Eunice Kennedy Shriver National Institute of Child Health and Human Development

NATIONAL ADVISORY CHILD HEALTH AND HUMAN DEVELOPMENT COUNCIL

MINUTES OF MEETING

September 18, 2015

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
***EUNICE KENNEDY SHRIVER* NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT**
NATIONAL ADVISORY CHILD HEALTH AND HUMAN DEVELOPMENT COUNCIL
SUMMARY MINUTES
September 18, 2015[1]

The National Advisory Child Health and Human Development (NACHHD) Council convened its 158th meeting at 1:30 p.m., Thursday, September 17, 2015, in Building 31, Conference Room 6, of the National Institutes of Health (NIH) in Bethesda, Maryland. The meeting was closed to the public from 1:30 p.m. to 3:16 p.m., as provided in Sections 552b(c)(4) and 552b(c)(6), Title 5, U.S.C., and Section 10(d) of Public Law 92-463, for the review, discussion, and evaluation of grant applications and related information. The meeting reconvened at 8:00 a.m. on Friday, September 18, 2015. This portion of the meeting was open to the public.

Dr. Alan Guttmacher, Chair, NACHHD Council, and Director, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), presided.

Council members present:
Dr. Diane Bianchi
Dr. Anne Case (virtual)
Ms. Barbara Collura
Dr. Bonnie Duran
Dr. Patricia Flynn (virtual –closed session)
Dr. Walter Frontera
Dr. Melissa Gilliam
Dr. Gregory Kopf (virtual)
Ms. Wendy Lazarus
Dr. Ruth Lehmann (virtual)
Dr. Ken Muneoka
Dr. Stephen Petrill
Dr. Piero Rinaldo
Dr. Frederick Rivara
Dr. Richard Shields (NABMRR Liaison)
Dr. George Saade
Dr. Paul Wise
Ms. Sheila Zimmet

Council members absent:
Dr. Patricia Flynn (open session)
Dr. Ruth Lehmann (open session)

Ex officio members present:
Dr. Patricia Dorn, Department of Veterans Affairs

[1] Members absent themselves from the meeting when the Council discusses applications from their own institutions or when a conflict of interest might occur. The procedure applies only to individual applications discussed, not to *en bloc* actions.

Invited guests:
Joe Laakso, Endocrine Society
Craig Fisher, American Psychological Association
Rachel Gandell, American College of Obstetricians and Gynecologists
James Baumberger, American Academy of Pediatrics
Mary Jo Hoeksema, Population Association of America

Others present:
Members of Staff, NICHD
Members of Staff, NIH

I. CALL TO ORDER AND INTRODUCTORY REMARKS

NICHD Director Dr. Alan E. Guttmacher welcomed Council members and staff. He announced that the meeting would be open to the public and that yesterday's meeting was closed to the public for the consideration of grant applications. The public portion was videocast. He introduced Dr. Richard Shields and welcomed him as the NABMRR Liaison member to the Council.

Dr. Shields introduced himself. He is at the University of Iowa as Chair of the Department of Physical Therapy and Rehabilitation Science, where he studies neuromuscular plasticity in those with spinal cord injuries. His recent work has indicated that muscles may be sending messages to the central nervous system though routes that don't involve the spinal cord.

Dr. Guttmacher also welcomed guests from several professional societies who would be joining the meeting throughout the day.

A. Review of Confidentiality and Conflict of Interest

NICHD Associate Director for Extramural Research, Dr. Della Hann, reminded Council members that material furnished for review and discussion during the closed portion of the meeting is considered privileged information. Advisors and consultants serving as members of a public health advisory committee may not participate in situations in which any violation of conflict of interest laws and regulations might occur. The responsible staff ensures that a Council member does not perform duties or render advice that might have a direct and predictable effect on the interests of an organization or institution in which he or she has a financial interest. In particular, Council members should not participate in the evaluation of grant applications for federal support that will affect the interests of such organizations or institutions. Dr. Hann reminded Council members that at the end of the closed session of the meeting, all members were required to certify that they had not been involved in any conflict of interest situations during the review of grant applications.

B. Council Minutes - Meeting of August 2015

Dr. Hann moved to approve the *Summary Minutes of Meeting* for the Minutes of the August 17, 2015, meeting. Dr. Bianchi asked that the minutes be amended to include her presence. Dr. Hann

agreed to amend the minutes and stated that they would be presented for vote at the next council meeting.

C. Future Meeting Dates

The Council agreed to the following future meeting dates:

January 21, 2016	(Thursday)
June 9, 2016	(Thursday)
September 21, 2016	(Wednesday)
January 19, 2017	(Thursday)
June 8, 2017	(Thursday)
September 22, 2017	(Friday)

II. NICHD DIRECTOR'S REPORT AND DISCUSSION

News from NIH

Dr. Walter Koroshetz, who had been serving as the Acting Director of the National Institute of Neurological Disorders and Stroke (NINDS), was appointed Director after a national search. Dr. Koroshetz has been leading the National Institutes of Health (NIH) efforts in the area of concussion research.

In August, Dr. William Riley, who was the Acting Director, was appointed Director of the NIH Office of Behavioral and Social Sciences Research and the Associate Director of NIH for Behavioral and Social Sciences.

Dr. Kay Lund, also joined the NIH this past August as the inaugural Director of the Division of Biomedical Research Workforce Programs, a position created in response to the 2012 report of the NIH Biomedical Research Workforce Working Group. Dr. Lund comes to the NIH from the University of North Carolina where she was the Sarah Graham Kenan Professor of Cell Biology and Physiology. She will be addressing workforce quality and diversity issues.

Dr. Sally Rockey retired from her post as the NIH Deputy Director for Extramural Research. She is now the inaugural Director of the Foundation for Food and Agriculture Research. This is the newly created foundation that will further the goals of the Department of Agriculture much like the Foundation for NIH does for NIH.

Dr. Thomas Insel, will step down as Director of the National Institute of Mental Health, effective November 1st. He will join the Life Sciences team at Alphabet (formerly Google) to lead a new effort focused on mental health. Dr. Bruce Cuthbert, will serve as the Acting Director while the national search for a new director is conducted.

Dr. Guttmacher also mentioned his own departure, announced this past August. He will be stepping down as Director of NICHD, with his last day on September 30th. Effective October 1st, Dr. Catherine Spong, currently the Deputy Director, will become the Acting Director of NICHD.

Dr. Guttmacher stated that Dr. Tabak, Principle Director of NIH, would discuss the congressionally mandated NIH Strategic Plan later in the meeting.

The National Children's Study (NCS) received an allocation of $165 million in Fiscal Year (FY) 2015. NIH redirected the funds, developing a plan in January 2015, that involved release of FOAs in February/March 2015, review of applications over the summer, and making awards in September 2015. Monies were allocated to research that continued to support the mission and the goals of the NCS.

For FY 2016, this effort will have a new name: Environmental influences on Child Health Outcomes (ECHO). The overarching goal will be to leverage extant cohorts to investigate the longitudinal impact of prenatal, perinatal, and postnatal environmental exposures on pediatric health outcomes with high public health impact. This program will support multiple synergistic, longitudinal studies by: using extant cohorts, representing various environmental exposures, sharing standardized research questions, and focusing on four key pediatric outcomes.

Additionally, this program will use the Institutional Development Awards (IDeA) program, that supports faculty development and research infrastructure enhancements in states that do not receive many NIH research funds, to create a Pediatric Clinical Trials Network across those states. This would help to address access gaps for rural children and would link IDeA state centers with experts in clinical trials. Credit for this concept goes to Lisa Kaeser, Director of NICHD's Office of Legislation and Public Policy.

Other updates include a notice regarding proposed changes to the Common Rule. It is available for public comment through the Federal Register at https://federalregister.gov/publicinspection. Comments are due by December 7th, 2015.

The NIH-Bill and Melinda Gates Foundation Global Health Meeting took place on July 8th. This is the second meeting since Bill Gates visited NIH in 2013. Activities in eight key areas were identified for the next 12 months. Areas involving NICHD include maternal and newborn health, contraceptive research, child health and development, pediatric pneumonia and indoor air pollution, and AIDS.

The Precision Medicine Initiative Working Group released a report on September 17, which recommended that individuals from all life stages be included in the recruitment of the one million person cohort, and that NIH consider the safeguards necessary to ensure the appropriate enrollment, retention, and protection of children, decision-impaired adults, and participants who may become incarcerated after enrollment.

News from NICHD

Dr. Guttmacher welcomed Dr. Della Hann in her role as NICHD's Associate Director for Extramural Research. She brings broad and deep knowledge of the extramural environment and the "big picture" view to the Institute's mission.

Dr. Guttmacher recognized Dr. Yasser El-Sayed, a Stanford investigator funded by NICHD's Maternal Fetal Medicine Units (MFMU) Network, who was given a $1 million donation by a

grateful patient after helping with her labor and delivery. Dr. El-Sayed will use that money to support the research activities of the MFMU.

The Intramural Research Program held a small competition for research projects supporting the Human Placenta Project again this year. It has been beneficial to both the institute and the Project.

There has been some structural reorganization within the NICHD Office of the Director (OD). The Office of Science Policy, Analysis, and Communications will become two offices: the Office of Science Policy, Reporting, and Program Analysis and the Office of Communications. The Office of Health Equity (OHE) will stay within the OD because of the important coordination function it performs across the intramural and extramural programs. However, the grants currently administered by OHE will move to the extramural program. The NCS Program Office will remain part of the OD while closeout activities continue and biospecimens are made ready for distribution to the scientific community. Lastly, the Associate Director for Clinical Research moved from the OD to the Division of Extramural Research.

Budget and Legislative Update

The Newborn Screening Saves Lives Reauthorization Act now requires that federally funded research using dried blood spots collected on or after March 18, 2015 be considered non-exempt human subjects research and follow the HHS Protection of Human Subjects regulations (45 CFR Part 46). Parental permission is required to use blood spots in research.

The Office of Behavioral and Social Sciences Research had a 20th anniversary celebration on the Hill; two NICHD grantees presented data.

On July 10, the House passed the 21st Century Cures Act (H.R. 6). It was received by the Senate on July 13 and referred to the Committee on Health, Education, Labor, and Pensions. This committee plans to introduce a different bill later this calendar year, which will represent the Senate's version of this Bill.

There is no FY 2016 NIH budget yet. The House and Senate have finished working on appropriations bills; they differ. Without action from Congress, sequestration caps will return in FY 2016. Without a continuing resolution, the government will not be funded beyond September 30. NICHD is preparing for the possibility of a shutdown.

III. REPORT OF THE DIVISION OF EXTRAMURAL RESEARCH (DER)

Report of the Director, DER

Dr. Hann presented the DER updates and introduced two new staff members. Dr. Ruben Alvarez is a Program Official in the Child Development and Behavior Branch focusing on language and bi-lingualism. Dr. Alvarez joins NICHD from the University of Tulsa, where he studied the human development and bi-lingualism. Dr. Candace Tingen is a Program Official in the

Gynecological Health and Disease program. She is a reproductive biologist with a background in cell biology. She came to NIH as an AAAS Policy Fellow and has also worked in the Office of Science Policy, Planning and Data Analysis at The National Institute on Minority Health and Health Disparities.

There are two new Scientific Review staff members: Dr. Sheri Hild and Dr. Priscah Mujuru. Dr. Hild was a Scientific Review Officer at National Center for Advancing Translational Sciences (NCATS) prior to joining NICHD. Her research prior to joining NIH focused on reproductive health. Dr. Mujuru was a Scientific Review Official at the Center for Scientific Review on the Nursing and Related Clinical Services study section. Her background is in Epidemiology.

There were two retirements this summer: Mary Plummer, Chief of the Office of Committee Management and CAPT H. Trent MacKay, MD, Chief of the Contraceptive Discovery and Development Branch. Recruitments for both positions are underway.

Dr. Hann provided an update on the Contraceptive Research Review. The Review Panel issued recommendations that were discussed at the January 2015 meeting of Council. The internal Contraceptive Working Group has been working to implement those recommendations. One area of focus has been improving coordination between contraceptive development research and behavioral research. NICHD will rename the branch to the Contraceptive Research Branch to help communicate the broader scope of science relevant to contraception

Dr. Hann presented data on NIH Research Project Grants, showing that while the number of extramural grant submissions has gone up, the success rate has continued to fall to 18 percent in 2014. NIH expects an even higher number of submissions for 2015 (close to five percent increase), meaning that the success rate will likely fall further. For NICHD, the success rate has also fallen since the budget doubling in the early 2000s. Currently the success rate is close to 12.5 percent. NICHD also expects a record number of submissions for 2015.

NIH is in the process of restructuring grant application instructions to keep the information as current as possible, reduce administrative burden, and clarify and simplify information on what is required to submit an application. There is currently a notice in the NIH Guide requesting input from the broader research community. Comments can be submitted through September 25th, 2015 at http://grants.nih.gov/grants/rfi/rfi.cfm?ID=47.

Dr. Hann also mentioned an effort aimed at clarifying NIH's long-standing expectations regarding rigor and transparency and how this is to be expressed in grant applications. A notice appeared in the NIH Guide earlier in the summer. The hope is that it will prompt applicants to consider issues that they may have previously down-played or ignored, which could have a detrimental effect on the quality of the science they produce. Changes will be made to the application itself, but also to the review criteria. Pending approval from OMB, revisions will be ready in Fall 2015 and apply to applications submitted beginning in January 2016.

Dr. Hann also highlighted the launch of the NICHD Data and Specimen Hub (N-DASH): www.dash.nichd.nih.gov. She thanked Dr. Rohan Hazra, who was instrumental in launching the project. N-DASH will be a home for NICHD-funded data. Currently users can browse and

download data from 14 studies, and investigators are encouraged to use this platform for sharing their data. Future plans include linking data sets to biospecimen collections.

Dr. Hann asked the Council for feedback on the August 2015 meeting. She noted that it is unusual to have an August meeting, and it was the first time the Council met entirely virtually. A Council member stated that the meeting went very well and would be a good approach if an additional Council meeting became a regular occurrence. Another Council Member stated that the reduction of travel burden was welcome.

IV. DIVISION OF INTRAMURAL RESEARCH PRESENTATION

Dr. Constantine Stratakis presented the Annual Report of the DIR.

He started by presenting the new members that were added to the Board of Scientific Counselors: P. Michael Conn, PhD, the Senior Vice President for Research and Associate Provost at Texas Tech University Health Sciences Center; Frances Jensen, MD, Professor and Chair of the Neurology Department at the University of Pennsylvania Perelman School of Medicine; Scott Rivkees, MD, Professor and Chair, Department of Pediatrics at the University of Florida; and Eric Vilain, MD, PhD, Chief of the Division of Medical Genetics, Department of Pediatrics, University of California, Los Angeles.

The NICHD DIR has 1100 employees, 69 principal investigators (PI), and more than 100 Clinical Protocols (two-thirds of which are at the NIH Clinical Center). It oversees medical training programs for pediatric and adult endocrinology, and reproductive endocrinology and infertility; the NICHD DIR also participates in the training of medical genetics fellows and residents at the NIH Clinical Research Center, and perinatal research and obstetrics trainees at Wayne State University, Detroit, Michigan.

In terms of personnel changes in the DIR, there have been two new appointments: Michael Collins, MD (NIDCR), was appointed Associate Director, Inter-Institute Endocrine Training Program; Maya Lodish, MD, was appointed Director of the Pediatric Endocrinology Training Program. As part of the Office of the Clinical Director reorganization mentioned at the June meeting, two new hospitalists have been hired. Jenny Blau, MD, is the Co-Chief, Internal Medicine and Assistant Deputy Program Director of the Inter-Institute Endocrinology Training Program. Andrew Demidowich, MD, is a Co-Chief, Internal Medicine and Liaison to the NICHD Medical Research Scholars Program.

The DIR reorganization, approved by the Council in June, has been approved by Dr. Francis Collins and the Department of Health and Human Services. It goes into effect October 1, 2015. The new Associate Scientific Directors (ASD), who will serve four-year terms starting October 1st, and members of the Group of Senior Advisors are as follows:

Dr. Brant Weinstein, ASD
Dr. Janice Chou, ASD
Dr. Gisela Storz, ASD
Dr. Juan Bonifacino, ASD
Dr. Joshua Zimmerberg, ASD

Dr. Chris McBain, Deputy SD
Dr. Forbes D. Porter, Clinical Director (CD)
Dr. Alan DeCherney, Deputy CD Academic Aff.*
Dr. Roberto Romero, Deputy CD Ob/Maternal-Fetal*
Ms. Francie Kitzmiller, Deputy, Admin & Budget*

Dr. Peter Basser, ASD
Dr. Tracey Rouault, ASD
Dr. Mary Dasso, ASD

Ms. Brenda Hanning, Deputy, Liaison & Training*

*Ex Officio

NICHD is currently recruiting tenure-track and midcareer investigators for Clinical and Translation Research in Pediatric or Women's Health (two positions), Cell/Developmental Biology, and Basic or Translational Neuroscience.

Dr. Stratakis also discussed DIR's training efforts. The bulk of trainees come in as postdoctoral fellows. A significant portion are summer and post baccalaureate trainees, as well. As a result of focused recruitment, NICHD placed ten students from groups traditionally underrepresented in science or from disadvantaged backgrounds into intramural labs. NICHD has a new electronic Annual Progress Review for all trainees and Individual Development Plans for all postdocs and clinical fellows. Most trainees go on to careers in research in academia and government or teach at the college level. Seventy percent of them are currently in the United States. Dr. Stratakis also discussed accomplishments and plans of past and current NICHD Scholars, and mentioned Dr. Kathryn Tabor, who won the Three-Minute Talks Competition (mentored by Dr. Harry Burgess). Her talk focused on neurons that modulate acoustic startle, a behavioral paradigm used to study anxiety and certain psychiatric conditions, including schizophrenia. Dr. Tabor looked at single genes in larval zebrafish that are found in neurons involved in the startle pathway to identify candidate genes that may be altered in humans with schizophrenia.

Dr. Stratakis then introduced Dr. Alan Hinnebusch, Head of the Section on Nutrient Control of Gene Regulation, who was recently elected to the National Academy of Sciences. Dr. Hinnebusch gave a scientific presentation focusing on the regulation of amino acid biosynthetic genes in budding yeast as a means of studying molecular mechanisms of gene regulation at the translational and transcriptional levels.

V. NIH STRATEGIC PLAN

Dr. Lawrence Tabak presented on the NIH Strategic Plan. Cromnibus H.R. 83-346 (enacted December 16, 2014) stated that NIH shall submit to Congress an NIH-wide five-year scientific strategic plan no later than one year after enactment. In addition, the 21st Century Cures Act requires NIH to develop and maintain a five-year biomedical research strategic plan within 270 days of enactment. The plan is to be used to identify research opportunities and develop individual plans with a common template for research activities of each IC. The Plan shall identify strategic focus areas that consider return on investment. This is to ensure that rare and pediatric diseases remain a priority, and ensure that maintaining the biomedical workforce remains a priority.

Dr. Tabak then reviewed what the goals of the NIH-wide Strategic Plan should and shouldn't be:

- Should be a living document that will guide NIH over the next 5 years
- Should articulate approaches and opportunities that are forward looking and inspirational
- Should identify major trans-NIH themes that will advance research

- Should not describe all the many important things that NIH does and will do in the future
- Should not address priorities of the individual Institutes, Centers, and Offices, since each of these has their own Strategic Plan

Dr. Tabak stated that the Strategic Plan was developed and discussed by NIH senior leadership and then each Center and Institute put forward a staff member to populate a Working Group. There were three NICHD staff on the Working Group. The NIH Advisory Committee to the Director and Working Group met twice to review the Plan; currently the recommendation is for additional emphasis on the interconnected nature of NIH's research, and the inclusion of clinical methodologies, data science, and workforce retention.

The draft framework of the Plan has several parts: an overview, areas of opportunity, and underlying principles.

The overview will state the NIH mission, describe the current NIH-supported landscape, and discuss constraints confronting the community in the face of lost purchasing power.

In the areas of opportunity there will be succinct descriptions of emergent opportunities for each, and specific examples from recent research, including fundamental science, health promotion/disease, and treatments/cures.

The underlying principles will describe the current status and emergent opportunities, as well as what NIH needs to realize these opportunities, highlight specific examples of recent breakthroughs, and discuss how this aligns with the HHS Strategic Plan. This includes setting priorities and enhancing stewardship.

NIH solicited feedback through a RFI and webinars, and had roughly 1,000 comments so far. It will also be discussed with 21 NIH Institutes, Centers, and Offices through October. Broadly, suggestions included issues such as emphasizing implementation science and interdisciplinary science, fixing peer review, expanding workforce training, using systems approaches, more explicit inclusion of behavioral and social sciences, and re-envisioning the role of participants as partners rather than patients.

The Strategic Plan is due to Congress in mid-December.

Dr. Tabak then asked the Council to provide feedback, either during the meeting or via email.

Council Discussion

Dr. Bonnie Duran stated that she agreed with an emphasis on implementation science. This approach would help specify what things are labeled "evidence-based", and would help clarify the role of medical context for specific recommendations. Dr. Duran also raised the issue of universal, selected and indicated approaches; universal approaches can worsen health disparities, according to data from the CDC.

Dr. George Saade stated that pregnancy is an ideal point to look at long-term health outcomes for the baby and the mother. Dr. Saade hoped that this would be reflected in the strategic plan. Dr. Tabak replied that this has been the emphasis during planning for ECHO.

Dr. Ken Muneoka asked if there had been any effort to shift the burden of research to academic institutions. NIH has been picking up more of the cost of research. Dr. Muneoka asked if there been discussion on how to reverse that trend. Dr. Tabak replied that there has been discussion of the need to renegotiate the contracts with research institutions. He stated that there are a variety of business models that universities use, so it would be hard to implement a universal solution; but, there is discussion of how to rebalance the investment in research. It may be possible to work together with universities to reach a new equilibrium over a period of time (perhaps a decade). There is a need to figure out how research can grow in an environment where resources will not be growing. Dr. Muneoka stated that the science suffers because the resources are going more and more to administrative costs and that takes away from funding for the science. Dr. Tabak replied that there has been an increase in administrative burden, mostly due to increased requirements. Dr. Tabak stated that reducing the administrative burden for universities could help to rebalance in a way that was favorable to research.

Ms. Wendy Lazarus stated that, as someone who uses NICHD research to determine policy, she is not sure what is being done to examine the effectiveness of workforce and other non-medical interventions on maternal and child health. Ms. Lazarus expressed that she would like to see something in the pipeline that will look at efficacy of new workforce models so that funding, perhaps from Medicaid, can be found for effective interventions. Dr. Tabak said that this is an issue that NIH handles in partnership with other HHS entities, to determine roles and responsibilities. Currently the interaction between agencies is working well. But moving forward, the challenge is to ensure that this issue isn't lost because it lies at the interface of several agencies. Ms. Lazarus said that she was referring more to the science rather than policy. Dr. Tabak replied that part of the challenge is determining who funds the science when it cuts across the mission of several agencies, but doesn't lie completely with one. There is a need to identify the issues that lie at the interface so that everyone is aware of them and they are not lost.

Dr. Melissa Gilliam asked how often the strategic plans are done and how big the changes are expected to be. Dr. Tabak said there was an attempt to craft one in 1992, but it was never released. In attempting to cover every contingency, it became unwieldy and was not useful. The current attempt is a new endeavor, and its success will depend on its impact and value. If there is no value, it probably won't happen again; if there is, it may become a regular occurrence. Dr. Gilliam asked why it is being done. Dr. Tabak replied that Congress wants there to be more transparency about how decisions are made and how funds are used, wants NIH to articulate its priorities and be accountable for achieving them, and wants NIH to put forward a clear statement of how it will tackle the most intractable medical issues and what it needs to do that. The goal is for NIH to get better at what it is already doing well.

Dr. Piero Rinaldo stated that the public sector is more aggressive than ever in its attempts to turn discovery into patents or intellectual property, and that this is not always coincident efforts to support public health. Dr. Rinaldo asked how the strategic plan takes this into account. Dr. Tabak replied that there are many kinds of partnerships. For example, the Accelerating Medicines Partnership, NIH, FDA, 10 pharmaceuticals companies and some non-profits have come together to study several highly prevalent conditions in "pre-competitive" space. Target discovery and validation is taking place free of intellectual property concerns. This is a paradigm shift and could be used to shape future opportunities. Dr. Tabak recognizes that intellectual property

concerns could make it harder to use this model for the next stages of drug discovery, but that it seems to work at least initially, and this is a great step forward in partnership models.

VI. RISK MANGEMENT

Mr. John Jarman presented NICHD's implementation of its risk management program. The Federal Managers Financial Integrity Act requires all federal agencies to document and assess their internal control processes for managing risk. Institute and Center (IC) Directors must attest annually that they have assessed their IC's risks and have plans in place to address any identified risks.

NIH identified 55 risks NIH-wide. In addition to these trans-NIH risks, NICHD also identified some additional IC specific risks. This process included identifying, mitigating, and monitoring risks associated with NICHD's scientific, programmatic, and administrative activities. Each risk has an assigned risk manager who identifies the policies and procedures that NICHD has in place to prevent the risk from occurring or detect it if it has occurred. The manager also documents the activities that they are engaged in to manage the risk.

Over a five-year period, NICHD conducted reviews of all identified risk categories to assess policies and procedures to ensure activities were effective. Additionally, some administrative risks, such as procurement credit cards, travel, and property, are tested annually.

Mr. Jarman presented several examples of outcomes from risk management activities. Some of these included identifying a need for back up storage facilities for bio-specimen repositories and including specific language in contracts for these repositories. NICHD also identified the need to have electronic access to records as a result of the partial closure of one of the leased facilities. Other activities also enhanced cash management of grant funds ensuring they were utilized properly and ensured that conditional gift funds were used only as the donor intended and in a timely manner. Positive outcomes were also seen in procurement, travel, and property management.

Mr. Jarman indicated that Enterprise Risk Management is a current focus of the Administration; it addresses the full spectrum of an organization's risks, including challenges and opportunities, and integrates them into an enterprise-wide, strategically-aligned portfolio view. Current IC/OD risks are often tilted towards administrative risks. Going forward, increased emphasis will be placed on scientific and programmatic risks.

Currently program risks, a key part of risk management, are not fully addressed within current IC/OD risk management programs but are addressed through other mechanisms. NIH will also seek to establish linkages between current risks and program risks.

Council Discussion

Dr. Diana Bianchi asked if there is a rapid response team to address unforeseen events. Mr. Jarman said there is a team for continuity of operations, mostly physical plant type events, and additionally there is a leadership team that gathers data to respond to inquiries about different issues. NICHD also uses its reporting chain to pass information along rapidly.

Dr. Hann added that the process of having Council meetings, which is the second tier of peer review, is a risk management process. It helps NICHD stay aware of potential risks and mitigate them, to ensure that NICHD is doing and funding work that truly supports its mission.

Dr. Guttmacher mentioned that the administrative tasks that Mr. Jarman oversees are essential to the success of NICHD, though it happens mostly behind the scenes. Dr. Guttmacher thanked him for his efforts and acknowledged Mr. Jarman's ability to recruit and mentor excellent staff.

VII. R35 DISCUSSION

Dr. Eugene Hayunga provided an update of the Working Group discussion since the last report on the R35 Outstanding Investigator Award. He compared the existing R35 award programs at three institutes: the National Cancer Institute, National Institute of General Medical Sciences and NINDS. The comparison looked at the purpose of the awards, eligibility requirements, other grant allocations allowed, and funding by time and amount.

Dr. Hayunga also mentioned several other award mechanisms focusing on the investigator: R37 MERIT Awards, Pioneer Awards (NIH Common Fund), Special Consideration for first renewal (some ICs), and Transformative Research Award Leadership program (NIH Common Fund). Dr. Hayunga stated that NICHD wants to balance potential benefits and costs of initiating its own R35 program. NICHD needs to consider improved support for outstanding investigators and the impact this will have on the payline and other NICHD programs. Dr. Hayunga thanked those at NICHD for analyzing data to address this question.

Based on previous discussion, the Working Group concluded that this mechanism was not for new or early career investigators, but instead would be more appropriate for investigators with a track record as researchers. The Working Group recommended that the R35 should be targeted to investigators who had at least one NICHD R01 and was in the 6th year of funding or beyond, irrespective of other NIH or NICHD grants. This is presently a pool of 245 investigators.

Assuming that those 245 investigators might apply during the last two years of their existing five-year R01, it was anticipated that approximately 100 of those eligible would apply and about 20 would be successful. In terms of potential first year costs, it was estimated that it would create a significant burden on review and the awards would cost approximately $22.5 million with unknown cost offsets, but they could potentially be in the range of $4.4 to $10.6 million. The effect on the payline could be about two percentile.

Council Discussion

Dr. Guttmacher informed the Council that this would be the last update for some time and that it is now up to the Council to determine how NICHD should proceed.

One Council member asked if there was a way to estimate the impact on diversity given the number and diversity of PIs who meet the eligibility criteria. This is a difficult question to answer because there are many unknowns. On the one hand, the awards would support a group of existing investigators who may not be as diverse as desired. On the other hand, increased resources might allow those investigators to hire a more diverse group of scientists in their labs. Additional resources might encourage investigators to take risks, both in terms of scientific exploration and in terms of giving a junior person an opportunity. Another Council member

voiced concern about how the R35 program would impact the payline and the impact that will have on underrepresented minorities.

Another Council member acknowledged the importance of rewarding excellent PIs, but that this would seem to come at the expense of other investigators. He then asked if the NCI had data on impact to other investigators. Dr. Hayunga replied that it was too early to tell, as the effects will be measured sometime after the awards had been made and NCI had only just started making awards. The Council member then asked about the other equivalent programs that had been mentioned in Dr. Hayunga's talk. Dr. Hayunga replied that the R37 is given to those who already have a funded R01, so it doesn't have additional costs. Dr. Hann interjected that the Pioneer Award comes from a separate pool of money, not the institute's.

One of the Council members who served on the Working Group stated that while he was initially enthusiastic about this type of award, he has become less so over time. This is particularly true given the presentation by Dr. Jon Lorsch at the previous Council meeting, where it was shown that the impact of the first R01 is much greater – in terms of productivity – than that of additional R01s. Therefore, he now feels it is more important to fund first R01s than to pursue the R35 funding mechanism.

Another Council member expressed a similar opinion: If NICHD pursues this model, then we are essentially providing support for already established PIs (many of whom received their awards at a time when paylines were higher) and thus we will not be addressing the problem with funding new investigators. This would seem to lock-in any inequity even further. And one other Council member stated that he has opposed this idea from the outset, because the perception of this funding model would be negative.

Dr. Guttmacher thanked those who contributed data to the effort, particularly Dr. Hayunga. Initially Dr. Guttmacher thought the idea sounded good, but as it was examined and discussed, it does not make sense to move forward at this point. It may be revisited in the future should paylines increase or other circumstances change.

VIII. NICHD EXTRAMURAL TRAINING PROGRAM UPDATE

Dr. Dennis Twombly presented an update on the NICHD training program. The overall objective of the review was to examine NICHD's formal training programs: Individual NRSA Fellowships (F30, Diversity-F31, Parent F31, F32); Institutional Training Grants (T32); Individual Career Development Awards (K01, K08, K23, K24, K25, K99-R00); Institutional Career Development Awards (K12 programs); and T15 / R25 Grants for Short Courses.

A 13-member Task Force consisting of representative NICHD Council members, NICHD staff and outside experts conducted the review.

There were six Task Force meetings, as well as NICHD Extramural Staff meetings and informal conversations. The Task Force prepared a written report (available on the public website) and a presentation to the Council.

The task force addressed seven overarching questions.

Question 1: Is the amount of funding NICHD commits to training awards the right amount? Are the allocations an appropriate percentage of the NICHD budget? How have these allocations evolved over time?

Data showed that NICHD spends five to seven percent of extramural budget on all training mechanisms. In FY 2014, NICHD supported 1,232 trainees at a cost of $74 million. The training budget is comparable to ICs of similar size. NICHD's budget rose rapidly during doubling years, reached a peak in 2003, but has declined by ~30 percent over past 10 years (in inflation-adjusted dollars). Based on this information, the Task Force believes that training is critical to attract and retain excellent new scientists and if possible, NICHD should increase funding to offset recent declines. Also, impending fiscal pressures warrant NICHD action.

Question 2: Is NICHD supporting the correct ratio of awards at different career stages, i.e., pre-doctoral/postdoctoral fellow/early faculty? Has this ratio changed over time?

According to the data, NICHD supports research training from pre-doctoral through early faculty stages. This includes clinical and Ph.D. and non-clinical trainees. Over the past 20 years, the number of awards at career (K) stage have more than doubled and pre-doctoral and postdoctoral awards have decreased by 25 to 40 percent. Based on this information, the Task Force recommends that more resources are allocated for fellowship stage, late-stage postdoc, and early faculty levels for those with PhD and other non-clinical degrees.

Question 3: Are there appropriate levels of commitment to the different training mechanisms? Are some mechanisms over- or underutilized?

NICHD spends far more on institutional programs (T32 and K12) than on individual awards (F and K), while other ICs place more emphasis on individual awards. Seventy-five to eighty percent of NICHD's overall training resources are in T32 and K12 programs. The K08 plus K23 for physician-scientists now constitutes 63 percent of the individual K portfolio. The K01 and K99 combined constitute 27 percent of the individual K portfolio. K24 awards support a large proportion of salary for well-funded investigators with limited additional impact on mentoring. Based on this information, NICHD should rebalance the training portfolio by shifting some funds from institutional programs to individual awards. NICHD should also consider increasing funding for K99-R00 program as a bridge to independence and reducing K24 mid-career awards or limit them to certain focus areas.

Question 4: Are the allocations to the fields supported by NICHD training appropriate for the NICHD mission, and are the types of training mechanisms appropriate for those fields? How does the current distribution compare with what NICHD has done in the past?

In general, NICHD does not target specific disciplines; most T32 programs, individual fellowships, and career awards are submitted in response to Parent FOAs. Funding strictly by payline can shift the portfolio in unintended fields/disciplines. K12 programs are solicited and funded via RFA with set-aside funds. The fields with the most funding include pediatrics, behavior, reproductive sciences, and rehabilitation. The fields with the least funding are pregnancy/perinatology, developmental biology, and intellectual and developmental disabilities.

The Task Force recommends conducting regular portfolio analysis and re-balance to fit NICHD needs, conducting a more detailed analysis of T32 and K12 portfolios to determine which subject

areas are over-represented or overlapping, using RFA or PAR to target specific fields, but only if well-justified, and basing R25 funding decisions on programmatic need rather than strictly by payline.

Question 5: How do we define success of NICHD training programs? Are NICHD training programs successful?

The goal of training programs is to develop the next generation of scientists and provide for the workforce. Success was defined as continuing in any research-related career (e.g., academia, industry, government). The key measures were employment type, grant applications, funded grants, and publications. Percent of trainees remaining in research careers ranges from 68 to 84 percent, with some programs more successful than others.

The Task Force recommends using a tiered/multi-faceted formula for gauging "success," identifying and scaling back those institutional programs that are less successful or not filling slots, and conducting an analysis of outcomes for postdocs and career awardees to assess the effect of combined programs (e.g., T32 and F32; K12 and K).

Question 6: Are there training/workforce needs that have already been addressed or that still need to be addressed by our portfolio of training awards?

Training funds are tighter and success rates are lower. Limited award funds must be leveraged across mechanisms, constituencies, and disciplines. Success rates for renewal T32 (45%) and K12 (65%) are far higher than for new T32 (17%) and new K12 (21%) applications. NICHD's existing commitments to ongoing institutional programs limit opportunities to cultivate scientists in novel or emerging areas and funding strictly by payline prevents proactive portfolio planning.

The Task Force recommends addressing the imbalance in success rates for new vs renewal T32 and K12, adopting strategies to enable more flexibility in selecting training awards by IC needs, using RFAs or PARs to promote areas where needs are justified, and developing new approaches for bridging to independence.

Question 7: Are there fiscal pressures or other factors in the near future that have potential to impact our mix of training programs?

The Biomedical Workforce recommends that all ICs should sponsor all mechanisms; NICHD joined the Parent F30 (dual degree) and Parent F31 (pre-doc) in FY 2014. F30s and Parent F31s are reducing awards and success rates for postdoc F32s and Diversity F31s. The NIH Physician-Scientist Workforce Working Group recommended increasing the relative proportion of individual vs. institutional awards and increasing K08/K23 salaries to $100,000, and research expenses to $50,000. If these steps are implemented, the number of awards will decrease by 40 percent; success rates will decrease from 30 percent to 17 percent. K99-R00 applications are increasing each year; success rates are down to 15%, which puts NICHD below NIH's target of 30 percent for a success rate.

The Task Force recommends giving priority to F32 and Diversity F31 fellowship applications, as opposed to F30 and Parent F31 applications, preserving K08/K23 success rates and awards by reducing K12 and K24 funding, and committing more funds to the K99-R00 program.

Council Discussion

Dr. Guttmacher thanked Dr. Twombly for the large amount of work that went into this effort. Dr. Guttmacher asked the Council to focus their discussion on issues that were not covered during Dr. Twombly's talk or if there is an objection to a particular recommendation.

Dr. George Saade said that he was part of the committee and agrees with all the recommendations. There was an additional issue that came to him after the Task Force met. Dr. Saade asked if there are mechanisms outside of the T and K mechanisms for training, particularly for clinical trials and clinical researchers; are there ways for clinicians to have a role in a clinical trial while being supported by training monies?

Dr. Rivara asked about reducing the duration of a K08 to 4 years instead of 5, thus saving money. Dr. Rivara also asked about cost sharing with the research institution; his impression is that there is less institutional commitment to K award winners, and thus K investigators have less support as they try to transition from K to R01.

Dr. Gilliam, who was also on the committee, asked about expanding the use of the K24 (or other mechanism) to try to bridge the gap from K23 to R01 to allow for career development support prior to obtaining the R01.

Dr. Stephen Petrill asked why pregnancy/perinatology, developmental biology, and intellectual and developmental disabilities are in the least funded category. Dr. Petrill asked if there was something the Council or the institute could do to increase opportunities in those fields.

Dr. Guttmacher stated that training issues would also be discussed in future Council meetings to determine next steps based on the information presented today.

IX. DRUG DISCOVERY & DEVELOPMENT IN NICHD POPULATIONS

Topic Overview

Dr. Christopher Austin presented an overview of Drug Discovery. To start, Dr. Austin displayed a graph showing the increase, over the last 30 years, of human conditions with known molecular basis. There are close to 5500, but only 500 have treatment options. Some of this is due to a time delay: target discovery to drug approval takes roughly 10 to15 years. Only three to four diseases move from untreatable to treatable per year. To change this, the approach should be the same as the Human Genome's strategy: use technology development to bend this curve.

NCATS is trying to increase the rate of drug development. Dr. Austin ran through the six steps of the drug development process: identify a target, create a testing system, or assay, test 100,000+ chemicals for activity on the target, and make modifications to active chemicals to ensure suitability for human use, test in animals for safety and effectiveness, and test in humans for safety and effectiveness. This process takes about 15 years and costs between $1 billion to $10 billion, with the cost driven by a 95-99% failure rate.

Dr. Austin brought up Eroom's Law (literally Moore's Law, backwards), which explains that the number of new drugs approved by the FDA, per billion US dollars (inflation adjusted) spent on research and development, has halved roughly every 9 years since 1950. This is a consistent

decrease in productivity when it comes to drug development over the last 60 years. Unless something changes, by 2050, the cost of a new drug will approach infinity, making discovery impossible. This is explained in a paper by Paul et al. (2010).

Dr. Austin stated that it is important to understand what the underlying principles are so that drug discovery goes from an empirical, phenomenological exercise into a predictive science. This is at the heart of what NCATS is trying to do by focusing on translational science, the field of investigation focused on understanding the scientific and operational principles underlying each step of the translation process. NCATS studies translation as a scientific and organizational problem.

Dr. Austin reviewed the NCATS mission, which is to be a catalyst for development and discovery. Each project is a case for using a technology in a new way, or for finding new technologies or processes. There are several pipelines through which companies or other investigators can interact with NCATS. Each project is set up to fill an unmet need, but also to provide insight into how the process can be improved.

Dr. Austin presented example collaboration with Dr. Kent Lai, an investigator at the University of Utah. This work focused on developing drugs for Galactosemia, a rare autosomal disease which has a mortality rate of 75 percent if untreated. They formed a joint project team, screened several thousand compounds (looking for a GALK inhibitor), and performed analytic chemistry to get the right molecule. This was something NCATS couldn't have done alone without Dr. Lai's subject matter expertise, nor would Dr. Lai have been able to accomplish it on his own.

Dr. Austin stated that NCATS is also focusing on patient-driven science. Each project was started because patients, or parents, came to NCATS and asked for research to begin because the disease populations were so small that no researchers had looked into the particular disorder.

NCATS also looks at ways to repurpose drugs that are already FDA approved. By repurposing, it is possible to cut off much of the discovery time, cost, and risk; drugs can be brought to clinical trial in just a year or two. The repurposing program looks to develop a repeatable process for finding targets for existing drugs instead of relying on the occasional medical observation driven discovery. NCATS has created a physical and electronic database of all the FDA approved compounds.

Dr. Austin said that NCATS is using a collaborative model with NCATS providing the drug development expertise and the Therapeutics for Rare and Neglected Diseases program, which has the disorder-specific knowledge. The collaboration is open to academics, non-profits, government labs, small businesses, and large pharmaceutical companies. Within this portfolio, the vast majority are developmental disorders and span a wide range of conditions. Dr. Austin gave the example of Niemann Pick Type C collaboration, which selected 2-hydroxpropyl-β-cyclodextrin as a pre-clinical candidate in February 2011, and is starting Phase II trials in October 2015. This has been so successful that a new company (Vtess) formed in Gaithersburg, Maryland to complete the clinical trials for this compound.

Dr. Austin also discussed the NCATS goal of developing an in vitro platform that uses human tissue to evaluate efficacy, safety, and toxicity of promising therapies (a vast improvement on mouse models, which don't translate well to human tissues). There are a number of steps from

having cells to getting functional organ-like tissues on a chip. Investigators at Harvard have engineered thin films of cardiac muscle tissue that, when exposed to mechanical stretch during growth, actually differentiates and responds to drugs in the way that attacked organs do. This model system is being used to study Barth Syndrome, using IPS derived Barth-cells and comparing them with tissues derived from normal cardiac tissue. Dr. Theresa Woodruff, an NICHD-funded investigator, also created a continuously cycling female reproductive system in vitro.

NICHD Investments in Drug Discovery

Dr. Anne Zajicek presented on the topic of NICHD investments in drug discovery. Dr. Zajicek briefly reviewed the history of NICHD, which began in 1962. One salient point is that in the past, it was thought that including children in clinical trials in children was unethical, now it is unethical to *not* enroll children.

This is not true of obstetrics, however; several drugs developed in the early 20th century are still a standard part of the obstetric formulary. The drug development pipeline for obstetrics is deficient. Cardiovascular disease, a mainstream medical condition, has 660 drugs in the pipeline. ALS, a neglected disease, has 34. Obstetrics has 17.

Dr. Zajicek stated that NICHD is developing drugs to fill unmet medical needs, and obstetrics is a key issue. The lack of research is driven by pharma's perception that there is high risk and little financial incentive for developing pediatric and obstetric drugs. Drug development initiatives span a number of NICHD branches.

Dr. Zajicek also reviewed the steps in the drug development process and touched on what a lengthy and expensive process it is. She also stated that NIH's role is not one of a drug manufacturer, rather it is to bring projects to the point where it has been de-risked enough that a pharma company is willing to move forward. So NIH has created several Cooperative Research and Development Agreements, which are partnerships between NIH and a pharmaceutical company to produce a commercially available product.

Dr. Zajicek discussed the drug development efforts of the Obstetric and Pediatric Pharmacology and Therapeutics Branch, which span grants in basic pharmacology, development of drug targets; pre-clinical models of drug response; pharmacogenomics; small clinical trials; pharmacoepidemiology; and formulations development.

Dr. Zajicek also mentioned the legislative efforts aimed at fixing the dearth of pediatric labeling of drugs. The 1997 FDA Modernization Act allowed a drug manufacturer to have an additional six months on a patent in exchange for performing pediatric studies. The 2002 Best Pharmaceuticals for Children Act gave six months of marketing exclusivity and included a role for NIH to perform research on drugs that were off patent. The 2003 Pediatric Research Equity Act required a pediatric trial for new drugs, but the indication needed to be the same for children as in adults.

The Best Pharmaceuticals for Children Act allowed NIH to prioritize drugs and therapeutic areas, sponsor pediatric clinical trials, and to submit clinical trial data to the FDA for consideration of label change. This was generally for drugs that were off patent. NIH prioritized trials by looking for therapeutic gaps, examining potential health benefits of the proposed

research, determining the adequacy of the infrastructure necessary to perform the research, and consulting with experts in pediatric practice and research. From this analysis an annual list of therapeutic areas and specific needs is published.

Dr. Zajicek stated that, as a result of examining infrastructure needs, it was decided to build a permanent network that could support multiple efforts. This is the Pediatric Trials Network, which has sites across the country.

Dr. Zajicek mentioned some of the successes of the drug development efforts, including: Pralidoxime, Propylthiouracil, Mercy TAPE Device to estimate body weight from measurement of the upper arm, Sodium Nitroprusside, Meropenem. Docket numbers have been assigned for two new trials for lorazepam for status epilepticus and ampicillin.

The data from these efforts are publically available, and many are in the N-DASH repository. The data in N-DASH is in SAS transport files, making it easily repurposed, unlike data hosted elsewhere, which is in pdf files.

Dr. Zajicek stated that the following drugs are likely to have labeling in 2016-17: Lisinopril, Lithium, Hydroxyurea (NHLBI Baby HUG), Diazepam, Vincristine, Actinomycin-D, Isotretinoin (neuroblastoma), Fluconazole, and Acyclovir.

Dr. Zajicek discussed a few cases/questions that illustrate how NICHD has worked through issues related to performing clinical trials in pediatric populations.

Dr. Zajicek summarized by saying there is a huge problem with a lack of formulations for pediatric research. For instance, there wasn't a formulation of intranasal oxytocin that could be given to children in a trial of intellectual disabilities. Other instances included a problem with formulation for a betamethasone trial and formulation problems with hydroxyurea.

Dr. Zajicek mentioned that metrics of success for these research efforts might include the number of publications, new practice guidelines, new drug labels, a wider range of validated pediatric and obstetric outcome measures in various therapeutic areas, or more studies successfully completed, with full recruitment and statistical power, and auditable and replicable data.

Dr. Zajicek stated that there are several outstanding issues. Some examples include a disconnect between basic and clinical pharmacology, a need for clinically relevant outcome measures, need for investigator understanding and implementation of good clinical practice, good laboratory practice and good manufacturing practice, a need for new clinical trial designs for small populations, incorporating validated database/electronic health records data, and a need for formulations.

Council Discussion

Dr. Gilliam asked how NCATS used the various funding mechanisms available to achieve NCATS' mission. Dr. Austin replied that most of the work actually goes on in the intramural environment. This allows for greater flexibility and change in response to changing needs.

Dr. Muneoka asked where cell-based therapies fit in. Dr. Austin replied that there is a group within NCATS that is focused on stem cell technologies, and translating therapies to the clinic.

Dr. Saade asked about how clinical trials might be accelerated in addition to the pre-clinical work being done at NCATS. Dr. Austin replied that most of NCATS' work is actually in the clinical end of the development spectrum. They are working to develop processes for testing drugs across the human lifespan.

X. NICHD VISION UPDATE

Dr. Caroline Signore gave an update on the NICHD vision. The visioning process began in 2011 with workshops. In 2012 NICHD published its Vision Statement for the next 10 years. Staff has been working on implementing it since 2013. The purpose of the Vision Statement was to identify the most promising scientific opportunities of the next 10 years across NICHD's mission. There were eight Scientific Vision Themes:

- Developmental Biology
- Developmental Origins of Health and Disease
- Pregnancy and Pregnancy Outcomes
- Reproduction
- Behavior and Cognition
- Plasticity and Rehabilitation
- Population Dynamics
- Conduct of Science

The Vision was not intended to be a prescription for NICHD activities, but an analysis of promising opportunities that will help inform future directions. The Vision statement is organized by chapters, corresponding to the eight themes. Each chapter concludes with opportunities that should happen in that area in the next 10 years, for a total of 23 opportunities.

Dr. Signore then discussed how NICHD is implementing the Vision in select emphasis areas, which are essential areas to NICHD, of great public health importance, have scientific opportunity and are critical for NICHD to undertake because others might not. Vision Emphasis areas for FY 2014-15 included developing new methods for intrauterine assessment of placental and fetal function; contraception research; and understanding long-term implications of assisted reproductive technologies (ART). Significant action has been taken for each of these emphasis areas.

In the area to develop new methods for intrauterine assessment of placental and fetal function, NICHD has awarded three RFAs totaling $46 million to support the Human Placenta Project. Also a SBIR grant was awarded to develop an algorithm to predict placental dysfunction and pregnancy complications from placental morphology measurements obtained via 3D ultrasound early in pregnancy.

Within Contraception Research, NICHD undertook a Review of Contraceptive Research and is now working to improve communication, scientific review, behavioral research, and funding mechanisms. At the NIH-Bill and Melinda Gates Foundation meeting a contraceptive research breakout session was held to explore opportunities for collaboration. Also, male contraceptive

research is moving forward with an upcoming multisite efficacy trial involving the male Contraceptive Clinical Trials Network's testing of nestorone/testosterone gel as a novel user-controlled male hormonal contraceptive and using novel androgen in repeat-dose studies as a possible "male pill".

In the third area, to understand long-term implications of ART an RFA for long-term outcomes of medically assisted reproduction was issued.

Dr. Signore then discussed the select pay, which was another way NICHD is trying to implement the Vision. A small, but meaningful amount of money is set aside for research grants in priority areas that just miss the payline. In 2014, two grants were funded. In 2015, four grant applications were nominated, but fiscal constraints prevented any awards from being made.

Dr. Signore gave some selected updates to the Vision and the 23 opportunities, showing how staff was moving the Vision forward in those areas.

Dr. Signore gave two examples of opportunities that have helped to achieve part of the Developmental Biology Theme. Two papers from NICHD-funded researchers were published to begin to address a comprehensive guide to molecular pathways and genomic/epigenetic regulation of developmental defects. Also within this theme, NICHD established the Stem Cell Interest Group to develop reproducible protocols for generating a variety of cell types from induced pluripotent stem cells, which fell under another opportunity to construct a library of pluripotent cells.

Under the Reproduction Theme, the Common Fund is sponsoring a Single Cell Analysis Program. This will help to characterize both female and male single germline cells.

For the Plasticity and Rehabilitation Theme, NICHD is part of the greater community working on the Robotics Initiative with NSF, NIH, USDA, NASA, and DoD to develop a range of robotics to enhance daily function of people with disabilities in their home settings and is involved in other activities to develop assistive robotic technology to achieve functional independence in humans; improve quality of life; assist with behavioral therapy and personalized care; and promote wellness/health.

Under the Conduct of Science theme, NICHD launched N-DASH to develop biorepositories and change the predominant model for data use to one of open access. Under this same theme, NICHD developed PregSource™ to involve the public in better reporting, identification, and definition of normal life processes.

In addition to these areas, Dr. Signore mentioned several areas under continuing development: identifying causes of stillbirth and preterm birth; determining risk and impact of concussion injuries; identifying bases and biologic markers of behavioral disorders; identifying causes of autism spectrum disorders; genetic and epigenetic interactions and gynecological disorders; male and non-hormonal contraception; and health care and independent living options for persons with disabilities.

Dr. Signore then asked the Council for their input on what new opportunities there might be, or any additional areas of emphasis for the Vision.

Council Discussion

One Council member asked what portion of the NICHD budget has been redirected to central issues in the Vision, other than the placental initiatives; and whether there been changes to funding or mechanisms to support these high priority areas. Dr. Signore replied that NICHD has always tried to support investigator-specific research first and not take money away from that to support Vision activates. Currently that's about 75 percent of NICHD's funding; less than one percent is going toward the Vision areas of emphasis. Dr. Guttmacher asked if there was a specific number that he thought it should be. The Council member suggested that funding should be proportional to the time and effort that went into the Vision development process and that Council could help by offering creative ways to use the Vision priorities to fund investigator-initiated research. The priorities are not only important, but were identified as being relatively neglected.

Dr. Spong noted that the Vision itself was for the entire community and is incredibly broad. Many topics were advanced because the field saw them as important and therefore addressed them despite a lack of specific funding. The areas presented were topics that were not being advanced. It may be possible to generate interest in priority areas without spending lots of money, perhaps by hosting conferences and generating interest in and understanding of the area. Dr. Guttmacher stated that NICHD is trying to further research efforts. Part of that is by using the institute's money. The other way is by using its influence to start or change the conversation, and raise issues that are being neglected. NICHD can certainly ask whether the percentage of investigator-initiated funding needs to be higher or lower.

Dr. Signore further explained that doing a before and after comparison would be challenging. It would be difficult to look at spending for the three emphasis areas in 2011 before the Vision process began and then compare with 2014 data, because funding was not tagged with codes for those particular areas.

Another Council member noted that while the concept of pregnancy was covered, this topic is very general. Additional considerations might include the management of women with specific conditions (preeclampsia, optimizing outcome if a baby is being born prematurely, management of labor or caesarian section), and including comparative effectiveness trials, to name a few.

And one other Council member recommended that NICHD should find ways to re-shape the field without reducing the spending level for investigator-initiated projects. Perhaps this could be done by setting up funding for high priority areas and letting investigators respond to funding collaborations that are based on Vision priorities. The member asked if there is a Visionary game plan that integrates NICHD's leadership potential beyond merely shifting funding. Dr. Guttmacher replied that there is no formal plan, but NICHD takes this into account when deploying resources, including staff effort. For example, enormous effort was expended to develop the scientific thinking behind the Human Placenta Project with the hope that this would then drive interest and attention—and it has. Dr. Spong further stated that there has been great interest by program staff to think differently about how NICHD funds research, and additional information about funding strategies will be presented at the next Council meeting.

XI. CONCEPT CLEARANCE REVIEW AND DISCUSSION

The Council heard short summaries of six concepts and unanimously endorsed each of them.

Dr. Katerina Tsliou of the Obstetric and Pediatric Pharmacology Branch presented the concept, Use of 3D Printing for Creation of Implantable Devices, which seeks to elicit solicitations for long-term implanted or bio-degradable devices. This concept would also support long-term follow up of children with these devices.

Dr. Marion Koso-Thomas of the Pregnancy and Perinatalogy Brach presented a request for the Recompetition of the Global Network for Women's and Children's Health Research Data Coordination Center.

Dr. David Weinberg of the Human Placenta Project presented the concept Assessing the Human Placental Structure and Function Using Existing Data Sets. Data generated from NICHD funded studies, not initially focused on the placenta, may have collected data that may shed light on the placenta's structure and function. The goal is to support a data mining effort that uses existing samples and data sets.

Dr. Brett Miller of the Child Development and Behavior Branch presented a request to renew funding for the Learning Disabilities Research Centers. The Centers supporting transdisciplinary research into reading, writing, and mathematics.

Dr. Alice Kau of the Intellectual and Developmental Disabilities Branch presented a concept for the Autism Centers of Excellence to fund Centers and Networks. Applicants will be encouraged to focus on adults with disabilities and interventions for comorbid conditions.

Dr. Melissa Parisi, Chief of the Intellectual and Developmental Disabilities Branch, presented a concept to fund applications for NICHD Genomic Clinical Variant Expert Curation Panels using a U24 cooperative agreement mechanism related to resource related research projects. NICHD has developed a Clinical Genomics Infrastructure, which will curate, collate, and classify genomic variants.

XII. CLOSING REMARKS

Dr. Spong thanked Dr. Guttmacher for all of the work he has done at NICHD and NIH in general. She highlighted his skills as a broad thinker, a careful planner, an excellent leader, and his incredible mentoring skills. Dr. Spong also mentioned his belief in the concept of a lifecourse as a viable scientific concept and his efforts to integrate that thinking into NICHD, as well as integrating it into his own life. Dr. Spong stated that the past year has been the most professionally rewarding in her capacity as Deputy Director.

Dr. Spong stated that she and Dr. Guttmacher worked closely as a team, and what has been started will continue. Projects will not stop mid-stream.

Dr. Guttmacher made some parting remarks, highlighting the thought that science and health are advanced when NICHD staff don't lobby for particular interests, but seek to advance the common good. Two major scientific initiatives highlight this: The Human Placenta Project and PregSource™. They are both initiatives focused on obstetrics, even though Dr. Guttmacher is a

pediatrician. He gave several other examples where the institute has advanced initiatives that have nothing do with pediatrics, even though this was his specialty. When thinking about who will be the next director, the specialty isn't that important. The director will need to address what is in the best interest of all rather than their particular specialty.

Dr. Guttmacher stated that while NICHD has a wonderful mission, the mission statement is still lacking. This is something he tried to do better, but will have to leave to his successors. He closed by thanking the Council and staff.

XIII. ADJOURNMENT

There being no further business, the meeting adjourned at 3:06 p.m. on Friday, September 18, 2015. The next meeting is scheduled for January 21, 2016.

Attachment: Council Roster Attachment I

I hereby certify that, to the best of my knowledge, the foregoing minutes and attachments are accurate and complete.[2]

/S/

Catherine Y. Spong 1/12/16
Catherine Y. Spong, M.D. Date
Chair, National Advisory Child Health and
Human Development Council
Acting Director, *Eunice Kennedy Shriver*
National Institute of Child Health and
Human Development

[2]These minutes will be formally considered by the Council at its next meeting, and any corrections or notations will be incorporated in the minutes of that meeting.

Eugene Hayunga, Ph.D.
Acting Branch Chief, Office of Committee Management, NICHD

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NATIONAL ADVISORY CHILD HEALTH AND HUMAN DEVELOPMENT COUNCIL
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