Department of Health and Human Services
National Institutes of Health (NIH)
Office of the Director (OD)
Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI)

Council of Councils Meeting
January 22, 2013

Meeting Minutes

I. WELCOME

James M. Anderson, M.D., Ph.D., Chair, welcomed participants, NIH staff members, and members of the public to the meeting of the Council of Councils. The meeting opened at 8:30 a.m. on Tuesday, January 22, 2013, in Building 31, 6th Floor, Room 10, on the NIH Campus, Bethesda, Maryland.

Dr. Anderson welcomed 10 new members and announced that one, Susan F. Goekler, Ph.D., was unable to attend the meeting. He also announced the appointment of Dr. Franziska Grieder as Director of the Office of Research Infrastructure Programs (ORIP). Following introductions and announcements from Robin I. Kawazoe, Executive Secretary for the Councils of Councils, Dr. Anderson reviewed the day's agenda.

A. Attendance

1) Council Members Present

Chair: JAMES M. ANDERSON, M.D., PH.D., Director, DPCPSI, OD, NIH
Executive Secretary: ROBIN I. KAWAZOE, DPCPSI, OD, NIH
EMERY N. BROWN, M.D., PH.D.,* Massachusetts Institute of Technology, Harvard Medical School, Massachusetts General Hospital, Cambridge, MA
LAVARNE A. BURTON, M.A., American Kidney Fund, Rockville, MD
CARLOS D. BUSTAMANTE, PH.D.,* Stanford University School of Medicine, Stanford, CA
F. XAVIER CASTELLANOS, M.D.,* New York University of School of Medicine, New York, NY
JANICE E. CLEMENTS, PH.D.,* The Johns Hopkins University School of Medicine, Baltimore, MD
STEVEN T. DEKOSKY, M.D.,* University of Virginia, Charlottesville, VA
RICHARD L. EHMAN, M.D., Mayo Clinic College of Medicine, Rochester, MN
JACK A. ELIAS, M.D., Yale University School of Medicine, New Haven, CT
RICHARD M. GREENWALD, PH.D., Simbex, iWalk, Dartmouth College, Lebanon, NH
BARBARA J. GUTHRIE, R.N., PH.D., F.A.A.N.,* Yale University, New Haven, CT
NANCY L. HAIGWOOD, PH.D.,* Oregon Health & Science University, Beaverton, OR
PETER J. HOTEZ, M.D., PH.D., Baylor College of Medicine, Houston, TX

JEFFREY A. KAUFMAN, M.B.A., Adenoid Cystic Carcinoma Research Foundation, Needham, MA
GRACE LEMASTERS, PH.D., University of Cincinnati College of Medicine, Cincinnati, OH
MARK O. LIVELY, PH.D., Wake Forest University School of Medicine, Winston-Salem, NC
K.C. KENT LLOYD, D.V.M., PH.D., University of California, Davis, Davis, CA
H. KIM LYERLY, M.D., Duke University School of Medicine, Durham, NC
CRAIG J. MCCLAIN, M.D.,* University of Louisville School of Medicine, Louisville, KY
JOYCE A. MITCHELL, PH.D., University of Utah, Salt Lake City, UT
ROBERT F. MURPHY, PH.D., Carnegie Mellon University, Pittsburgh, PA
REGIS O'KEEFE, M.D., PH.D., University of Rochester School of Medicine and Dentistry, Rochester, NY
REGINA RABINOVICH, M.D., M.P.H., Global Health Consultant, Seattle, WA
JAMES E. SCHWOB, M.D., PH.D.,* Tufts University School of Medicine, Boston, MA
TERRIE (FOX) WETLE, PH.D., Brown University Medical School, Providence, RI
GILBERT C. WHITE, II, M.D.,* Blood Research Institute, BloodCenter of Wisconsin, Milwaukee, WI

*Appointments are still pending review of financial disclosures and conflict-of-interest statements. These members did not vote at the January 22, 2013 meeting.

2) **Liaisons**

JANINE A. CLAYTON, M.D., Director, Office of Research on Women's Health, DPCPSI, OD
ROBERT EISINGER, PH.D., Director, Scientific and Program Operations, Office of AIDS Research, DPCPSI, OD (representing Director Jack Whitescarver, Ph.D.)
FRANZISKA B. GRIEDER, D.V.M., Ph.D., Director, Office of Research Infrastructure Programs, DPCPSI, OD
ROBERT M. KAPLAN, PH.D., Director, Office of Behavioral and Social Sciences Research, DPCPSI, OD
DAVID M. MURRAY, PH.D., Director, Office of Disease Prevention, DPCPSI, OD
ELIZABETH L. WILDER, PH.D., Director, Office of Strategic Coordination, DPCPSI, OD

3) **Ex Officio Member**

LAWRENCE A. TABAK, D.D.S., PH.D., Principal Deputy Director, NIH

4) **Presenters in Attendance**

CHRISTOPHER AUSTIN, M.D., Director, National Center for Advancing Translational Sciences, NIH
DANIEL H. GESCHWIND, M.D., PH.D., David Geffen School of Medicine, University of California, Los Angeles

TERRY MAGNUSON, Ph.D., Sarah Graham Kenan Professor, Chair, Department of Genetics, Vice Dean for Research, School of Medicine, University of North Carolina, Chapel Hill

RONALD MARGOLIS, Ph.D., Senior Advisor, Molecular Endocrinology, Division of Diabetes, Endocrinology, and Metabolic Diseases, National institute of Diabetes and Digestive and Kidney Diseases

WILLIE MCCULLOUGH, Ph.D., Program Director, Division of Construction and Instruments, ORIP, DPCPSI, OD

OLEG MIROCHNITCHENKO, PH.D., Health Scientist Administrator, Division of Comparative Medicine, ORIP, DPCPSI, OD

5) NIH Staff and Guests

In addition to Council members, presenters, and Directors, others in attendance included NIH staff and interested members of the public.

B. Meeting Procedures

Ms. Robin Kawazoe reviewed the following:

- Council members are considered Federal employees during Council meetings and are therefore subject to the rules governing Federal employees.
- Each Council participant has completed and submitted a financial disclosure form and conflict of interest statement as a Federal requirement for membership on advisory councils. Financial disclosures are used to assess real and perceived conflicts of interests, and Council members must recuse themselves from the meeting during discussion of items for which conflicts have been identified.
- Time has been allotted for discussion between the Council and presenters, but time for comments from other meeting attendees is limited. The public can submit comments in writing; instructions are available on the DPCPSI Web site and in the *Federal Register*.
- Council members should not speak on the Council's behalf or on activities not yet cleared by Council.
- Approved meeting minutes will be posted on the DPCPSI Web site.

C. Future Meeting Dates

Council meetings will be held on May 14 and September 24, 2013. Council meetings in 2014 will be held on January 31, June 20, and September 5.

II. OVERVIEW OF THE OFFICE OF BEHAVIORAL AND SOCIAL SCIENCES RESEARCH (OBSSR)

Dr. Robert Kaplan, OBSSR Director, began his presentation by briefly describing his academic career, which focused on developing quality-adjusted survival analyses to better compare various aspects of population health, and how this work aligned with the

mission of NIH and other agencies. When he first began his career, quality of life was rarely measured, and survival analyses focused on traditional indicators, such as life expectancy, that did not adequately characterize population health status or distinguish, for example, healthy, active individuals from those in a coma. Now studies of quality of life generate approximately 10,000 publications per year, the concept of quality-adjusted life year is a common component of medical training, and federal health initiatives, such as the Healthy People initiative, increasingly incorporate quality of life into their objectives. Both Dr. Kaplan's academic work and the overall change in focus toward both quality and quantity of life map well to the mission of NIH, which includes the application of fundamental knowledge "to extend healthy life and reduce the burdens of illness and disability."

These changes have also guided Dr. Kaplan's vision for new directions taken by OBSSR. These directions can be grouped into three overarching categories.

The Next Generation of Measurement and Data

A wide range of OBSSR activities focus on new technologies and systems approaches to measurement, data collection, and data visualization, and particularly to approaches for analyzing Big Data. Sample projects include the development of approaches to capture all types of environmental exposures to increase the ability to study combinations of genetic and environmental determinants of health, a tool to improve and collect data on adherence to medications, unobtrusive monitoring tools to collect data and monitor health in older persons living alone, and models to determine how disasters or public health emergencies might affect communities and traffic patterns. OBSSR held a conference on data visualization, and it continues to be interested in data harmonization, for example in electronic health records, the Patient-Reported Outcomes Measurement Information System (PROMIS), and the NIH Toolbox.

Delivering Services in a Reforming Health Care System

A report recently released by the Institute of Medicine (IOM) noted that the United States spends approximately twice as much per capita on health care as other member countries in the Organisation for Economic Co-operation and Development (OECD), but that several categories of US health outcomes are worse. The IOM report compared health outcomes in the US to those in 16 counties with highly successful economies. Although the United States has an advantage with respect to stroke mortality, control of blood pressure and cholesterol levels, and elder care, Americans are at a significant disadvantage, and in many cases fare the poorly with respect life expectancy from birth, and probability of reaching age 50. This results from a variety of factors, including higher rates of injury, non-communicable disease, and communicable disease, regardless of socioeconomic status. Although some problems can be attributed to the health care system, behavior plays a large role in many of the causes underlying these statistics. For example, Americans consume more calories, are more likely to become sexually active at an earlier age, and are less likely to wear helmets or seat belts in comparison to peers in other wealthy economies. Although there are large socioeconomic disparities in the US, wealthy non-Hispanic white Americans still have poorer health outcomes than peers in

comparison countries. OBSSR supports a large amount of work focused on correlates of health outcomes.

Training the Next Generation of Research Investigators

OBSSR has been sponsoring a group of medical schools who are revising their curricula to incorporate more behavioral and social science. Changes in the medical school curriculum, as well as expected revisions of the Medical College Admission Test (MCAT), will likely lead to changes in undergraduate curricula. However, Ph.D. programs remain focused on training new professors, when approximately half of new Ph.D. holders move into fields outside of academia, and training is discipline-specific and includes out-of-date measures. In addition, the number of postdoctoral fellows supported by the federal government is lower in behavioral and social sciences than in other disciplines. OBSSR is working on ways to modernize Ph.D. programs to train candidates in team and systems science and to prepare them for a range of job opportunities.

Discussion Highlights

- OBSSR's efforts in promoting a healthy lifestyle focus on a range of behaviors both in primary and secondary prevention. The Office is interested in the continuum from optimal health to poor outcomes, and it is looking at efforts to prevent early behaviors that might lead to adverse outcomes. Several OBSSR communications activities, including the OBSSR web site, aim to disseminate study findings and promote public discussion of health behaviors.

- NIH and OBSSR have already begun addressing some recommendations in the IOM report, for example the harmonization of measures and data collection.

- Socioeconomic status and neighborhood have large effects on health. For example, poverty is an overriding determinant for many conditions noted in the IOM report, and for the first time, global health benchmarks are being used to assess population health in the United States.

- Mental illness is placing a large burden on health care systems, not only in industrialized nations, but also in developing ones. Mental health thus will become a major issue in global health.

- The K–12 curriculum should be revised to incorporate social and behavioral health issues, particularly because education is one driver of health outcomes.

- Training in probability and statistics should be improved. Revising K–12 education to include probability and statistics can improve both the training of potential researchers and the numeracy and scientific literacy of the general public. Applications can also help individuals better understand risk.

- The increasing focus on Big Data should not come at the expense of knowing how to analyze small sample sizes. Computational and statistical sciences will have to work together, as traditional statistical approaches do not work well with machine learning.

- Efforts to refine Ph.D. education in behavioral and social scientists should include ways to foster collaboration among disciplines so that all sciences are working together. Examples include collaborations between quantitative and basic scientists, between behavioral and social sciences and medicine, and between behavioral and social scientists and systems scientists and technology developers. Some Council members cautioned against emphasizing team science at a predoctoral level because of hesitation on the part of many departments to hire individuals trained in multidisciplinary programs. However, a move from discipline-specific predoctoral training into multidisciplinary doctoral training might be easier for individuals trained in quantitative sciences than for those trained in laboratory science.

- Postdoctoral tracks focused on careers outside academia should be developed.

III. REMARKS BY THE NIH PRINCIPAL DEPUTY DIRECTOR

Dr. Lawrence Tabak began his remarks with an update on the FY2013 budget. Like other federal agencies, NIH is operating under a continuing resolution through March 27. Although the passage of the American Taxpayer Relief Act on January 1 averted the threat of an immediate reduction in NIH spending, a new sequester will be ordered on March 1 that will cut NIH spending and be implemented on March 27 if no budget resolution has been achieved. Congress may agree to replace the sequester with a balanced approach to long-term spending and budget deficits. ConsequentlyNIH is not ramping down in anticipation of a sequester, but it continues to operate with caution as is standard under continuing resolutions.

Dr. Tabak also updated the Council on the integration of NIH research activities focused on substance use, abuse, and addiction. He reminded the Council that the Scientific Management Review Board (SMRB) had recommended that NIH establish a new institute focused on substance use, abuse, and addiction-related research. Another option considered by the SMRB was a functional integration of existing research resources, rather than creation of a new Institute that would replace the National Institute on Drug Abuse (NIDA) and the National Institute of Alcohol Abuse and Alcoholism (NIAAA). In the 2 years since then, a task force has conducted several analyses, and NIDA and NIAAA have worked on their own to coordinate their research. Another internal group has assessed potential gaps in the current substance abuse and addiction research portfolios of all Institutes and Centers (ICs) across NIH and developed a draft integrated strategic plan that will augment, not replace, the ICs' strategic plans.

Following this review and extensive consultation with stakeholders, the NIH Director, decided that it is more appropriate for NIH to pursue a functional integration, rather than a major structural reorganization in this area. A steering committee composed of leadership from NIDA, NIAAA, and the National Cancer Institute (NCI) will implement the functional integration, and the NCI, NIAAA, and NIDA advisory councils will

perform second-level reviews of joint research activities. In addition, NIH will create metrics to serve as an initial blueprint and to aid in ongoing evaluation and monitoring of investments in the functional integration of research activities. As specific programs are identified for investment, program-specific metrics will provide additional means for monitoring. Dr. Tabak will report to the NCI, NIDA, and NIAAA advisory councils on the progress of integration activities, and NIH has begun its search for a permanent NIAAA Director.

Dr. Tabak then discussed a communications initiative that NIH has implemented to create a cohesive NIH identity, assess and describe the value of NIH-supported research, and address various stakeholders with competing interests. NIH has been described as "one of the best-kept secrets in Washington," because less than 10% of Americans surveyed know what NIH is. In addition, each IC has its own public identity, resulting in a fragmented approach to communications with the public. NIH has created a communications toolkit, including a new logo, core messages, fact sheets and presentations, operating procedures for media activities, and guidelines on working with grantee institutions and stakeholder organizations. NIH also is hosting a series of meetings, collaborating on local and national events, and coordinating announcements from multiple institutions.

The remainder of Dr. Tabak's remarks focused on the implementation of recommendations from working groups convened by the Advisory Council to the Director (ACD) to identify ways to sustain the future of biomedical research in the United States; ensure the diversity of the workforce; and, to optimize the management, integration, and analysis of large biomedical datasets. These recommendations were reported to the ACD at its June 2012 meeting and implementation plans were described at the December 2012 ACD meeting.

The working group on the biomedical research workforce was convened in response to the increasing difficulties new scientists face in launching traditional, independent careers in academia. The number of new Ph.D.s has increased, even as more established investigators are staying in the workforce longer. In addition, many Ph.D. graduates are entering science-related careers outside of tenure-track academia, and other potential Ph.D. graduates turn away from research careers because they view the career as less attractive. To implement the working group's recommendations to address these challenges, NIH has established a Biomedical Research Workforce Initiative to develop innovative training approaches, introduce trainees to a wider range of science-related career choices, and adjust NIH support for postdoctoral stipends. The initiative also seeks to create a comprehensive tracking system to collect data on trainees and guide decision-making. The working group and initiative focus on Ph.D. scientists. NIH will soon establish an ACD working group on clinician-scientists.

A working group on diversity in the biomedical research workforce was precipitated by an August 2011 *Science* paper that highlighted the disparity in success rates for grant applications among black or African American investigators, compared with those in other groups. NIH recognizes that scientific progress is accelerated by having a diverse workforce and the broad range of perspectives that creates. The working group

emphasized collective responsibility and the large amount of work and various initiatives needed to build trust among the communities from which potential researchers might be recruited, ensure fairness in peer-review, and establish collaborations with extramural partners. The Diversity Initiative also will build infrastructure to increase diversity and establish a nationwide monitoring network, augmenting diversity efforts already under way. NIH is creating a steering committee to ensure that diversity is a core consideration of NIH governance, and recruitment is under way for a permanent Chief Officer for Scientific Workforce Diversity.

The ACD working group on data and informatics called for NIH to ensure that cultural changes within the agency recognize the key role informatics and computation will play in every IC's mission. As with efforts to ensure diversity, commitment to informatics and computation is a collective responsibility among all ICs, and it will require a collaborative environment, both within NIH and throughout the extramural community. NIH is implementing the Big Data to Knowledge initiative (BD2K) to enable biomedical researchers to maximize the value of biomedical data, and it is implementing InfrastructurePlus to create an adaptive environment. Both initiatives will be led by trans-NIH Data Councils, which will report to the NIH Director and be led by the NIH Chief Information Officer and a new Associate Director for Data Science. The governing boards will be established within the next month, and recruitment for the Associate Director for Data Science is under way.

Discussion Highlights

- NIH continues to seek ways to be more efficient and have a higher impact with its resources, and both IC and overall NIH leadership are continually reevaluating priorities. Stakeholders will need to continue to make a case for the value of NIH.

- The working group on clinician-scientists should take a holistic view of the clinician-scientist to include, for example, dentists, veterinarians, and nurses.

- The National Center for Biotechnology Information has been highly successful and sets a standard, but its focus is limited to genomics and DNA sequencing. The proposed initiatives in data science will be broader in scope.

- NIH is working to form partnerships with industry, particularly for mobile health and database integration.

IV. UPDATE ON PLANNING FOR A COMMON FUND INITIATIVE

Dr. Anderson reviewed DPCPSI's planning process, through which the Council narrows down a list of brainstormed ideas by clearing concepts for further development. He noted that at the September Council meeting, Council members had asked to see concepts again when they were developed more fully, especially if those concepts had been cleared with a majority "maybe" vote. Following this review, Dr. Ronald Margolis, of the National Institute of Diabetes and Digestive and Kidney Diseases, presented a proposal for a

Common Fund initiative to begin in 2014. Development of this concept has involved consultation with several experts from NIH, academia, industry, and other countries.

The concept to "deorphanize the druggable genome" is based on the understanding that a subset of genes in the human genome encodes proteins that are involved in disease and can be bound or modulated by small compounds. On the basis of the categorization of known targets into families, researchers have been able to predict a larger druggable genome, called an orphan proteome, which includes a vast number of unidentified targets. The proposed concept will deorphanize this proteome by gathering more information about unannotated proteins within protein families related to the druggable genome. Efforts so far have been hindered by a focus on what is already known, a dearth of mechanistic studies on the functions of unannotated proteins, a lack of understanding of their roles in physiology and disease, and the lack of a comprehensive, curated, searchable database on the druggable genome. In addition, the pharmaceutical industry has abandoned several efforts to expand the druggable genome. Computational approaches, technological advances in data collection, new multidisciplinary fields and collaborative communities, and the potential for synergies arising from the application of basic biology to chemistry can move this field forward.

The proposed initiative will likely have two arms. One will involve a multidisciplinary approach to the unannotated proteome, whereas the other will focus on the development of a knowledge base that: provides consolidated, fundamental knowledge; stimulates hypotheses; and aids in the identification of new drug targets. Potential outcomes include new publications, R01 grant applications, and investigational new drug applications, as well as an enduring, informatics-based, accessible knowledge base and a pool of newly annotated potential targets. It is expected that public-private partnerships will facilitate the eventual transfer of this initiative out of the Common Fund.

Discussion Highlights

- The proposed initiative will have a wide focus that includes new classes of targets and proteins that are accessible to standard pharmaceutical interventions.
- Council members provided useful input including the recommendation to focus on areas which are expected to have the highest impact.
- The initiative will start with known methods and challenge investigators in the community to identify and exploit new and emerging technologies. As illustrated by work with the Knockout Mouse Project, the initiative also can interact with existing programs.

V. CONCEPT CLEARANCE: RESEARCH FACILITIES IMPROVEMENT PROGRAM

The National Primate Research Center (NPRC) program supports eight centers nationwide. These centers house a total of 27,000 non-human primates and support 1,000 research projects per year. Several of these projects involve translational research, and

approximately 40% of the research conducted at the centers focuses on HIV/AIDS. A longstanding collaboration among the ORIP Division of Construction and Instruments (DCI), the ORIP Division of Comparative Medicine (DCM), and the NIH Office of AIDS Research (OAR) has provided funds to modernize laboratories and animal housing facilities at the NPRCs in support of HIV/AIDS research on non-human primates.

Dr. Willie McCullough, of DCI, presented this concept for Council approval. The funding opportunity would aim to increase the size of animal facilities; increase, renovate, and maintain or repair laboratory facilities; and support the purchase and installation of fixed equipment. OAR would continue to provide funding through a request for applications limited to the eight NPRCs. A total of $4 million across two to five awards is anticipated for FY2013.

Discussion Highlights

- The offering of new funding competitions for this program depends on whether OAR has the funds to support new awards.
- Expansion at one NPRC does not come at the expense of other NPRCs.
- During the past 4 years, NPRCs have collaborated and built a consortium to coordinate resources. For example, they are linked to a common database, and one major accomplishment, the Animal Locator database, can be used to find an animal housed at any of the eight NPRCs.
- This funding opportunity focuses specifically on HIV/AIDS research, which is done primarily in macaques. Because chimpanzees are not used for HIV/AIDS research, this funding opportunity would not be affected by the IOM's recommendations on the use of chimpanzees in research. However, it is possible that NPRCs house chimpanzees that will be phased out of research, thus increasing the capacity to house other non-human primates. It will take considerable funds to convert the chimpanzee housing space for use to house other non-human primates. How to fund the repurposing of facilities should be discussed at some point.

Vote

A motion to approve the funding concept was forwarded and seconded. The motion passed unanimously.

VI. RODENT PORTFOLIO AT THE DIVISION OF COMPARATIVE MEDICINE

A. Overview

Dr. Oleg Mirochnitchenko, of DCM, provided a brief overview of the Division's rodent portfolio. About 18% of the DCM budget is devoted to rodent research, primarily through resource centers, resource-related research grants, and training grants. Among these resources is the Rat Resource and Research Center, housed at the University of Missouri. This Center distributes rats, cell maintenance protocols, and rat embryonic stem cell lines

in support of grants supported by 14 ICs. The Center also coordinates with other centers and develops new technologies and disease models. Other initiatives include the Knockout Mouse Project Repository, the Peromyscus Genetic Stock Center, and the National Gnotobiotic Rodent Resource Center. DCM also supports hypothesis-driven research projects that use rodent models, for example, to explore the biology of stem cells. Future development of the rodent portfolio will include support for studies of the human genome, collaborations to determine whether rodent models are appropriate for a research question, the promotion and facilitation of partnerships with other ICs to continue support for trans-NIH initiatives, and continued creation of an informatics system that will allow the identification and evaluation of existing model resources.

B. Mutant Mouse Research: Modeling Human Disease and Health

The core mission of the Mutant Mouse Regional Resource Centers (MMRRCs) is to input, archive, and distribute genetically engineered mouse strains and embryonic stem cell lines. The four regional centers have a total of more than 3,800 strains and lines and have filled more than 7,200 orders in support of projects funded by 15 ICs. The Centers also provide quality control, as well as consultations on colony management, breeding schemes, and genotyping schemes. They therefore offer many advantages to researchers and facilities, such as securing against the loss of strains, facilitating compliance with the NIH sharing policy, and assisting with disaster plan management. The MMRRCs also work with international groups. For example, they led the development of an article describing practices common to repositories throughout the world. This article was published in *Mammalian Genome*.

Dr. Terry Magnuson, of the University of North Carolina at Chapel Hill (UNC-CH), noted that each MMRRC has a unique research focus. The MMRRC at UNC-CH aims to employ systems genetics programs and predictive mouse biology to develop better models for human health and disease. Projects include:

- A collaboration with the UNC-CH's Computer Science department to develop a strain certification program using a universal mouse genotyping array of 80,000 single nucleotide polymorphisms (SNPs).

- A project exploring the role of epigenetics in gametogenesis, uncovering an essential role for the SWI/SNF chromatin remodeling complex during male meiosis.

- Collaboration with the UNC-CH Center for Excellence in Genome Sciences, which is supported by the National Human Genome Research Institute and the National Institute of Mental Health, to explore interactions between mouse strain and diet and their effects on adult behaviors.

- Collaboration with the National Gnotobiotic Rodent Resource Center to develop mouse models with germ-free or selectively colonized guts, which will aid studies of host-microbial interactions, physiological and pathophysiological responses to bacteria, and the functional effects of microbes.

- The Collaborative Cross, which has performed pair-wise crosses of three wild-derived strains and five common laboratory-derived strains, in all combinations, to maximize genomic variability with diverse, genetically reproducible mouse populations. This project has involved communication with mouse laboratories from around the world. The Collaborative Cross complements the Knockout Mouse Project, for example on studies of regulatory variation and host responses to pathogens, and it has enhanced studies on genetic disposition to breast cancer. In celebration of the tenth anniversary of the Collaborative Cross, the February 2012 issues of *Genetics* and *G3* were devoted to papers about the project.

Discussion

- Information on genotype, phenotype, and SNPs associated with models generated by the UNC-CH MMRRC are placed in a public database maintained by the Computer Science department. The models are also available to the public. About 50 to 100 lines generated by the Collaborative Cross are complete and are being used in studies.

- The MMRRCs serve as archives for reference populations. In some cases, investigators also can come to centers to generate mutations, and once they identify specific mutant strains, they can order them from the Center.

VII. REVIEW OF GRANT APPLICATIONS

This portion of the meeting was closed to the public, in accordance with the provisions set forth in Sections 552(b)(c)(4) and 552(b)(c)(6), Title 5, U.S. Code and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix).[1] Members were instructed to exit the room if they deemed that their participation in the deliberation of any matter before the Council would represent a real or perceived conflict of interest. Members were asked to sign a conflict-of-interest/confidentiality certification to this effect. The *en bloc* vote for concurrence with the initial review recommendations was affirmed by all Council members present. During the closed session, the Council concurred with the review of 317 ORIP applications with total direct costs of $135,674,659.

VIII. INCLUSION OF WOMEN AND MINORITIES IN ORIP-SUPPORTED RESEARCH

In compliance with requirements by the 1993 NIH Revitalization Act to ensure that women and minorities are included in NIH-supported research, ORIP prepared a report on inclusion in its research activities. ORIP reported that for FY 2011 and FY 2012, ORIP did not support any NIH-defined clinical trials and projects that included human subjects. The Science Education Partnership Awards, the Small Business Innovation Research awards, and the Small Business Technology Transfer awards, were exempt from tracking. Thus ORIP did not have any reportable activities.

[1] For the record, it is noted that members absented themselves from the meeting when the Council discussed applications (a) from their respective institutions or (b) in which a conflict of interest may have occurred. This procedure applied only to applications that were discussed individually, not to "en bloc" actions.

A Council member pointed out one typographical error in the report. Otherwise, a motion was forwarded to approve the inclusion report and certify that its data are correct. The motion passed unanimously.

IX. REPORT FROM THE WORKING GROUP ON THE USE OF CHIMPANZEES IN NIH-SUPPORTED RESEARCH

Drs. K.C. Kent Lloyd and Daniel Geschwind, co-Chairs of the Council of Councils Working Group on the Use of Chimpanzees in NIH-Supported Research, reviewed the background, organization, and recommendations of its report to the Council. The efforts that would eventually lead to the working group's report began in December 2010, when NIH asked IOM to review the use of NIH-owned and NIH-supported chimpanzees in research. In a report issued in December 2011, the IOM committee recommended that three basic principles guide the future use of chimpanzees:

- The knowledge gained must be necessary to advance the public's health;
- There must be no other research model by which the knowledge could be obtained, and the research cannot not be ethically performed on human subjects; and
- The animals used in the proposed research must be maintained either in ethologically appropriate physical and social environments or in natural habitats.

Use of chimpanzees would be deemed appropriate only if the research satisfied all three principles and the research-specific criteria.

Dr. Francis Collins, NIH Director, accepted the IOM recommendations, and in February 2012, DPCPSI established the Council of Councils Working Group on the Use of Chimpanzees in NIH-Supported Research. This working group was charged with:

- Developing a plan for implementation of the IOM's guiding principles and criteria.
- Analyzing currently active NIH-supported research using chimpanzees to advise on which studies currently meet the principles and criteria defined by the IOM report and advising on the process for closing studies if any do not comply with the IOM recommendations.
- Advising on the size and placement of active and inactive populations of NIH-owned or –supported chimpanzees that may need to be considered as a result of implementing the IOM recommendations.
- Developing a review process for considering whether the potential use of the chimpanzee in NIH-supported research is scientifically necessary and consistent with the IOM principles.

A request for information (RFI) was published in the *NIH Guide for Grants and Contracts* and the *Federal Register*. The Working Group divided its tasks among four interactive subgroups, gathered information from the RFI, expert interviews, consultants,

and field trips, and held regular meetings. Updates were provided to the Council at its June 2012 and September 2012 meetings. The Working Group report includes findings from the Working Group's deliberations and issues 28 recommendations addressing the Working Group's charge:
[http://dpcpsi.nih.gov/council/pdf/FNL_Report_WG_Chimpanzees.pdf].

Working Group Findings: Review of Currently Active NIH-Supported Research Using Chimpanzees

The Working Group performed this review early in its process to make recommendations on whether currently funded research projects were consistent with the IOM principles and criteria for use of chimpanzees. Some projects that were compliant with IOM principles were conditionally approved, pending the Working Group's definition of "ethologically appropriate." The Council concurred with the findings of the review during closed sessions of the Council of Councils on September 5, 2012, October 29, 2012, and January 8, 2013. The Working Group report provides summary level information about these projects.

Recommendations: Ethologically Appropriate Physical and Social Environments

"Ethologically appropriate" was used as a key concept in the IOM report but it was noted that the report and the literature offered no generally accepted definition of the term. As part of their deliberations, Working Group defined ethologically appropriate environments as "environments that not only allow, but importantly, promote the full range of natural chimpanzee behaviors." The Working Group report presents 10 recommendations on ethologically appropriate physical and social environments based on this definition.

Recommendations: Size and Placement of Research-Active and Research-Inactive Populations of NIH-owned and NIH-supported Chimpanzees

Discussions about the size and placement of NIH-owned and NIH-supported active and inactive chimpanzee populations were informed by the Working Group's assessment of future research needs. The Working Group presented nine recommendations in their report to reflect these positions.

Recommendations: Review Process for Future Proposals to Use Chimpanzees in NIH-Supported Research

The Working Group's recommendations regarding a process to review future research were informed by their assessment of potential future research needs and by the IOM's suggestion that an independent review committee be established. In addition to preparing nine recommendations on the review process, the Working Group also proposed a decision tree, based on the IOM principles and criteria, and a benefit-burden matrix, to help guide an independent oversight committee as it determines whether the use of chimpanzees should be permitted in a research project proposed for NIH support.

Next Steps

Following approval of the report by the Council, NIH will issue a request for information and collect public comments for 60 days. Following review of these comments, the NIH Director will make a final decision.

Additional Recommendations by the Council to be Forwarded to the NIH Director

The report is final and cannot be modified. However, Dr. Anderson invited Council members to note any additional issues or recommendations, which he will include in a letter to the NIH Director.

Council members noted the following recommendations or concerns:

- The Working Group's statement regarding *ad hoc* members of the independent oversight committee should be strengthened to emphasize the importance of including expertise in the research area being considered. Because of remaining questions and issues regarding hepatitis viruses, the Council recommends that experts in hepatitis be included on the independent oversight committee until these questions are resolved. The ensuing discussion highlighted to Council that the need for content experts, including for example in hepatitis research, was already included in the report.

- Questions arose about which subspecies of chimpanzees are addressed by the Working Group's report. The IOM defines the chimpanzee species as *Pan troglodytes*, and that report and the efforts of the Working Group focused on *Pan troglodytes*. It should be noted that requirements might differ for *Pan paniscus*, which also could be proposed for research. Breeding plans for the colony of 50 chimpanzees should consider subspecies of *Pan troglodytes*. Zoos and protection plans should include strong efforts to avoid hybridization of these subspecies.

- Scientific importance is one of the principles proposed for the independent oversight committee to consider as it reviews whether the proposed use of chimpanzees in NIH-supported research meets the IOM principles and criteria. Because study sections that evaluate the scientific merit of an application also assess animal use, the two reviews could generate mixed messages and some confusion. The ensuing discussion highlighted to Council how the function of the Oversight Committee will differ from the independent review group conducting the scientific review of the proposal. It was pointed out that the specific role of the Oversight Committee should minimize the potential for mixed messages or confusion.

- The Working Group proposes that the independent oversight committee conduct its review following approval of an application by the IC Director to ensure maximum transparency and consideration of the maximum amount of information. In addition, this ensures that such review is done at the level of NIH, rather than local committees. However, the inclusion of members of the public on this committee, as recommended by IOM, could raise other issues, such as how to ensure confidentiality of privileged information.

Council Discussion, Approval of the Report, and Dissolution of the Working Group

Discussion Highlights

In addition to the suggestions or issues noted above, Council members also discussed the following issues:

- Legal and practical limitations will have to be addressed to allow NIH-owned chimpanzees to be retired. The Working Group envisions a gradual phase-out to allow investigators to complete approved research, but it acknowledges that projects might be completed before facilities are available.

- Council members questioned whether a determination by the Oversight Committee that research proposed in chimpanzees could be performed ethically in humans meant that the research was approved in humans. The Working Group clarified that the Oversight Committee would take a broader view of the proposed research and determine whether it *could* be done ethically in humans, and an IRB would take a closer look in the context of human subject protections.

- Use of materials collected as part of routine care of the chimpanzee could be exempt from review by the Oversight Committee. However, determinations of the extent of burden of a proposed study on chimpanzees would also take into account the type and duration of a procedure that could prolong a veterinary examination.

- In line with recommendations by IOM, the Working Group concluded that the review process should be independent of current review processes.

- Council members discussed the pros and cons of where to place the Oversight Committee in the overall review process and suggested that NIH determine the best location.

Approval of the Report

A motion to approve the report of the Working Group on the Use of Chimpanzees in NIH-Supported Research was forwarded and seconded. The motion passed unanimously (13 for, 0 against, 0 abstentions).

Having fulfilled its charge, the Working Group was dissolved.

X. NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES—A VISION FOR THE FUTURE

Dr. Christopher Austin, newly appointed Director of the National Center for Advancing Translational Sciences (NCATS), began his remarks by noting that NCATS leadership is still gathering information and building on work done by the SMRB and an ACD working group. A strategic plan is expected to be completed by early summer.

Although biomedical science has seen many advances, the transition of these advances into improvements in human health remains inefficient, and the systems for clinical trials and development of drugs and devices are in crisis. Even when advances are translated into demonstrably useful interventions, uptake of these interventions is poor. Americans are unhealthier, and public and private funders of the biomedical research enterprise are impatient. NCATS was formed in December 2011 to "catalyze the generation of innovative methods and technologies that will enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions." The Center includes the Cures Acceleration Network and three components—the Clinical and Translational Science Awards (CTSA) program, the Office of Rare Diseases Research, and the National Center for Translational Therapeutics—that were once housed in other ICs.

From its inception, NCATS has been viewed as a catalyst and a collaborative entity. The Center aims to catalyze and augment collaboration not only among NIH ICs, but also between NIH and academia, the pharmaceutical and biotechnology industries, venture capitalists, patient advocates, and other stakeholders in biomedical research. Thus NCATS projects are all collaborative, dual-use projects. These projects have specific deliverables to move them through the development pipeline, but they are grounded in new paradigms and technological developments to improve the process of translation. The projects are all disease agnostic and based on science that is an intermediary between mechanistic research and commercialization.

Among the preclinical projects and initiatives is the NCATS NIH Chemical Genomics Center, which involves 200 collaborations with investigators worldwide to develop new technologies and paradigms in chemical genomics, with a focus on rare and neglected diseases. Another is the Assay Guidance Manual eBook, which was originally developed as a quantitative biology manual for high-throughput screening and lead optimization at Eli Lilly & Company, was revised as a manual for all scientists, and is now posted on the NCATS Web site.

Several projects are designed either to speed up the conventional drug development pipeline or to repurpose approved drugs for other clinical uses. For example, NCATS has compiled a compendium of approved drugs for repurposing, facilitated collaborations to develop human pyruvate kinase activators into anti-cancer agents, collaborated with the Leukemia and Lymphoma Society to identify a compound that kills chronic lymphocytic leukemia without killing normal B cells, and initiated a project to establish template agreements between NIH and drug companies to allow academic investigators access to compounds for proof-of-concept studies. In addition, NCATS' Therapeutics for Rare and Neglected Diseases Program (TRND) supports collaborations between the NCATS Division of Preclinical Innovation and extramural laboratories to push potential drugs for rare and neglected diseases to a point in the pipeline where drug companies are willing to take over their development. For example, a TRND project on sickle cell disease is addressing the problems of chemical, target, clinical, and regulatory risks.

The majority of the budget in the NCATS Division of Clinical Innovation (DCI) supports the CTSA program, which has achieved its initial intent to develop academic homes for

clinical and translational science with awards at approximately 60 academic medical centers. The program is now evolving to focus on innovation in research methods, resources, and services to improve the quality, safety, and efficiency of translational science. A complementary initiative within the NCATS Office of Rare Diseases Research (ORDR) is the Rare Disease Clinical Research Network, which focuses on groups of diseases that have common mechanisms or affect common cell types.

Discussion Highlights

- To utilize resources most efficiently and facilitate the eventual transition of NCATS-supported preclinical development projects to other organizations, particularly in the biotechnology/pharmaceutical sector, projects are designed with milestones and time points that they must meet to merit continuation. However, it is still difficult to transition some projects, as some collaborators prefer for the project to stay with the Center as long as possible.

- The pharmaceutical industry wants to work with academic scientists to increase its pool of ideas, but at present, there are too many hurdles to collaborations between the two sectors and NCATS is working to surmount those. Contacts at pharmaceutical companies are excited about the idea of template agreements.

- Many of the goals Dr. Austin envisions for CTSAs involve efforts they have started to take on themselves.

- Dr. Austin's vision for NCATS accomplishments include academic-industrial collaborations to make translation and commercialization of advances as seamless as possible, innovating regulatory steps such as IRB harmonization, efforts to reduce toxicological hurdles, and efforts to increase interoperability of informatics systems.

- NCATS can learn from and repurpose process work from other collaborations. For example, lessons can be learned from the collaboration between Baylor College of Medicine and the Bill and Melinda Gates Foundation on Chagas disease, as well as from Human the Physiome Project funded by the European Union.

XI. CLOSING REMARKS

Dr. Anderson thanked Council members and speakers for their contributions at this meeting. The next Council meeting will be held on May 14, 2013.

XII. ADJOURNMENT

Dr. Anderson adjourned the meeting at 4:55 p.m. on January 22, 2013.

XIII. CERTIFICATION

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

3-28-2013

James M. Anderson, M.D., Ph.D.
Chair, NIH Council of Councils
Director, Division of Program Coordination,
Planning, and Strategic Initiatives (DPCPSI)
Office of the Director
National Institutes of Health

Date

3/28/2013

Robin I. Kawazoe
Executive Secretary, NIH Council of Councils
Deputy Director, DPCPSI
OD, NIH

Date