
*Eunice Kennedy Shriver* National Institute of Child Health and Human Development

# NATIONAL ADVISORY CHILD HEALTH AND HUMAN DEVELOPMENT COUNCIL

## *MINUTES OF MEETING*

January 23, 2014

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**
**PUBLIC HEALTH SERVICE**
***EUNICE KENNEDY SHRIVER* NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT**
**NATIONAL ADVISORY CHILD HEALTH AND HUMAN DEVELOPMENT COUNCIL**
**SUMMARY MINUTES**
**January 23, 2014**[1]

The National Advisory Child Health and Human Development (NACHHD) Council convened its 152nd meeting at 8:00 a.m., Thursday, January 23, 2014, in Building 31, Conference Room 6, of the National Institutes of Health (NIH), Bethesda, Maryland. The meeting was open to the public from 8:00 a.m. to 12:00 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 1:00 p.m. until 3:30 p.m.

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

**Council members present:**

Dr. Diana Bianchi
Dr. PonJola Coney (Remote)
Dr. Gordon Cutler
Dr. Bonnie Duran
Dr. Walter Frontera
Dr. Richard Greenwald
Dr. Reneé Jenkins
Dr. Frances Jensen (Remote)
Ms. Wendy Lazarus
Dr. Ruth Lehmann
Dr. Kimberly Leslie
Dr. Ken Muneoka
Dr. Piero Rinaldo
Dr. George W. Rutherford
Dr. Yoel Sadovsky
Dr. Richard K. Wagner (Remote)
Dr. Paul Wise
Dr. Carmen Green, National Advisory Board on Medical Rehabilitation Research. Liaison

Council Roster (attached)

**Council member absent:**
Dr. Jere Behrman

**Ex officio members present:**
Dr. Jay D. Kerecman, Uniformed Services University of the Health Sciences, Department of Defense

**Ex officio members absent:**
Dr. Patricia Dorn, Department of Veterans Affairs
Dr. Michael Lu, Maternal and Child Health Bureau, Health Resources and Services Administration, DHHS

[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 were:**
Members of Staff, NICHD
Other Members of Staff, NIH

**Others present were:**

Mr. Ethan Jorgensen-Earp, American Academy of Pediatrics
Mr. Joe Laakso, Endocrine Society
Dr. Rich Cohn, Health Sciences Research

## I. Call to Order and Introductory Remarks

Dr. Guttmacher welcomed Council members and staff. He announced that the meeting would be open to the public on Thursday morning, January 26, and closed to the public in the afternoon to discuss grant applications. He stated that the Institute will continue to allow members the option to participate in one meeting a year through electronic means via Adobe Connect technology as an alternative to attending meetings in Bethesda, Maryland. He stated that three members of the Council would be participating in the meeting as virtual attendees through Adobe Connect and that the general public was also welcome to view the open session from remote sites via NIH Videocast.

Review of Confidentiality and Conflict of Interest

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

Council Minutes—September 19, 2013, Meeting

The minutes were approved unanimously as written.

The following are future meeting dates:

| | |
|---|---|
| June 5, 2014 | (Thursday) |
| September 18, 2014 | (Thursday) |
| January 22, 2015 | (Thursday) |
| June 4, 2015 | (Thursday) |
| September 17, 2015 | (Thursday) |

## II. NICHD Director's Report and Discussion

Dr. Guttmacher's report covered news from the NIH, the NICHD, and a legislative update.

News from the NIH

Dr. George Koob was appointed Director of the National Institute on Alcohol Abuse and Alcoholism, and Dr. Philip E. Bourne was appointed the NIH Associate Director for Data Science. Dr. Bourne will work across the NIH Institutes and Centers (ICs) on issues related to big data, including storage, confidentiality, and data sharing.

The three scientists who shared the 2013 Nobel Prize in Physiology or Medicine and the three scientists who shared the prize in Chemistry have all been NIH grantees.

The BRAIN Initiative is gathering momentum within the NIH. The Initiative is offering six funding opportunities in fiscal year 2014. The science that comes from the initiative promises to be rich. Dr. Gregory Farber of the National Institute of Mental Health would provide a fuller summary later in the meeting.

Bill Gates, co-chair and trustee of the Bill & Melinda Gates Foundation, visited NIH on December 2 to deliver the annual David E. Barmes Global Health Lecture. In his talk, "Why the Future Needs Biomedical Innovation," he mentioned the NICHD, the only Institute to be mentioned by name during his talk. The Directors of four NIH Institutes—the NICHD, the National Cancer Institute (NCI), the National Institute of Allergy and Infectious Disease (NIAID), and the National Institute on Biomedical Imaging and Bioengineering (NIBIB)—met with Mr. Gates before the lecture. The NICHD shares Mr. Gates's interest in early nutrition, preterm birth, and contraception.

The NIH is investigating ways to make the Biographical Sketch (biosketch) submitted by grant applicants more useful. There is growing concern that the biosketch format does not provide the most accurate assessment of the applicant's past performance. Past performance is an important part of a review and is a valuable indicator of future success, but investigators who publish in the most prestigious journals—*Cell*, *Nature*, and *Science*—may be at too much of an advantage. Busy reviewers do not always read the cited work, but they may assume the science is excellent based on the publication. Also, the biosketch can undervalue team science, where a team member can make an important contribution but not be the first or last author.

One suggestion is to replace the 15 peer-reviewed publications on the biosketch with a narrative description of the applicant's five most significant contributions to his or her field. This would focus the review on actual contributions and accomplishments, as opposed to academic pedigree.

The NIH is also discussing how to better use core facilities supported by the NIH. The cores exist around the world and provide access to instruments, technologies, and consultation services. The cores may be supported by an academic or private institution's own funding, government funding, or both. There is variability in how they are managed and organized, and some are redundant, even the cores that exist within the NIH.

The institutions that have cores, both inside and outside the NIH, are concerned about issues such as costs, management, audits, and the space the cores require. The NIH can help to improve efficiency and maximize funding by working with the principal investigators (PIs) and the cores. Some institutions with cores have partnered with their business schools to improve management and make them more efficient. The NIH will also identify ways to incentivize ICs and institutions to share cores.

News from the NICHD

NACHHD members Dr. Diana Bianchi and Dr. Yoel Sadovsky were recently elected to the Institute of Medicine (IOM). Dr. Louis Muglia, a member of the Board of Scientific Councilors, was also elected. Dr. Guttmacher extended congratulations to them.

NICHD intramural PI Dr. Todd Macfarlan received the Presidential Early Career Award for Scientists and Engineers for his research on mechanisms of mammalian epigenome reprogramming. Two NICHD extramural investigators, Dr. Thomas Fazzio and Dr. Sallie Permar, also received the award. Dr. Maddox received the 2013 Department of Health and Human Services Career Achievement Award for advancing the national research agenda and improving global health.

Dr. Guttmacher, National Children's Study Director Dr. Steven Hirschfeld, and NIH Director Dr. Francis Collins contributed a perspective piece on the National Children's Study to the *New England Journal of Medicine*. The study is currently under review by the IOM, which is expected to issue its report within a few months.

The NICHD, the Bill & Melinda Gates Foundation, the Global Alliance to Prevent Prematurity and Stillbirth, the March of Dimes, and the WHO have been working to develop an approach to reduce preterm birth worldwide. Representatives of the group published an article in the December issue of *Lancet Global Health* to get out word of the effort to the scientific community.

The NIH and the Food and Drug Administration worked together on the Best Pharmaceuticals for Children Act as part of the effort to study safe and effective dosing for children. It is uncommon to have drug studies geared specifically to children; usually dosages are extrapolated from adult doses. The NICHD puts in substantial funding to this research each year and is the leading agency on this effort within the NIH. Sodium nitroprusside, a drug for high blood pressure, is the first drug to receive new labeling under the process set up by the Act. More studies are now underway to evaluate safe and effective doses of other drugs for pediatric patients.

NICHD Communications has placed a much greater emphasis on social media. The Institute has Facebook and Twitter accounts and is rapidly accruing followers. The tweets and Facebook messages are geared toward lay and professional audiences. Dr. Guttmacher welcomed suggestions from the councilors on any aspect of the effort and asked councilors to become followers.

The search for a new Deputy Director to replace Dr. Maddox is underway. The National Center for Advancing Translational Sciences Director, Dr. Christopher P. Austin, is chair of the search committee. The Deputy Director must be a leader and a person of vision, somebody with management and interpersonal skills. The NICHD is accepting applications for the position through the end of February. Because the best candidates are not reading the help wanted ads, it is important that Council members encourage qualified people to apply. Dr. Guttmacher asked councilors to email the names of potential candidates to him. Candidates must have a M.D. or a Ph.D.

Legislative Update

The PREEMIE Act was reauthorized as part of a three-bill package that included the Pediatric Research Consortia and the Chimps Act. The PREEMIE Act allows the HHS Secretary to establish an Advisory Committee on Infant Mortality. Within 1 year of enactment, a research plan will be developed for conducting and supporting research, education, and programs on preterm birth. The PREEMIE Act does not appropriate any new funds.

The NICHD staff continues to be involved in Congressional briefings. On the day of the NACHHD meeting, for example, the NICHD staff was briefing the House Equality Caucus on lesbian, gay, bisexual, and transgender issues.

Dr. Guttmacher said that the funding issue appears to be taking a turn for the better, with increased funding over fiscal year (FY) 2013 levels. The NICHD expects to have about half of the FY 2013 funding cuts restored in FY 2014. The NICHD will not receive as much funding as it did in FY 2012, but Dr. Guttmacher expressed hope that the NIH will return to past funding levels in future years.

The National Children's Study will receive up to $165 million in FY 2014. The NIH can recapture any of those funds that are not spent on the study. It is expected that the National Children's Study will not spend up to $165 million this year, so each of the Institutes is expected to receive some of the unspent funding.

Other appropriations bills include the following clauses that apply to NIH:

- Federal Advisory Committees candidates cannot be asked about their politics as part of the appointment process.
- The NIH must present a detailed business plan for the BRAIN Initiative, including how the ICs will collaborate on the effort.
- Congress requests a report in FY 2015 on how to accelerate commercialization of therapies to patients, and requests a workshop on this subject.
- The NIH Director must improve efficiencies, including in communication activities, by doing it in a more centralized fashion and less through the individual ICs.

- Plans to scrutinize extramural grantees receiving more than $1.5 million must be extended to intramural investigators receiving more than $1.5 million.
- The NIH Director must review scientific priority setting.
- Travel and conference regulations remain in place.
- Federal employees receive a 1 percent pay raise for the first time in 4 years.

The most recent budget agreement sets the funding ceilings through FY 2015, so there is no risk before then of a government shutdown. The President's budget is expected to come out in late February or early March. There is no threat of sequester before FY 2016.

Discussion

A councilor asked whether the lecture by Bill Gates will be available online. (It is, and it has more than 1,000 views and can be viewed at http://videocast.nih.gov/summary.asp?Live=13311&bhcp=1)

Dr. Reneé Jenkins asked whether proposed changes to the biosketch will help or hurt new investigators. Dr. Guttmacher said that the changes were meant to address the disadvantages that the new investigator faces in applying for funding. The biosketch tends to favor people who have longer curricula vitae and more first-author credits. That is why the NIH is considering having the applicant list five areas of accomplishment rather than listing publications. However, some have expressed concern that listing accomplishments would also favor senior investigators. One suggestion is to reduce the five areas down to two. Other groups, such as the Howard Hughes Medical Institute, have implemented changes similar to the one under consideration at the NIH and have found it helps new investigators. Dr. Catherine Spong said that the idea is to allow a middle author, often a young investigator, to explain exactly what he or she had contributed to a paper. This should help the young investigator.

Dr. Guttmacher said that the roles of the first and last authors used to be clear before laboratories began working together on an investigation. It is not as clear now.

Dr. Piero Rinaldo said that it might be just as difficult for junior faculty to come up with five major accomplishments. Senior faculty will still have an easier time to excel on that measure.

Dr. Carmen Green said that these changes may not fix the problem of bias and may even enhance it.

Dr. Guttmacher said that the positive bias toward investigators who publish in *Cell, Science,* or *Nature* tends to favor basic research over clinical research. The change in the biosketch might be especially helpful for those study sections that consider both basic and clinical work.

Dr. Ruth Lehmann said that publications are a good gauge of the investigator's ability, in her view. She asked whether this is an attempt to fund people rather than projects. Dr. Guttmacher said it was not. However, the discussion of funding people versus projects will come up later in the meeting.

Dr. Sadovsky said that the issue is to find objective criteria of success and promise. He asked whether there are other measures that the NIH could find. He suggested the NIH should join with other groups that are investigating this question, including Elsevier, Thomson Reuters, and Google Scholar.

Dr. Guttmacher said they have discussed ways to partner with other groups to measure success and promise. But it is a challenge to find or develop tools and criteria that can identify the applications most likely to be successful and to advance science. Whatever criteria they decide upon, it must be used NIH-wide.

Dr. Guttmacher asked members to email him with any further ideas on this discussion

Dr. Kimberly Leslie asked whether the NIH could establish set-asides for new investigators. Dr. Guttmacher said the NIH does have differential paylines for young investigators, but there is still an imbalance. The biosketch is meant to help even the playing field more.

Dr. Gordon Cutler said investigators in other countries are impressed at the boldness of the National Children's Study. If the study gets up and running, will there be a way to extend it after the participants reach 21 years of age? Also, this study will present enormous management issues. Does the NIH have experience with retaining participants who did not volunteer, but were enrolled by their parents? To keep people in a trial through adolescence and into adulthood will require great skill on the part of the investigators and their teams. They will have to maintain a strong emotional bond with the participants. How will the NIH manage this?

Dr. Guttmacher said that it will be a management challenge and will require that frontline personnel establish good relationships with the participants in order to retain them. Data from the first 5 years of the child's life will be especially important, and retention during that time will be the highest priority. But retention until the child turns 21 is also important.

It is not clear whether this study could go beyond 21 years as it is currently designed. Congress did not want to fund a study with no end date, so the study will stop at 21 years. That said, it may be possible in 20 years to see whether there is a way to keep it going. The Framingham study went beyond its original shelf life.

The Report of the Director is available in full on the NICHD website:
http://www.nichd.nih.gov/about/advisory/nachhd/Documents/directors_report_201401.pdf

## III. Report of the Director, Division of Extramural Research (DER)

Government Shutdown and Furlough Impact

Dr. Catherine Spong, Director, Division of Extramural Research, presented an overview on the activities of the DER. She began her report by stating that the government shutdown, coming on the heels of Hurricane Sandy and sequestration, adversely affected morale and disrupted scheduled meetings, study sections, and receipt dates. More than 200 meetings of the Center for Scientific Review were canceled, affecting 11,000 grant applications.

When the government restarted, reviewers and program officers took extraordinary steps to review all the applications in time for the January Council meeting. Many people worked over the holidays to get

this done. Also, many of the meetings were held electronically. Most of the applications meant to come to the Council today have arrived on time. There is one review that was not completed in time for today's Council meeting. It will be presented to the Council soon and, assuming the Council approves it, should go out with this latest round of funding. Dr. Spong thanked everybody involved in the effort to review all of the applications in time for this round of funding.

The Human Placenta Project

The aim of this project is to understand human placental structure and function in real time and to improve the technology for real-time assessment of placental development in both normal and abnormal pregnancies. New technologies developed as part of this project will be used to develop noninvasive markers to predict and prevent adverse pregnancy outcomes. The study will also look at the relationship between the placenta and long-term health.

The project will begin in the spring or summer with a meeting of experts who will help decide how to address the study's objectives.

NICHD Contraceptive Research Review

The NICHD will review its contraceptive research to review the accomplishments of the program and consider the needs for the future. The review will consider the NICHD's programs; the balance of basic, clinical, translational, and behavior research; whether the workforce has the appropriate capability now; and whether there will be a pipeline of researchers to continue contraceptive research in the future.

National Center for Medical Rehabilitation Research (NCMRR) Review

The NCMRR is changing its role to become the coordinator and cofounder of rehabilitation research across the ICs. This means more of the rehabilitation research will be done by other ICs. For oversight, the plan is to form an NACHHD subcommittee, chaired by Dr. Ken Muneoka, to oversee NCMRR activities. This new plan will mean more work for the Council. Dr. Spong asked members to forward suggestions and opinions on the plan.

At the conclusion of her report, Dr. Spong introduced Dr. Rohan Hazra, Medical Officer, Maternal and Pediatric Infectious Diseases Branch, who presented the council members with an update on the Data and Specimen Archiving and Sharing Working Group.

Data and Specimen Archiving and Sharing

Dr. Hazra's report is based on the findings of the NIH Data and Specimen Archiving Working Group, which had been charged with developing recommendations for archiving and sharing data and specimens from sunsetting studies. The working group's goal was to develop a way to make data from NIH-funded studies available to the wider research community.

The Working Group did an extensive review of models and best practices, to borrow from those that worked best. The NIH Data and Informatics Group set out goals that the Working Group adopted. The

goals included advancing science through the sharing of data, promoting new methods and software to share data, and increasing the workforce to accomplish these goals. The Big Data to Knowledge Initiative is working with data but not with specimens. The IOM has also been working on increasing the sharing of clinical data, so this is a very timely topic.

One question is whether there is an existing NIH data and specimen archive that they could expand upon or whether they should establish a new one. There are both technical requirements, such as data design, and nontechnical requirements, such as the organization and governance structure. The nontechnical considerations are expected to be the more challenging, because it must be clear how clinicians provide their data and specimens and how others access that information and material. The Working Group is still working on this and will next make recommendations to the NIH leadership.

Discussion

Dr. Cutler asked whether Working Group members consulted with the NIA about their database. Geriatricians have raved about its setup and the fact that outside investigators have access. Dr. Hazra said the Working Group is familiar with the NIA database and had looked at it. They had not invited more input from the NIA, but likely would do so.

Dr. Bonnie Duran asked whether the Working Group had taken into account communities who object to data sharing. In particular, some communities may be small enough that it would be difficult to maintain confidentiality.

Dr. Hazra said that the Working Group is beginning with studies in which participants and investigators want the data to be shared. But the issues are complicated, particularly around genetic data and stigmatizing data. Some data should not be shared or should be shared only in controlled ways. It is likely that not all data will be made widely available.

Dr. Maddox said this shows that the Institute needs to have the communities involved in the studies right from the beginning.

Dr. Walter Frontera asked how the NICHD plans to coordinate rehabilitation research efforts across the ICs, now that coordination is the new role of the NCMRR.

Dr. Guttmacher said that NICHD leaders have discussed the issue of coordinating this research with other ICs. Some issues arise because of the nature of rehabilitation research; others are related to how the NIH functions. One of the first steps is to invigorate the trans-NIH committee and define the referral policies. One issue is how to administer the grants. The other issue is for the NIH to find a new home base for investigators who have been working with the NCMRR.

Dr. Cutler said that every group handles data in different ways, so it would be important to find ways to standardize data collection so that every research group has the same basic data. Dr. Spong said that is a good point and that a number of groups are trying to identify common data elements for clinical trials right now.

## IV. Concept Clearance Review and Discussion

Dr. Maddox introduced this section of the meeting by saying that new concepts that require special funding or set-aside dollars are brought to Council, providing a chance for the public and the Council to comment.

Council discussed and unanimously endorsed five concepts as detailed below.

Isolation, Purification, and Synthesis of Human Milk Oligosaccharides with Antimicrobial Activity

Dr. Gilman Grave said that this is a request for applications (RFA) with set-aside funds using the R43 Small Business Innovation Research (SBIR) Grant and the R41 Small Business Technology Transfer (STTR) mechanisms.

NICHD-supported investigators have discovered that some oligosaccharides in human milk have antimicrobial activity against enteric bacteria and viruses and appear to have market potential. This RFA is meant to encourage small companies to develop synthetic procedures to produce batches of human milk oligosaccharides in kilogram quantities so that the NICHD can ramp up preclinical testing.

Dr. Sadovsky asked whether this RFA concerned only the oligosaccharides or whether it would include the antimicrobial potential of other components of human milk. Dr. Grave said it includes only oligosaccharides. There are 200 oligosaccharides, and several have been found to have antimicrobial properties. Small companies could also create new non-natural oligosaccharides that do not exist in nature that would provide tighter binding to some microbes.

A councilor asked whether the oligosaccharides are conserved in other species. Dr. Grave said that he did not know, but that that was a great question.

Dr. Cutler asked whether there are companies that have the capacity and interest to pursue this project. He also asked whether the RFA allowed large companies to apply. Dr. Grave said the NICHD may consider developing partnerships with larger companies, but there are some smaller companies already interested and this RFA could be a way to find more.

Tools for Assessment and Improvement of Neurologic Outcomes

Dr. Rosemary Higgins said the goal of this RFA is to develop tools and technology for assessment and improvement in brain and neurological outcomes for pregnancies and infants. This is for SBIR and STTR set-asides.

Dr. Jay Kerecman said this is an important and interesting concept. He asked whether there are any plans to encourage design firms to evaluate the birthing environment. He noted that many hospitals are moving to single-bed rooms as a way to encourage family bonding, even though there is no evidence that the single-bed arrangement is a better one.

Dr. Higgins said that is an important question but beyond the scope of this RFA.

Dr. Frances Jensen asked whether this RFA will include late preclinical studies that could involve animals. It might be important to specify whether animal studies could be funded. Dr. Higgins said the RFA will include translational studies, so it could include animal studies.

Reducing HIV Risk Behaviors in Individuals Who Experienced Childhood Maltreatment

Dr. Lynne Haverkos said this RFA is to find links between early maltreatment of children and their later risk of HIV infection. It is meant to reduce HIV risk of individuals maltreated as children or young adults. The RFA is dependent upon funding from the R21.

Dr. Green asked whether this RFA focuses on children or adults and whether it focuses on certain types of maltreatment, such as sexual abuse or mutilation.

Dr. Haverkos said the RFA would focus on adolescents and young adults who are at risk but not infected. The RFA does not specify the types of maltreatment.

Dr. Green cautioned that it could be a problem not to specify the type of maltreatment. The literature suggests that different types of maltreatment create different outcomes. There are also ethical considerations for a study in which the researcher has knowledge of maltreatment. Also, an individual who has experienced maltreatment may not be able to truly consent to participation in the study. Those are challenges that need to be addressed.

Dr. Haverkos said that those who worked on the RFA have thought about these issues, which always exist when studies involving sexual activity are involved. Confidentiality is always a big issue in these studies. She said they will focus on a particular population, such as sexually abused children. These studies may be done either inside or outside the United States.

NIH/UNICEF/OGAC Collaboration: Increasing Access and Uptake of HIV Testing and Counseling (HTC) and Appropriate HIV-Related Services for Adolescents Living in Low- and Middle-Income Countries

Dr. Bill G. Kopogiannis said the purpose of this collaborative RFA is to increase access to and use of HIV counseling by adolescents ages 10 to 24 years in low- and middle-income countries and to link HIV-infected adolescents to treatment, care, and support. The grant mechanism is R01. It will focus on income-limited settings outside the United States.

Dr. George Rutherford said that young married women are already being identified because they are tested when they become pregnant. NICHD should focus on other young people—young women who are not pregnant and people who are aging into the at-risk age group. Dr. Kopogiannis said they will look at those populations.

Pediatric HIV/AIDS Cohort Study (PHACS)

Dr. Lynne Mofenson said this RFA is a competing renewal to continue the observational cohorts developed during the first two competitive funding cycles. PHACS is trying to determine the long-term safety of in utero exposure to antiretroviral drugs in HIV-exposed but uninfected infants, children, and adolescents. It is also examining the effects of HIV and its treatment on perinatally HIV-infected children, adolescents, and young adults.

Thirty papers have been published so far as a result of this study, including one study finding that children who were exposed to tenofovir in utero may have decreased bone mineral density as adolescents. This and other findings show the need to continue to study this population as they age.

Dr. Bianchi asked how studies are singled out for concept clearance. Dr. Maddox said these ideas come from NICHD scientists who bring them to the leadership for consideration. The proposals are evaluated based on available funding and the state of the science. The leadership brings projects it approves to the NACHHD for input. The projects just presented have been approved by the leadership.

Dr. Spong said that staff has developed proposals that target SBIR and STRR dollars, because there are not very many applications in those areas.

## V. NIH BRAIN Initiative: New Tools for Brain Research Funding Opportunity Announcements

Dr. Gregory K. Farber, Director, Office of Technology Development and Coordination, National Institute of Mental Health explained that President Barack Obama announced the BRAIN (Brain Research through Advancing Innovative Neurotechnologies) Initiative in April 2013. The NIH, the National Science Foundation, and the Defense Advanced Research Projects Agency are the three federal agencies involved in the $100 million project.

The NIH project will map the brain's circuits, measure fluctuating patterns of activity, and attempt to answer the question of how these circuits give rise to cognitive abilities. There are many new technologies that can help them to tackle this problem. The NIH has initial funding of $40 million for this project.

The NIH Advisory Committee to the Director (ACD) convened a Working Group following the April announcement. The Working Group convened a series of meetings with experts. Among the areas they covered were molecular approaches, computation, big data, and human experimentation. The Working Group wrote an interim report that the ACD has approved. NIH Director Dr. Francis Collins accepted the recommendations. The Working Group made nine recommendations:

- Generate a census of cell types
- Create structural maps of the brain
- Develop new large-scale network recording capabilities

- Develop a suite of tools for circuit manipulation
- Link neuronal activity to behavior
- Integrate theory, modeling, statistics, and computation with experimentation
- Delineate mechanisms underlying human imaging technologies
- Create mechanisms to enable collection of human data
- Disseminate knowledge and training

Among the principles that cut across recommendations are to use appropriate experimental systems, cross interdisciplinary boundaries, integrate spatial and temporal scales, establish platforms for data sharing, validate and disseminate technology, and consider the ethical implications of neuroscience research.

The NIH has set up five implementation teams from among the ICs that have interest in the brain. Their charge is to use the recommendations to suggest funding opportunity announcements. Six funding opportunity announcements (FOAs) have been released. All of the FOAs will be managed by a project team and will also have a steering group. Intramural scientists are allowed to apply for funding through these FOAs.

The NIH has created a website to enhance communication among the awardees. The NIH has sent emails to its listservs, and program staff have presented at meetings. There is a website to find out more at http://www.nih.gov/science/brain/.

The European Union also is carrying out its own project focusing on computational models and is funding it with €1 billion. The American effort will not duplicate the European effort, and there is an opportunity for synergy with the European effort.

Discussion

Dr. Cutler said that he is interested in the translational aspect of this project, including finding gene variants that could be targets for new drugs. One very basic question is whether one gene variant could conceivably be responsible for producing highly intelligent people. He suggested that it might make sense to sequence the genomes of unusual individuals.

Dr. Farber said that is not a focus of the BRAIN Initiative, although it is a valuable approach. The focus is on tools and technology. The approach that Dr. Cutler suggests is one that is supported across the NIH in the regular course of research.

Dr. Jensen asked who among the NICHD staff would represent the NICHD on this Initiative. She asked whether they are the same staff who are working on the NIH Blueprint for Neuroscience Research. She also said that it might make sense to further leverage the $40 million available to the NIH for this Initiative by funding investigators who are already doing this type of research.

Dr. Guttmacher said that a number of NICHD staff members are involved in the Initiative and in the NIH Blueprint for Neuroscience Research. More may become involved as the Initiative develops.

The NICHD is focusing on the human development aspect of brain research. The Initiative overlaps with the NIH Blueprint for Neuroscience Research. Also, it will be important to develop a business plan for the BRAIN Initiative.

Dr. Leslie noted that the $40 million set aside for the BRAIN Initiative seems small compared with the European budget. Dr. Farber said that this is the first year of the effort and that funding will likely grow. Dr. Guttmacher said the $40 million for the NIH effort should be seen as a planning grant and is expected to grow as the project continues. Also, the amount government-wide to start the project is $110 million.

Dr. Lehmann said she found the data sharing to be an interesting component. She asked whether data from all funding mechanisms related to brain research would include data sharing. Dr. Farber said that planning to do that is underway. Concrete plans should be available in 12 months.

Ms. Wendy Lazarus asked how the NICHD can ensure that the child development focus is maintained. Dr. Guttmacher said the NICHD staff would do that, as will staff members from other ICs who are involved. That said, it will be up to the scientific community to what extent issues related to development will be prioritized.

Dr. Paul H. Wise asked how the NIH would ensure there is a good public understanding of the findings; there is a danger that the findings could be misrepresented or misinterpreted. Dr. Farber said that they have invited private industry and patient advocacy groups to the next meeting of the Working Group to provide them information about the Initiative.

## VI. Payline versus Select Pay

Dr. Guttmacher said that the way paylines are handled varies among the ICs and evolves over time. Some ICs stay within a payline. Others have a broader range within which they fund grant applications, allowing the IC to fund a project that doesn’t score as well but that fits with other projects that are being funded.

One problem with paylines is that some study sections have better applications than others. Another problem is that study sections vary in their collective ability to recognize good science. In addition, paylines may put emerging areas of science at a disadvantage.

How can the NIH evaluate the performance of study sections to make sure the NIH is funding the best science? Should the publication and citations of the studies that come out of that study section be evaluated? Should patents attributed to funded applications reviewed by a study section to help evaluate the study section be the metric? Should retrospective case studies of important scientific discoveries be done to see whether there are common characteristics of early work that ultimately lead to important outcomes? Are there newer analytics that the NIH could use? Is there a way to supplement the judgment of scientists with analytics to detect rapidly emerging ideas and to enable an earlier investment?

Discussion

Dr. Rutherford said it might be easier to evaluate applications from the opposite perspective; that is, what predicts a poor study? What do studies that have no publications and no follow-up grant have in common?

Dr. Guttmacher said that is a good idea, and it also makes sense to evaluate the science that the NIH does not fund but that does well with other funding. How many of those projects result in scientific breakthroughs?

Dr. Rinaldo said that abstracts and posters should not be a measure of excellence for research. Also, using the number of times a study is downloaded can be misleading if the study appears in a journal that provides free downloads rather than one that does not. Invited presentations are a good measure of excellence.

Dr. Green said the number of invited presentations may not be a good measure of excellence, because women and minorities are less likely to be invited to give presentations. Also, the NIH should analyze the performance of different study sections.

Dr. Green also said that she is concerned about using the number of times an article is downloaded as a sign of excellence. People who are outside the country will have a harder time downloading articles because of the cost, which could disadvantage certain studies. Whatever metrics it uses to measure scientific excellence, the NIH should be careful to not further marginalize groups of scientists.

Dr. Richard Wagner said one question is how much value should be put on funding high-risk, high-reward, and high-priority projects. Once that is decided, then what remains should be within the payline.

Dr. Leslie said that the NCI has a payline but also sets aside funding that the program officers have more discretion over. The program officers divide that money among applicants who don't meet the payline but are highly rated. The program officers are making more funding decisions.

Dr. Guttmacher said that does raise the question of whether the NIH should move away from the payline and allow the staff to make more funding decisions.

Dr. Lehmann said that moving away from the payline toward greater reliance on program officers would be a dangerous thing to do. Also, she said she is concerned about the junior investigators, who are good scientists who get their first R01. But it is very difficult for them to get their second R01. They are told that the money must go to the more senior PIs. The junior PIs may want to do something really novel, to branch out from their mentors, but the lack of funding will drive them from the ranks of investigators because they cannot wait 10 years for funding.

Dr. Guttmacher said this is a very important point that has been recently discussed at the NIH. He asked that that issue be deferred until the next discussion on the agenda, which asks whether it is better to fund people or projects.

Dr. Richard Greenwald said he agreed with a point made earlier about looking at the projects that do not succeed. But he also cautioned that failure is part of innovation and that projects that fail are not necessarily bad projects. The NIH should be careful not to discourage all risk-taking.

## VII. Funding People versus Projects

Dr. Guttmacher said that within the extramural program, the NICHD emphasizes the project rather than the person in its funding decisions. The intramural program focuses more on funding people.
Dr. Guttmacher said that the NICHD has made some efforts to recognize and fund promising or accomplished extramural investigators. One example of that is the NICHD Pioneer Awards.

Dr. Guttmacher said that person-centered funding has several potential advantages:

- Enhanced flexibility for the investigator
- Promotion of risk-taking
- Longer duration of support
- Solid level of support
- Less focus on project details in the application

The NICHD does have merit awards that recognize the individual scientist and provide a secure source of funding for a longer period of time. He asked whether the NICHD should use more money to recognize early-career investigators whose stars are rising and, if so, how it should do so.

Discussion

Dr. Cutler said that both intramural and extramural funding mechanisms work well; both produce Nobel Prize winners. He said he is in favor of using more of both approaches (person- and project-oriented) for extramural and intramural investigators. He suggested setting aside a certain percentage of person-oriented funding to be given to extramural investigators as a secure source of funding. This would relieve the investigator of having to write new grants. Alternatively, intramural investigators should be encouraged to apply for extramural money. They would not be allowed to get additional funding this way. But the advantage to intramural investigators is to show their ability to win NIH funding. This would give each intramural investigator an opportunity to leave the NIH, if he or she wants.

Dr. Bianchi said there are workforce issues that must be taken into consideration. More senior investigators are losing NIH funding, and that impacts training grants and mentoring. How does the NICHD take into account personnel needs when making funding decisions? Dr. Guttmacher agreed and said that when the senior investigator loses funding, it creates anxiety in the younger investigators.

Dr. Sadovsky added that “young” does not equal “bright,” nor does “old” equal “not bright.” There is a need to support both young and tenured investigators. He said the NICHD should have more merit awards. There is a risk to giving funding by chronological age instead of by idea. Instead, the same measures of excellence should apply to all investigators.

Dr. Jensen said it is important to find ways to keep the mid- and senior-level investigators in the scientific workforce. They are the mentors and trainers of the next generation of scientists. Many senior investigators are involved with long-term projects that might not be as exciting to study sections. An emphasis on innovation could cause senior investigators to bounce to new topics, potentially reducing the chance of having translational research, since translational research may not seem innovative and important findings may not make it to the bedside quickly.

Dr. Jenkins asked whether there is data to indicate that senior investigators are losing out on funding. She said that the diversity of the workforce should be important to develop. It is important to try to determine funding priorities, but it is difficult to do without any data.

Dr. Guttmacher said the discussion is aimed, in part, at determining a way to ensure diversity. When the NIH funds projects, it can see how that affects the diversity of the science. When the NIH funds people, it can more reliably achieve diversity of the workforce. The Division of Program Coordination, Planning, and Strategic Initiatives has analyzed the person-oriented funding of the Pioneer Awards and found that the investigators supported are more productive than investigators funded with an R01.

Dr. Leslie suggested designating NICHD scholars who exemplify the best of NICHD-related science. This would provide person-oriented funding and would raise the visibility of the NICHD.

Dr. Duran said that institutes of higher education used to set aside a set amount of money for research and a set amount for teaching. Has the NIH made a statement on that?

Dr. Guttmacher said that the NIH focuses on things it can influence. The NIH is aware of funding cuts within the academic institutions but does not have much influence there.

Dr. Muneoka said the aim should be to fund the best science. Program officers should be more involved in deciding who gets funding. The NICHD should take advantage of the smart people who are administering the program.

Dr. Cutler said he was struck at how many clinical investigators want to do long-term translational projects but had a difficult time getting funding. Basic scientists who do not appreciate the importance of translational research are evaluating the applications of clinical investigators. He suggested getting a better balance in the membership of the study sections to represent all of the kinds of research.

Dr. Cutler also said there is a certain amount of unpredictability when choosing applicants for funding.

## VIII. Comments of Retiring Members

Dr. Guttmacher presented retiring members of the NACHHD certificates and letters of appreciation for serving on the Council and invited each member to provide remarks.

Dr. Wagner said he has been impressed with the NICHD staff’s dedication to children under difficult conditions. He said they are an inspiration.

Dr. PonJola Coney said it has been an honor and privilege to serve on the board. The experience was stimulating and humbling. She thanked the staff for making the Council meetings successful.

Dr. Rutherford said it has been an honor to be on Council and that he has been impressed by the professionalism of everyone at the meetings. The breadth of research at the NICHD is impressive and he was gratified to see the portfolio continue to expand during his tenure.

Dr. Cutler said it has been an honor and privilege to serve. He said the NIH is one of the great institutions of the world. He urged the NICHD and the NIH to continue to do more work to find targets for new drugs.

Dr. Sadovsky said serving on the Council has been an honor and humbling at the same time. He said the NICHD has huge responsibilities, and the staff is doing the right thing for many people.

Dr. Guttmacher said he appreciated the breadth of perspective and wisdom the five departing councilors brought to the table and said the NICHD staff would call on them in the future. He also asked them to stay in touch and pass along any new ideas they may have. He said retired councilors should remain the NICHD's eyes and ears in the scientific community.

## IX. Review of Applications

A total of 1,424 applications were assigned to the Institute. Applications that were transferred out, withdrawn, noncompetitive, unscored, or not recommended for further consideration by the initial review groups were not considered by the Council. The Council reviewed 671 applications requesting $252,835,462 in requested total costs. The Council favorably recommended 671 new, renewal, and supplemental research and training grant applications, with requested total costs of $252,835,462.

## X. Adjournment

There being no further business, the meeting adjourned at 3:30 p.m. on Thursday, January 23, 2014. The next meeting is scheduled for June 5, 2014.

Attachment: Council Roster

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

/s/ 05/28/2014

Alan E. Guttmacher, M.D. Date
Chair, National Advisory Child Health and Human Development Council
Director, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

Mary Plummer
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.