration of Ventilation (M+SD)				
On ventilator or death by day 7 (%)				
Pneumothorax (%)				
Any air leak (%)				
Postnatal steroids for BPD (%)				
Necrotizing enterocolitis ≥2 (%)				
PDA requiring surgery				

	Early CPAP/Early Extubation	Prophylactic Surfactant
Delivery Room Management	Resuscitate using CPAP. If necessary, initial PPV settings PIP 15-25, PEEP 5. Transport on CPAP If intubated for resuscitation, give surfactant within 1 hour of age. Do not intubate unless indicated by NRP guidelines	Intubate and give surfactant within 1 hour of age Transport with PPV according to SOC
Upon NICU Admission	Randomize within 2 hours to Pulse Oximeter	Randomize within 2 hours to Pulse Oximeter
Intubation Criteria	**Not Required. May intubate for ANY of these criteria** • FiO_2 >.50 required to maintain indicated SpO2 $\geq$ 88% (using the altered Pulse Oximeters) for one hour • $PaCO_2$ > 65 torr (art. or cap. samples, if venous $PaCO_2$ > 70 torr) documented on a single blood gas • Hemodynamic instability defined as a low blood pressure for gestational age and/or poor perfusion, requiring volume and/or pressor support for a period of 4 hours or more. **If intubated, give surfactant within the first 48 hrs if in respiratory distress**	**Reintubation Criteria** **Standard of Care**
Extubation Criteria	**Attempt extubation within 24 hours of fulfilling all of the following criteria:** • $PaCO_2$ < 65 torr with a pH > 7.20 (arterial or capillary samples) • An indicated SpO2 $\geq$ 88% with an FiO2 $\leq$ 50% • Mean airway pressure (MAP) < 10 cm H_2O, vent rate $\leq$ 20 bpm, amplitude < 2X MAP if on HFV • Absence of clinically significant PDA • Hemodynamically stable	**Keep intubated and ventilated until criteria met. Attempt extubation within 24 hours of fulfilling all of the following criteria** • $PaCO_2$ < 50 torr and pH > 7.30 (arterial or capillary samples) • FiO2 $\leq$ 35 with SpO2 > 88% • Mean airway pressure (MAP) < 8 cm H_2O, vent. rate $\leq$ 20 bpm, amplitude < 2X MAP on HFV • Absence of clinically significant PDA • Hemodynamically stable
Repeated Surf Doses	Subsequent doses may be given at the manufacturer's recommended dose up to a total of 4 doses.	
Intubation	Intubation may be performed at any time for the occurrence of repetitive apnea requiring bag and mask ventilation, clinical shock, sepsis, and/or the need for surgery	
CPAP D/C	In room air for at least 1 hour	
CPAP Resumption	At any time	
Duration of Intervention	14 days	14 days

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From: Higgins, Rosemary (NIH/NICHD)
To: Spong, Catherine (NIH/NICHD)
Subject: Re: Support trial
Date: Wednesday, January 12, 2005 2:50:57 PM

I think so

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Spong, Catherine (NIH/NICHD) <spongc@dir49.nichd.nih.gov>
To: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
Sent: Wed Jan 12 13:41:43 2005
Subject: Re: Support trial

I didn't followup
Did we circulate it to the group?

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
To: Spong, Catherine (NIH/NICHD) <spongc@dir49.nichd.nih.gov>
Sent: Wed Jan 12 13:36:42 2005
Subject: Support trial

Cathy
When Dr. Laptook presented at the last MFMU steering committee meeting, there was concern (from Dr. Rouse) regarding overlap. We had sent the protocol to you - any feedback or concerns about overlap?
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

From: Higgins, Rosemary (NIH/NICHD)
To: petrie@rti.org
Subject: SUPPORT_IRB-Oximeter Status doc (2)
Date: Friday, January 07, 2005 12:19:00 PM
Attachments: SUPPORT_IRB-Oximeter Status doc (2).doc

SUPPORT TRIAL
IRB/Oximeter Status-

January 6, 2005

Center	IRB Status	Oximeters Ordered	Oximeters Received
Case	Waiting for IRB Approval	**Yes**	**Yes**
UT-Dallas	Waiting for IRB Approval	**Yes**	**Yes**
Wayne State	?		
Miami	?		
Emory	Approval at one site	**No**	
Cincinnati	Approved at one site	**Yes**	**Yes**
Indiana	Provisional Approval	**Yes**	
Yale	Waiting for IRB Approval	**Yes**	**Yes**
Brown	Received IRB Approval	**Yes**	**Yes**
Stanford	Waiting for IRB Approval	**No**	
UAB	Received IRB Approval	**Yes**	**No**
UT-Houston	?	**Yes**	**Yes**
Duke	Waiting for IRB Approval	**Yes**	
Wake Forest	Waiting for IRB Approval	**Yes**	**Yes**
Rochester	Waiting for IRB Approval	**Yes**	**Yes**
UCSD	Received IRB Approval	**Yes**	**Yes**

From: Higgins, Rosemary (NIH/NICHD)
To: "bkh@rti.org"
Subject: Re: SUPPORT Trial
Date: Thursday, January 06, 2005 9:51:09 AM

Ok
Great!!
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Hastings, Betty J. <bkh@rti.org>
To: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
Sent: Thu Jan 06 09:50:06 2005
Subject: RE: SUPPORT Trial

Wade told me that there is a letter coming from Masimo today (not sure what it is) but when I receive it, I will send it and tell the sites they can begin.
Thanks.
Betty

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Thursday, January 06, 2005 9:48 AM
To: Hastings, Betty J.
Subject: Re: SUPPORT Trial

Then I guess we can start, right?
Will you send something out?

Thanks. A lot!
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Hastings, Betty J. <bkh@rti.org>
To: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
Sent: Thu Jan 06 09:43:42 2005
Subject: RE: SUPPORT Trial

Yes, they have been shipped to several of the sites and I finally received the serial numbers from Masimo so I am able to supply the color codes to the sites. In fact, I shipped the randomization envelopes to UCSD yesterday.

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Thursday, January 06, 2005 9:40 AM

To: Hastings, Betty J.
Subject: Re: SUPPORT Trial

Thanks Betty

Any further word on oximeter availability?

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Hastings, Betty J. <bkh@rti.org>
To: ahensman@wihri.org <ahensman@wihri.org>; mbball@leland.stanford.edu <mbball@leland.stanford.edu>; grisbyca@email.uc.edu <grisbyca@email.uc.edu>; ellen_hale@oz.ped.emory.edu <ellen_hale@oz.ped.emory.edu>; gaynelle.hensley@utsouthwestern.edu <gaynelle.hensley@utsouthwestern.edu>; Georgia E McDavid <Georgia.E.McDavid@uth.tmc.edu>; auten002@mc.duke.edu <auten002@mc.duke.edu>; linda_reubens@urmc.rochester.edu <linda_reubens@urmc.rochester.edu>; lucmille@iupui.edu <lucmille@iupui.edu>; mcollins@peds.uab.edu <mcollins@peds.uab.edu>; Nancy.Miller@UTSouthwestern.edu <Nancy.Miller@UTSouthwestern.edu>; Nancy Newman <nxs5@cwru.edu>; npeters@wfubmc.edu <npeters@wfubmc.edu>; pat.gettner@yale.edu <pat.gettner@yale.edu>; ae5357@wayne.edu <ae5357@wayne.edu>; rbridge@ucsd.edu <rbridge@ucsd.edu>; risa.demetrio@sharp.com <risa.demetrio@sharp.com>; kathy.arnell@sharp.com <kathy.arnell@sharp.com>; Reverett@med.miami.edu <Reverett@med.miami.edu>; wrich@ucsd.edu <wrich@ucsd.edu>; Personal Email Personal Email Lenora Jackson <Lenora.Jackson@uc.edu>; Estelle E. Fischer <estelle.fischer@cchmc.org>; Holly Mincey <minceyhl@email.uc.edu>; Jody Shively <jody.shively@cchmc.org>; Kate Bridges, MD <Kathleen.Bridges@cchmc.org>
CC: nfiner@ucsd.edu <nfiner@ucsd.edu>; Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>; Das, Abhik <adas@rti.org>; Petrie, Carolyn <petrie@rti.org>; Poole, W. Kenneth <poo@rti.org>
Sent: Thu Jan 06 09:38:44 2005
Subject: SUPPORT Trial

I wanted to let you know that the latest version of the Manual of Operations and the forms (all dated 1/4/2005) has been posted on the Neonatal Web Site. Please let me know if you would rather receive an electronic version of this material.

Thanks.
Betty

Betty Hastings

RTI International
Statistic Research Division
P.O. Box 12194
Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7740
Fax: (919) 485-7762
bkh@rti.org

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT Agenda
Date: Tuesday, January 04, 2005 1:07:57 PM

Many thanks Rose and a very Happy New Year to you and your family.
Be well
Neil

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, January 04, 2005 9:54 AM
To: 'nfiner@ucsd.edu'
Cc: 'petrie@rti.org'
Subject: Re: SUPPORT Agenda

Neil
I will have carolyn add it to the agenda and we will get copies for the attendees.
Happy new year!!
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Neil Finer <nfiner@ucsd.edu>
To: Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>
Sent: Tue Jan 04 12:52:16 2005
Subject: RE: SUPPORT Agenda

Good idea
Thanks
Neil

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, January 04, 2005 3:39 AM
To: 'nfiner@ucsd.edu'
Cc: 'petrie@rti.org'
Subject: Re: SUPPORT Agenda

Neil
We should also see where folks are with their respective irb's.
Thanks
Rose

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Neil Finer <nfiner@ucsd.edu>
To: Betty Hastings <bkh@rti.org>; Michele Walsh <mcw3@cwru.edu>; Wade Rich <wrich@ucsd.edu>; Higgins, Rosemary (NIH/NICHD) <higginsr@mail.nih.gov>; Avroy A. Fanaroff, M.D. <aaf2@po.cwru.edu>; Donovan, Edward (DONOVAEF)

<edward.donovan@chmcc.org>; Shahnaz Duara <sduara@miami.edu>; Wally Carlo, M.D. <WCarlo@PEDS.UAB.EDU>; Neil Finer <nfiner@ucsd.edu>; Ken Poole <poo@rti.org>
CC: Maynard Rasmussen, MD <Maynard.Rasmussen@sharp.com>
Sent: Mon Jan 03 21:04:28 2005
Subject: SUPPORT Agenda

Hello Everyone and Happy New Year
I have outlined a brief agenda below for our meeting next week. I have invited Cynthia Cole form Harvard, who is applying for funding for the POST-ROP Trial. As you know William Tarnow Mordi has obtained funding for the Australian arm, and other is Canada and the UK are pursing funding. I thought that it would be productive to have Cynthia there, She will talk for 15 minutes to us about here plans etc

Agenda:
SUPPORT Committee at Steering Committee - Tuesday Jan 11, 2:00 - 3:00 PM

1. Review of Protocol changes and Manual - Wade Rich and Betty Hastings
2. Review of Secondaries - status of each -
   MRI - Hintz
   Pulmonary Follow-up - Stevens
   Asthma Gene - Schibler
   Surfactant Gene - Cotton
   Ancillary - Episodic Desaturations - Martin - Case-Western and UCSD
3. Oximeter status - Maynard Rasmussen, Wade Rich
4. In-services - site visits
5. Cynthia Cole - Discussion of POST-ROP Trial

Please add any other items that you think appropriate
Be well and travel safe
Neil

From: Higgins, Rosemary (NIH/NICHD)
To: joseph.volpe@tch.harvard.edu
Subject: NICHD NRN protocol review request
Date: Monday, December 27, 2004 11:23:00 AM

HI,

The Neonatal Research Network Steering Committee has recently approved a project titled

NEUROIMAGING AND NEURODEVELOPMENTAL OUTCOME: A SECONDARY TO SURFACTANT POSITIVE AIRWAY PRESSURE AND PULSE OXIMETRY TRIAL (SUPPORT)

This is a secondary study to a previously approved SUPPORT Trial. I am wondering if you could confidentially review this protocol by January 24, 2005. If so, please let me know and I can send it to you with the primary SUPPORT protocol and instructions for review.

Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD)
To: terrie.inder@rch.org.au
Subject: NICHD NRN protocol review request
Date: Thursday, December 23, 2004 1:55:00 PM

Hi Dr. Inder
The Neonatal Research Network Steering Committee has recently approved a project titled

NEUROIMAGING AND NEURODEVELOPMENTAL OUTCOME: A SECONDARY TO SURFACTANT POSITIVE AIRWAY PRESSURE AND PULSE OXIMETRY TRIAL (SUPPORT)

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Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD)
To: andrew.whitelaw@bristol.ac.uk
Subject: NICHD Neonatal Research Network Protocol Review Request
Date: Thursday, December 23, 2004 1:54:00 PM

HI,

The Neonatal Research Network Steering Committee has recently approved a project titled

NEUROIMAGING AND NEURODEVELOPMENTAL OUTCOME: A SECONDARY TO SURFACTANT POSITIVE AIRWAY PRESSURE AND PULSE OXIMETRY TRIAL (SUPPORT)

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Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD)
To: dmf@itsa.ucsf.edu
Subject: Neonatal Research Network protocol review
Date: Thursday, December 23, 2004 1:53:00 PM

HI,

The Neonatal Research Network Steering Committee has recently approved a project titled

NEUROIMAGING AND NEURODEVELOPMENTAL OUTCOME: A SECONDARY TO SURFACTANT POSITIVE AIRWAY PRESSURE AND PULSE OXIMETRY TRIAL (SUPPORT)

This is a secondary study to a previously approved SUPPORT Trial. I am wondering if you could confidentially review this protocol by January 24, 2005. If so, please let me know and I can send it to you with the primary SUPPORT protocol and instructions for review.

Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Neil Finer
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: MRI SUPPORT Secondary
Date: Wednesday, December 22, 2004 6:44:01 PM

Thanks and Good luck Rose
All the best for the Holidays.
Neil

----- Original Message -----
From: Higgins, Rosemary (NIH/NICHD)
To: Abbot Laptook (E-mail) ; Carlo Waldemar (E-mail) ; Charles Rosenfeld ; Dale Phelps ; Ed Donovan ; Ehrenkranz Richard (E-mail) ; Jobe Alan (E-mail) ; Lemons Jim (E-mail) ; Michael O'Shea ; Michelle Walsh ; Neil Finer ; Oh William (E-mail) ; Poole Kenneth (E-mail) ; Ronald GOldberg ; Shahnaz Duara ; Shankaran Seetha (E-mail) ; Stevenson David (E-mail) ; Stoll Barbara (E-mail) ; Tyson Jon (E-mail) ; Walid Salhab
Cc: petrie@rti.org
Sent: Wednesday, December 22, 2004 1:55 PM
Subject: MRI SUPPORT Secondary

Hi,
I have the votes in from the MRI Secondary to SUPPORT study. There are 14 yes votes and 1 no vote, so this protocol will go to the advisory board and for outside review. I will also try to obtain funding as many have suggested.

Thanks
Rose

Rosemary D. Higgins, M.D.
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
NICHD, NIH
6100 Executive Blvd., Room 4B03B
MSC 7510
Bethesda, MD 20892
(For overnight delivery, use Rockville, MD 20852)
301-435-7909
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD)
To: Petrie, Carolyn
Cc: jobea0@chmcc.org
Subject: RE: NRN SC meeting Jan 11 & 12, 2005
Date: Wednesday, December 22, 2004 9:51:00 AM

Alan should attend SUPPORT, benchmarking, and nec

The others are really optional, so its fine.
Rose

-----Original Message-----
From: Petrie, Carolyn [mailto:petrie@rti.org]
Sent: Wednesday, December 22, 2004 9:36 AM
To: Higgins, Rosemary (NIH/NICHD)
Subject: FW: NRN SC meeting Jan 11 & 12, 2005

-----Original Message-----
From: CHMCC Groupwise [mailto:alan.jobe@chmcc.org]
Sent: Wednesday, December 22, 2004 9:35 AM
To: Petrie, Carolyn
Subject: Re: NRN SC meeting Jan 11 & 12, 2005

Looks OK - I will get there about noon on the first day. You might check
with Rose to see if she wants me to be at a session that I would miss by the
late arrival - and switch for one of the later ones.

Have a good holiday

Alan H. Jobe, MD, PhD
Professor of Pediatrics
Division of Pulmonary Biology/Neonatology
Cincinnati Children's Hospital Medical Center
3333 Burnet Avenue, ML#7029
Cincinnati, Ohio 45229
ph: 513-636-8563
fax: 513-636-8691
E-mail: alan.jobe@cchmc.org

From: Duara, Shahnaz
To: Hastings, Betty J.; rbridge@ucsd.edu; brenda.H.Morris@Uth.tmc.edu; cotte010@mc.duke.edu; vanmeurs@leland.stanford.edu; kurt.schibler@cchmc.org; Jobea0@chmcc.org; susie.buchter@oz.ped.emory.edu; Vineet.bhandari@yale.edu; Walid.Salhab@UTSouthwestern.edu; wcarlo@peds.uab.edu; alaptook@wihri.org; aaf2@po.cwru.edu; barbara_stoll@oz.ped.emory.edu; dale_phelps@urmc.rochester.edu; dstevenson@stanford.edu; edward.donovan@chmcc.org; jlemons@iupui.edu; jon.e.tyson@uth.tmc.edu; moshea@wfubmc.edu; nfiner@ucsd.edu; richard.ehrenkranz@yale.edu; goldb008@mc.duke.edu; sshankar@med.wayne.edu; Duara, Shahnaz; Walid Salhab, MD; Charles Rosenfield, MD; M.D. William Oh; Michele Walsh, MD; Everett, Ruth; ahensman@wihri.org; mbball@leland.stanford.edu; ellen_hale@oz.ped.emory.edu; gaynelle.hensley@utsouthwestern.edu; Georgia E McDavid; auten002@mc.duke.edu; linda_reubens@urmc.rochester.edu; lucmille@iupui.edu; mcollins@peds.uab.edu; Nancy.Miller@UTSouthwestern.edu; Nancy Newman; npeters@wfubmc.edu; pat.gettner@yale.edu; kathy.arnell@sharp.com; Wade Rich; grisbyca@email.uc.edu; Rebecca Bara; Risa Demetrio; balexanba@hotmail.com; Lenora Jackson; Estelle E. Fischer; Holly Mincey; Jody Shively; Kate Bridges, MD
Cc: Higgins, Rosemary (NIH/NICHD) [E]; Willinger, Marian (NIH/NICHD) [E]; Poole, W. Kenneth; Berberich, Mary Anne (NIH/NHLBI)
Subject: RE: SUPPORT Trial
Date: Tuesday, December 07, 2004 5:33:46 PM

Great - go, Neil!

Shahnaz

-----Original Message-----
From: Hastings, Betty J. [mailto:bkh@rti.org]
Sent: Tuesday, December 07, 2004 2:16 PM
To: rbridge@ucsd.edu; brenda.H.Morris@Uth.tmc.edu; cotte010@mc.duke.edu; vanmeurs@leland.stanford.edu; kurt.schibler@cchmc.org; Jobea0@chmcc.org; susie.buchter@oz.ped.emory.edu; Vineet.bhandari@yale.edu; Walid.Salhab@UTSouthwestern.edu; wcarlo@peds.uab.edu; alaptook@wihri.org; aaf2@po.cwru.edu; barbara_stoll@oz.ped.emory.edu; dale_phelps@urmc.rochester.edu; dstevenson@stanford.edu; edward.donovan@chmcc.org; jlemons@iupui.edu; jon.e.tyson@uth.tmc.edu; moshea@wfubmc.edu; nfiner@ucsd.edu; richard.ehrenkranz@yale.edu; goldb008@mc.duke.edu; sshankar@med.wayne.edu; Duara, Shahnaz; Walid Salhab, MD; Charles Rosenfield, MD; M.D. William Oh; Michele Walsh, MD; Everett, Ruth; ahensman@wihri.org; mbball@leland.stanford.edu; ellen_hale@oz.ped.emory.edu; gaynelle.hensley@utsouthwestern.edu; Georgia E McDavid; auten002@mc.duke.edu; linda_reubens@urmc.rochester.edu; lucmille@iupui.edu; mcollins@peds.uab.edu; Nancy.Miller@UTSouthwestern.edu; Nancy Newman; npeters@wfubmc.edu; pat.gettner@yale.edu; kathy.arnell@sharp.com; Wade Rich; grisbyca@email.uc.edu; Rebecca Bara; Risa Demetrio; Personal Email; Lenora Jackson; Estelle E. Fischer; Holly Mincey; Jody Shively; Kate Bridges, MD
Cc: higginsr@mail.nih.gov; [SCRN] Willinger, Marian; Poole, W. Kenneth; Berberim@nhlbi.nih.gov
Subject: SUPPORT Trial

The DSMC met on December 6, 2004 to review the protocol for the SUPPORT Trial. The attached memo contains their recommendation for moving forward with this Trial.

Thanks.
Betty

<<DSMC Report 12-6-04.doc>>

Betty Hastings

RTI International
Statistic Research Division
P.O. Box 12194
Research Triangle Park, NC 27709-2194
Telephone: (919) 485-7740

Fax: (919) 485-7762
bkh@rti.org

From:	Wally Carlo, M.D.
To:	Higgins, Rosemary (NIH/NICHD) [E]
Cc:	Hickman, Leslie (NIH/NICHD); Donna Thrower; Monica Collins
Subject:	RE: Additional Pulse Oximeters
Date:	Friday, September 24, 2004 11:41:27 AM

Great! I will send it to you. wally

From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Friday, September 24, 2004 10:39 AM
To: Wally Carlo, M.D.
Cc: Hickman, Leslie (NIH/NICHD)
Subject: RE: Additional Pulse Oximeters

We need a letter signed by you and your business official so that we can approve this. Thanks
Rose

> -----Original Message-----
> **From:** Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]
> **Sent:** Friday, September 24, 2004 11:43 AM
> **To:** Higgins, Rosemary (NIH/NICHD)
> **Cc:** Wally Carlo, M.D.; Monica Collins; Donna Thrower
> **Subject:** Additional Pulse Oximeters
>
> Dear Rose: As we discussed, I estimate that we will need more pulse oximeters. Could we go ahead and buy four pulse oximeters with the carry over funds? We are usually high enrollers in the Network and estimate that we will need even more pulse oximeters in the future. Thanks. Wally

From:	Wally Carlo, M.D.
To:	Higgins, Rosemary (NIH/NICHD) [E]; mcw3@po.cwru.edu; nfiner@ucsd.edu; sduara@miami.edu; poo@rti.org; edward.donovan@cchmc.org
Cc:	jobea0@chmcc.org
Subject:	RE: SUPPORT
Date:	Monday, September 20, 2004 9:55:34 AM

Particular thanks to Ed and his team for a very organized and informative training. wally

-----Original Message-----
From: Higgins, Rosemary (NIH/NICHD) [mailto:higginsr@mail.nih.gov]
Sent: Monday, September 20, 2004 8:53 AM
To: 'mcw3@po.cwru.edu'; 'nfiner@ucsd.edu'; 'sduara@miami.edu'; Wally Carlo, M.D.; 'poo@rti.org'; 'edward.donovan@cchmc.org'
Cc: 'jobea0@chmcc.org'
Subject: SUPPORT

I want to extend a sincere thanks to the SUPPORT subcommittee members for their commitment and dedication to this trial. I think the training meeting
was excellent and the level of enthiusiasm was outstanding! Your hard work
is greatly appreciated!!
Thanks so much!!
Rose

Sent from my BlackBerry Wireless Handheld

Incoming mail is certified Virus Free.
Checked by AVG anti-virus system (http://www.grisoft.com).
Version: 6.0.766 / Virus Database: 513 - Release Date: 9/17/2004

Outgoing mail is certified Virus Free.
Checked by AVG anti-virus system (http://www.grisoft.com).
Version: 6.0.766 / Virus Database: 513 - Release Date: 9/17/2004