



Eunice Kennedy Shriver National Institute
of Child Health and Human Development

NATIONAL ADVISORY CHILD HEALTH
AND HUMAN DEVELOPMENT
COUNCIL

MINUTES OF MEETING

June 9, 2016

**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
June 9, 2016¹**

The National Advisory Child Health and Human Development (NACHHD) Council convened its 160th meeting at 8:00 a.m., Thursday, June 9, 2016, in Building 31, Conference Room 10, of the National Institutes of Health (NIH) in Bethesda, Maryland. The meeting was open to the public from 8:00 a.m. to 12:30 p.m. As provided in Sections 552b(c)(4) and 552b(c)(6), Title 5, U.S.C., and Section 10(d) of Public Law 92-463, for the review, discussion, and evaluation of grant applications and related information, the meeting was closed to the public from 1:30 p.m. until 4:45 p.m.

Dr. Catherine Spong, Chair, NACHHD, and Acting Director, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), presided.

Council members present:

Dr. Anne Case (virtual)	Dr. Ruth Lehmann
Ms. Barbara Collura	Dr. Stephen Petrill
Dr. Patricia Flynn	Dr. Piero Rinaldo
Dr. Melissa Gilliam	Dr. Frederick Rivara
Dr. Gregory Kopf	Dr. George Saade
Ms. Wendy Lazarus	Ms. Sheila Zimmet

Council members absent:

Dr. Walter Fontera

National Advisory Board on Medical Rehabilitation Research Council Liaison

Dr. Richard Shields (virtual)

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.

Ex officio members present:

Dr. Aaron Lopata, Chief Medical Officer at Health Resources Services Administration

Non-voting Council members present:

Dr. Atul Butte

Dr. Richard Krugman

Dr. DeWayne Pursley

Ms. Lesli Rotenberg

Non-voting Council members absent:

Dr. Timothy Shriver

Others present:

Dr. Della Hann, Director, Division of Extramural Research (DER), NICHD

Dr. Constantine Stratakis, Director, Division of Intramural Research (DIR), NICHD

Members of Staff, NICHD

Members of Staff, NIH

Invited Guests:

Ethan Jorgensen-Earp, American Academy of Pediatrics

Joseph Laakso, Endocrine Society

Craig Fisher, American Psychological Association

I. CALL TO ORDER AND INTRODUCTORY REMARKS

NICHD Acting Director, Dr. Catherine Spong, welcomed Council members, guests, and staff. She announced that the meeting would be open to the public for the morning portion and closed to the public in the afternoon for the consideration of grant applications. The public portion was VideoCast.

A. Review of Confidentiality and Conflict of Interest

NICHD DER Director, Dr. Della Hann, reminded Council members that at the end of the closed session, all members were required to certify that they had not been involved in any conflict of interest situations during the review of grant applications. Advisors and consultants serving as members of a public health advisory committee may not participate in situations in which any violation of conflict of interest laws and regulations might occur. Therefore, Council members may not perform duties or render advice that might have a direct and predictable effect on the interests of an organization or institution in which he or she has a financial interest. In particular, Council members should not participate in the evaluation of grant applications for federal support that will affect the interests of such organizations or institutions. Dr. Hann also advised

Council members that material furnished for review and discussion during the closed portion of the meeting is considered privileged information.

B. Council Minutes – Meeting January 21, 2016

Dr. Hann moved to approve the *Summary of Meeting Minutes* for the January 2016 sessions of Council. The *Minutes* documents were approved unanimously, as written.

C. Future Meeting Dates

The Council agreed to the following future meeting dates:

August 22, 2016 (virtual)	(Monday)
September 21, 2016	(Wednesday)
January 19, 2017	(Thursday)
June 8, 2017	(Thursday)
September 22, 2017	(Friday)

II. NICHD DIRECTOR'S REPORT AND DISCUSSION

News from NIH

A number of new positions have been announced at NIH. Dr. Eric Dishman has been named the director of the NIH Precision Medicine Initiative (PMI). Dr. Dishman previously served the NIH Director in an advisory capacity. Prior to coming to NIH, he was a vice president and fellow of Intel Corporation's Life Sciences Group. Dr. Dishman will start the last week of June.

NIH is seeking a PMI Chief Technology Officer to assist the PMI Director with data challenges. Applications were due June 24, 2016. NIH is funding the world's largest biobank to support PMI; Mayo Clinic was awarded \$142 million to establish a repository and provide infrastructure to store bio specimens.

The position of Environmental Influences on Child Health Outcomes (ECHO) Program Director was awarded to Dr. Matthew W. Gillman of Harvard University. Dr. Gillman has extensive experience leading large cohorts. He will assume his duties July 2016. ECHO is also seeking a Senior Program official to assist the newly appointed Director. Applications were due June 20, 2016.

Applications for the Institutional Development Award (IDeA) were due April 15, 2016. Applications were robust, and grants are to be awarded by the end of the fiscal year. Oversight of these awards fall under Dr. Gillman; NICHD has a special role to play in this as part of the IDeA Pediatric Trials Network.

Dr. Patricia Flatley Brennan, R.N., PhD was named Director of the National Library of Medicine (NLM). She is currently the professor at the School of Nursing and College of Engineering at the

University of Wisconsin Madison. Dr. Brennan has many accomplishments to her credit; this includes developing an electronic network to reduce isolation and improve self-care among home care patients. Dr. Brennan will start in the summer of 2016.

Maureen M. Goodnow, PhD is now NIH Associate Director for AIDS Research and Director of the NIH Office of AIDS Research. She is a professor of pathology and immunology at the University of Florida in Gainesville. As part of her role, she will be working closely with all of the NIH Institutes and Centers to pursue new tools for preventing HIV infection including vaccines, improve treatments and ultimately a cure. Dr. Goodnow will join July 2016.

A Cancer Moonshot Blue Ribbon Panel is being named to help guide Vice President Biden's National Cancer Moon Shot Initiative. It will serve as a working group of the presidentially appointed National Cancer Advisory Board and will provide scientific guidance from thought leaders in the cancer community. There will be an online platform to collect ideas from the public. Dr. Spong encouraged all to submit ideas about cancer research. Cancer Moonshot ideas are due July 1, 2016 at cancerresearchideas.gov.

A working group called the Red Team made recommendations on reducing risk and promoting patient safety at the NIH Clinical Center. The themes from this Red Team report included fortifying a culture and practice of safety and quality, strengthening leadership for clinical care quality, oversight and compliance, realigning authority with responsibility to ensure optimal leadership of the Clinical Center, and addressing sterile processing of all injectable products.

Many of the recommendations will be implemented or are currently being implemented. These include establishing a hospital board and an NIH Office of Research Support and Compliance as well as retaining some companies that specialize in quality assurance for manufacturing and compounding. The recently established hospital board will be led by Laura Ferise, Executive Vice President and Chief Operating Officer, at New York Presbyterian. The NIH Office of Research Support and Compliance will be directed by Dr. Catherine Zoon. Dr. Zoon was previously the Director of the Center for Biologics Evaluation and Research. Additional recommendations from the Red Team included centralizing the authority for intramural clinical care and research and having a leadership team with expertise and experience in hospital management and patient care. To that end, there will be a nationwide search for a physician CEO with this type of experience.

NIH continues to affirm its support of basic scientific research. NIH IC Directors recently wrote a letter in the journal *Science* reiterating this support.

The Gabriella Miller Kids First Pediatric Research Initiative, based out of the Office of the Director, has reissued a previous initiative. The goals of this initiative are to identify samples for whole genome sequencing that will help illicit the contributions to childhood cancers and structural birth defects. Just as with the previous announcement, the clinical and genetic sequence data are going to become part of the Kids First data resource.

NIH conducted a workshop with the Bill and Melinda Gates Foundation this spring. The workshop was attended by Dr. Francis Collins and Mr. Bill Gates. Maternal and child health topics were discussed, and NICHD was heavily involved.

News from NICHD

Dr. Spong was part of a delegation that went to Brazil to meet with a number of health officials about the Zika virus. The delegation included officials from NIH, CDC, and FDA. NICHD staff have been heavily involved in a number of Zika-related workshops and activities. Staff have also been involved with Senate hearings on the matter. For its part, NICHD has released a Rapid Funding Announcement (R21); applications being accepted on a rolling basis began April 2016. The goal is to review applications each month to allow grants to be awarded in a timely manner. Dr. Spong mentioned that the Council will participate in the second level of peer review for these applications electronically, as needed. NICHD has also, in coordination with NIEHS and NIAID, commissioned a multi-site, multi-country cohort study to understand Zika and its role in pregnancy. A workshop to identify strategies for evaluation, management and treatment of children who are exposed to Zika virus in pregnancy is being planned for September of this year. The only local transmission to occur in the United States is in Puerto Rico; all other instances so far have been travel-related. Some modeling done by the Center for American Progress estimated that more than 2 million pregnant women in the United States could be at risk for Zika this summer and fall. As a result, Zika has become a high priority item for NICHD.

A workshop to address opioid use in pregnancy as well as Neonatal Abstinence Syndrome (NAS) occurred April 4-5, 2016. The workshop goals were to address gaps and understand considerations when screening for opiate use in pregnancy. Participants discussed the complications of pregnancy associated with opiate use and the most appropriate treatments for pregnancy, as some of these said treatments do carry adverse sequela. The workshop also addressed how to best manage infants suffering from NAS.

The Human Placenta Project is another major initiative at NICHD; the goal is to understand human placental development, structure, and function in real time. The third annual meeting was held in April and highlighted a number of advances seen over the past two years.

The National Center for Medical Rehabilitation Research (NCMRR) is home to two Presidential Early Career Award for Scientists and Engineers awardees- Drs. Elizabeth Skidmore and Ervin Sejdic. NCMRR also held a workshop May 25 – 26, 2016 that identified gaps, discussed infrastructure need, and emphasized career development opportunities across NIH.

Dr. Spong presented NICHD research that evaluated data sharing by the Institute; Dr. Sarah Glavin and the Office of Science Policy Reporting and Program Analysis (OSPRA) spearheaded this evaluation. The NIH Data Sharing Policy NOT-OD-03-032 has been in place since 2003 and requires a data sharing plan for certain types of applications. The plan can take on many forms- it can follow a request-receive model (where a researcher requests data from the study PI), or PIs can choose to deposit their data in an archive/enclave/website. NICHD developed DASH as a data sharing mechanism to facilitate data sharing for NICHD supported work. To conduct its evaluation of data

sharing at NICHD, OSPRA selected grants that were funded in 2009 to allow for some time for these results to be published. The original applications were reviewed and characterized by their data sharing plan. OSPRA then identified a “main finding” publication and searched for publically accessible data. Of these grants, 78 percent had plans that were compliant and 22 percent had no plan or the plan was not compliant. 99 percent of those who planned to use an archive did. Some grantees that planned to use the request-receive model or had no data sharing plan at all decided to leverage an archive. The actual compliance rate ranged from 60 to 88 percent. Main findings were published an average six to seven years after grants started. All of the 17 studies associated with a clinical research network were compliant- 76 percent of these share data via an archive or website. These data suggest that NICHD is doing a good job with data sharing but there is room for improvement.

NICHD is currently in the middle of a review by the Office of Health Equity. Chaired by Dr. Melissa Gilliam, the working group (comprised by NIH and NICHD staff and others) will help identify critical areas of focus. The final report will be available in September.

The Office of Health Equity currently has an Acting Director, Dr. Jean Flagg-Newton. Dr. Regina James, previous Director, has taken a new position at the National Institute of Minority Health and Health Disparities.

NICHD has successfully moved to 6710 Rockledge Drive. A Council meeting will be held there in the future. Dr. Spong thanked Mr. Rodney Rivera for his work on ensuring a smooth transition.

Budget and Legislative Update

The President’s proposed budget for NIH for fiscal year 2017 includes \$33.14 billion for NIH. This is a combination of mandatory and discretionary funds. NICHD is slated for \$1.338 billion, and it is unclear when the budget will be passed. On June 7, 2016, the Senate Subcommittee on Labor, HHS, Education appropriations reported out a bill proposing funding agencies for FY17 including a \$2 billion increase for NIH. The House has not yet announced when it will take up its version of the bill. If there is a continuing resolution, the Senate still has to agree with the two-year sequestration agreement, which results in less money in FY17 than FY16.

Council Discussion

A question was asked about the search for a new NICHD Director. Dr. Spong responded that the search is ongoing and the decision is with Dr. Collins.

III. REPORT OF THE DIVISION OF EXTRAMURAL RESEARCH

Report of the Director, DER

Staff Updates

Dr. Della Hann presented the DER updates and introduced five new staff members who joined the NICHD Extramural Program: Dr. Karen Lee in the Child Development and Behavior Branch, Dr. Daniel Johnston, Chief of the Contraception Research Branch, Dr. Bill Duval, Division of

Extramural Research, Ms. Barbara Johnson, in the Office of Committee Management, and Ms. Hazel Alsol in the Grants Management Branch. Summer trainees and volunteers include Ms. Ronna Popkin in the Population Dynamics Branch and Mr. Dean Allen in NCMRR.

Two NICHD staff members also transitioned from NICHD Extramural. Dr. Tiina Urv transitioned to NCATS, and Mr. Paul Gresham transitioned to the FDA. Two additional staff, Susan Tolivasa and Carol Sheredos, are retiring.

Funding the Best Science

Dr. Hann discussed funding the best science and started with a presentation on grant application success rates. The year 2003 marked the end of the doubling of the NIH budget. The application success rate was at 30 percent at that time. In subsequent years, NIH grant success rates dropped and have now settled at 18 percent. NICHD follows a similar pattern. The success rate in 2003 hovered at 28 percent and has now dropped to 11.5 percent. The number of awards has also fallen. Dr. Hann reported that the Institute has lost its funding “momentum” since 2003.

Dr. Hann then reviewed the characteristics of scored applications. NICHD’s funding portfolio is skewed in favor of human studies (unlike the rest of NIH). Our requested budgets for grants is also higher due to the fact that the cost of human studies is more expensive at NICHD than the rest of NIH.

Dr. Hann explained that the unique number of applicants applying for funding yields a funding rate. For R01 grants, the number of people applying for NIH grants in any given year is increasing (up 28 percent since 2003); however, the number of awards has dropped, as has the funding rate. A similar pattern is witnessed at NICHD; there has been a 61 percent increase in the number of people applying for R01 grants and yet the number of awards issued continues to decrease.

The same is true of R21 grants. On an NIH level, more people are applying, yet the funding continues to drop (this in turn has resulted in a drop in funding rate). The pattern is more dramatic at NICHD. More applicants continue to apply for grants, while the funding rate at NICHD has fallen to five percent.

Patterns for P01 differed. There was no significant increase in the number of applicants NIH-wide. This was not the case at NICHD. In 2009, there was a dramatic increase in the number of applicants. The award rate remained stable at NICHD. A number of Institutes at NIH are no longer issuing P01s, and the number of P01s being issued has decreased significantly. This represents a shift at NIH.

Dr. Hann presented a slide on paylines that was initially presented in January. The payline has decreased from 28 percent in 2000 to nine percent in 2015, and the application rate continues to rise. NICHD has one of the lowest paylines of the Institutes and Centers that publish paylines. This is not due to changes in scoring over time. When funding practices were compared across ICs, it was determined that NICHD rarely funded beyond its payline. A slide alluding to the number of citations per award by percentile score range showed that applications scored in the

20th and 30th percentiles are, in fact, good science. However, NICHD's current payline is at the 9th percentile. This means that NICHD is unable to fund a lot of good science.

To improve the payline, Dr. Hann recommended tightening referral guidelines and transfer acceptance, communicating priorities, implementing strategic use of FOAs for big projects, and implementing stricter methods for large grant acceptance. Each branch has been developing three to seven priority topics considering developing vision documents, strategic plans, and assessing portfolios. The plan is to post priorities on the website within the next month. This approach will allow NICHD to have a little more flexibility for discretionary funding. NICHD should also assess the acceptance of large grants and participation in FOAs and be more strategic about investments in general.

Fair Labor Standards Act (FLSA)

Dr. Della Hann reported that on July 6, 2015, the Department of Labor produced a Notice of Proposed Rulemaking in order to update overtime rules. The current threshold sits at \$23,660. The proposal suggested that the threshold for overtime be \$50,440.

Dr. Collins had discussions with the Department of Labor regarding this issue. The final threshold number was settled at \$47,476, effective December 1, 2016. Many postdocs will therefore become eligible. In three years, the threshold will be raised again to \$50,440.

NIH has decided to increase stipends for NRSA postdocs so that all of them are at or below the threshold. Extramural institutions must now decide how to manage the rule change.

Council Discussion

Dr. Ruth Lehmann asked Dr. Della Hann if there were any data available on RFAs. Dr. Hann responded that she has yet to investigate RFAs; Dr. Spong mentioned that 25 to 30 percent of NICHD's monies are disbursed as RFAs- other institutes are as high as 50%.

Dr. Stephen Petrill asked a follow-up question about funding the best science and wanted to know how young investigators were impacted. Anecdotal evidence suggests that students are opting out of academic careers. This is an ongoing discussion across the NIH; Dr. Hann suggested that NIH needs to re-evaluate how to train new investigators.

Dr. George Saade asked if NICHD was worried about basic research and if basic science funding will come at the expense of clinical trial research. Dr. Hann replied that both are in fact priority areas for NICHD. Dr. Saade stated that the change in postdoc salaries may negatively impact clinical trial research since these studies tend to cost more money. He added that such studies were badly needed because in clinical areas such as obstetrics, there is no evidence base. Dr. Hann again stated the goal was to maintain balance.

Dr. Ruth Lehmann asked if Dr. Hann's proposed prioritized funding strategy to combat the low payline would come at an expense of basic science funding. Dr. Lehmann is concerned that it may be possible to be too strategic. Dr. Hann says that there must be a balance between research priorities (which will evolve) and basic research. She also affirmed that priority areas will not

close the door on novel research and basic science. However, all activities are ultimately limited by the payline.

Dr. Melissa Gilliam asked for more detailed data on grant applicants. Dr. Hann stated that the data originated from the Office of Extramural Research. Dr. Gilliam would also like a little bit more data on the applicants themselves. Dr. Gilliam added that she would like to know how many of these individuals are re-applicants.

IV. GLOBAL HEALTH UPDATE

Dr. Vesna Kutlesic, Director of the NICHD Office of Global Health (OGH), provided an overview of the NICHD global health research portfolio. OGH leads cross-cutting, interagency global health initiatives in line with NICHD's mission. This includes building and maintaining global health partnerships and collaborations; conveying research evidence relevant to multi-sector global health program and policy development; and assisting the Institute's components in enhancing their international research portfolios.

The United States Government (USG) is the largest funder of global health programs and research in the world, spending approximately 10 billion dollars per year. Dr. Francis Collins, the NIH Director, has identified global health research as one of the five top priority areas of his tenure. A 2013 *JAMA* article by Dr. Roger Glass, Associate Director of Global Health at NIH, discussed the potential benefits to the health of the US population of funding the best peer-reviewed science globally. In FY15, NIH funded 7,195 foreign awards across 24 Institutes and Centers; these were either direct foreign awards or domestic awards with foreign components. NIAID currently ranks first in the total number of foreign awards- NICHD ranks sixth.

NICHD's estimated total dollar and in kind expenditure for foreign awards and other global health activities for FY 2015 was approximately \$115M. This included 286 "foreign" grants and projects in 138 countries (including unincorporated territories e.g., Hong Kong, Puerto Rico, etc.). Approximately 61 percent of the foreign awards at NICHD were R01 grants. Key scientific areas of interest included: maternal, neonatal, and child morbidity and mortality; healthy pregnancy outcomes, reproductive health, family planning; HIV/AIDS (including prevention, mother to child transmission); infections, malaria, tuberculosis, hepatitis B; gastrointestinal diseases, diarrhea in children; food insecurity, nutrition, breastfeeding; and training activities for researchers, physicians, nurses, etc. A more detailed description of NICHD-funded global health research and activities can be found in the 2015 NICHD International Activities Catalog.

Dr. Kutlesic identified several reasons why it is important for NICHD to fund global health research. First and foremost, disease and disability have no borders. Recent health crises, such as the Ebola and Zika virus outbreaks, underscore the unique vulnerabilities infants, children, and pregnant women face during public health emergencies. Fragile health systems worldwide demonstrate the need for capacity building for effective emergency response. Poverty also has an impact on health that can be averted with early, evidence-based interventions.

Dr. Kutlesic then highlighted NICHD global health collaborations, including a new phase of cooperation between NIH and the Bill and Melinda Gates Foundation (BMGF). Mutual scientific

priority areas include maternal and newborn health, contraceptive research, child health and development, pediatric pneumonia and indoor air pollution, HIV/AIDS, malaria, tuberculosis, and HPV/cervical cancers, among others. In addition, NICHD scientific staff has also participated in technical working groups as part of the Public Law 109-95: Assistance for Orphans and Other Vulnerable Children in Developing Countries Act, and the US National Academies, “Investing in Young Children Globally” Forum. Furthermore, in February 2015, OGH organized a NICHD Global Health Consultation on the intersection of child neurodevelopment, nutrition, and inflammation, which included 80 researchers and representatives from multiple NIH ICs, BMGF, HHS OGA, CDC, USAID, WHO, World Bank, Sackler Institute, and Grand Challenges Canada.

NICHD has a diverse global health research portfolio in keeping with the Institute’s broad mission. More recently, this includes the NIH Zika Cohort Study (ZIP), a multi-site, multi-country prospective observational cohort study aimed at assessing the strength of the association between Zika infection during pregnancy and adverse maternal/fetal outcomes, while controlling for potential confounders. NICHD has also issued a rapid funding announcement for Zika virus-related complications. Another example of NICHD-funded global health research includes the Global Network for Women and Children’s Health Research, which supports research aimed at developing cost-effective and sustainable interventions that address the major causes of perinatal morbidity and mortality of women and children in several low and middle income countries. Furthermore, the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network seeks to reduce mother-to-infant transmission of the HIV virus, as well as to evaluate vaccines and pharmacological treatment in several countries. Other NICHD-funded global health research includes the Biomarkers of Nutrition for Development (BOND) Project, Positive Outcomes for Orphans Study, and Partnership for HIV/AIDS Research, to name a few.

Council Discussion

Dr. Patricia Dorn asked about how global health research priorities at NICHD are determined, and whether the NIH grant application process is the same for foreign scientists. Dr. Kutlesic responded that global health research priorities at NIH are determined through a number of different channels including through the White House, Congress, HHS Secretary’s Office, NIH OD and NICHD Directors’ Offices, as well as from NIH scientific staff, the broader scientific community, the general public, among other sources. Moreover, the NIH grant application and peer review process is similar for foreign and domestic applicants, but some research opportunities are only open to researchers who are US citizens.

Dr. Frederick Rivara asked about injuries as a research priority area worldwide. Dr. Kutlesic responded that the global burden of injuries has been identified as an important research priority in recent years. NICHD’s National Center for Rehabilitation Research (NCMRR) and the Pediatric Trauma and Critical Illness Branch (PTCIB) manage research grants related to injury and rehabilitation. Furthermore, in July 2015, NICHD organized a Global Injury Prevention Meeting aimed at identifying research priorities, which included several grantees from the Fogarty International Center’s Global Injury and Trauma Research Training Program.

V. STATEMENT OF UNDERSTANDING

The statement was read by Mr. Bryan Clark. This is an annual requirement. This is an agreement between NICHD and the Advisory Council. To help achieve the goals of the Institute, the National Advisory Child Health and Human Development Council is charged with the responsibility of advising, consulting with, and making recommendations to the Director of NICHD, on matters relating to the research and research support activities and functions of the Institute. The roles and responsibilities of the Council members include secondary review of grant applications, with a focus on NICHD scientific program priorities and program balance.

There are no changes to the text from last year. It is especially important for new members to review. Sections include the following: Council Membership, Structure Secondary Review of Grant Applications (Summary Statements), Administrative Decisions and Actions that Do Not Require Council Recommendation, Options Available to the Council, Expedited Review of Meritorious Applications, Interim Review (that will occur in August of this year), Concept Review (During Open Session), as well as Emergency Procedures.

Council Discussion

There were no questions regarding the Statement of Understanding. Dr. Frederic Rivara moved to approve the Statement. The document approved unanimously.

VI. OFFICE OF SCIENCE POLICY, REPORTING, AND PROGRAM ANALYSIS 101

Dr. Sarah L. Glavin presented on the Office of Science Policy, Reporting and Program Analysis' (OSPRA) role which is to understand, analyze, and report on all of NICHD's activities. This includes extramural and intramural research, research training infrastructure, as well as other activities. Much of the focus revolves around different types of planning, such as research and operational planning and key collaboration. The Referral and Program Analysis Branch receives the grants and identifies applications for certain key topics by coding all the grants. This allows the branch to manage and track grants. While NIH-wide reporting systems do exist, each Institute has nested coding within the larger system to allow for more detailed tracking.

Portfolio analysis data are to identify research gaps, areas of saturation, potential collaborations, trends over time, and research connections. This, in turn, drives administrative and policy initiatives. OSPRA also monitors publications to investigate the impact of NICHD's work. For example, OSPRA monitors training outcomes. Program evaluation, monitoring, and assessment are key activities. For example, the office has recently investigated data sharing, clinical center collaboration, and public health campaigns.

Data are folded into reports for various stakeholders within and outside of the government. Types of reports include scientific category reporting, narrative reports, as well as Congressional justifications. Reports generally go to Congress, NIH, HHS, OMB, the White House, and others.

Council Discussion

Dr. Richard Krugman asked about how he could get in touch with OSPRA. Dr. Glavin says he can email her directly.

Ms. Barbara Collura inquired about the impact of the Congressional ban on embryo research and if OSPRA could accommodate such an inquiry. Dr. Glavin responded that they have not looked at the issue but could investigate to help start the conversation.

VII. ABCD STUDY

Dr. Gaya Dowling, Project Director, presented on the Adolescent Brain Cognitive Development (ABCD) study, which is a study of 10,000 children, ages 9 and 10, whom will be followed for 10 years. The study will assess factors that influence individual brain development trajectories and outcomes. This project was initiated by the National Institute of Drug Abuse, the National Institute on Alcohol Abuse and Alcoholism and the Cancer Control and Population Sciences Division of the National Cancer Institute- all of whom comprise the Collaborative Research on Addiction at NIH, or CRAN. A detailed governance structure, consisting of working groups, an IRB, an external advisory board, and cross-agency committees, has been established.

Dr. Dowling began her presentation describing why this type of research is important. Research objectives include: characterizing individual developmental trajectories; developing national standards for the trajectory of brain development in youth; dissecting the gene vs. environment dichotomy (enhanced by the recruitment of 800 twin pairs) to better understand what factors truly impact development and how; examining the effects of physical activity, sleep, screen time, as well as sports and injuries on brain development; studying the onset and progression of mental disorders and substance abuse; and understanding how exposure to different substances like alcohol, marijuana, nicotine, and caffeine impact developmental outcomes.

Experts came together in 2014 to help develop a framework for this study. After several symposia and RFIs, FOAs were released in January of 2015. Cooperative Agreements were leveraged instead of contracts. 13 awards were disbursed to institutions and centers across the country- there are 19 research sites across the country, with the University of California San Diego serving as both the coordinating center and data informatics center.

In FY16, the consortium was funded at \$30 million, with NICHD contributing \$1 million. Since then, PIs have met and now received IRB approval. Researchers are also refining the protocol and informatics strategy. The ABCD governance structure has also been established. An external advisory board (one of many advisory boards) has also been assembled, in addition to an NIH Collaborators Group that meets monthly. The former is responsible for overseeing the study and reviewing the study protocol and lend scientific guidance. A separate, ABCD Observational Study Board focuses on consent, bioethics, participant burden as well as confidentiality. There are six working groups that focus on substance abuse, health and mental health, culture and environment, as well as biomarkers and mobile technology. Other groups are responsible for recruitment and retention, data quality, informatics, etc. A community advisory group will also be launched.

The ABCD Protocol centers on a school-based strategy for recruitment. The schools are not involved in the study but will be leveraged in order to obtain a demographically balanced sample. Dr. Dowling emphasized the role of the school in parent outreach- the study will partner with several organizations to target the schools. The twin cohort, which will be recruited in

Colorado, Minnesota, Missouri, and Virginia, will be established outside of the school-based strategy.

The ABCD Assessment Protocol includes bio specimens, substance use, neurocognition, mental health, culture and environment, mobile tech and passive data, structural MRI, as well as Resting State and Task-Based fMRI. The key was to assemble assessments in a way that were not over-burdensome for the children. Bio specimens including saliva and blood samples that will be collected every other year. Baby teeth will be collected where possible. Participants will receive neurocognitive assessments at baseline on an iPad. The study will also leverage parental questionnaires.

The ABCD study is committed to an open science model via the NIH Data Archive (formerly NDAR). Raw clean data in addition to curated cleaned data will be released.

Council Discussion

Dr. DeWayne Pursley asked if there are similar studies being conducted. Dr. Dowling responded that there is interest in a “little” ABCD study starting at the neonatal stage. There are a lot of discussions about collaborating with a number of international investigators. Dr. Della Hann mentioned “Add Health” as another source of data.

Ms. Wendy Lazarus commented that toxic stress has impact on brain function and if that element is being incorporated into study. Dr. Dowling responded that stress and trauma in fact part of the study

Dr. Melissa Gilliam asked a question about sampling for homeless youth. Dr. Dowling responded they will be captured but will be a challenge because of movement. Dr. Gilliam then asked about how the study will address sexual identity and orientation and their health needs. Dr. Dowling replied that more questions around this topic will launch after baseline.

Dr. Patricia Flynn stated that she has concerns about the distribution of the sites nationally- specifically the “deep south” that seems to be omitted. Dr. Flynn stated that the poorest youth live in these areas and valuable information will be missed. Dr. Flynn then asked what the site selection was based on and asked if targeted site selection is possible in the “deep south”. Dr. Dowling responded that this was a result of going with a cooperative agreement approach and that sites were based on the location of the applicants, so study organizers were unable to specify sites. Dr. Patricia Flynn requested that the group consider targeting areas in the “deep south”.

Dr. Atul Butte asked when recruitment will start. Dr. Dowling stated that recruitment will start this September. Dr. Butte then asked if this study will sync up with Precision Medicine. Dr. Dowling responded that it is still unclear.

Dr. Stephen Petrill asked about genotyping. Dr. Dowling stated that there is currently no funding for genotyping. That said, they hope to plan for genotyping in the future.

VIII. ZIKA VIRUS UPDATE

Dr. Nahida Chakhtoura started by giving a background on the Zika virus and its discovery in 1947. An outbreak occurred in French Polynesia in 2013 and 2014. In May 2015, the virus arrived in Brazil, and the first case of microcephaly occurred in September of that year. The virus has travelled to other parts of the Caribbean and South America. Chile and Uruguay do not currently have local transmission. It is expected that *Aedes aegypti* and *Aedes albopictus* mosquitos will carry the virus to the United States.

While microcephaly can have multiple causes, data now point to Zika as the causative agent in these cases. There are differing modes of transmission of Zika, including mother to infant, as well as sexual transmission. As a result, the CDC updated its recommendations to address reproductive age women (and their sexual partners) as well as pregnant women. There is range of adverse outcomes including miscarriage, stillbirth, fetal brain abnormalities, and eye abnormalities. Other teratogenic effects of Zika include absent brain structures, fetal brain disruption sequence, cerebral calcifications, brain asymmetry, as well as other neurologic issues. There may also be future neuro-developmental issues in these infants, as well.

Adverse fetal outcomes are not limited to microcephaly; a JAMA Ophthalmology article in February 2016 documented scarring of ocular tissue in all the infants studied. The first cohort study that came about in March 2016 found that of 42 Zika-positive women, 29 percent encountered fetal abnormalities, and 17 percent had microcephaly atrophy or calcification on the ultrasound. This paper also suggested that the risk is not limited to the first trimester.

The diagnostic challenge is that most adults are asymptomatic. The cross-infection with dengue also makes diagnosis difficult. A paper by Dr. Driggers showed that even though the individual was infected at 12 to 13 weeks gestation, she remained positive for up to 10 weeks after that. This is in line with other data from Dr. O'Connor's lab that suggests a longer duration of viremia due to the fetal component. Dr. Nahida Chakhtoura stressed that nothing is known about asymptomatic women at this stage.

The scientific community is trying to understand how Zika kills developing human brain cells; human cortical neural progenitor cells may be the target. Researchers at the University of South Florida found that the virus caused cell death in cortical neural progenitor cells. The virus attenuates their growth causing dysregulation and cell death. Zika also impairs growth in human neurospheres and brain organoids.

A mouse model has been developed. Dr. Michael Diamond has found that Zika caused placental damage and fetal demise in mice. In immune-deficient mice, the fetus usually died after 13 days of life. These models could potentially be used for a treatment vaccine and for further understanding of the infection.

Another group documented results of a Brazilian strain of the virus in experimental models, and they also witnessed cell death. The Zika virus was able to cross the placenta, target cortical progenitor cells, and cause cell death by apoptosis and autophagy.

More studies continue to document Zika and its impact on the placenta. Another group found that type III interferons produced by human placental trophoblasts was able to confer protection against Zika infection. This was case in the full term placenta. Another group from Emory used a

Puerto-Rican strain and found that the Zika virus was able to directly access the placental compartment, causing damage. It is still unclear what the receptor cells are in humans at this time.

There are several theories as to why Zika is exhibiting now. One theory is that the virus itself has evolved over time, or that the new generations of humans are especially susceptible. There is also the question of pre-existing immunity in areas where there is dengue. Research gaps related to Zika include risk of infection in pregnancy, sequelae of Zika exposed and infected infants without microcephaly, diagnostics, and the long-term reservoirs for Zika.

With the help of Dr. Spong, NICHD has launched a Zika PAR-16-106 Rapid Assessment of the Zika Virus Complications (R21). Eight institutes have signed on. There is also the Zika Cohort Study- a multi-site, multi-country prospective observational cohort study to determine the risk of Zika infection during pregnancy on maternal and fetal outcomes while controlling for potential confounders. Ten-thousand women are to be enrolled starting at four sites (additional sites will be added). There will be a standardized protocol and data collection, as well as coordination with NIAID and NIEHS. The plan is to enroll the women during the first trimester- women may or may not be infected at time of enrollment. Symptomatic, asymptomatic and non-infected women will be followed through pregnancy and potentially up to a year after birth.

Council Discussion

Dr. Spong thanked Dr. Chakhtoura for her efforts.

Dr. Barbara Collura asked about the funding constraints. Dr. Spong responded by saying that this is a priority area-NICHD must conduct Zika research, regardless of funding constraints. As a result, the Institute may not be able to improve its payline as planned. Much of what has been obligated is directed at NIAID and vaccine research. NICHD has a working relationship with NIAID, but this lack of funding for NICHD could be a real problem.

Dr. Aaron Lopata asked about neonatal research and Zika infection. The ZIP study plans to address this issue in the cohort as well by collecting bio samples post-partum. The infants will be followed every three months for at least a year (or perhaps longer) to see what happens if they are infected directly from vector or through the mother.

IX. CONCEPT CLEARANCE REVIEW AND DISCUSSION

Dr. Hann introduced the concept clearance section of the meeting by saying that the presenters would describe broad areas of investigation, but would not go into detail to avoid any potential conflict of interest.

Dr. Min Lee explained that this concept clearance is for a chemical. The Contraception Research Branch (CRB) seeks the Council's approval for the manufacturing of high quality drug substances being tested in protocols conducted by the clinical contraception clinical trials network so the development of new and or improved contraceptive methods is the primary goal of the CRB. This initiative is a renewal. The goal of this initiative is to ensure the continuous manufacture and supply of contraceptive drug substances produced under current good

manufacturing practice protocols, to support ongoing planned contraceptive trials in support of CRB's mission. In the near term, CRB plans to manufacture chemical substances for studying male contraception. . Additionally, CRB seeks more molecules to be produced to support the production of other contraceptive agents.

Council Discussion

Dr. Krugman asked for how long this has been going on and asked about the cost of the contract. Dr. Lee responded that the chemical has been around for 20 years, and that the contract is valued at about \$700,000-\$800,000 per year.

Dr. Gregory Kopf asked about the type of facility being used and if they performed quality control at that facility. Dr. Lee responded that they have in-house quality assurance and quality control.

Dr. Kopf also asked about particle size distribution. Dr. Lee responded that another contractor is responsible for milling.

Council concurred unanimously.

X. 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).

XI. 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 618 HD-primary applications requesting \$196,081,262 in direct costs and \$255,772,530 in total costs.

ADJOURNMENT

There being no further business, the meeting adjourned at 4:45p on Thursday, June 9, 2016. The next meeting is scheduled for August 22, 2016.

Attachment: Council Roster

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

/S/

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

8/1/16
Date

Kimberly Witherspoon
Committee Management Officer, NICHD

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.