Eunice Kennedy Shriver National Institute of Child Health and Human Development

NATIONAL ADVISORY CHILD HEALTH AND HUMAN DEVELOPMENT COUNCIL

MEETING MINUTES

January 23, 2020

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

January 23, 2020[1]

The National Advisory Child Health and Human Development (NACHHD) Council convened its 172nd meeting at 8:00 a.m., Thursday, January 23, 2020, in Building 6710B, Conference Room 1425 & 1417, of the National Institutes of Health (NIH) in Bethesda, Maryland. The meeting was open to the public from 8:00 a.m. to 11:55 a.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 was closed to the public from 1:00 p.m. until 4:00 p.m.

Diana W. Bianchi, M.D., Director, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), presided.

Council members present:
Diana W. Bianchi, M.D. (Chair)
Michael Boninger, M.D.
Susan Bookheimer, Ph.D.
Michele Caggana, Sc.D., FACMG
Catherine Gordon, M.D., M.Sc.
Carmen L. Neuberger, J.D.
Annette Sohn, M.D.
Clifford Tabin, Ph.D.
Alyce Thomas, RD
Alan Thevenet N. Tita, M.D., Ph.D., M.P.H.
Rebeca Wong, Ph.D.
Anthony J. Wynshaw-Boris, M.D., Ph.D.

Council members absent:
None

National Advisory Board on Medical Rehabilitation Research Council Liaison:
Kenneth Ottenbacher, Ph.D., OTR

***Ex officio* members present:**
Patricia Dorn, Ph.D.
Aaron M. Lopata, M.D, M.P.P.

Department of Defense
MAJ Barbara K. Bujak, Ph.D., PT, DPT

Observers (pending members) present:
John P. Coughlin, M.D.
Kathleen B. Egan, Ph.D.
Lucky Jain, M.D.
Missy D. Lavender, M.B.A.
Adam C. Resnick, Ph.D.

[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.

Acting Executive Secretary
Alison Cernich, Ph.D., Deputy Director, NICHD
Others present:
Constantine Stratakis, M.D., D.Sc., Director, Division of Intramural Research, NICHD
Caroline Signore, M.D., M.P.H., Deputy Director, Division of Extramural Research
Lisa Kaeser, J.D., Director, Office of Legislation and Public Policy
Members of Staff, NICHD
Members of Staff, NIH

Invited guest:
Juliane Baron, Executive Director, Federation of Associations in Behavioral & Brain Sciences

I. CALL TO ORDER AND INTRODUCTORY REMARKS

Dr. Bianchi began the meeting at 8:01 a.m. by recognizing the contributions of Stephen A. Foley, M.D., who has retired from the Council.

Dr. Cernich read the confidentiality instructions.

A. Review of Confidentiality and Conflict of Interest

Dr. Cernich reminded Council members that all members were required to read, agree to, and sign the confidentiality and nondisclosure rules for special government employees on the Council member website before evaluating any NIH grant applications. At the meeting, Council members also received a conflict-of-interest certification form, which they were required to sign before the closed session of the review of applications. Dr. Cernich also reminded Council members that they are required to recuse themselves and leave the room if there is a specific discussion involving any organizations or universities for which they are in conflict, in addition to those listed on the Council Action document. Council members are not allowed to serve on any NIH peer review panels while serving as Council members. It is NIH policy that individuals may not serve on both the first and second levels of peer review.

B. Council Minutes

Dr. Cernich moved to approve the September 2019 meeting minutes. The minutes were approved unanimously.

C. Future Meeting Dates

Dr. Cernich reviewed the future meeting dates:

June 11, 2020
September 10, 2020
February 3, 2021

II. NICHD DIRECTOR'S REPORT AND DISCUSSION

Dr. Bianchi delivered the Director's report.

Budget Update

NIH received $41.7 billion for fiscal year (FY) 2020, with NICHD receiving $1.5 billion. This represented a 3% increase for both NIH and NICHD. NICHD will also receive money from the

Office of the Director for projects such as the Helping to End Addiction Long-term (HEAL) Initiative and the INCLUDE (INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndromE) project.

The federal fiscal year begins on October 1. Preparation for the next annual budget begins shortly after the new fiscal year begins.

- By early winter, the NIH institutes and centers (ICs) prepare justification for their budgets to send to Congress.
- The President releases the executive budget in February.
- The House and Senate hold their appropriations hearings in March or April.
- In the late spring or early summer, Congress amends and votes on the final budget.
- By September 30, the budget should be passed by both the House and the Senate and signed by the President.

Although this is the budget schedule, NIH has received its final budget by September 30 only once in the past 22 years. When the budget is not signed by September 30, the government operates on a continuing resolution.

NICHD Strategic Plan Implementation

The strategic planning process had three goals:

- Identify scientific priorities.
- Identify potential partnerships and collaborations.
- Inform investments in research, training, and infrastructure.

NICHD is now working on implementing the strategic plan and determining how to make progress on each objective within the plan's themes and goals. Some of the plan's goals will be phased in depending on available resources and scientific opportunities. NICHD is developing metrics to measure progress. Examples of metrics could include increasing the number of new investigators in a field and increasing workforce diversity. To ensure transparency, Dr. Bianchi will provide regular progress reports to the Council.

Maternal Mortality

Every 12 hours, a woman in the United States dies of complications from childbirth. About 60% of these deaths are preventable. There are racial/ethnic and age disparities in maternal mortality: African American, American Indian, and Alaska Native women and women more than 35 years old have higher incidences of maternal mortality. About one-third of the deaths occur during pregnancy, another third during delivery or within one week of birth, and the remaining third up to one year after birth.

Interest in maternal health has increased among members of Congress. NIH Director Francis Collins, M.D., Ph.D.; National Institute on Minority Health and Health Disparities Director Eliseo J. Pérez-Stable, M.D.; National Heart, Lung, and Blood Institute Director Gary H. Gibbons, M.D.; and Dr. Bianchi were among those who attended a meeting of the Black Maternal Health Caucus on Capitol Hill on December 11.

The causes of maternal death vary depending on when the death occurs. For example, hemorrhage and amniotic fluid embolism are more common on the day of delivery. Infections

are more common between 7 and 42 days postpartum, while cardiomyopathy is a concern 43–365 days postpartum. Dr. Collins has established a trans-NIH task force to address the causes of pregnancy-related deaths.

Consistent with its mission and strategic plan, NICHD allocates the most funding of all the ICs for maternal health—$25.7 million in FY 2018. The Secretary of Health and Human Services (HHS) is coordinating the Centers for Disease Control and Prevention (CDC), the Health Resources and Services Administration (HRSA), the Agency for Healthcare Research and Quality (AHRQ), the Food and Drug Administration, the Indian Health Service, and NIH to develop an action plan for research. The Surgeon General is developing an action plan for communities. The Patient-Centered Outcomes Research Institute (PCORI) will hold a workshop in March. NICHD is working with the NIH Office of Research on Women's Health on a comorbidities workshop to take place May 19–20, 2020.

Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC)

The task force, authorized by the 21st Century Cures Act, submitted its report and 15 recommendations in September 2018. Key recommendations included the following:

- Change the culture that has limited scientific knowledge of therapeutic product safety, effectiveness, and dosing for pregnant and lactating women.
- Protect pregnant women through research, not from research.
- Remove pregnant women's designation as a vulnerable population in the Common Rule.
- Expand the number of clinicians and researchers with expertise in obstetric and lactation pharmacology and therapeutics.
- Remove regulatory barriers to research.

NICHD has established four working groups, covering research and training, drug discovery, communications, and regulatory issues, to address the recommendations. The working groups will report their progress toward an implementation plan at the February 3 PRGLAC meeting. The implementation plan will include costs and timelines, the agencies and stakeholders to be involved, what new or existing programs are needed, and how to evaluate implementation of the recommendations.

Earlier in January, Dr. Bianchi met with the co-leaders of ConcePTION, a European Union public–private partnership involving 88 organizations that is creating evidence-based information on medications taken during pregnancy and breastfeeding. The 5-year initiative will:

- Use de-identified data from health resources.
- Develop procedures and tools to collect digital data and samples from pregnant women.
- Create the first Europe-wide human milk biobank for research.
- Develop tools to predict which drugs are likely to be transferred to human milk.

Joint Meeting with the Bill & Melinda Gates Foundation

Dr. Bianchi attended the annual joint consultative meeting on global health with the Gates Foundation on December 20. The discussions encompassed topics that fall within NICHD's Global Network for Women's and Children's Health Research. The meeting included working groups on maternal, neonatal, and child health; nutrition and growth; neurodevelopment; and contraception. The goal is to develop milestone-driven collaborations between NIH and the foundation.

Maternal and neonatal infections are a major cause of death in mothers and infants. The Global Network is discussing a partnership with the Gates Foundation and the Foundation for the National Institutes of Health (FNIH) to expand the Azithromycin-Prevention in Labor Use Study (A-PLUS) to enroll 34,000 women at eight research sites in sub-Saharan Africa, South Asia, and Latin America. The study will assess whether a prophylactic oral dose of azithromycin given during labor will reduce maternal death or sepsis within 6 weeks of delivery and neonatal death or sepsis within the first 28 days of life.

Staff Updates

- AAAS Science & Technology Policy Fellow Niteace Whittington, Ph.D., is working in the NICHD Office of Science Policy, Reporting, and Program Analysis.
- Science Director Dr. Stratakis will leave NICHD in June to become the executive director and chief scientific officer of the Research Institute of the McGill University Health Centre (MUHC) and director of research for the MUHC system.

The following leadership positions, in addition to the position of Scientific Director, are open:

- Director, National Center for Medical Rehabilitation Research. The search is underway, and an appointment recommendation is expected to be sent to Dr. Collins by April.
- Director, Division of Intramural Population Health Research. A search committee is being formed. The position will be advertised for 60 days, likely beginning in February. Interviews are expected to take place in early spring.

Action Item: Council members should encourage qualified individuals to apply for the vacant positions.

Council Discussion

Dr. Tita asked about NICHD's plan for maternal health. Dr. Bianchi estimated that the trans-NIH research plan to address maternal mortality and severe maternal morbidity will be completed by end of March, likely too late for a funding opportunity announcement (FOA) to be issued this fiscal year. NICHD has not received additional funds for maternal health, so the funding would have to come from another part of the budget. In the spring, the HHS Secretary will release a maternal health plan that will include research.

Dr. Sohn asked whether NICHD would partner with the Gates Medical Research Institute (MRI), which has an interest in maternal and child health. Dr. Bianchi said that NICHD has not yet discussed that possibility with the Gates MRI, but NICHD will work with the Gates Foundation on issues related to human milk.

Ms. Thomas asked whether the priority is to reduce preventable maternal deaths. Dr. Bianchi said that that is the goal. NICHD will talk to officials in states such as California that have reduced maternal mortality and in Georgia, which has had success with telehealth. The institute also plans to look at states that have poorer maternal health outcomes to understand the causes. Studies will focus on biobehavioral outcomes, healthcare, biomarkers, and more.

Action Item: Council members should send suggestions for where to focus to reduce the number of preventable maternal deaths. The plan is being drawn up now, so Council members should do so soon.

Dr. Jain asked whether maternal health is in the strategic plan and whether some of the maternal health initiatives could be fast-tracked. Dr. Bianchi said that NICHD has had a longstanding interest in maternal health and mortality and is a leader in the field. Maternal health and mortality are embedded in the plan's healthy pregnancy section.

III. INTRODUCTION OF NEW MEMBERS

Dr. Cernich invited the new members to introduce themselves.

Dr. Resnick is the director of the Center for Data-Driven Discovery in Biomedicine at Children's Hospital of Philadelphia. His interests involve pediatric cancers and the developmental context of pediatric disease.

Ms. Lavender is the chief executive officer and founder of Renalis, a foundation to help women with pelvic health conditions. Her work focuses on fibroids and endometriosis.

Dr. Jain is the George W. Brumley, Jr. professor and chair in the Department of Pediatrics and the Division of Neonatology at Emory University. He is a neonatologist whose work focuses on fetal lung transition after birth.

Dr. Bujak is a U.S. Army major and a physical therapist with the Clinical and Rehabilitative Medicine Research Program with the U.S. Army Medical Research and Development Command at Fort Detrick. Her Ph.D. is in health promotion education and behavior.

Dr. Coughlin is a pediatric surgeon at Johns Hopkins All Children's Outpatient Care Center in Tampa, Florida.

Dr. Egan has an adult son, David, who has Down syndrome. She has been a longtime advocate for the inclusion of people with disabilities.

Following the introductions, Dr. Bianchi noted that Dr. Egan's son, David, has contributed to the Down syndrome field by taking part in numerous research studies and by being an advocate for himself and others. She presented a certificate of appreciation to Dr. Egan to give to Mr. Egan. Dr. Bianchi thanked the entire Egan family for their work in support of research related to Down syndrome.

IV. DIVISION OF EXTRAMURAL RESEARCH (DER) REPORT

Dr. Signore presented the DER report.

Trends in Extramural Funding

Dr. Signore presented data for competing Research Project Grant (RPG) funding, which showed a decrease in success rates from approx. 15% in FY 2010 to 11.5% in FY 2015. Among the steps NICHD took to improve the success rate were funding more clinical trials through FOAs, developing stricter methods for accepting large grants, and more clearly communicating research priorities. Grant funding has grown in the last several years, as has the competing RPG application success rate, which was 19.5% for FY 2019.

DER also enhanced clinical trial oversight. As of 2018, NICHD has required an assessment of every clinical trial's level of risk, using criteria such as the trial's complexity and cost, the

feasibility of recruitment and retention, and the prior experience of the principal investigator. Of the 130 clinical trials that NICHD supported, program staff deemed 94 to be low risk, 29 to be medium risk, and 7 to be high risk.

Staff Updates

- Rita Anand, Ph.D., has retired from the Scientific Review Branch. Her accomplishments included establishing the study section that covered the gamut of pediatrics, including neonatology, adolescence, and critical care.
- Kathryn Adams moved from the Department of the Army to join DER as a health science policy analyst. She will assist with clinical trials and clinical research.
- Alberta Boah is a new grants management specialist in the Grants Management Branch. She previously worked at the National Center for Advancing Translational Science (NCATS).
- Valerie Cotton has joined the Developmental Biology and Structural Variation Branch as the program manager for the Gabriella Miller Kids First Pediatric Research Program.
- Derek McLean, Ph.D., of the Scientific Review Branch will chair the Reproduction, Andrology, and Gynecology Committee.
- Lisa Neal has been appointed chief of the Office of Committee Management.

NICHD is also searching for a person to fill the position of senior policy advisor for clinical research, and two branches have openings for branch chief. Five different scientific branches are seeking candidates to serve as program officials.

Council Discussion

Dr. Tita asked what proportion of the budget goes to DER. Dr. Signore said that 80% of the NICHD budget goes to extramural programs; the remaining 20% goes to staffing and the intramural program. She noted that the information she presented included only competing research project grants.

Alexis Clark, M.P.P., said that the data shown to the attendees did not include the noncompeting grants, which total about $550 million. Those grants are the largest part of the extramural budget. Competing grants total about $200 million. Mechanisms such as P50s, U54s, and training grants are not research project grants and were not included in Dr. Signore's presentation.

Dr. Caggana asked whether the number of grant applications has changed. Dr. Signore said that the number of applications had increased over time in the past, a factor in the declining success rate. It was pointed out that in more recent years, our efforts to control the number of incoming applications had been successful in reducing the number of applications coming in.

V. NICHD VISION FOR MULTISITE CLINICAL TRIAL INFRASTRUCTURE

Dr. Cernich said that NICHD has four guiding principles for support of clinical trials:

- Enhance rigor and reproducibility.
- Promote infrastructure to support a wider range of investigators.
- Facilitate data sharing.
- Facilitate the involvement of diverse populations in multisite clinical trials.

NICHD developed these principles in line with Goal 6 of the strategic plan: to improve oversight and management of clinical trials. Adhering to these principles ensures good stewardship of public funds, increases accountability, and helps NICHD maintain the public trust.

NICHD is laying out a new vision for multisite clinical trial infrastructure but is committed to supporting and completing all active protocols as they were designed. Possible models of clinical trial infrastructure include the following:

- A centralized approach in which NICHD supports the infrastructure; any qualified investigator can use it.
- A consortia approach in which investigators self-select to form a clinical trial consortium with its own infrastructure that includes clinical sites and a data coordinating center.

The power of cloud computing must be harnessed. The cloud allows data computation at an unprecedented scale, storage of large and diverse data, easier access and reuse, and easier sharing with other researchers.

NICHD is conferring with other ICs that have more experience with cloud computing. One approach is to use existing resources, such as the NIH Science and Technology Research Infrastructure for Discovery, Experimentation, and Sustainability (STRIDES) Initiative, which offers discounts on computing, storage, and cloud-related services. NICHD is also working with the NIH Associate Director for Data Science on how to connect datasets in the cloud and find new ways to pilot discovery.

Request for Information (RFI) on the NICHD Vision for Multisite Clinical Trials Infrastructure

Dr. Bianchi said that the RFI solicited comments on NICHD's vision for supporting multisite clinical trial infrastructure. NICHD held a webinar in November to provide information on the institute's rationale and guiding principles as well as to put forward the two models—centralized and consortia—as examples of a possible infrastructure.

NICHD received 79 responses to the RFI. Responses came from institutions of higher education and affiliated hospitals, nonprofit organizations, professional societies, and data coordinating centers. The 16 individuals who responded included principal investigators, academicians, patients, and patient advocates. One entity coordinated several of the pelvic floor disease responses.

The responses supported having an infrastructure for clinical trials, with preferences for:

- Multiple models of clinical trial infrastructure.
- Multiple clinical trial sites to account for diverse and rare disease populations.
- Core sites with a specialty and well-trained staff.
- An environment that provides research training.
- Diversity of research organizations that can have access to the infrastructure.
- Mentoring for young investigators.

The RFI responses expressed a general preference for the central resource, but there were also recommendations for a hybrid model that combines aspects of the centralized and consortia models. Respondents who supported the centralized model said that centralization makes standardization across trials easier and allows for economies of scale. However, a data

coordinating center may have difficulty managing numerous sites, and there are special considerations for global health research. Another suggestion was to invest in developing common data elements.

Dr. Bianchi also made the following points:

- NICHD's support for clinical trials requires a modern infrastructure that allows for data storage, sharing, analysis, and reuse. The institute has made a start with the Data and Specimen Hub (DASH), which has been well-received by researchers.
- NICHD will do a landscape analysis of the best clinical practices across NIH, including looking at resources such as StrokeNet and the National Clinical Trials Network.
- NICHD will also consider creating a dedicated clinical trials study section to enhance external peer review.

Council Discussion

Dr. Wong said that the *All of Us* Research Program has many of the same goals that this multisite clinical trial infrastructure does. She asked whether there is a connection between this proposal and the Research Program. Dr. Cernich said that the Research Program is developing a longitudinal data platform, not a clinical trials platform. However, the program is adopting things that NICHD can adopt, such as SNOMED Clinical Terms. Dr. Bianchi also noted that the Research Program is not yet enrolling children, who are among NICHD's principal constituencies. The program has enrolled 5,000 pregnant participants but has minimal data on them.

Dr. Dorn asked whether NICHD has consulted with the Department of Veterans Affairs Cooperative Studies Program (CSP), which conducts large clinical trials across multiple sites. Dr. Cernich said that the NIH equivalent of the CSP is the NCATS Clinical and Translational Science Awards (CTSA) Program. NICHD can sometimes use the CTSA model, but it does not work well for many NICHD trials, such as those involving neonates or pregnant women. Dr. Bianchi said that NICHD's populations include women, children, and people with disabilities, so the system must include those populations.

Dr. Tita asked how much of NICHD's funding is directed to the networks. Dr. Signore said that the networks are among NICHD's top-funded programs. Dr. Bianchi estimated that the networks receive around $50 million annually.

Dr. Tita said that he approves of the proposal to take a more centralized approach to the clinical trials. That approach would not preclude investigator-initiated projects. The networks can train young investigators and assist established investigators.

Dr. Tita asked how many sites the networks will encompass. Dr. Bianchi said that the NICHD staff are still in the planning stage, but one idea is to have seasoned network investigators work with less experienced investigators, particularly those who are under resourced or where the opioid crisis has hit. NICHD already has a partnership with the Institutional Development Award (IDeA) states.

Dr. Jain asked whether NICHD is funding an adequate number of clinical trials and what the maximum number of trials that NICHD could fund is. Dr. Bianchi said that NICHD is gathering data on the total number of trials it is funding. There are new opportunities because of advances in technology; for example, healthcare is already incorporating findings from machine learning.

Dr. Tita asked whether there will be some version of each of the existing networks when NICHD rolls out its new plan. Dr. Bianchi said that no decision has been made, but NICHD will continue to need expertise related to NICHD's populations, such as expertise on pediatrics and obstetrics.

Dr. Tita said that many of the centers invest their own money in the work—a factor that should be recognized. Dr. Bianchi said that the existing network sites are contributing funding. The budget is getting slightly larger, but there are many projects to fund. One strategy is to partner more with outside organizations, such as industry groups and the Gates Foundation.

VI. FOOD FOR THOUGHT: RESEARCH ON OPTIMAL NUTRITION FOR PRETERM INFANTS

Mandy Brown Belfort, M.D., M.P.H., presented her research on maternal milk diets as an effective clinical intervention in the neonatal intensive care unit (NICU).

With medical advances, even the smallest preterm babies are now surviving. But some preterm babies face chronic health challenges, leading to efforts to place greater emphasis on improving outcomes. During the 1980s and 1990s, there was more literature published on the critical role of nutrition—both macronutrients and micronutrients—on fetal brain development. Many key developmental processes occur between 24 weeks' gestation and full-term birth.

Through magnetic resonance imaging, Dr. Belfort showed how much the fetal brain develops between 28 weeks' and 38 weeks' gestation. During this time, the fetal brain triples in size and goes from a smooth structure to one with nearly fully developed gyri and sulci. A baby born within this window is undergoing the same development as the fetus that is safely in the mother's womb, but without nutrition from the placenta and under more stressful conditions.

During Dr. Belfort's neonatal fellowship, the emphasis in the NICU was largely on brain injury and hemorrhage as the cause of adverse neurodevelopmental outcomes. She wondered what role nutrition plays, but there was little literature on the topic. Dr. Belfort reasoned that the timing of receiving specific nutrients would be important for reducing adverse neurodevelopmental outcomes.

Dr. Belfort's 2011 study found that weight gain during the baby's first week in the NICU produced better neurodevelopmental outcomes as measured by the Bayley Mental Developmental Index (MDI) at 18 to 22 months. Weight gain after the first week produced a lower score on the MDI.

Weight gain and growth are important to better outcomes, but half of the preterm babies discharged from the NICU are below the 10th percentile in weight; one-quarter are below the third percentile.

Human milk contains the right amount of proteins, calories, minerals, and non-nutrient bioactive molecules, such as growth factors, for the full-term baby. Most babies in the NICU are fed intravenously with a combination of commercially available formulas and fortifiers, maternal breast milk, and pasteurized donor human milk. The nutrient guidelines are based on what the reference fetus would need at each week of gestation. What is optimal for the fetus may not be optimal for a preterm baby who is under stress and whose intestines are immature.

A study published in 2012 showed that preterm infants who were fed fortified maternal milk gained less weight and had a smaller head circumference than those who were fed preterm

formula. The question was why deficits accumulate more for those babies who got maternal milk.

Dr. Belfort analyzed the content of 1,600 milk samples from mothers whose infants were in the NICU. The results showed wide variations in protein, carbohydrate, and fat content. Dr. Belfort found that the more protein a baby ingested, the more they grew; the more fat a baby ingested, the more weight the baby gained. She also noted that infants being fed intravenously cannot signal when they are hungry, when they are full, and whether they need to feed more frequently or for longer because of a growth spurt.

Dr. Belfort has just begun recruiting preterm infants for the NOURISH Study, which will use a point-of-care human milk macronutrient analyzer to test the mother's milk and fortify the milk as needed. The babies' weight, length, and head circumference will be tracked and compared with a control group. The study will also use magnetic resonance imaging to evaluate the impact of protein and energy content on brain development.

The NICU presents an opportunity to optimize nutrition and development during this critical period of brain growth by feeding preterm babies what they need when they need it. If the intervention works, it will be a way to provide preterm infants a human milk diet that meets or approximates target protein and energy intakes.

VII. JUSTIN'S JOURNEY: THE BENEFITS OF THE PRENOURISH STUDY FOR NICU INFANTS AND FAMILIES

Valencia Joyner Koomson, Ph.D., M.Eng., and her preterm son, Justin, took part in the preNOURISH Study for NICU Infants and Families. When Dr. Koomson gave birth in her 28th week, Justin, weighing only 3 pounds and 3 ounces, was placed in the NICU.

The preNOURISH Study served as a lifeline by helping enhance Justin's ability to thrive, combatting the family's feelings of helplessness, providing the opportunity to actively participate in his care, and providing assurance that he was receiving quality care.

Dr. Koomson and her husband agreed to participate in the study for several reasons: The staff and the study team were attentive, kind, and patient; it was an opportunity to help improve care for other infants; participants from diverse backgrounds are needed so that results apply to the entire population; and the Brigham and Women's Hospital is at the forefront of medical research and has an institutional review board that maintains rigorous standards. These factors convinced her family that Justin's participation would facilitate his growth and development.

Dr. Koomson showed photos of her son at 1 week old, when he was still in the NICU and gaining 1 ounce per day. At 2 months, he was home and weighed 6 pounds. Subsequent photos at 7 months, 15 months, and 19 months provided visual evidence of his growth. At 19 months, he weighed 28 pounds.

VIII. EXTENDING NICHD'S WORK THROUGH PARTNERSHIPS

Ms. Kaeser said that NICHD has legislative authority to enter into agreements with other entities, including private companies and nonprofit organizations.

Before entering into a collaboration or partnership, NICHD asks the following:

- Would it further the NICHD mission?
- Would it allow NICHD to do something that the institute could not do on its own?
- Are NICHD's role and the role of the partner clearly defined?
- What are the costs?
- Has NICHD leadership vetted the concept?
- Does the timeline required for drafting the agreement and obtaining approval work for the project?

Agreements and collaborations may be trans-NIH. One example is the NIH Pediatric Research Consortium (N-PeRC), which brings ICs together to harmonize pediatric research activities across institutes. N-PeRC is already showing results, including in the area of the transition of adolescents to adult healthcare.

NICHD enters into collaborations with other federal agencies in a variety of research areas, including autism, birth defects, and Down syndrome. One example of an interagency agreement is the one between NICHD and the Department of Defense for the Limb Loss and Preservation Registry.

Agreements can include technology transfer, gifts, contracts, and personnel agreements. Some common types of technology transfer agreements are material transfer agreements, cooperative research and development agreements, and clinical trial agreements. Cooperative research and development agreements involve handing off research to a private company. However, agreements are not a back door way to get funding when a grant application has been unsuccessful.

NICHD can accept gifts and donations that further its activities, but only if there are no strings attached.

Public–private partnerships include a memorandum of understanding to capture the roles and responsibilities of the partners. The partnership must further the NICHD mission, must include a partner with shared goals, and is time limited. One example of a public–private partnership is the one with Mars, Inc.'s WALTHAM Petcare Science Institute, which supports research on human–animal interaction. One of the findings this partnership has produced is that adolescents with type 1 diabetes became more disciplined about checking their own blood glucose when they started caring for pet fish.

NICHD has partnered with 20 organizations to develop and launch PregSource®, a crowd-sourced Web portal to gather data on the natural history and variations of human pregnancy. Pregnant women can answer questions and add information almost daily, including information about the medications they take. PregSource® will help produce data on normative pregnancies. Partners include nonprofits, professional societies, and other ICs. *All of Us* launched a pilot project to enroll 100 pregnant *All of Us* participants in PregSource®. The hope is to have children born to participants also join the program.

NICHD also has partnerships through FNIH, a 501(c)(3) organization that is not part of NIH but that supports the NIH mission. NIH cannot solicit funds, but FNIH can. FNIH tends to engage in large-scale projects. FNIH's work has included the Alzheimer's Disease Neuroimaging Initiative (ADNI), which aims to speed up clinical trials by providing researchers with biomarkers.

NICHD will continue to enter into a range of agreements to augment and strengthen its science with other NIH ICs, federal agencies, nonprofit and industry organizations, professional

societies, and foundations. The NICHD strategic plan envisions more partnerships to enhance NICHD's work and reach.

IX. CENTER FOR SCIENTIFIC REVIEW UPDATE

Noni Byrnes, Ph.D., Director of the Center for Scientific Review (CSR), said that CSR's mission is to ensure fair, efficient, independent, and timely reviews; free from inappropriate influences.

CSR has 247 scientific review officers (SROs), 18,000 reviewers, and more than 200 study sections. It oversees 1,450 annual review meetings and more than 75% of NIH's 82,600 applications. CSR reviews the majority of R01, Small Business Innovation Research/Small Business Technology Transfer, and F grant applications for the NIH. It also handles special initiatives, program announcements, and requests for proposals.

CSR Priorities

CSR's top priority is to ensure quality peer review. The review process should be free of bias and have stated criteria and a scoring system to judge applications. The study section members must be able to judge scientific relevance and merit, recognize emerging scientific areas, and have the right breadth of knowledge. Reviewers are trained and their work is evaluated.

The underlying principles are to be transparent and data driven, involve stakeholders, and be open about how decisions are made. To help ensure transparency, CSR recently established its Office of Communications and Outreach. The office has established a social media presence, which has sparked interaction with stakeholders and has helped CSR shape new policies. CSR has also redesigned its website, making the site easier for new investigators to navigate. Additionally, all study section description and overlap statements were recently updated. Overlap statements are there to make the referral process more transparent to investigators.

CSR is working to broaden representation on its advisory council by including members at earlier career stages. CSR Advisory Council Working Groups have revamped the Early Career Reviewer Program and have developed a reviewer integrity training module that is being piloted now and should be ready for use in all June and July study section meetings. A working group is considering how peer review criteria could be simplified to allow greater focus on scientific impact and reduce reviewers' administrative tasks.

The preliminary findings from the CSR anonymization study found that anonymization had little effect. An external contractor completed the study by reviewing 1,200 previously reviewed applications. The contractor found that the scores of African American applicants did not change when their names were redacted. Redaction appeared to reduce the scores of White applicants, but the effect size was small. Even when the applications were anonymized, more than 20% of reviewers could correctly identify the investigator. CSR will make the de-identified data available for further analysis and will publish its results.

Working with the National Institute of General Medical Sciences and the NIH Chief Officer for Scientific Workforce Diversity, CSR will conduct a pilot training on potential biases for SROs and reviewers. The pilot is about to begin and refinements will be made before rollout for all CSR reviewers and SROs in late 2020 or early 2021.

CSR has redesigned the incoming study section chairs' orientation training and provided the revamped training to 88 incoming chairs last year. The training includes case studies and vignettes that were developed by prior chairs.

CSR has a new evaluation framework for study sections: Evaluating Panel Quality in Review (ENQUIRE). ENQUIRE is a two-step process that begins with assembling a group of senior scientists with broad interests who will review scientific clusters and focus on the question of how well the scientific scope of the study sections aligns with the current state of the science. The second step is the process evaluation: A process working group focuses on the question of whether the study section function supports optimal identification of high-impact science.

Each year, 20% of CSR study sections will be evaluated, so that every study section will be reevaluated every 5 years. CSR will continue to use feedback to refine the process. One item critical to success is to match applications and reviewer expertise to the redefined scientific content of the study section.

CSR's other initiatives include reaching out to scientific societies and seeking reviewer recommendations through a single interface that SROs can easily access.

Council Discussion

Dr. Bookheimer asked whether the anonymization study looked at gender. Dr. Byrnes said that the study examined gender and other variables, such as race, ethnicity, and institution.

Dr. Bookheimer asked about the success rate of grant applications based on gender and being a member of an underrepresented group. Dr. Byrnes said that there is an ongoing evaluation of those factors. One-third of applicants are women. Their success on type 1 applications is about the same as men's. Women do less well on type 2 applications. The study sections are 42% women. Dr. Byrnes said that she is encouraging the SROs to recruit more associate professors, more of whom are women.

Dr. Bookheimer said that her personal observation is that female reviewers are more likely to change their scores following the discussion than are male reviewers. She suggested that CSR investigate whether her observation is correct.

Dr. Bianchi asked about a paper showing that certain topics, including pregnancy, do poorly in peer review. Dr. Byrnes said that NIH is re-analyzing the data from that paper. The authors may not have considered all the variables when drawing their conclusions. CSR does have a pregnancy study section and a community health study section; and proposals in these areas are not competing with other topic areas in the first level of review, conducted by CSR. One possibility is that institutes that have more R01 funding were compared with those that had less funding. Dr. Bianchi said that NICHD has a large number of noncompeting grants, which could make its funding look artificially low.

Dr. Sohn asked whether the reforms around selection of reviewers and training of reviewers will extend to the special emphasis panels. Dr. Byrnes said that CSR has started to tackle that issue with new policies and staff training. Women represent only 32% of the membership of special emphasis panels. The aim is to have 50% of the panel membership be women.

Dr. Wynshaw-Boris asked what percentage of study section chairs are women. Dr. Byrnes said that she doesn't know off-hand, but it is somewhere between 30% and 40%. However, women

are vastly underrepresented in some study sections, such as structural biology and chemistry, and are overrepresented in nursing.

Dr. Tita asked whether the time to complete a review could be shortened. Dr. Byrnes said that the council structure of advisory councils, meeting three times per year, is limiting but CSR has had rapid reviews in urgent cases and is committed to doing this when needed. Rapid review is possible on a small scale but difficult on a large scale. Also, much less time is spent in review than in making the award. Dr. Cernich said that NICHD did rapid reviews and continuous submissions to address the Zika virus. When the institute is on a continuing resolution, as was the case earlier this fiscal year, NICHD does not have the funds available to make awards.

Dr. Jain asked whether Dr. Byrnes is concerned about having an adequate pipeline of reviewers and experts for the study sections. Dr. Byrnes said that CSR is trying to relieve the administrative burden, but she is not concerned with the pipeline. She is concerned about having a small group of reviewers who serve many times every year. CSR must broaden study section membership by not having the same scientists serve for multiple panels every round, every year.

Dr. Jain asked how Dr. Byrnes rated the clinical trial review panels. Dr. Byrnes said that the main problem with the clinical trials reviews that CSR has heard from reviewers is that they are cumbersome. A working group is examining the reviews with an eye to simplifying the process.

X. Concept Clearance Review and Discussion

The Council reviewed the following 10 concepts:

Centers of Excellence in Endometriosis Research. Lisa Halvorson, M.D., said that the request is to support novel and collaborative research to address critical gaps in understanding endometriosis.

Genomic Predictors of Pregnancy Loss. Dr. Halvorson said that only 30% of conceptions result in live births. This project will attempt to identify genetic predictors of pregnancy loss, to assist with pregnancy counseling. Dr. Caggana asked whether the project would include more than genomic predictors or whether it could include environmental influences. Dr. Halvorson said that it will be broader than genomics alone and could include epigenetics. Dr. Wynshaw-Boris asked whether the genetic testing would include both parents and the fetus. Dr. Halvorson said both parents' blood will be analyzed. The analysis may also include some pregnancy tissue. Study participants will be people who have lost a prior pregnancy.

Development of Fertility Regulation Methods by Small Business. Christopher Lindsey, Ph.D., said that this initiative seeks to foster innovative research by small businesses to translate innovative science to safe and effective nonhormonal contraceptive products for men and women.

The T32 Postdoctoral Training in the Pediatric Clinical Pharmacology Program. George P. Giacoia, M.D., said that this program will help ensure a diverse workforce in pediatric clinical pharmacology. Dr. Gordon asked about the program's funding. Dr. Giacoia said it will be funded through the Best Pharmaceuticals for Children Act (BPCA). Dr. Gordon asked whether the program will consider the spectrum of pediatrics from neonates through adolescence. Dr. Giacoia said that it will.

Program Project Grants for HIV Research. Denise Russo, Ph.D., said that the goal is to stimulate collaborations among individuals to promote better research outcomes than would be expected from a single R01 or multiple isolated R01s. Dr. Sohn said that she appreciated that the concept highlights tuberculosis, which is a huge killer in the developing world. Dr. Sohn asked whether HIV-exposed but -uninfected infants will be included in this work. Dr. Russo said that they will. Dr. Sohn asked whether junior investigators who are not U.S. citizens could be part of the program, noting that there are multiple ways for junior investigators outside the country to participate but that she was not sure whether they must be U.S. citizens. Dr. Russo said she would provide the answer to Dr. Sohn after the meeting.

Catalyzing Innovation in Pediatric Pharmacology Clinical Trial Design and Resource Access. Perdita Taylor-Zapata, M.D., said that this initiative will provide a consultative resource for investigators planning robust clinical pharmacology trials. The initiative will provide access to the BPCA Pediatric Trials Network Data Coordinating Center to develop nontraditional clinical trial designs in pediatric therapeutics.

Maternal and Pediatric Precision in Therapeutics Hub. Dr. Taylor-Zapata said that this initiative will be a hub of pharmacology expertise and basic science research and will provide a technology platform that can be used by NICHD clinical trials, investigator-initiated programs, and other NIH-wide clinical programs to advance the understanding of pharmacology in children and lactating women. Dr. Tita asked whether this initiative is similar to the Obstetric-Fetal Pharmacology Research Centers (OPRC) Network. Dr. Taylor-Zapata said that this initiative is an outgrowth of the OPRC Network's efforts. NICHD wants to capture the network members' expertise and advance their findings.

Multisite Clinical Trial Infrastructure in Pregnancy and Lactation. Dr. Signore said that the initiative will provide critical infrastructure to support multisite clinical trials in pregnancy and lactation. The program will support a data coordinating center and multiple clinical centers. Dr. Tita suggested that the initiative be large enough to incorporate 150,000 to 200,000 pregnant women, be adequately funded, and allow for long-term follow-up studies.

Elucidating the Role of Nutrition in the Care and Development of Preterm Infants. Andrew Bremer, M.D., Ph.D., said that this initiative will address the knowledge gaps in nutrition in the care of preterm infants. Dr. Caggana asked whether the initiative will include preterm infants who have other anomalies. Dr. Bremer said that the initiative will include those infants.

A Comparative Effectiveness Study of Pharmacological Therapies in the Treatment of Neonatal Opioid Withdrawal Syndrome. Buprenorphine is emerging as another potential therapy to treat opioid withdrawal. This initiative will use existing clinical trial networks to compare treatment with methadone and morphine to treatment with buprenorphine in neonates with opioid withdrawal syndrome.

Council Discussion

The Council concurred unanimously on each of the concepts.

Dr. Bianchi thanked members of the public for attending the meeting, either in person or through the videocast. She adjourned the open session of the meeting at 12:09 p.m.

XI. CLOSED SESSION

This portion of the meeting was closed to the public in accordance with the determination that it concerned matters exempt from mandatory disclosures under Sections 552b(c)(4) and 552b(c)(6), Title 5, U.S. Code and Section 10(d) of the Federal Advisory Committee Act as amended (5 U.S.C. Appendix 2).

XII. REVIEW OF APPLICATIONS

The session included a discussion of procedures and policies regarding voting and confidentiality of application materials, committee discussions, and recommendations. Members absented themselves from the meeting during discussion of and voting on applications from their own institutions or other applications in which there was a potential conflict of interest, real or apparent. Members were asked to sign a statement to this effect. The Council considered and approved 499 HD-primary applications requesting up to $149,598,799 in direct costs and $205,283,459 in total costs.

XIII. ADJOURNMENT

There being no further business, the meeting adjourned at 4:00 p.m. on Thursday, January 23, 2020. The next meeting is scheduled for June 11, 2020.

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

/Diana W. Bianchi, M.D./ — April 13, 2020
Diana W. Bianchi, M.D. — Date
Chair, National Advisory Child Health and Human Development Council
Director, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

_____ — _____
Eugene G. Hayunga, Ph.D. — Date
Acting Committee Management Officer, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development
Attachment: Council Roster

[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.