



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

**NATIONAL ADVISORY CHILD HEALTH
AND HUMAN DEVELOPMENT
COUNCIL**

MINUTES OF MEETING

January 21, 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
January 21, 2016¹**

The National Advisory Child Health and Human Development (NACHHD) Council convened its 159th meeting at 8:00 a.m., Thursday, January 21, 2016, in Building 31, Conference Room 6, of the National Institutes of Health (NIH) in Bethesda, Maryland. The meeting was open to the public from 8:00 a.m. to 1:00 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 1:45 p.m. until 4:00 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. Diana Bianchi	Dr. Ken Muneoka
Dr. Anne Case	Dr. Stephen Petrill (virtual)
Ms. Barbara Collura	Dr. Piero Rinaldo (virtual)
Dr. Bonnie Duran	Dr. Frederick Rivara
Dr. Patricia Flynn	Dr. George Saade
Dr. Walter Frontera (virtual)	Dr. Paul Wise
Dr. Melissa Gilliam	Ms. Sheila Zimmet
Dr. Gregory Kopf	
Ms. Wendy Lazarus	

Council members absent:

Dr. Ruth Lehmann

National Advisory Board on Medical Rehabilitation Research Council Liaison

Dr. Richard Shields

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
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

Rebecca Nathanson, American College of Obstetricians and Gynecologists

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 - Meetings of August 27, 2015 and September 19, 2015

Dr. Hann moved to approve the *Summary of Meeting Minutes* for the August and September 2015 sessions of Council. The *Minutes* documents were approved unanimously, as written.

C. Future Meeting Dates

The Council agreed to the following future meeting dates:

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

An August tele-meeting date will likely be necessary; the particular date will be determined in the next few months.

II. INTRODUCTION OF NEW MEMBERS

Dr. Spong welcomed five new non-voting Council members:

- Dr. Atul Butte, Director, Institute for Computational Health Sciences, University of California, San Francisco
- Dr. Richard Krugman, Distinguished Professor, Pediatrics/Child Abuse, University of Colorado School of Medicine
- Dr. DeWayne Pursley, Chief, Department of Neonatology, Beth Israel Deaconess Medical Center
- Ms. Lesli Rotenberg, General Manager, Children's Programming, Public Broadcasting Service
- Dr. Timothy Shriver, Chairman and CEO, Special Olympics

The new members presented brief overviews of their research and professional interests. All stated they were looking forward to serving on the Council and future interactions with other Council members and NICHD staff.

III. NICHD DIRECTOR'S REPORT AND DISCUSSION

News from NIH

NIH's five-year Strategic Plan was finalized and sent to Congress in December 2015. As a result of input, a fourth objective, Excelling as a Federal Science Agency by Managing Results, was added.

The Precision Medicine effort continues to move forward. A number of funding opportunities related to this effort are available, some with deadlines in February.

National Children's Study (NCS) funds for FY16 have been redirected to the Environmental Influences on Child Health Outcomes (ECHO) program, which will leverage extant cohorts to investigate longitudinal impact of a variety of factors on pediatric health outcomes with high health impact. Funds from ECHO will be used in part to create the Institutional Development Award (IDeA) States National Pediatric Clinical Trials Network, which will address medical access gaps in rural children through a national network for pediatric research at IDeA locations. A number of funding opportunities related to this effort are available, some with deadlines in March and April.

The NCS Data Archive will be open to public users within a few months. Additional data will be released in May and October 2016. A variety of study material will be available on the Archive website.

As part of the Gabriella Miller Kids First Pediatric Research Initiative, supplemental funding was released for whole genome sequencing on birth defect and childhood cancer cohorts (trios). A second funding opportunity has been released with letters of intent due in March.

NICHD's participation in The NIH-Gates Foundation collaboration is moving forward on the topics of Infectious Disease and Maternal, Newborn and Child Health with staff involvement in several working groups.

News from NICHD

NICHD non-human primate operations at Poolesville will close. NICHD will transfer approximately 100 animals per year over the next three years to other facilities.

The Office of Health Equity (OHE) was realigned as a result of the review of the NICHD's Office of the Director. Grants from this office were transferred to the Division of Extramural Research. NICHD is now working to develop a new role for OHE and will convene a working group of Council to assist.

A Rehabilitative Research at NIH meeting will be held May 25-26, 2016. It will be free and open to the public.

The Human Placenta Project, whose goal is to understand the role of the placenta during pregnancy, released three RFAs in 2015 and made 19 awards totaling \$46 million. The third Human Placenta meeting will be held April 14-15, 2016. It will be free and open to the public.

NICHD's PregSource™, a crowd-sourced, interactive mobile app, now has 20 partner organizations. The app will gather information, in real time, about common pregnancy experiences. This will help researchers build a more complete picture of normal variation during pregnancy.

Budget and Legislative Update

The NIH received \$32 billion for fiscal year (FY) 2016, a 6.6 percent increase from FY15. The NICHD received a 4 percent increase this year, for a total of \$1.34 billion. The National Center for Medical Rehabilitation Research budget will be approximately \$70 million.

NICHD's \$51.4 million increase will be spent on required increases, grants from the October 2015 Council that otherwise would have been paid with FY15 funds, leaving only \$6.7 million of the increase for the remainder of the fiscal year.

Congressional Report language asked NICHD to plan a scientific workshop on anhydramnios and provide an update in the FY17 budget for the workshop and how it relates to the Human Placenta Project. Additionally, NIH was asked to submit, within a year, a report on the feasibility of a multi-year study of children and adults with Trisomy 21. Congress also asked for an increase in the number of NRSA and other training awards proportional to the IC budget increase, and an update in the FY17 budget on how NIH will use its Strategic Plan as part of its resource reallocation process.

In December 2015, Dr. Lisa Freund, Chief of the Child Development and Behavior Branch, and others provided a legislative briefing on Understanding the Developing Brain.

Council Discussion

Dr. Frederick Rivera asked about the funding for ECHO, stating that he had thought the NCS money had only been allocated for a single year. Dr. Spong stated that the initial monies of \$165 million were allocated to ECHO due to language in the appropriations that allowed it to be spent on research that met the goals of the NCS. The language was the same this year, and it is anticipated that it will remain that way for the next 7 years.

Dr. Gregory Kopf asked if there was interest in including other organizations (e.g., USAID) into the NIH-Gates collaboration. Dr. Spong stated that she was not sure, as the collaboration was initiated at the top level.

Dr. Melissa Gilliam asked what "report language" means. Dr. Spong said that this is language that comes from Congress asking NIH to do something or respond to something.

Ms. Wendy Lazarus asked for more information about what was behind the increase in funding for NIH and what it means for the future. Dr. Spong speculated that there is a lot of interest and goodwill for the work NIH does, and expressed a hope that it will continue.

IV. REPORT OF THE DIVISION OF EXTRAMURAL RESEARCH

Report of the Director, DER

Dr. Della Hann presented the DER updates and introduced four new staff members who joined the NICHD Extramural Program: Valerie Cotton, Developmental Biology and Structural Variation Branch; Sue Marden, National Center for Medical Rehabilitation Research; Kimberly Witherspoon, Office of Committee Management; and Jerusha Murugen, Office of Global Health Research.

Four NICHD staff members also transitioned into the extramural research program: Della White, Populations Dynamics Branch; Ruth Brenner, Pediatric Trauma and Critical Illness Branch; Eric

Lorenzo, Maternal and Pediatric Infectious Disease Branch; and Reiko Toyama, Developmental Biology and Structural Variation Branch.

Dr. Hann also acknowledged Lynne Havercos, a Medical Officer in the Child Development and Behavior Branch, who recently retired.

Dr. Hann recognized three summer interns of the DREAM Program: Chinagozi Ugwu, Reon Holloway, and John Dougherty.

NIH and NICHD: Costs and Success Rates

The success rate of NIH research project grants have decreased from above 30% to below 20% between 1998 and 2014, even as the number of applications have increased. NICHD's success rate went from a peak above 30% in 2000, to about 11.5% in 2015 while the number of applications have almost doubled. In addition, the average cost of awards has risen, though buying power is the same now as it was in 1998.

Implementing Council Working Group Recommendations

As recommended by review of the Office of the Director, grants from the Office of Health Equity have migrated to the DER and staff have successfully integrated into appropriate branches.

NICHD research training and career development awards (NRSA, K, and T awards) were reviewed by a working group. Recommendations included: shifting support from institutional support awards to individual awards (K12 to other K awards), increasing the success rate for the K99-00, and increasing salary for K08 and K23 awards (physician-scientist trainees). Shortly after this recommendation was issued, NIH mandated an increase in salary for K08 and K23 awards. Currently, NICHD supports the K12 mechanism to a greater extent than any other Institute. In order to accommodate the recommended changes and cover the salary increases, NICHD will implement gradual reductions to the K12 programs over time.

Updates

Adolescent Brain Cognitive Development Project (ABCD)

This project has a goal of longitudinally following 10,000 children, beginning at age 9-10, to assess factors that influence individual brain development trajectories and outcomes. A detailed governance structure, consisting of working groups, an IRB, an external advisory board, and cross-agency committees, has been established.

Zika Virus

The Zika virus, which is transmitted by mosquito, is suspected as a causal factor for microcephaly. The first infection was in May 2015 in Brazil. To date, there have been 15 cases in the United States. HHS has initiated a coordinated response, stepped up surveillance and lab activities, established sample sharing, planned a workshop for March 2016, and had the CDC

issue a travel advisory on January 16, 2016. There are a number of knowledge gaps that, by leveraging international and internal infrastructure, research will address.

Stewardship of Clinical Trials

A number of recent reports have been issued touching on the stewardship of clinical trials at NIH. Currently, data are supposed to be shared on clinicaltrials.gov within 12 months of the end of data collection, along with a narrative summary of the findings. NICHD put out an RFI on enhancing the timely data sharing of NICHD-funded studies, to encourage compliance with data sharing regulation. Dr. Hann noted that NICHD DASH is one place that data can be shared by NICHD-funded investigators.

Council Discussion

Dr. Anne Case asked whether the reduction in K12 awards would be achieved by reducing the number of institutions receiving them or the number of individuals supported at each institution. Dr. Hann stated that, at first, the reduction would come from the number of individuals supported at a given institution. NICHD might also choose to limit the number of new institutions receiving K12 awards.

Dr. Diana Bianchi asked how being funded through the F grant mechanism correlates with later funding success. Dr. Hann stated that those who receive the F and K awards are more likely to stay in the field and obtain later grants compared to those fellows on institutional awards.

Dr. Richard Krugman asked how instances of abuse would be dealt with in the ABCD study, because, with a cohort of 10,000, it is likely that approximately 100 new instances of abuse will occur every year. Dr. Hann deferred to Dr. Susan Weiss, from the National Institute on Drug Abuse. Dr. Weiss stated that the study had researchers who were experienced in these issues, and the participants signed confidentiality forms. All information children provide is confidential unless there is an immediate need, such as an indication that they may harm themselves or someone else. Thresholds for divulging that information are still being established, and will be dealt with by several levels of review.

Ms. Sheila Zimmet stated that it was her understanding that the obligation to report abuse, such as in cases of abuse by the parent, outweighs confidentiality, and that this is usually stated in the consent forms. Dr. Weiss confirmed that this was correct.

Dr. Melissa Gilliam asked about efforts to capture teen pregnancy and timing of the onset of pregnancy. Dr. Weiss replied that pregnancy and pubertal hormones will be monitored.

Dr. Walter Frontera asked how low the K12 funding would be cut to in the future. Dr. Hann responded that a level has not been set and stated that reductions will be made to individual awards as they come up for re-competition.

Dr. Timothy Shiver asked whether children with developmental disabilities would be included in the ABCD study since the exclusion of this population leads to a large knowledge gap, and stated that, for this reason, exclusion seems unacceptable. He further asked to what extent psychosocial issues will be monitored over the course of the study. Dr. Susan Weiss replied that there will be

some limitations to the inclusion of those populations, if they are unable to complete the study measures. Dr. Frederick Rivera stated that the ABCD sample of 10,000 should be a random, representative sample of children across the United States. Dr. Weiss replied that the sample will be close to a national sample in terms of race and ethnicity and rural versus urban areas, but the study is limited by study site location. Dr. Rivera asked why, if there are 19 sites across the country, the sample couldn't be representative. Dr. Weiss responded that cost was the issue because children would then have to be paid to travel to the study sites. Within the locale of the study sites, an attempt is being made to make the sample representative.

Dr. George Saade stated that NICHD has several cohorts from whom data was gathered during pregnancy and the perinatal period, and who also consented for later follow up. This should be kept in mind by those wishing to gather longitudinal data on those from pregnancy through age 10. Dr. Hann agreed there are many interesting, consented cohorts and significant resources were expended in developing them. This is why data sharing efforts are so important. To maximize success, investigators need to be willing to share previously collected data which she mentioned earlier.

Ms. Sheila Zimmet asked if there were any studies currently being conducted on lead exposure, given the recent news from Flint, Michigan. Dr. Hann stated that the Secretary's office reached out and NICHD is part of the ongoing effort.

V. NATIONAL CENTER FOR MEDICAL REHABILITATION RESEARCH (NCMRR) UPDATE

Dr. Alison Cernich thanked the Council for the chance to speak and presented an update of the work at NCMRR.

NCMRR was established in 1990 following the Americans with Disabilities Act to promote rehabilitation research with the NIH, and coordinate efforts through the Trans-NIH Medical Rehabilitation Coordinating Committee across the NIH. NCMRR in FY15 had a budget of \$66 million, including monies set aside by NICHD.

NCMRR is currently developing a Rehabilitation Research Plan that includes action items that cross the interests and mission of the NIH. Input was sought from an advisory board, then from the NIH community and finally from the public. Some priorities will be reshaped to be less specific, so that the investigator community will have more flexibility. The final Plan will be sent to Congress in September of 2016.

NCMRR is planning a Rehabilitation Scientific Meeting with an agenda produced by the Trans-NIH Medical Rehabilitation Committee, available on the NCMRR website.

Dr. Cernich thanked the federal partners (Veterans Affairs, Department of Defense, National Science Foundation and others) that make up the Advisory Board for their critical input.

Council Discussion

There were no questions for Dr. Cernich from the Council.

VI. UPDATE ON PRECISION MEDICINE

Dr. Josephine Briggs, Director of the National Center for Complementary and Integrative Health, provided an update on the Precision Medicine Initiative (PMI).

The mission of the PMI is to use research, technology, and policy to empower patients, researchers, and providers to work together toward the development of individualized treatments. The Initiative is taking a broad look at the many drivers of health and well-being.

The promise of PMI is that it will result in more therapies like Zelboraf and Kalydeco, treatments that target a portion of the populations with metastatic melanoma and cystic fibrosis, respectively. Another area of promise is that genetic information will provide a better idea of who will benefit from a treatment.

PMI will be realized through changes in participant partnerships, electronic health records, technologies, genomics, and data science. Clinical research needs to engage patients as partners in the research process to achieve results. This is often hindered by recruitment at the start and retention over time, perhaps because research questions need to be broadened to include issues most relevant to patients. PMI is attempting to use new model of participant engagement.

PMI is looking for new ways to drive clinical research. It is taking advantage of mobile technologies to interact with people and track an increasingly large amount of health information. PMI is also looking to better use electronic health record data, which requires researchers and the organizations maintain the EHRs to agree on data syntax, semantics, and transmission methods. Centralized data storage for patients and researchers is also being explored.

The ACD received a report on PMI in December 2015.

PMI will recruit one million volunteers to participate as a longitudinal cohort, who consent to be re-contacted for sub-studies. It is anticipated that it will take 3-4 years to fully recruit participants, with enrollment to start by the end of calendar year 2016. Participants will also be asked if they would be willing to bring in other family members, boosting both recruitment and engagement.

The core data set will include self-report measures, baseline health exam, EHR data, biospecimen data, and mHealth data (passively collected data from cell phones, wearable sensors). Data will come in part from five to seven large health care provider organizations participating, overseen by a coordinating center.

Pilot studies for enrollment and interfacing with participants will be conducted this year, with funding to be awarded in the early part of this year.

The FY16 budget for PMI is coming primarily from NIH, with some additional monies from the FDA and the Office of the National Coordinator for Health Information Technology.

Council Discussion

Dr. Melissa Gilliam asked if underrepresented populations would be defined and if PMI's definitions of various populations would be influenced by how people self-identify. Dr. Briggs stated that one of the main deliverables in the first few years will be focus groups and quantitative research determining participants' attitudes about being engaged in clinical research.

Dr. Diana Bianchi asked how pregnant women will fit into PMI, as little was said about them in the initial working groups. Dr. Briggs recognized that pregnancy is a stage of the life cycle where the potential for engagement was very strong. A working group will address that.

Dr. Anne Case asked about attrition rates, which might differ depending on whether participants were self-enrolled versus recruited by health care providers. This could impact the longitudinal data, which is the most valuable. Dr. Briggs stated that the use and utility of mobile devices will be critical to the cost effectiveness of the effort. Other components of longitudinal data do not need to be expensive (e.g., EHR data). Much attention is being paid to make sure studies are cost effective.

Ms. Wendy Lazarus asked how the reliance on mobile technologies will impact the ability to reach under-served populations. Dr. Briggs stated that the mobile phone use is high even in those populations, and incentives might be focused on providing minutes or other tangibles. The Council member stated that using intergenerational engagement could be a powerful force: bringing in the Millennials who would then bring in and help retain the older members of their family.

VII. LEG 101

Ms. Lisa Kaeser, Director of the NICHD Office of Legislation and Public Policy, presented on the functions of the Office of Legislation and Public Policy, which acts as a legislative liaison, public liaison, manages public-private partnerships, and controlled correspondence. Ms. Kaeser highlighted some of the little known facts about the appropriations and legislative processes.

While many believe that NIH staff can tell Congress how much money it needs, the Anti-Lobbying Act prohibits Federal employees from using appropriated funds to lobby Congress. The NIH Director, however, is invited annually to present before the Appropriations committee regarding NIH's research accomplishments and challenges.

Along with annual bills to fund the Federal agencies, the Appropriations Committee releases reports with directives, or "significant items", which dictate areas of priority for NIH. NIH staff do not decide what directives Congress includes in those reports; these are not known until they are publicly released.

While Congress makes annual appropriations and can pass legislation defunding specific projects, it has rarely done so. Ms. Kaeser's office does get frequent inquiries about specific programs or research projects, however.

NICHD runs no research advocacy organizations. There is a voluntary coalition, the Friends of NICHD, which advocates on behalf of NICHD to Congress. NICHD staff provide information to them as requested.

NIH staff may not propose new legislation and suggest hearings. Staff can, however, with clearance from HHS, and upon request from Congress, provide technical assistance on proposed legislation, answer questions for the record following hearings, and provide responses to correspondence from Members of Congress.

Authorizations and appropriations differ; authorization bills allow Congress to increase funding, but NIH doesn't actually get the money until the Appropriations Committees decide which areas, agencies, and programs will receive additional funding.

Council Members are special government employees. As such, Council can talk to Congress during hours not spent as a special government employee (and after each Council meeting has adjourned) as long as government funds are not used.

Council Discussion

Dr. Richard Krugman asked about the \$2 billion increase that NIH received for FY16 and whether it is related to the money set aside for the 21st Century Cures legislation, which he thought was being funded out of oil money. Ms. Kaeser replied that 21st Century Cures bill is a large, bipartisan NIH-FDA reauthorization bill passed by the House last summer to accelerate the discovery, development, and delivery of treatments and cures for disease. One of its components was to specify how the mandates could be paid for. The Senate is taking up portions of the House bill, but so far nothing has passed.

VIII. FUNDING THE BEST SCIENCE

Dr. Spong gave a presentation about NICHD funding and strategies so NICHD can fund the best science.

The NICHD payline is among the lower end of Institute paylines, having decreased from 28.2% in 2000 to 9% in 2015. This is coupled with an application rate that continues to rise due in part to the allowance of unlimited resubmissions.

As a percent of NICHD's budget, R01s make up the vast majority at 36%. R21s, Centers, and Contracts each make up about 6%. About 65% of NICHD funded studies focus on humans and 35% on animals. This is the opposite of the other Institutes where the ratio is 60% animal and 40% human. In addition, NICHD R01s are more costly than R01s from other institutes and have increased more over time relative to other ICs.

When funding practices were compared across ICs, NICHD has a lower proportion of funding beyond its published payline. About half of the Institutes publish a payline and those that publish a payline are more likely to allocate funds to funding mechanisms in proportions similar to NICHD than those Institutes without published paylines. The NIH Strategic Plan makes some recommendations for making funding decisions, including considering principal investigator (PI) minimum time, considering limiting the number of grants per PI, and select pay that funds the best science.

An internal analysis found that to move the NICHD payline, approximately \$10 million is needed for each percentage point. There are many ways to effect this change and these were

discussed. Options for improving the payline at NICHD include: tightening referral guidelines, tightening transfer acceptance from other ICs, moving to accepting clinical trials only by Funding Opportunity Announcement, employing stricter methods for large grant acceptance, and limiting the number of solicitations on which NICHD is listed. Additionally, Council may want to consider more stringent requirements for PIs receiving more than \$1 million, limitations on long-standing grants and duration of awards, and make P01s by Funding Opportunity Announcement. NICHD could also choose not to use some funding mechanisms, which could free up some money. The required PI effort level could also be raised for every grant.

In summary, NICHD is trying to be more strategic about what it funds, and Council input is welcome.

Council Discussion

Dr. George Saade asked what the return on investment was for different funding mechanisms. Dr. Spong replied that this depends on how success is defined. This is usually done by the number of publications and the ability of the PI to obtain other funds. Those data are currently being compiled. Dr. Saade said that for him, a useful metric of return on investment was impact for patients and he doesn't see that kind of impact for some funding mechanisms. Dr. Spong replied that changes in practice can be measured for clinical trials, but NICHD funds many scientific areas that are important, but that won't have a direct clinical impact. NICHD is interested in examining, where applicable, how research impacts clinical practice, either through the introduction of a new practice or cessation of one for which evidence is lacking.

Dr. Patricia Dorn asked what PI level of effort was being considered for the R01 and what the impact on grant number would be. Dr. Spong stated this is open for discussion and wanted to know what Council thought. She posed the question: how many grants can an individual handle?

Dr. Patricia Dorn stated that one way to determine the level would be to look at what was proposed, ask whether the level of effort proposed is appropriate, and then ask whether that level of effort is enough to warrant being designated a PI. Dr. Spong said that this was important, and that study section does look at that. Mandating a specific amount of effort, however, would limit the number of applications a PI could submit.

Dr. Melissa Gilliam observed that the pressure to be funded is what drives the submission of multiple grants and that artificially limiting the number of grants a PI may receive might only increase that pressure. Dr. Gilliam asked how diversity might be impacted if the P01 mechanism were trimmed. Dr. Spong asked if Dr. Gilliam would limit the number of grants a PI could receive. Dr. Gilliam replied that she would not penalize someone if they were writing good grants, if the objective is really to fund the best science. Decreasing the number of grants or the amount of time of funding will only increase the time spent writing grants.

Dr. Anne Case stated that it is hard to know what to do with the data presented until metrics are developed, as Dr. Saade mentioned. Dr. Case suggested that multiple approaches may be better than a single rule for grant number or duration.

Dr. Gregory Kopf mentioned that the cost difference for human research funded by NICHD compared with other ICs is important to investigate and could be a source of cost savings. Dr. Spong replied that delving into that issue is important, and may depend on how the various ICs use different funding mechanisms.

Dr. Richard Krugman asked for clarification about indirect costs, and, since they run about one third of direct costs, whether they might be worth examining. Dr. Spong replied that NICHD has no control over indirect costs. They are set through NIH-HHS discussion, and NICHD has no input. A Council member asked if Council could provide input. Dr. Hann stated that she was not aware of any way Council could provide input into that process.

Dr. Piero Rinaldo stated that PI level of effort assumes 100% availability, but most PIs have protected time and asked if factoring that in would better inform discussions around effort limits. Dr. Spong replied that this was a very good point.

Dr. Ken Muneoka noted that NIH says that the maximum level of effort is reached at \$1 million and if the average R01 is for \$250,000, it seems obvious this funding level should be the limit. Dr. Spong replied that NIH hasn't set \$1 million as a firm limit, but rather Council should discuss those grants when \$1 million is reached.

Dr. Atul Butte mentioned that it is easy to reach the \$1 million threshold if you are overseeing a big project where most of the money is used outside of the lab, i.e., one's lab only has a small piece of the work. Dr. Butte also asked about those grants that are not renewed, and whether there would be time and cost savings to look at the annual reports a year before the grant ends and potentially cancel it. Dr. Spong replied that those reports are examined closely, and sometimes they are cancelled, or given a no-cost or mid-cost continuance for the last year.

Dr. Paul Wise stated that looking at level of effort and cutting grant size avoids making a strong determination of what is and isn't good science. He recommends examining whether funding is really supporting the direction the science has to go and to think harder about the measures of success. Dr. Spong thanked Dr. Wise and said that NICHD is looking at those metrics and will be coming back to Council with them.

IX. DIR PRESENTATION: NEURAL CODES FOR THE SENSE OF TASTE

Dr. Constantine Stratakis introduced Dr. Mark Stopfer, a part of NICHD's Developmental Neuroscience Program. Dr. Stopfer's work uses animal models (locusts, moths, and fruit flies) of the neural development of olfaction and taste, which govern a variety of brain functions across many species.

Dr. Stopfer's lab uses a variety of tools to study the basic rules that populations of neurons use process information, specifically about taste and olfaction. It is commonly thought that there are four basic tastes that are processed through labeled line coding using direct connections from specific receptors to specific brain areas – e.g. receptors for sweet to brain areas for sweet. This has been difficult to test, however, because vertebrate taste receptors have a complicated

underlying mechanism and recording from taste brain areas is technically challenging. Dr. Stopfer's approach uses simple model systems, mainly from insects.

The lab delivers stimuli to the moth's proboscis in a computer liquid delivery system so that the precise timing of taste delivery to the proboscis can be known and linked with electrophysiological recordings of many neurons in the maxillary nerve.

Dr. Stopfer found that gustatory receptor neurons (GRN) respond to different number of tastants (e.g., some just sucrose, some from across taste categories). GRN can respond to some tastants in a taste category, but may not respond to others in the same category. They also show a diversity of temporal responses (e.g., a GRN may respond to several taste categories, but fire with different patterns of excitation and inhibition depending on the taste chemical). The data gathered were sufficient for a computational model to discriminate between specific taste chemicals, not just the four basic taste categories, using just the electrophysiological recordings.

From the GRNs, information is relayed to interneurons in another brain area. These neurons respond to seemingly every taste, but with different firing patterns. They are more broadly tuned, inhibit one another, and receive information from multiple receptor types. Computational modeling of the recordings also permitted rapid classification of tastants, even more accurately than the GRN data.

In summary, it appears that each tastant is encoded uniquely, meaning that there aren't just a few basic taste categories. Tastes are encoded in a combinatorial, spatio-temporal fashion; this means that one has to look at a whole population of cells to know what tastant is being encoded. In addition, there is no evidence that taste is processed by labeled lines. A review of the literature suggests similar mechanisms may exist in other species including vertebrates.

Dr. Stopfer concluded by thanking the scientists who performed some of this work, including Sam Reiter, Chelsey Campillo Rodriguez, and Kui Sun.

Council Discussion

Dr. Gregory Kopf asked if desensitization plays a role in fine tuning of neural pathways for taste. Dr. Stopfer responded that they have not looked at plasticity within the circuit yet, but that there is a response decrement over the course of many trials and that it may play a role in discrimination.

Dr. Diana Bianchi asked if it was possible to examine changes to this circuit across the lifecycle. Dr. Stopfer replied that the moth would not be the best developmental model, but drosophila, which the lab also uses, could be used to examine developmental changes.

Dr. Ken Muneoka asked about the role of inhibitory input to the circuit. Dr. Stopfer replied that there are populations inhibitory second order neurons and that the complex pattern of firing across the population of second order neurons is due to the interplay of excitatory and inhibitory neurons.

Dr. Richard Shields asked if there was an optimal taste exposure that might, epigenetically, have downstream effects on other parts of the brain. Dr. Stopfer replied that it hard to know what an optimal exposure would be. In addition, these neurons seem to respond to everything. This

suggests that the system is meant to describe everything it encounters and that brain plasticity can then kick in.

Dr. George Saade asked whether anything is known about how early developmental exposures affects brain areas responsible for hunger and satiety. Dr. Stopfer replied that nothing is known about the gustatory system, but that within the olfactory system, caterpillars can be trained to prefer an odor that carries over to the moth. The mechanism is still unknown, however.

X. 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. The Council heard short summaries of each of the five areas of investigation and unanimously endorsed each of them.

Dr. Tonse Raju proposed an initiative for mentored specialized clinical investigator development awards for the Maternal Fetal Medicine Units Network and the Neonatal Research Network. Only specific centers will be invited to submit applications for fellows and junior faculty who are already working in one of the Networks. It is meant to enhance the research independence of the applicants as they learn to conduct large clinical trials. Four of the seven recipients of these awards are now faculty at major research institutions.

Dr. Min Lee proposed re-competition for the Contraceptive Research Centers Program. Originally established by Congress in 1993, there is still a critical need for family planning approaches for men and women. The primary objective is to support research into the development of safe and effective new or improved contraceptive approaches for men and women. Dr. Patricia Flynn asked what accomplishments the Centers have made to date. Dr. Lee responded that the vaginal ring had been funded by the Center, as well as some of the clinical trials for emergency contraception. A Council member asked if the cost for each was known. Dr. Hann replied that it varied across the programs.

Dr. Nahida Chakhtoura proposed an initiative to improve the knowledge base for treating and preventing sexually transmitted infections (STI) and HIV in youth through research aimed at understanding the interaction between HIV, STI, and adolescent reproductive development and the use of contraception.

Dr. Gilman Grave proposed the re-competition of the Pediatric Scientist Development Program. First established in 1986 to address concerns that trainees needed additional training in molecular biology to be competitive, this initiative now helps trainees to deal with the large body of knowledge related to the “-omics” revolution. To date 175 scientists have been trained, 86% of whom continue on in pediatric development. Dr. Diana Bianchi noted that these awards are more like individual development awards and less like a K12, even though it may be counted that way in the statistics.

Dr. Karen Winer proposed the re-competition of the Child Health Research Career Development Awards. These awards were established in 1990 to train junior faculty who are physician scientists in basic research to more successfully compete for NIH funding. Trainees are uniquely able to bridge the gap between basic research and clinical science; the majority of awardees continue a career in academic pediatrics, and 70% have successfully applied for NIH funding.

XI. COMMENTS OF RETIRING MEMBERS

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

Dr. Paul Wise said that it had been a privilege to participate in the work of the Institute and Council, thanked Dr. Spong for her leadership, and the Council for an informative and educational experience.

Dr. Ken Muneoka echoed Dr. Wise's statement, and additionally thanked Dr. Alan Guttmacher.

Dr. Bonnie Duran also thanked leadership and the Council, and indicated that her experience on Council had taught her a great deal. Dr. Duran suggested that part of the reason NICHD's research may be more expensive is because of the large effort put forth around community engagement, a necessary feature to much of the work NICHD is working towards.

Dr. Diana Bianchi thanked Dr. Spong, the Council and Dr. Guttmacher for the opportunity to serve. She also acknowledged the NICHD staff, especially Paul Gresham, Sandi Delcore, Sandra Sheriff, and others. Dr. Bianchi appreciated how data driven the Council was, and expressed hope that this continues. She would have liked to have more time to interact with Council and strategize. She mentioned that NICHD is at the halfway point for the Strategic Vision and she suggested that this is an appropriate time to review the themes and perform a gap analysis.

XII. 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).

XIII. 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 757 HD-primary applications requesting \$212,119,627 in direct costs and \$294,153,236 in total costs.

ADJOURNMENT

There being no further business, the meeting adjourned at 4:45p on Thursday, January 21, 2016. The next meeting is scheduled for June 9, 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
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.