Eunice Kennedy Shriver National Institute of Child Health and Human Development

NATIONAL ADVISORY CHILD HEALTH AND HUMAN DEVELOPMENT COUNCIL

MEETING MINUTES

January 24–25, 2019

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 24–25, 2019[1]

The National Advisory Child Health and Human Development (NACHHD) Council convened its 169th meeting on Thursday, January 24, and Friday, January 25, 2019, at 6710B Rockledge Drive, Conference Rooms 1425–1427 of the National Institutes of Health (NIH) in Bethesda, Maryland. The meeting was open to the public from 1:00 p.m. to 4:30 p.m. on January 24 and from 9:00 a.m. to 12:40 p.m. on January 25. 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 1:40 p.m. until 5:00 p.m. on January 25.

Dr. Diana W. Bianchi, 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.
Atul J. Butte, M.D., Ph.D. (remote)
Stephen A. Foley, M.D.
Melissa L. Gilliam, M.D., M.P.H.
Catherine Gordon, M.D., M.Sc.
Richard D. Krugman, M.D.
DeWayne M. Pursley, M.D., M.P.H.
Lesli Rotenberg
Timothy P. Shriver, Ph.D.
Annette Sohn, M.D.
Clifford Tabin, Ph.D.
Alyce Thomas, RD

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.

Observers (pending members) present:
Susan Bookheimer, Ph.D.

Ad hoc reviewer:
Rebeca Wong, 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.

Others present:
Della M. Hann, Ph.D., Director, Division of Extramural Research, and Associate Director for Extramural Research, NICHD
Constantine Stratakis, M.D., D.Sc., Director, Division of Intramural Research, NICHD
Members of Staff, NICHD
Members of Staff, NIH

Invited guests:
James Baumberger, M.P.P., American Academy of Pediatrics
Matthew Mariani, American Academy of Pediatrics

I. DAY ONE CALL TO ORDER AND INTRODUCTORY REMARKS

Dr. Bianchi began the meeting at 1:00 p.m. The meeting was videocast live.

A. Review of Confidentiality and Conflict of Interest

Dr. Hann reminded Council members that all members were required to read and sign the confidentiality agreement and nondisclosure rules for special government employees on the Council member website before evaluating any NIH grant applications. 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. Hann also reminded Council members that 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, those members are required to recuse themselves from the discussion and leave the room. Council members are not allowed to serve on the NIH peer review panel 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. Hann moved to approve the September 13–14, 2018, meeting minutes. The minutes were approved unanimously.

C. Future Meeting Dates

Dr. Hann reviewed the future meeting dates:

June 11, 2019
September 19, 2019

II. NICHD DIRECTOR'S REPORT AND DISCUSSION

Dr. Bianchi provided the Director's report.

Scientific Workshops/Meetings

The workshop on Menstruation: Science and Society, organized by the Gynecologic Health and Disease Branch, was held on September 20–21 in Bethesda, Maryland. Conditions such as endometriosis affect at least 10% of women. This extremely painful condition can lead women to use opioids for relief. Areas that were explored included endometrial biology, comparative studies in other mammals, menstrual blood as a biofluid, menstruation as a diagnostic tool, and global health. Publication of the workshop topics discussed in a peer-reviewed journal is in preparation.

Another growing area, known as "femtech," uses digital health applications to improve women's health in areas such as fertility solutions, period- and pregnancy-tracking software, nursing care software, and women's sexual wellness and reproductive health care. Dr. Bianchi noted that women's issues are somewhat less represented in the NIH research portfolio than research relating to men in general. Femtech represents an opportunity for research on women's health.

For a societal issue at the global health level, Dr. Bianchi referred to a March 8, 2017, article in *Time Magazine* by Meghan Markle, titled "How Periods Affect Potential," which highlighted the stigma surrounding menstruation, especially in low-resource settings. The lack of access to hygiene supplies, proper sanitation facilities, and open dialogue leads to girls failing or dropping out of school. The article encouraged breaking this cycle of "period poverty." Dr. Bianchi recommended watching the movie *Pad Man*, a true story about an Indian entrepreneur who invented the machine that provides low-cost sanitary pads to women in rural India.

Societal issues regarding menstruation are also present here in the United States. The vast majority of states tax feminine hygiene products (the "tampon tax"), and a July 22, 2018, article in the *New York Times* reported that a member of Congress asked for reimbursement from the Committee on House Administration for menstrual products for his staff members, since the Committee pays for toilet paper but not feminine supplies. On the day of the workshop, NICHD created the hashtag #NICHDMensesScience. The Twitter response has been positive, and it is helping change the conversation from shame to talking about coping strategies.

The 5th Annual Human Placenta Project (HPP) Meeting was held in Bethesda on November 13–14, 2018. It highlighted the amazing progress that has been made as a result of NICHD's $80 million investment. Presentations by HPP grantees described significant progress in developing novel methods for placental assessment, and there were moderated discussions of translational challenges as well as the global challenges and opportunities for HPP. This meeting produced five demonstrations and more than 30 posters.

Dr. Bianchi reported on the 4th Bill & Melinda Gates Foundation (BMGF) and NIH Collaborative Meeting, which is held annually to discuss future areas of collaboration between the BMGF and NIH, the two largest funders of biomedical research in the world. NICHD is involved in two working groups: the Contraception Working Group (co-chaired by Dr. Dan Johnson) and the Maternal Neonatal Child Health (MNCH) Working Group (co-chaired by Dr. Bianchi and Dr. Sindura Ganapathi). The MNCH scientific focus areas include the following:

Adverse Pregnancy Outcomes

This focus includes a possible collaboration on a clinical trial using the infrastructure of the NICHD Global Network to improve perinatal outcomes. In addition, NICHD and BMGF collaborated on the Women First: Preconception Maternal Nutrition study, for which the primary study has been published and secondary analyses are underway.

A significant focus is on the Data and Specimen Hub (DASH), which is a publicly available centralized resource for researchers to store and access de-identified data from studies supported by NICHD. DASH not only helps investigators meet NIH's data sharing requirements for their studies, it also provides a resource for investigators to conduct secondary analyses. DASH was launched in August 2015. Currently, on DASH, 111 studies are available on 29 study topics. There have been more than 16,400 users, 110 data requests, and 10 data use publications.

Growth and Nutrition

Focus areas include maternal nutrition during the periconceptional, gestational, and perinatal periods; factors that affect feeding, such as lactation performance, prematurity, and low birth rate; predictors of adverse outcomes for infants and young children in low-resource settings; and resource development, including developing new tools to assess nutritional status and related outcomes.

Neurodevelopment

NIH reported on data harmonization and analysis of the Environmental influences on Child Health Outcomes (ECHO) study and the NIH Baby Toolbox of neurodevelopmental assessment tools for assessing children from birth to age 3.5 years. One area of great interest to BMGF is the NIH HEAL (Helping to End Addiction Long-term) Initiative's HEALthy Brain and Cognitive Development Study, which looks at a cohort of pregnant women and offspring to examine the impact of opioid and other exposures on brain and cognitive development. NICHD is co-funding this study, which is being conducted largely by the National Institute on Drug Abuse (NIDA).

NICHD Research Initiatives of Note

The Placental Atlas Tool (PAT), released in October 2018, is a Web-based resource freely accessible to all interested researchers. PAT gathers placental molecular datasets into an integrated resource and provides the analytical tools for secondary analysis to encourage a systems biology approach to placental research, facilitate hypothesis generation, and identify potential biomarkers and therapeutic agents. It provides a number of key functionalities, including robust analytics, an image explorer to browse and search placental images, and a workspace area that provides researchers with a secure environment to save, manage, and analyze data available through PAT for secondary analyses.

The Trans-NIH Pediatric Research Consortium (N-PeRC) is an effort to harmonize efforts in child health research across the 27 NIH Institutes and Centers (ICs). Four bimonthly meetings have been held since the launch of this consortium in June 2018. The group has identified gaps and opportunities for collaboration in areas including development of safe pediatric drugs and devices; data sharing, for which it is hoped additional funds will be identified to create a federation for DNA sequencing data and build on infrastructure to link pediatric datasets across NIH; trans-NIH training to grow the pediatric workforce; and the transition from adolescence to adulthood. N-PeRC should enhance NIH communication about pediatric research as NIH will now speak with one voice about childhood research.

The HEAL Initiative launched in April 2018 as a trans-agency effort to develop faster scientific solutions to stem the national opioid misuse/addiction crisis, with an emphasis on non-pharmacological ways to treat pain. In fiscal year (FY) 2018, NIH doubled funding for the opioid crisis research from $600 million to $1.1 billion, which was made possible by congressional support. The NICHD-funded Advancing Clinical Trials in Neonatal Opioid Withdrawal Syndrome (ACT NOW), a new study to evaluate treatment options for newborns with opioid withdrawal syndrome, is now formally included in HEAL. Recent funding announcements focus on biomarkers, novel targets for treatment, and -omics.

The NIH INCLUDE (Investigation of Co-occurring conditions across the Lifespan to Understand Down syndromE) Project received a significant increase in funding from Congress, thanks in large part to the inspiring testimony of Mr. Frank Stephens, who provided a deeply personal account of his own life with Down syndrome and how it has affected him and his family. Each year, more than 6,000 infants with Down syndrome are born in the United States. Over the past 25 years, their lifespan has doubled from 30 to 60 years. NIH funding for research on Down syndrome was fairly low from 2008 until 2015 but is now on the rise. The FY 2018 budget

legislation for NIH included language to "develop a new trans-NIH initiative to study trisomy 21" which will have the unique double benefit of not only providing a deeper understanding of Down syndrome, but also a deeper understanding of shared common conditions, such as Alzheimer's disease, leukemia, and autism. The INCLUDE project will have three components to address key quality of life issues: conducting targeted, high-risk, high-reward basic science studies on chromosome 21; assembling a large study population of individuals with Down syndrome; and including individuals with Down syndrome in existing clinical trials. NICHD is funding projects in all three of these areas. The total funding support across NIH for INCLUDE is $22.2 million for 49 awards. In addition, funding announcements for FY 2019 are planned and the following two workshops are in development: Planning a Virtual Down Syndrome Cohort Across the Lifespan and The State of the Science for Meaningful Clinical Trials in Down Syndrome.

Staffing Updates

- Dr. Elizabeth Baden has been hired as the NICHD Chief of Staff. This is a new position designed to help ensure consistent communication across NICHD and implement the strategic plan. Dr. Baden will also serve as Executive Secretary for new working groups of the NICHD Advisory Council and N-PeRC.

NICHD is hiring for a number of positions:

- Deputy Director. The search committee is completing its first round of interviews.
- Executive Officer. A search committee has been charged, and the application window will soon open.
- Extramural Branch Chief Positions: Pregnancy and Perinatology, Obstetrics and Pediatrics Pharmacology and Therapeutics, and Child Development and Behavior
- Medical and Program Officers in the Division of Extramural Research

Council Discussion

Council members had no questions or comments.

III. REPORT OF THE DIVISION OF EXTRAMURAL RESEARCH

Dr. Hann reported on the Division of Extramural Research (DER).

HEAL Initiative

NICHD's participation in HEAL initiatives includes signing on to 24 Funding Opportunity Announcements (FOAs) (7 on opioid use disorder and 17 on pain) and leading one FOA as part of the ACT NOW program in conjunction with the ECHO Program. There are about 50 NIH FOAs for HEAL and NICHD is on nearly half of these ensuring that the populations essential to the NICHD mission are represented.

Impact Analysis

NICHD undertook an analysis of its 10 largest programs in the extramural portfolio. This effort involved creating a standardized methodology of over 20 quantitative metrics to identify the downstream impact of NICHD's largest programs and their effect on public health. One way to gauge impact is to look at whether the research is used in clinical practice. To determine this, the impact analysis looked at practice guidelines and the references cited by these guidelines. From this it was possible to follow the impact of these NICHD programs by looking at the grants

acknowledged in the references. The impact analyses indicated that all of the 10 programs were being cited in practice guidelines. Understandably, the more clinically oriented programs had the largest number of guideline citations. The impact analysis also looked at UpToDate Guidelines, which confirmed that publications from NICHD programs are being used in this clinician-friendly reference.

The impact analysis also allowed for content analysis using the Relative Citation Ratio (RCR). In conducting these analyses, it was possible to compare published NICHD papers with other NIH papers and papers from the field (not NIH). An example of this content analysis was shown. In it, one could discern 15 distinct cluster areas, such as respiratory complications and hypoxic ischemic encephalopathy, hypothermia, and sepsis. Again, the saturation of publications from the NICHD program papers was very positive.

This analysis will provide valuable data in working with program staff. It allows NICHD to see where the program is having an impact and to focus an informed dialogue to shape the programs going forward.

Staff Updates

- Dr. Della White left the NICHD Population Dynamics Branch and moved to a position at the National Center for Complementary and Integrative Health.
- Dr. Tonse Raju retired as Chief of the Pregnancy and Perinatology Branch.
- Dr. Lisa Freund retired as Chief of the Child Development and Behavior Branch.
- Dr. Sujata Bardhan has joined the Intellectual and Developmental Disabilities Branch.
- Ms. Christiane Robbins joined the Scientific Review Branch.
- Dr. Christopher Lindsey joined the Contraception Research Branch.
- Dr. James Coulombe was promoted to the Chief of the Developmental Biology and Structural Variation Branch.

Dr. Hann said that DER is hiring and she encouraged all attendees to spread the word. The URL is https://www.nichd.nih.gov/about/jobs.

Council Discussion

Dr. Michael Boninger, noting that these data indicate the percentage of papers from grants that are cited by more than one guideline, asked whether there are data on outcomes of publications per grant. He wondered whether there is a quantitative measure for citations or a percentage of grants in specific categories. Dr. Hann said that in the clinical area, there are networks, so the collection of grants being assessed is not individualized. Dr. Bianchi said that percentages were used, because some of the older programs have more publications. It is very hard to compare networks that have been in existence for many years with those that have been funded for a shorter period of time, so it is better to use percentages than to try to look at specific publications per grant. This provides a better indication of the return on investment of these large programs versus the typical R01 versus everything in the extramural branch. The analysis has made clear that some of these programs are having a significant impact on clinical guidelines.

IV. UPDATE ON STRATEGIC PLANNING

Dr. Bianchi provided an update on the strategic planning process and invited the Council's active engagement in this discussion.

Overview of Strategic Planning Activities

The initial goals of strategic planning are to identify scientific priority areas in which NICHD can either lead or be a partner/collaborator at NIH. Additional decisions regarding funding and training opportunities will follow.

A timeline for stakeholder input (Phase I) and plan development (Phase II) has been devised. After Council input at this meeting and public comment, the plan finalization is projected to be in the spring of 2019.

The plan is defined by the three core principles of transparency, decisions informed by evidence, and stakeholder participation. Other principles include inclusion of women, children, and people with disabilities in research and the alignment of extramural and intramural research.

Transparency is critical for enabling internal and external stakeholders to look at NICHD's portfolio with a fresh perspective. The review and refocus of NICHD's science and alignment of resources with scientific priorities are designed to improve the health of the populations that NICHD serves. To this end, the strategic planning process was launched at the January 2018 meeting of this Council, a website accessible to the public was established and frequently updated, and the goals and objectives of the plan were clearly outlined in multiple venues.

To ensure that decisions are informed by evidence, NICHD collected key NICHD data, including a bibliometric portfolio analysis, a review of NICHD/NIH strategic and internal scientific research plans, and an analysis of the impact of selected networks and centers within DER. A listening session was held at the September 23, 2018, meeting of this Council, and a Strategic Planning Working Group was formed. This working group included NICHD staff and 53 outside experts, one-third of whom were young investigators, who represent the future of NICHD. They provided diverse perspectives with different insights into the problems.

Stakeholder participation has also been robust. NICHD held an interactive live public webinar that engaged more than 300 participants and received 119 email questions and ideas at nichdstrategicplan@nih.gov. Thirty-five patient and family organizations attended a meeting of the Friends of NICHD. General public input has also been encouraged through the use of Facebook and Twitter pages. The level of NICHD's social media activities to engage the public in the strategic planning process has resulted in 59,624 impressions, with the majority of promotional efforts occurring on Twitter.

These efforts collectively yielded more than 270 great ideas, of which about 50 were prioritized for further consideration by the Intramural and Extramural Working Teams. These teams considered the magnitude of a problem that NICHD would address as a priority, looking at whether it was something that NICHD is uniquely suited to do and how it would affect NICHD's position in the scientific community and NICHD's relationship with stakeholders. Feasibility was also a consideration, with a goal of making significant progress in the next five years.

A final set of six themes, goals, and opportunities was consolidated and is being presented for further consideration at this meeting and via the Request for Information (RFI) process. Certain concepts are "woven" into the fabric of the strategic plan. The "warps" correspond to the scientific priority areas, and the "wefts" refer to concepts that are embedded in all NICHD priority areas, such as inclusion of NICHD populations, nutrition, health disparities, infectious diseases, prevention and global health. The themes were developed while keeping in mind that NICHD is not just about child health but also about human development. The goal is to focus on the NICHD population, which is women, children, and people with disabilities, in every endeavor.

Dr. Bianchi reviewed the six research themes:

1. **Understanding Early Human Development:** The goal is to enhance knowledge of genes and regulatory networks at the single- and multi-cell levels during preconception, conception, and gestation to understand human development, improve fertility, and reduce pregnancy loss. Scientific opportunities include the following:
    a. Develop novel ways to characterize early development stages.
    b. Categorize and profile single cells to better define their role.
    c. Explore the influence of environmental exposures on early development.
    d. Identify the full range and function of cell types present during development.
    e. Understand the developmental factors at the cellular level that contribute to miscarriage, stillbirth, birth defects, and other congenital conditions.

2. **Setting the Foundation for a Healthy Pregnancy and Lifelong Wellness:** The goal is to improve pregnancy outcomes to maximize the lifelong health of the woman and her children. Dr. Bianchi noted that Congress has not put much focus on pregnancy, most likely because it is seen as a time-limited condition. This theme tried to make the connection that a long-term view of a healthy pregnancy ultimately leads to a healthier population. Scientific opportunities include the following:
    a. Support research on early indicators of risk or threats to maternal health during pregnancy.
    b. Understand how pregnancy-related conditions contribute to maternal mortality and influence health and wellbeing later in life.
    c. Determine potential targets for interventions by studying genotypic, phenotypic, exposure, and other biomarkers.
    d. Utilize datasets to understand the course and complications of pregnancy.
    e. Support or conduct studies of the placenta.
    f. Identify and validate targets for preventing preterm birth and related adverse events.

3. **Promoting Gynecological, Andrological, and Reproductive Health:** The goal is to enable women and men to manage fertility and minimize the impact of gynecological and andrological conditions. Dr. Bianchi noted that NICHD funds $30 million in male reproductive research. Scientific opportunities include the following:
    a. Improve basic biological understanding of male and female reproductive organs.
    b. Utilize integrated genetic and phenotypic exposure data to understand underlying mechanisms of health conditions.
    c. Focus on the science of pediatric gynecology, especially as it relates to congenital conditions or complex pediatric gynecological conditions.
    d. Understand the basic biology of healthy reproductive development.
    e. Develop solutions for infertility and ensure options for men and women to manage their fertility.
    f. Identify modifiable factors to solve infertility.

4. **Identifying Sensitive Time Periods to Optimize Health Interventions:** The goal is to understand sensitive time periods during development and rehabilitation when prevention and treatment strategies may have their greatest impact. Dr. Bianchi explained that this involves the timing of interventions, including *in utero* interventions. Scientific opportunities include the following:
    a. Focus on change brought on by normal development or by injury or disease.
    b. Understand sensitive time periods in which an exposure to a disease or an event or the use of a particular intervention will have the greatest impact.
    c. Identify the timing and mechanisms of plasticity in early developmental stages.

   d. Investigate the mechanisms that determine the initiation and termination of these sensitive time periods, including different periods during gestation.
   e. Identify sensitive time periods after disease or injury when plasticity is high to inform the timing of prevention and management, including early interventions for intellectual, developmental, and learning disabilities and therapeutic approaches in critical care and rehabilitation settings.
   f. Explore factors that can promote or hinder health during these sensitive time periods, such as nutrition, sleep, early exposure to infectious diseases, early language interventions, and technologies.
   g. Enhance the ability to target interventions by looking at social determinants in conjunction with biological factors that influence these sensitive time periods.

5. **Improving Health During the Transition from Adolescence to Adulthood:** The goal is to improve the transition from adolescence to adulthood by identifying behavioral, social, environmental, and biological factors that enhance health, especially for adolescents with disabilities or other chronic conditions. Scientific opportunities include the following:
   a. Identify the behavioral, social, environmental, hormonal, endocrine, and genetic factors that contribute to adolescent development.
   b. Incorporate lifestyle factors, such as diet, sleep, or exposure to social media, as a focus of the environmental and behavioral aspects of this opportunity.
   c. Consider the impact of the medical transition from pediatric to adult care, especially for children with disabilities or other chronic diseases.

6. **Ensuring Safe and Effective Therapeutics and Devices:** The goal is to develop, test, and validate safe and effective therapeutics and devices, specifically for the NICHD populations of pregnant and lactating women, children, and individuals with disabilities. Dr. Bianchi observed that, for example, there is a gap in knowledge about the long-term effects of tubal ligation. Scientific opportunities include the following:
   a. Consider and address specific needs of these populations through their inclusion in the development, testing, and validation of therapeutics and devices.
   b. Evaluate medications and safe and effective dosing in these specific populations to allow for better treatment.
   c. Utilize data such as electronic health records and datasets to discover potential adverse events, positive outcomes, or common comorbidities in these populations.
   d. Enable implementation efforts in health systems by supporting acceptability and adherence research to ensure that interventions can be meaningfully used in these populations.

For each of these six research themes, there are many potential partners for NICHD among the ICs at NIH. For example, in the area of adolescent transition to adulthood, NICHD could partner with N-PeRC, NIDA, the National Institute of Mental Health (NIMH), the National Institute of Allergy and Infectious Diseases (NIAID), and the National Institute on Alcohol Abuse and Alcoholism (NIAAA). The critical questions are in which areas NICHD should lead and in which areas it should partner.

Dr. Bianchi noted that a number of institutes at NIH focus on neuroscience. The question is whether NICHD should focus on neuroscience when four other institutes at NIH are already doing so. Should NICHD partner in various ways with other ICs, or is there a better way for NICHD to carve out areas that are unique to it? Dr. Bianchi noted that just recently, the Director of NIMH talked with her about ways to address the applications on pediatric violence that NIMH

receives but is not sure what to do with. It is important for NICHD to think critically about the dual challenge of defining the specific priorities that it wants to be known for while not sacrificing everything else. Currently, the NICHD focus is so broad that initiatives go to other ICs, because they have more clearly articulated their priorities. The present discussion should focus on what is missing, what should be added, and where NICHD goes from here.

V. ADVISORY COUNCIL DISCUSSION ON STRATEGIC PLANNING

Mr. Scott Wheeler of Strategy Arts facilitated this portion of the meeting by leading the discussion on each of the six themes that will be part of the RFI. He described the process as being at a critical point to finalize the details. He asked Council members to think about partnerships, training that will be needed, infrastructure, technology, and metrics to track and accelerate progress. Articulating what the priorities are is essential to moving on to the next phase of the project. Mr. Wheeler said that the process has included all the information from the Council, the public, and the Extramural and Intramural Working Teams. All of these data went to the Strategic Planning Committee, and a number of reports have been generated. After this session, the Council's comments and input from the RFI, which is still open, will go back to the Strategic Planning Committee, which will adjust the themes. Then it will go to the Working Teams to plan the details of each priority. Dr. Bianchi said that much of the input received at this point might be related to future funding announcements or major projects that will translate to the implementation of specific measureable objectives. Implementation is a major goal.

During the discussion, Mr. Wheeler displayed each of the six themes as they appear in the RFI.

Council Discussion on the Strategic Plan as a Whole

Dr. Susan Bookheimer, noting that she was speaking on behalf of the directors of the Intellectual and Developmental Disabilities Research Centers across the country, said that research into the basic neuroscience of intellectual and developmental disorders should be a leading priority of NICHD and that this basic research should move into other areas that have been mentioned, such as transition to adulthood. At least one in six individuals is affected by an intellectual or developmental disability, so this is a critical issue. Cognitive neuroscience has been mentioned in this discussion, and it is covered to some extent by other ICs, but developmental neuroscience, the basics of brain development, is critical to the NICHD mission but something that the other ICs are not nearly as invested in. A focus on intellectual and developmental disabilities should be a major goal for NICHD. Some of the recent findings for treatment should also play a major role. Research into nucleotides will give us the ability to treat single gene disorders and is a beginning of personalized medicine, and NICHD is the only institute that can do it.

Dr. Timothy Shriver endorsed Dr. Bookheimer's comments. He said that he appreciated and was sensitive to the interlocking nature and complexity among the NIH ICs, but at the big picture level, he suggested that the NICHD strategic plan is focused on NICHD being known for the best work on pregnancy, reproduction, and maternal health. This is fine, but NICHD should also be known for work on intellectual and developmental disabilities. Dr. Shriver said that the vast enterprise of medicine does not understand, prioritize, or even recognize the importance of intellectual, developmental, and emotional disabilities in its work, nor does it include this population adequately in research. The average scientist, looking at NICHD's research priorities, should be able to conclude that NICHD has placed intellectual and developmental disabilities in a prominent place. This is a lonely field for investigators and a difficult field to advance and find funding for, and the strategic plan should make clear that NICHD focuses on intellectual and developmental disabilities.

Dr. Richard Krugman said that the budget increase would provide the ability to address some of these priority areas. He asked how the area of violence as it relates to children is being addressed through this process, noting that of the six research themes, four specifically focus on groups other than children, and the other two are not targeted to children particularly. Dr. Bianchi said that she had a summary of some of the initial objectives that are lining up with some of these themes. She noted that for Theme #5 (improving health as children move into adulthood), the impacts of violence, trauma, and injury and related specific objectives within that area are included.

Dr. Krugman asked whether, going forward, the organizational structure of NICHD branches and offices would change or simply adapt to the new priorities. Dr. Bianchi said that no decisions on whether to organize branches around themes have yet been made. This will be looked at once the science is decided, and requires approval by the U.S. Department of Health and Human Services (HHS).

Mr. Wheeler said that in terms of the warp and weft of the strategy, there are many things that could be called out individually, and efforts to figure out how to weave the things that are important to all of the communities into all of the themes are ongoing. The challenge is to explain what is a priority for NICHD and where it can have the most advantage in the most areas for the most people while also not being so specific that people feel excluded.

Dr. DeWayne Pursley said that while crosscutting considerations, such as the concepts of prevention, therapy, and intervention, are important, another consideration should be disparity, which is alluded to in the introduction but does not appear anywhere in the themes. It is important to be intentional in talking about disparities because of the risk of missing major opportunities when the focus is on the composite and not on how specific subgroups are affected. This needs to be specifically inserted.

Dr. Annette Sohn noted that there has been much discussion of “our populations” and who they are. NICHD covers 18% of pediatric research, but in some of the other ICs, the question is whether children are just an afterthought, perhaps being grouped into a longitudinal cohort that happens to contain a few children, whereas NICHD can truly say, “Children are our focus.” The developing brain from conception through adolescence is very important in the way in which it influences the entire lifespan, and it is hard to separate all of these things out. It must be made clear that NICHD is the advocate for these populations.

Dr. Boninger noted that reading the document and watching Dr. Bianchi’s presentation are two different experiences, because the weave is not something that comes out from the document. It is important to get the weave to be able to more clearly describe the constituents that NICHD uniquely represents.

Dr. Bianchi said that 25% of both the NIMH budget and the National Institute of Dental and Craniofacial Research budget is child health research. Child health research is only 55% of the NICHD budget, with about 30% going to reproductive research and 18% going to intellectual disabilities research. The challenge is in how to navigate this landscape while simultaneously promoting child health. A major reason that N-PeRC was formed was to leverage these budget considerations. Autism is a major focus for NIMH. The question is whether to partner with NIMH or decide that autism is an area where NICHD should have its own focus. NCATS deals with rare disorders. It is not that NICHD does not want to support those things, but how does NICHD leverage its budget to put its money where its priorities are?

Dr. Bookheimer said that intellectual and developmental disabilities research is not really the province of any of the other ICs. There is considerable cross talk about these disorders, so while NIMH is funding adolescent/adult work in autism, most of the work related to the animal models is done by NICHD, which none of the other ICs are equipped to or want to do. NIMH has declined to do candidate gene research, which is a big problem for intellectual disabilities research. NICHD is where the foundation for this research comes from.

Dr. Bianchi said that this excellent feedback is essential in helping identify specific areas where NICHD can lead.

Mr. Wheeler said that the explanation of the weft is very important. NICHD must refine how that concept is communicated in the plan so that Council members can ensure that the right things are being called out.

Council Discussion on Each of the Research Themes

Research Theme #1: Understanding Early Human Development

Dr. Clifford Tabin said that the area where NICHD can lead in neuroscience is in developmental neuroscience. That is something that no other IC covers, and basic developmental mechanisms for neurobiology are a foundation for the type of information needed to address the issues that have been presented. However, speaking as a basic scientist, Dr. Tabin said that basic fundamental science percolates all through the plan but is not a focus of the plan. There is a real absence of specifically saying that NICHD will fund research to lay the foundation for future knowledge that will benefit child health. For example, mouse models for looking at genes in autism provide the type of information that is fundamental to making scientific advances, yet the plan only briefly refers to understanding model organisms. The plan should specifically focus, under "Opportunities," on exploiting a diverse set of model organisms to address fundamental science and problems on a variety of levels, leading to insights that will inform human child health research. If this draft were the final version, it would have a chilling effect on the basic science community funded by NICHD, because this type of basic research is not a focus for the future. Understanding basic scientific principles is critical for all the themes, and it should be specifically stated.

Dr. Bookheimer said that this draft is written as though there is a strong emphasis on cells, but there are multiple levels of understanding in neuroscience in terms of genes, gene expression profiling, and new techniques for networks. This should be written in a broader way to incorporate multiple levels of understanding, from genes to cells to organoids to systems to networks.

Research Theme #2: Setting the Foundation for a Healthy Pregnancy and Lifelong Wellness

Dr. Catherine Gordon suggested that with the emphasis on pregnancy in women, teen pregnancy has gotten lost. She noted that this would be an opportunity to look at the effects of teen pregnancy on the mother and the fetus, on outcomes, and on opportunities for prevention.

Dr. Boninger said that in terms of rehabilitation, this theme would be a unique context in which to consider lifelong illness people with disabilities and to include people who acquire disabilities.

Dr. Krugman said that the words "violence" and "sexual abuse" rarely appear, because no one talks about or wants to deal with these issues. These words must be expressly spoken, or these issues will be ignored.

Dr. Shriver said that this theme would be a good context in which to mention equity issues surrounding underrepresented populations and emphasize an inquiry into the distinctive factors

affecting people who have been subjected to inequitable socioeconomic conditions. Mr. Wheeler said that there had been many discussions of equity considerations and how to bring this forward. Dr. Bianchi added that health equity issues were a major discussion in the working group, so it certainly has been captured in a crosscutting way.

Dr. Bookheimer said that in terms of models of pregnancy, there are important animal models on maternal health as it relates to autism. Basic research on maternal health should also be included here.

Ms. Alyce Thomas said that it was good to see nutrition woven into all six themes, but because of its wide-ranging effect on everyone—certainly including teens and pregnant women—the importance of good nutrition should not only be mentioned across themes but also have the importance of nutrition research addressed.

Dr. Sohn noted the need for pharmacovigilance during pregnancy, not simply for substances but also for medications that doctors may have prescribed for their patients, may have been validated in initial clinical trials, but when given to large populations either in the United States or globally, end up being associated with birth defects or abnormal adverse events for the women or their babies.

Dr. Gordon added that vigilance is needed for not only medications given during pregnancy but also supplements that seem benign but are not.

Dr. Butte noted that there should be consideration of the role of imaging and other non-invasive testing during pregnancy.

Research Theme #3: Promoting Gynecological, Andrological, and Reproductive Health

Dr. Bookheimer said that she did not see in this section the potential effect of fertility treatments, such as multiple births and potential negative consequences for child cognitive development and developmental disabilities, in both the short and long terms.

Dr. Gordon noted that it should be made clear that endometriosis is quite different between adolescents and adults and that there should be a big “shout-out” to pediatric gynecology, because this area should be the domain of NICHD.

Dr. Shriver observed that one of the values of a strategic plan is as a communication tool, and he said that it did not appear to him that there is new, emerging science that has led to this theme being considered a “big opportunity” to make a great breakthrough. The last two items particularly appear simply to be continuing the study of pregnancy and fertility, as opposed to representing a critical scientific significant tipping point.

Dr. Bianchi said that she would like this to be a “big idea” session. This is a moment to think big and be aspirational. That is part of the RFI. NIH Director Francis Collins, M.D., Ph.D., specifically said that he expects to see some aspirational goals from this plan.

Dr. Tabin said that this should be framed not only on breakthroughs that are available to be built on but also on what the breakthroughs of the future will be.

Dr. Foley said that it was unclear whether the focus is on pediatric pelvic pain or pelvic organ dysfunction and how that relates to fertility or just generally. Dr. Bianchi said that we have to address the pediatric and adolescent populations as well as the adult population. Dr. Foley said that he considered polycystic ovary syndrome (PCOS) to have a huge impact on pediatric and adolescent populations and wondered whether it should be in this area, but the condition is

hugely important for fertility, and if it could be picked up in a pediatric population, it would be a big deal. Dr. Gordon agreed with Dr. Foley, noting that PCOS affects 6% to 10% of premenopausal women.

Dr. Bianchi asked whether this could be framed as a big, aspirational goal, like identifying predictive biomarkers in girls. Dr. Gordon suggesting framing it as better understanding biomarkers in adolescents versus biomarkers in adults that could predict numerous outcomes, such as fertility or cardiovascular morbidity and mortality.

Dr. Foley said that some of the reasons that the condition is not treated in this young population are "fat prejudice," in which a person is fat and therefore judged as someone who just watches too much TV; and a lack of a biomarker that confirms that a person has the condition. There is a lack of research into this condition. There may be something simple available. Dr. Foley said that he does a lot of high-density lipoprotein (HDL) and HDL2 evaluations on young children and that they tend to have lower values, though this is anecdotal. If there were a confirmatory biomarker that would allow earlier intervention, it would lead to better treatment, greatly decreasing the number of fertility issues later on.

Dr. Bianchi noted that understanding a condition earlier in the lifespan leads to earlier treatment and detection. She said that although the six themes are broader by intention, PCOS would clearly be covered under this theme.

Research Theme #4: Identifying Sensitive Time Periods to Optimize Health Interventions

Dr. Bookheimer said that this is an important theme. It was unclear whether this theme is meant to include prenatal as well as postnatal periods, but both are very important. This is where neuroscience plays out, and neuroscience issues should be mentioned explicitly. There are clearly critical periods in neuroscience prenatal development and there is gene expression work to validate that. This information should be woven in.

Dr. Sohn said that she was surprised not to see adolescents here, particularly because adolescence is a period of so much brain maturation that will affect the rest of their lives. The adolescent period is not identified here. Dr. Sohn wondered whether brain development and maturation might be an area where NICHD could take a bigger lead. She noted that Theme #5 very much relates to adolescents and that perhaps this could be covered there, but she suggested that since this theme covers sensitive time periods, it should be made clear that the theme is not just about early childhood.

Dr. Shriver said that he was struck by the mention of "development interrupted by injury or disease" and asked whether, in this day and age, people with genetic disorders or lifelong issues see themselves as people with diseases. How this is framed could be an opportunity to sensitize people's thinking on how this is viewed medically, as well as socially and culturally.

Dr. Rebeca Wong observed that Dr. Bianchi's presentation used the word "critical" instead of "sensitive" and suggested that "critical" was a better word in this context. Dr. Bianchi said that there had been some ambiguity about this, so the words have been used interchangeably. She said that this was helpful guidance and appreciated advice about which word would be better to use.

Dr. Gordon cautioned that in looking at Themes #4 and #5, it is important to ensure that adolescents are not missed, because Theme #5 is about the transition from adolescence, but it does appear that adolescents have been missed in Theme #4. Theme #4 could focus on the continuum of exposures and would be a good context in which to bring up violence.

Dr. Butte was concerned that there will be more descriptive studies than interventional studies, because interventions take a long time to assess. He wondered about the role for biomarkers and a faster way to tell when the intervention might be successful than just waiting or expecting to see a difference. He suggested that societal and individual biomarkers would be needed to test the success of life course interventions, rather than waiting to determine this over the entire life course.

Dr. Bianchi said that she was looking at a document with some of these themes called out. Under Theme #4, one of the subthemes says, "Identify the timing and mechanisms of neuroplasticity in early developmental periods, including fetal development."

Research Theme #5: Improving Health During the Transition from Adolescence to Adulthood

Dr. Shriver said that although he was under the impression that there is a significant priority in this theme for understanding this transition for people with intellectual and developmental disabilities, there was no specific mention of disability in the draft of this theme. He suggested the need to clarify that these transitions affect different populations differently and that this transition period is a particularly, if not the most, stressful and challenging time for people with intellectual disabilities. The prominence of this message should be elevated in this theme.

Dr. Sohn said that it was important for NICHD to bring brain neuroscience and cognition into this, as well as partnering with other groups in certain niche areas. Adolescence by definition is a multidisciplinary area of life with many different exposures and risk factors. For example, the transition for adolescents who have been treated with drugs their whole lives, such as for HIV or cystic fibrosis, will have different themes in terms of independence versus caregivers versus treatment. This is a topic of great interest, certainly in the global HIV world.

Dr. Wong, noting that this theme does not mention sexuality, observed that this transition period can be a time of confusion about sexual identity, and she wondered whether this topic was discussed for inclusion in the theme. Mr. Wheeler said that this topic had not been called out a lot, and he appreciated Dr. Wong bringing it up.

Dr. Foley again noted the importance of biomarkers in this theme to provide opportunities for early interventions. Dr. Gordon agreed on recognizing biomarkers in the patient and the family. This transition period is not being well-studied.

Research Theme #6: Ensuring Safe and Effective Therapeutics and Devices

Dr. Boninger said that he liked this theme, and he suggested including the many transformative technologies in the commercial marketplace, which are not being as effectively utilized for the NICHD populations as they should be. This is an area where NICHD is uniquely suited to contribute, and some wording about this should be added.

Dr. Bookheimer suggested that the title should refer to the development of novel therapeutics with the new technologies that are available. The current title seems to focus more on existing treatments and their effects rather than on novel therapeutics.

Dr. Butte suggested including a look at innovative models.

Dr. Sohn asked whether there had been discussion of private/public partnerships around this theme. Mr. Wheeler said that there had been a lot of discussion about it and that it will be further elucidated after the themes are refined. Dr. Sohn suggested a partnership with the Medical Research Institute (MRI) in Boston, which is specifically looking at translational science for drug development for specific diseases, as well as vaccine development. MRI is already a partner of

NICHD with overlapping interests, so this relationship would be different from simply putting out requests for grant proposals. A variety or multiple types of partnerships would be beneficial.

Dr. Pursley said that this is an area where there is benefit to identifying newborns specifically, because although there has been development of drugs and therapeutics for children, newborns as a population have been almost totally excluded from it for many reasons, including being a small, high-risk population that adds liability to the study and requires biomarkers to identify impact. There would be benefits to specifically identifying newborns in this theme.

Dr. Bianchi again asked the Council to identify some truly aspirational, outrageous goals if there were a pot of money available. For an example, she cited the artificial womb, which has already been created in sheep but could not have been funded at NIH, because it was so "out there." Council members took a few minutes to consider some big topics.

Dr. Butte suggested developing a safe, effective, evaluated, ethical, affordable system for gene editing to cure genetic diseases.

Dr. Boninger suggested developing technologies that make physical or cognitive disabilities invisible, such as prosthetics that are not easily recognized as prosthetics, like contact lenses instead of glasses. This would fit within Theme #6. Dr. Boninger added that the NICHD target populations (pregnant women, children, and people with disabilities) are uniquely discriminated against in research, and he suggested the field of "advocacy science," which is developing scientific studies to eliminate this disparity in these populations.

Dr. Krugman said that millions of children annually experience violence, neglect, or physical, emotional, or sexual abuse and that some of them take a path to become violent or sexual offenders themselves. But others will not take such a path and will just live with their own past trauma. Many survivors develop chronic health issues such as depression, suicidal ideation, obesity, or eating disorders, while others survive with no sequelae at all. The natural history of the impact of these early traumas is not known. Dr. Krugman suggested the need to better elucidate the impact of the natural history of these situations.

Dr. Tabin suggested a focus on regenerative biology, which relates to NICHD, because the platforms for regenerative medicine are fundamental embryology and fundamental developmental biology. He said that knowledge of stem cells should make it possible to learn how to regrow limbs. He suggested using NICHD to bring together stem cell biologists, tissue engineers, and developmental biologists to develop regenerative advances. Dr. Bianchi said that NCMRR has a limb loss registry, and she wondered about combining the collection of people who have experienced limb loss with some of the themes, such as developing devices in Theme #6 by including a stem cell biology approach. It would be remarkable to go from the basic cellular biology of making a limb to studying limbs that are not developing properly in humans and treating them. Dr. Tabin emphasized that this would require having the fundamental biological knowledge to begin with.

Dr. Bookheimer suggested having universal prenatal genetic screening. She also suggested using translational and integrative research methods to find a "bio-common" pathway in autism, rather than using a single model and coming up with an answer that works only for that one model. This would be a study of many genetic and nongenetic models using common biomarkers to find a common pathway.

Ms. Thomas had three suggestions: elucidate how unhealthy eating patterns affect not only the fetus but subsequently the long-term health of the child and the adult and turn the fetal origin of chronic diseases from theory to fact, devise an effective method to have children and adolescents

choose healthy foods, and determine the ideal diet for gestational diabetes. In light of the fact that the name "NICHD" might not clearly articulate the breadth of the institute's populations, she asked whether there had been any discussion of changing the name. Dr. Bianchi said that the topic had been discussed. It involves congressional approval and is a very complicated question. The name must also be short enough to be useful, but Dr. Bianchi said that she is open to consideration of names that might better represent the populations on which NICHD focuses.

Dr. Foley suggested developing a biomarker to ensure that every child with PCOS was treated at 9 years of age instead of 29, particularly considering the number of metabolic syndromes that are associated with PCOS. He also agreed that it would be very helpful to know the best diet for gestational diabetes.

Dr. Wong suggested research on addiction among children, particularly research to help counteract the negative effects of the addiction to constant dependence on mobile and social media. Starting with children would be a great breakthrough.

Dr. Sohn had two suggestions: Use models of brain development to guide the development and timing of an intervention to modify adolescent risk-taking behavior for addictions to many things, such as alcohol, substances, sex, or tobacco; and explore whether NICHD is in a position to help transfer the structures and ethical tools to other countries so that the countries could develop DASH-type data sharing globally. In the HIV world, it is very difficult to share data. If there were a way to learn from what NICHD has done in DASH, it would be a great way to transfer knowledge as well as technology.

Dr. Shriver said that if science were close to understanding the developmental triggers for the onset of autism and schizophrenia, the next step would be to develop a way to, if not prevent those underlying neurological vulnerabilities, stop them from developing further. A second idea would be to examine the role of positive relations on human development. Little is known about the biology, genetics, or epigenetics of why some people respond so resiliently to specific traumas such as violence and disease while others do not. People with intellectual disabilities have enormous resiliency, but it is not known why, nor is it known how to help someone from a biological or epigenetic point of view to become resilient. It would be valuable for NICHD to work on understanding resilience in children. Dr. Shriver suggested that while it is important to study disease, more study should be done on healthy development.

Dr. Pursley suggested finding the mechanisms by which social factors are transformed into biological outcomes. There has not been substantive progress in identifying genetic or epigenetic contributions. Pediatricians could better address these issues if they understood the mechanisms and if there were interventions designed to mitigate the factors.

Dr. Kenneth Ottenbacher suggested developing a device or method to eliminate birth defects and deaths related to oxygen deprivation.

Dr. Gordon agreed with the need to identify early biomarkers for PCOS, which is a common condition but is not commonly diagnosed, because it is hard to come to a consensus on what it is and because there are so many morbidities that can lead to mortality. She also seconded the need to understand the addiction to devices and what that means for child and adolescent long-term health.

Dr. Bianchi said that the Council feedback has been enormously helpful. She emphasized that the plan is still a draft document and will incorporate suggestions. Dr. Bianchi said that there appears to be confusion regarding Research Theme #5 (improving health during the transition from adolescence to adulthood) and Research Theme #4 (identifying sensitive time periods to

optimize health interventions). She asked whether the Council would recommend that issues related to more typical adolescent development, for example, go into Theme #4 and that Theme #5 focus on issues related to the transition to adulthood.

Dr. Gordon agreed with Dr. Bianchi's suggestion to bring more clarity to the two themes, because it would bring the whole spectrum of exposure, even through the fetal period, into Theme #4. She noted that transition is such a huge issue in itself that it deserves its own theme.

Dr. Bianchi said that the next day, the Council would hear more about the NICHD operational planning process and the process by which the scientific FOAs are created. This would be discussed in the concept clearance session. Once these "warp" (scientific) themes have been decided, then as staff members bring forth concepts we can ask whether areas such as nutrition, health disparities, or global health have been addressed.

Dr. Tabin said that the plan is a matrix with only one axis labeled. Once the other axis is labeled, the staff can work better at the intersections.

Dr. Shriver suggested that in considering the various themes and goals, such as Theme #6, people might be more inspired if they can see what the picture of success is, not just the picture of inquiry. Perhaps a category about hoped-for progress in each of these areas should be added.

Dr. Bianchi thanked the Council for the rich discussion and the staff for all the hard work, which will inform what will be a transformative plan.

VI. DAY ONE ADJOURNMENT

Dr. Bianchi adjourned the first day of the meeting at 4:30 p.m.

VII. DAY TWO

VIII. DAY TWO CALL TO ORDER AND INTRODUCTORY REMARKS

Dr. Bianchi called the meeting to order at 9:00 a.m. She announced that to inform the revision of the mission and vision of NICHD, a working group composed of two members of the NICHD Advisory Council (Dr. Gordon and Ms. Lesli Rotenberg) and one member of the National Advisory Board for Medical Rehabilitation Research (Richard Ellenson) had been created. This group will work with NICHD staff to propose new mission and vision statements and bring the outcome of their discussion back to the full Council at the June meeting for consideration and a final recommendation to the Director.

IX. UPDATE ON RESEARCH CAREER DEVELOPMENT AND NEW INVESTIGATORS

Dr. Bianchi introduced Dr. Dennis Twombly, NICHD Deputy Director of Extramural Policy.

Dr. Twombly said that NICHD uses a number of funding mechanisms, including individual National Research Service Award (NRSA) fellowships (F30, Diversity-F31, Parent F31, and F32), institutional training grants (T32 grants, which go to departments or institutions to support about six slots), individual career development awards (K01, K08, K23, K24, K25, and K99-R00, which are individual mentor awards), institutional career development awards (K12 programs, which, unlike the other K awards, give funding to institutions, which then choose the investigators), and T15/R25 education grants. The key indices in evaluating the awards are funding commitments, numbers of awards, success rates, and outcomes of former fellows and

trainees. Dr. Twombly noted that NICHD had undertaken a review of its formal training programs in 2015 and that the recommendations were approved at the Council's September 2015 meeting.

The various fellowships and career awards are designed to take the recipients from the training stage as graduate and medical students (T32, F30, Parent F31, and Diversity-F31), through their postdoctoral transitions (T32, F32, Intramural Research Training Awards, K99-R00, and K12), and on into the time when they become independent faculty members (K01, K08, K23, and K25).

In the transition stage, the K99-R00 award is a particularly popular pathway to independence, because it is a two-phase award: Once investigators get a job, their institution can apply for the R00 part of the award, thus providing these young investigators with their first independent grant. In the transition phase, the K12 is awarded as a two- to four-year grant. In the independent stage, NICHD limits its K01 awards to rehabilitation research, child abuse and neglect, and population research in order to bring these fields along. Similarly, the K08 and K23 awards are for physician-scientists and require that applicants have clinical credentials to be considered.

The NICHD training budget ranges between 6% and 8% of the extramural budget. Between 1990 and 2014, NICHD committed more money to K12 grants than to individual K grants. An FY 2014 comparison with other institutes found that NICHD was investing a significantly larger proportion of funds in K12 awards (38.3%) and a significantly smaller proportion of funds in individual K awards than other Institutes were.

In light of these findings, NICHD decided to maintain its overall training commitment at approximately 6% of the extramural budget but to realign its training programs in keeping with its 2015 review and NIH biomedical workforce and physician-scientist workforce recommendations. For NRSA programs, NICHD now (as required by NIH) supports all fellowship mechanisms, including F30 and Parent F31; has increased success rates for individual F31 and F32 fellowships, which had fallen to a very low 10%; and has increased the relative proportion of individual fellowships versus institutional training grants (T32). For career development awards, NICHD has increased K08/K23 salary awards to $100,000, increased success rates for individual career development awards, increased success rates for the K99-R00 program from 16% in 2014 to 36% in 2018, and increased the relative proportion of individual K awards versus the institutional K12 awards.

To accomplish these changes, NICHD reduced K12-allocated slots as they came up for renewal and shifted funds from K12 to individual K awards. This has been a critical change, because when potential applicants saw low success rates, they were not motivated to apply. NICHD is now seeing more interest from applicants. More slots are being taken from the institutional T32 grants and being moved to individual fellowship awards, where success rates are better. NICHD paylines have also been enhanced for Early Stage Investigators (ESIs), an ESI being defined as "an R01 applicant who is within 10 years of receiving a terminal doctoral degree or end of clinical training and has not yet received a major independent NIH grant as a PD/PI." There has been a dramatic increase in NICHD awards to ESIs, from approximately 30 in 2017 to more than 60 in 2018, with a commensurate increase in ESI-awarded direct costs, from approximately $20 million to $40 million.

Finally, Dr. Twombly described the NIH Extramural Loan Repayment Programs under which, for qualifying research areas, NIH repays 25% of qualified debt per year, up to a maximum of $35,000, and covers the resulting taxes. The debt must exceed 20% of the base salary. In 2018, NICHD funded 100 of these awards at a cost of approximately $5 million.

Council Discussion

Dr. Boninger said that there had been some discussion that the K12s were needed because of a shortage of physicians in the rehabilitation area. There might be a misconception in the rehab world that the four rehab K12s will no longer be funded after this last cycle. Dr. Boninger asked whether there is a criterion being used to decide the institute's needs with regard to K12s and how close NICHD is to hitting its target. He noted that the rehab grants are unique, because they are focused not only on physicians as clinicians but also on occupational and physical therapists. Dr. Twombly said that there were eight K12 programs overall. In the case of the rehab group, the four K12s were merged into one Request for Applications (RFA), with a slight reduction in slots, but he was not aware of the long-term plan for NCMRR. Alison Cernich, Ph.D., who was present at the meeting, said that NCMRR is also looking at these data and can look at them again to see what the trajectory with the K12s and the individual Ks is. NCMRR is also looking at new models, such as funding opportunities for early career R03s that will get pilot data for an R01. NCMRR is trying to expand its career awards outside of K12 awards and make clear to the community that the K12 program, which is coming up for renewal soon, might not continue to be funded, but this is still being evaluated.

Dr. Dorn asked, for ESIs who are within that terminal degree stage, what the metrics are for deciding to bring in more individuals for funding who are within that window. Dr. Twombly said that the intent was to bring the success rate for ESIs closer to that of experienced investigators. He asked Ms. Alexis Clark, NICHD Budget Officer and Chief of the Financial Management Branch, to comment on those metrics. Ms. Clark said that R01s are the only grants that count for ESIs. An investigator could be an ESI and get an R21 grant, which does not take away preferential status. The investigator can hold onto that grant until receiving an R01 equivalent grant. NICHD Branches now have more funding discretion since the process was changed from a very strict payline to a pool. The pool is somewhat similar to payline percentile allocations, but because of the NIH Next Generation Researchers Initiative and the emphasis on ESIs, NICHD has broadened its score range. Now NICHD has included funds for ESIs up to the 25th percentile, and it is expected that Branches will fund these ESIs or explain why not. There is no mandate to fund ESIs if there are concerns with the science or other portfolio concerns, but Branches have been provided with money to fund ESI grants.

Dr. Butte noted that it was mentioned that because of low success rates, researchers became discouraged and did not apply for grants. He asked whether these applicants went to another institute or simply did not apply at all. He wondered whether the actual applicant numbers have ever gone down. Dr. Twombly said that applications for career awards have gone down in the past few years due to discouragement. Generally, if there is no T32 or K12 program, people either are supported by their mentors or do not apply.

Dr. Hann noted that one of the fears is that these young investigators will get discouraged and leave research, which is not a problem unique to NICHD. NIH has acknowledged the problem and has set a high expectation for ICs to support new investigators.

Dr. Butte asked what percentage of trainees never gets a major award of any kind. Dr. Twombly said that this is hard to generalize. As part of the analysis of these programs, NICHD looked at outcomes of fellowship and other recipients. Of those who had individual K awards, 80% applied for funding and were successful. Those in the K12 award category did not do anywhere near as well. The reality is that the individual K awards for physician-scientists were instrumental in their success at becoming independent investigators. Those with F31 and F30 fellowships did pretty well. Individuals with F32 fellowships had very good outcomes. The T32 programs are mixed, with only some having good outcomes. The struggle is with how much time is needed to

support these young investigators and with what mechanisms to keep them in the research program.

Dr. Bianchi said that the overall commitment of NICHD to training has not changed but that how NICHD spends its money on training is changing as NICHD considers the best mechanisms to make young investigators successful.

X. HEALTH AND DEMOGRAPHIC DISPARITIES IN RECOVERY FROM HURRICANE KATRINA: THE KATRINA@10 PROGRAM—WITH A SPECIAL FOCUS ON VIETNAMESE AMERICANS

Dr. Bianchi introduced Dr. Mark VanLandingham, Thomas C. Keller Professor and Director of the Center for Studies of Displaced Populations at the Tulane University School of Public Health and Tropical Medicine.

Dr. VanLandingham said that the Katrina@10 research program is an interrelated set of three primary data collection projects from him and two other researchers (Dr. Mary Waters and Dr. David Abramson) that focus on specific subpopulations that were uniquely affected by Hurricane Katrina. The program explores how the trajectories of long-term recovery differ among these subpopulations and compares these trajectories with those of well-studied mainstream populations. The program also looks at how the effects of predisposing factors (such as poverty) and degrees of impact (such as flooding depth) differ among the three subpopulations and seeks to elucidate the determinants of long-term recovery in domains such as mental and physical health, socioeconomic status, and community and social roles. The program will determine how well its theoretical model predicts recovery across its three cohort studies. Strengths of the program include its breadth (two studies focus on the entire city and region), its depth (three cohort studies of uniquely affected populations), the data (longitudinal for all three cohorts with pre- and post-exposure for two cohorts), the duration (short-term [1- to 2-year], medium-term [5-year], and long-term [10-year] perspectives), and a very experienced team.

The five studies in the P01 include Resilience in Survivors of Katrina Projects (RISK), Gulf Coast Child and Family Health Study (GCAFH), Broad Impacts (Displaced New Orleans Residents Study Analysis), New Demographics (NEW NOLA), and Katrina Impacts on Vietnamese Americans in New Orleans (KATIVA NOLA), which is the study that Dr. VanLandingham co-leads with Dr. Mai Do. Dr. VanLandingham gave a brief summary of the first four studies before more fully describing KATIVA NOLA.

KATIVA NOLA began as a study of how immigrants fared in America. People who decide to migrate are not random; they exhibit certain characteristics. In 2003, 709 Vietnamese nationals and immigrants were surveyed to examine the impact of emigration on health status. In 2005, 125 Vietnamese immigrants were interviewed before Katrina and then re-interviewed after Katrina to assess post-disaster recovery. The illustrative finding was that the trajectory of post-Katrina recovery for Vietnamese Americans is much stronger than for similarly affected groups. Why did the Vietnamese Americans do so well? Why were they able to remain resilient and move on to recovery? Dr. VanLandingham suggested that culture, described by social scientists as “the symbolic system of beliefs, values, and shared understandings that render the world meaningful and intelligible for a particular group of people,” could be the missing piece that explained this resilience. Being Vietnamese American made them part of a community with a shared history that provided perspective. They had a history from their parents and grandparents of surviving and overcoming great challenges and a frame of insularity with a strong distrust of

government and corporate institutions, having lived with bad government in Vietnam and being used to doing things on their own.

Dr. VanLandingham said that the next steps for the study are to try to quantify and operationalize culture in terms of how cultural consensus and the perceived benefit from affiliation with a particular ethnic group lead to community resilience and on to recovery from disturbing events. The study will also be expanded to focus on cognitive decline among Vietnamese American elderly, in collaboration with the National Institute on Aging (NIA).

Dr. VanLandingham thanked NICHD for its support of demography and other social sciences and said that interdisciplinary and longitudinal approaches are crucial for successfully studying how major disasters affect health and development.

Council Discussion

Dr. Shriver asked for more information about how the subpopulations were identified and selected, how children were chosen, and whether there were any with special needs. Dr. VanLandingham said that each of the three cohorts is collecting the same data and that there is a children's module. For the two studies with pre-Katrina participants, those participants were opportunistic and chosen for different reasons unrelated to children. Dr. Shriver asked whether there is any monitoring or selection of children with special needs. Dr. VanLandingham said that the researchers are collecting data on children moving forward and are monitoring how the children are doing, including children with disabilities. Dr. Shriver said that it would be helpful if Dr. VanLandingham would forward more information on this.

Dr. Constantine Stratakis asked whether repeated exposure to trauma builds resilience, how to balance what happens post-trauma with the need to build resilience, and whether there is any concern that the next generation of Vietnamese Americans, who have not been exposed to adversity, will not respond the same way. Dr. VanLandingham said that he was very interested in the trauma part, noting that before Katrina, many terrible things had happened to this population. However, his Vietnamese American colleagues talked him out of exploring the trauma piece, fearing that participants would find it too hard to discuss, so this was a missed opportunity. There are two hypotheses about earlier trauma: It either makes people resilient or depletes their reserves. Those trauma questions are certainly being asked now.

Dr. Stratakis asked how the next generation of Vietnamese Americans would change. Dr. VanLandingham said that the study came at the right time for the Vietnamese American community, because it was a solidified community. If Katrina had happened a generation later, the community would be much more Americanized; but at the time, it was very much a Vietnamese community. Dr. Stratakis noted that this research has implications for researchers on how to deal with kids who have been exposed to trauma, how they build resilience, and how they deal with trauma. The answers are as yet unknown.

Ms. Rotenberg congratulated Dr. VanLandingham on his collaboration with other researchers and scientists and wondered whether any further collaborations are being considered. She noted the research of Dr. Nadine Burke Harris on adverse child experiences, which has many connections to Dr. VanLandingham's research. Ms. Rotenberg suggested that it would be interesting to follow up on the idea of the "cultural assets" that specific subpopulations bring to dealing with resilience, and she asked whether other connections are being made with other researchers looking at these issues. Dr. VanLandingham said that he had contacted a physician who is now working on Alzheimer's disease in the Vietnamese American community.

X. VOICE OF THE PARTICIPANT

Dr. Bianchi introduced Ms. Cam-Thanh Tran to provide the voice of the participant. The Advisory Council regularly asks participants to speak at the meeting.

Ms. Tran said that the Vietnamese American community in New Orleans East shares a special bond because they all originally came from northern Vietnam before relocating to South Vietnam to escape religious persecution after Vietnam was divided into two states. In 1975, after the fall of Saigon, they left their villages along the coast of South Vietnam and came to the United States, settling into a community in east New Orleans at the invitation of the Catholic Church.

After Hurricane Katrina hit, most Vietnamese Americans evacuated to Houston, Dallas, or Atlanta. During this time, Father Vien Nguyen, pastor of their New Orleans Catholic church, traveled to these cities to visit his parishioners. The priest wanted the people to come back, and he promised them that there would be a mass every Sunday at 10:00 a.m. People began to drive back for this mass, after which Fr. Nguyen would offer lunch and strategize with his parishioners about what to do next. They decided to pool their efforts and talents and return to rebuild their community. They faced challenges in getting water and energy turned back on and having to live in tents, because the Federal Emergency Management Agency (FEMA) would not provide trailers. A major setback—when the mayor used his executive power to open a landfill close to the community—became a galvanizing moment, which brought the community together as the elders and youths stood together as one community to protest FEMA's decision. After Katrina, two strong organizations, the Community Development Corporation (CDC) and the Vietnamese American Young Leader Association, were formed to meet the needs of the community.

Ms. Tran introduced herself to the Council. Her family came to the United States in 1975. She grew up in Denver, became an elementary school teacher, and got married. After Katrina hit, she and her husband, who was from New Orleans, went to help his family rebuild. She volunteered at the church, became a part of the founding staff of the CDC, and was a project manager in charge of opening a charter school and a cultural center. When Dr. VanLandingham arrived in 2010, he recruited her as a project manager, and now she is the Assistant Director of the Center for Studies of Displaced Populations at Tulane University.

Ms. Tran says that she acts as a "cultural broker" for KATIVA NOLA, doing various community outreach events to keep participants motivated and informed and show appreciation for their participation in the study. KATIVA NOLA sends culturally appropriate Tet cards to all respondents and collaborators to celebrate the Vietnamese Lunar New Year, engages in community service, and recently organized an exhibition celebrating the notable Vietnamese American women in New Orleans, a population that does not get a lot of recognition. KATIVA NOLA takes every opportunity to "toot its own horn" with newsletters and outreach about its accomplishments and involvement with the community.

A cultural broker can help mitigate mishaps, such as a recent incident in which Dr. VanLandingham asked Ms. Tran to review a brochure to be sent to the Vietnamese American community. The picture on the front was inadvertently culturally inappropriate, appearing to be an image from a communist propaganda poster promoting hard labor; the cover was then made more culturally appropriate.

Ms. Tran concluded by suggesting that a cultural broker builds bridges to connect two different cultures and find commonality through respect and understanding. She encouraged investigators who are working with a different culture to use a cultural broker who understands the culture and can help calm ruffled feathers and solve problems.

Council Discussion

Dr. Sohn opined that second-generation children are generally more assimilated and are essentially cultural brokers in their own families. She asked how Ms. Tran interacts with the second generation and what role they play in the research. Ms. Tran said that she always tells members of the younger generation that they need to learn their history by interviewing their parents and grandparents. They might complain that their grandparents do not like to talk about things, but the reality is that when the door is opened, the grandparents are very forthcoming. Ms. Tran offers help on how to interview, which can be as simple as asking, "What happened in Vietnam while you were growing up?" It is very important for the younger generation to be in touch with the older generation.

Dr. Shriver said that sometimes the challenge is in how to change the culture if there is a negative perception about something or someone. He asked how the Vietnamese American culture perceives children with intellectual or developmental disabilities and whether there is a strategy to help shift the culture if that is called for. Ms. Tran said that the key is having understanding. There used to be a taboo about having a disabled child, and family members would hide the child, sometimes because they felt that they were to blame and sometimes to protect the child. Now they are educated to understand that having a disabled child is normal and that the child must be helped to be part of the community.

Dr. Bianchi thanked Ms. Tran and said that this shows the importance of cultural brokers to research.

XII. OVERVIEW OF THE NICHD INITIATIVE PLANNING PROCESS

Dr. Hann provided an overview of the NICHD Initiative Planning Process, which, internally at NICHD, is called operational planning. The NIH budget dedicates about 20% of the budget to research project grants for targeted research, with the majority of the budget going toward investigator-initiated research. In comparison, NICHD funding for extramurally targeted research in 2018 was about 10%.

The planning process begins with a concept, which describes the basic purpose, scope, and objectives of a potential solicitation of grants or contracts. This typically involves NICHD setting aside funds to stimulate research in a defined area to accomplish specific objectives.

Concepts come from a variety of sources, including Program Officers who identify scientific needs; internal conversations that identify gaps; public health needs; priorities important to NIH, ICs, and Branches; review of portfolios to identify where new initiatives are needed; and meetings, both internal and external, to discover concepts that will stimulate the field. In considering the initiatives that come out of this wide-ranging process, NICHD looks at the goal of the initiative, whether it addresses a gap or represents a recurring issue, the cost and the type of grant mechanism needed, and whether it is something that NICHD should fund or is better suited to one of the other ICs.

It is typically a two-year process to bring an initiative to its final stages. Once a concept or idea has been developed, it is presented at the operational planning process for approval or disapproval to proceed. Initiatives that are approved are brought to the Council. If an initiative is approved, an FOA is prepared. This is a complicated and time-consuming process. The FOA is vetted at multiple levels of the institute before being sent to the NIH Office of External Research (OER) for further vetting. The FOA must be "on the street" for 60 days, which is considered the minimum amount of time needed for an investigator to prepare a decent-quality application. Peer

review takes several months, after which the initiative comes back before the Council for review in closed session and then to the NICHD Director for approval to fund. During this two-year process, there are multiple opportunities for input and modifications of the initiative. There could be breakthroughs that change the landscape of the particular science, or there could be governmental changes that affect the initiative.

Initiatives are prepared by program staff and presented to leadership and all staff at biannual operational planning meetings. In late spring 2019, NICHD will hold meetings for FY 2021 initiatives. Usually 20 to 30 initiatives are presented and evaluated based on the clarity of the goal, the extent to which it addresses an important gap or opportunity, the extent to which it is a Branch or NICHD priority, and what funds are needed.

Council Discussion

Dr. Krugman asked why the Council does not see the initiatives that do not make the cut. Dr. Hann said that it is not that simple. Some initiatives are being reconsidered and are not actually dead. Sometimes the idea is something that NICHD wants to encourage but not fund at this time. Usually, if there is a passionate idea, it will not be summarily dropped.

Dr. Krugman asked how one feeds into the mechanisms for generating initiatives beyond coming from Program Officers. Dr. Hann said that the ideas come from a very wide range of sources and then are considered internally on the described pathway to concept clearance. Program Officers get ideas from everywhere, including from looking at progress reports in the portfolio and seeing what needs to be done.

Dr. Bianchi said that although NICHD commits a certain amount of research funds to targeted research, the Council is empowered to ask whether it is really needed at this point. This is a very serious responsibility of the Council, because that decision is what can make less money available for investigator-initiated research.

XIII. NICHD INCLUSION DATA

Dr. Eugene Hayunga reported that the NIH Revitalization Act of 1993 (the Act) requires that the Advisory Council of each IC comment on how the IC has complied with the section of the Act requiring that the NIH Director "ensure that women and members of minorities and their subpopulations are included in all human subject research" by including them in Phase III clinical trials, not allowing cost to be an acceptable reason to exclude them, and initiating programs to recruit these populations into clinical studies.

Dr. Hayunga gave a brief summary of the *Triennial Advisory Council Report Certifying Compliance with the NIH Policy on Inclusion Guidelines* for 2016–2018, which was included in the materials for the Council's consideration and will be posted in the public record.

Dr. Hayunga gave an overview of enrollment in FYs 2016, 2017, and 2018. In FY 2018, NICHD had 1,121 research projects, of which 30 were Phase III clinical trials, which is similar to the other two years. In FY 2018, the total enrollment in all NICHD extramural and intramural research projects was 1,293,100 individuals, of whom 778,357 (60.2%) were women, which is a similar percentage to those of the previous two years. The large percentage of females is due to the number of female-only trials. Enrollment data for FY 2018 by race and ethnicity also showed substantial inclusion of minorities. Dr. Hayunga cautioned that the ethnicity data are aggregate data, so they do not compare with U.S. data. The inclusion of women and minorities is based on self-identification, which accounts for those individuals listed as "unknown."

Dr. Hayunga said that the report also highlighted inclusion policy changes related to the 21st Century Cures Act, research related to intellectual and developmental disabilities, health disparities research, intramural research, and projects and publications addressing sex/gender and racial/ethnic differences. For the future, NICHD will continue monitoring, with attention to milestones required for projects. NIH will analyze and display enrollment data using Research, Condition, and Disease Categorization (RCDC) terminology and will gather more detailed data on the inclusion of children across the lifespan.

Dr. Hayunga concluded by noting that the data clearly indicate substantial inclusion of women and minorities across a broad spectrum of NICHD-supported research. He added that the NIH inclusion policy is science-driven to ensure that results are generalizable to all populations. It is based on ethics and justice so that all groups share in the benefits of being included in research.

Council Discussion

Dr. Boninger asked how many studies either cannot recruit women or minorities because of scientific considerations or are studies that have this type of diversity recruitment as a specific goal. Dr. Hayunga said that there are no data on studies with recruitment of women and minorities as a specific goal. However, not recruiting women and minorities is a key feature of peer review, and such studies would be flagged and not given an award until that issue is resolved. This would also be reflected in the review score. Some might argue that there is no need to include these populations in studies where it is known that there is no difference between, for example, men and women in the particular science being studied, but those studies would still be encouraged to include these populations as a matter of general justice.

Dr. Boninger said that it would be important to see that peer review really does move the needle for recruitment of minorities and women, and he suggested that it would be interesting to have some data on the percentage of studies affected. Dr. Hayunga said that the numbers were never bad to begin with. When this requirement was instituted in 1994, some editorials opined that it would bring research to a halt. In reality, the data showed that far more than 90% of applications were already in compliance.

Dr. Pursley noted that in the FY 2018 data by race, 14% of individuals were identified as "Unknown, Not Reported," and he asked what barriers might account for this lack of self-identification in a certain demographic group. Dr. Hayunga said that there are not specific data on this, but it might be useful to look at individual studies where people might not want to be stigmatized by a particular disease. This could be looked into further.

Dr. Shriver asked why the two sections in the report on intellectual disabilities are separate. Dr. Hayunga said that they are not separate but were included that way to highlight different things. Dr. Shriver asked how intellectual disabilities relate to the overall inclusion compliance data. Dr. Hayunga said that this would require a deeper dive into the data. There is a new analytical tool that should facilitate the ability to pull out specific studies using the RCDC codes.

Dr. Shriver asked what it would take to have people with intellectual disabilities added to the inclusion guidelines along with women and minorities. Is it a matter of legislation, scientific consensus, advocacy, or a combination thereof? Dr. Hayunga said that inclusion is a priority for NICHD and his office continues to look at this group. The report presented today is based on the legislative requirement for inclusion of women and minorities, but people with intellectual disabilities are a matter of great interest to NICHD and will be followed with or without legislation. Dr. Hann added that the intent is to use this new tool to analyze the research on the

population with intellectual disabilities and see how it compares with the inclusion of women and minorities.

Dr. Butte said that his understanding is that this covers recruitment into studies but not samples in biobanks or data already accumulated. Dr. Hayunga says that this report is about prospective studies. Dr. Butte asked whether this framework was still the right framework for NICHD to capture people who are chronically underrepresented in research. Dr. Hayunga said that NIH is about scientific discovery and finding gaps in scientific knowledge. NIH is sensitive to the interests of various groups and operates within that context.

Dr. Butte asked whether there is an NIH-wide framework that continually updates this process. Dr. Hann said that there are groups at NIH, such as the Office of Research on Women's Health (ORWH), Office of Extramural Research (OER), and the National Institute on Minority Health and Health Disparities (NIMHD), that have a coordinating committee to try to develop additional tools. Nevertheless, congressional legislation is the fundamental piece, and in this report, NIH is specifically trying to show compliance with congressional mandates.

It was moved and seconded to approve the *Triennial Advisory Council Report Certifying Compliance with the NIH Policy on Inclusion Guidelines* for 2016–2018. The motion passed unanimously.

XIV. CONCEPT CLEARANCE REVIEW AND DISCUSSION

NICHD staff presented the following concepts for review:

Repository of Mouse Models for Cytogenetic Disorders (Dr. Melissa Parisi, Intellectual and Developmental Disabilities Branch). Dr. Bookheimer asked how many mice would be required and whether this is a very long-term project. She wondered whether, although it is restricted to Down syndrome, it could be expanded to other very important disorders for people with intellectual developmental disabilities. Dr. Parisi said that this repository already exists and has been funded for about 20 years. Currently, the number of strains available for Down syndrome is about six, three or four of which are in active production and are being distributed on a regular basis to investigators, with an emphasis on investigators who are NIH-funded and who get the mice for free. Whether it can be expanded to other disorders is a consideration. Right now, it is limited to Down syndrome because of the demand for the mice and the large investigator community that focuses on Down syndrome. New strains of mice that have recently been developed may prove to be better models for some of the Down syndrome-related projects that are under development.

The next four concepts were about the INCLUDE project. Dr. Parisi gave an overview of each project, saying that this is a transformative research award for Down syndrome, which has not been well-studied. This is a trans-NIH initiative to study trisomy 21, with 18 ICs involved in this project. NICHD is serving as the Institute of record for clearance of these initiatives on behalf of all other Institutes.

INCLUDE Project Transformative (Dr. Parisi, Intellectual and Developmental Disabilities Branch). Dr. Sohn asked whether, given that NICHD is acting as the institute of record for these concepts and clearly will be taking a leadership role, the NIH Director is providing additional resources to NICHD to support this. Dr. Hann said that additional resources are being provided.

INCLUDE Project Clinical Trial Readiness Awards (Dr. Parisi, Intellectual and Developmental Disabilities Branch). The Council members had no questions about this concept.

INCLUDE Project Clinical Trials for Co-Occurring Conditions in Down Syndrome (Dr. Parisi, Intellectual and Developmental Disabilities Branch). Dr. Butte, noting that this is a massive enterprise, asked whether any of these data are going into one single place where investigators will be able to learn from open data. Dr. Parisi said that the INCLUDE project is modeled on the Cancer Moonshot, so requirements for any successful application will include broad, extensive, and early data sharing. This data sharing will be facilitated through FOAs that will include specific, targeted initiatives related to data sharing coordination. The intent is to build on and leverage existing NIH resources for data coordination, harmonization, and sharing. Several workshops are planned for 2019, including one focused on building a cohort for Down syndrome participants across the lifespan, and these data sharing issues will be an important focus of that workshop. Dr. Butte noted that many clinical trials fail and that it is important to know why they fail, so data sharing is very important. Dr. Parisi said that one of the reasons that prior clinical trials in the Down syndrome community have not been successful is that they have been small, with inadequate sample sizes. There is also a significant placebo effect, which, in some cases, has masked potential subpopulation responses to given drugs. Another workshop planned for 2019 is for identifying strategies that will be successful. There are also a couple of beneficial resources available to the NIH community, such as the NCATS-supported recruitment and trial innovation centers that are part of the Clinical and Translational Science Awards (CTSA) Program and the DS Connect registry.

INCLUDE Project Competitive Supplements for Research in Down Syndrome (Dr. Parisi, Intellectual and Developmental Disabilities Branch). The Council members had no questions about this concept.

Data Sharing for Demographic Research (DSDR) Infrastructure Program (Dr. Rebecca Clark, Populations Dynamics Branch). Since this is a reissue, Dr. Butte asked whether there is a group that has this already. Dr. Clark said that there is, but it is an open competition, and there was one competitor last time. Dr. Butte asked why DASH would not do that. Dr. Clark said that all DSDR holdings are cross-posted on the DASH portal. DASH does not have the capacity to provide the kinds of services that DSDR requires, but any contractor interested in applying for the RFA is welcome to do so. There are human subjects protection and privacy considerations. If NIH or an NICHD contractor held these data, the holder would be required to provide the data in response to the Freedom of Information Act (FOIA). The original investigators and their institutional review boards (IRBs) will not allow these highly sensitive data to be stored in a repository that is subject to the FOIA. Dr. Wong asked whether this is an NIH-wide initiative. Dr. Clark said that other institutes do have their repositories. This archive for NICHD is mostly demographic research and includes almost anyone from NICHD who wants to deposit NICHD-related data, and the Child Development and Behavior Branch does deposit considerable data. Dr. Wong asked whether there is an intention to use best practices from other institutes to overcome some of the contractor issues. Dr. Clark said that those discussions do occur, particularly with NIA. This is an RFA for an R24 grant, so some of those protections are built into the grant mechanism. The current holder of the grant does amazing work on deductive disclosure and mitigating risk and has a strict data use agreement with significant punishments for people who leak private data. A federal government entity could not write a data use protection like that.

Study of Pregnancy and Neonatal Health (SPAN) (Dr. Edwina Yeung, Division of Intramural Population Health Research). The Council members had no questions about this concept.

Obstetric-Fetal Pharmacology Research Centers (OPRC) (Dr. Zhaoxia Ren, Developmental Biology and Structural Variation Branch). Dr. Sohn asked how the investigators choose which

drugs to study. Dr. Ren said that this is a renewed initiative. The applicants propose concepts in line with priority guidelines and identify critical scientific needs.

Contraceptive Clinical Trials Network Sites for Male and Female Contraceptive Development (Dr. Diana Blithe, Division of Intramural Population Health Research). Dr. Krugman asked whether this was part of the Cures Act.

U.S. Children with Perinatal HIV Who Were Born Internationally (Dr. Bill Kapogiannis, Maternal and Pediatric Infectious Disease Branch). Dr. Sohn asked whether issues such as undocumented families and delays in access to care are included. Dr. Kapogiannis said that this would include populations who have challenges with status.

Pediatric HIV/AIDS Cohort Study (PHACS) 2020 (Dr. Denise Russo, Maternal and Pediatric Infectious Disease Branch). The Council members had no questions about this concept.

Council Discussion

Each of the concepts was approved unanimously.

XVI. CLOSING REMARKS

Dr. Bianchi adjourned the meeting for lunch prior to the closed session.

XVII. DAY TWO 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).

Update: Division of Intramural Research (Closed to Extramural)

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 412 primary applications requesting $111,777,583 in direct costs and $153,332,406 in total costs.

Remarks

XVIII. ADJOURNMENT

There being no further business, the meeting adjourned at 4:00p.m. on Friday, January 25, 2019. The next meeting is scheduled for June 11, 2019.

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

/s/ 4/9/2019

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 Hayunga, Ph.D.
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.