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
September 5, 2012

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 Wednesday, September 5, 2012, in Building 31, 6th Floor, Room 6, on the NIH Campus, Bethesda, Maryland.

Dr. Anderson thanked Dr. Louise Ramm, former Director of the Office of Research Infrastructure Programs (ORIP), for her efforts in assuring the smooth transition of programs from the National Center for Research Resources (NCRR) to DPCPSI. Dr. Ramm has begun a 1-year appointment at the University of Maryland School of Medicine.

Dr. Anderson also announced the selection of Dr. Janine Clayton as the new Director of the Office of Research on Women's Health (ORWH). Dr. Clayton had been serving as Acting Director of the Office since the retirement of founding Director Vivian Pinn, M.D. A board-certified ophthalmologist, Dr. Clayton has served as Deputy Clinical Director of the National Eye Institute and the Deputy Director of ORWH.

Ten members are rotating off the Council. Dr. Anderson acknowledged them and thanked them for their service: Dr. Stephen Barnes; Ms. Elizabeth Concordia; Dr. David Crabb; Dr. Daniel Geschwind; Dr. Mae Gordon; Dr. Jean McSweeney; Dr. David Valle; Mr. John Walsh; Dr. Gary Westbrook; and Dr. Luther Williams.

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
STEPHEN L. BARNES, PH.D., University of Alabama at Birmingham
LAVARNE A. BURTON, M.A., American Kidney Fund, Rockville, MD
ELIZABETH B. CONCORDIA, M.A.S., University of Pittsburgh Medical Center, Pittsburgh, PA
DAVID W. CRABB, M.D., Indiana University School of Medicine, Indianapolis, IN
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[1]
DANIEL H. GESCHWIND, M.D., PH.D., David Geffen School of Medicine, University of California, Los Angeles
MAE O. GORDON, PH.D., Washington University School of Medicine, St. Louis, MO
RICHARD M. GREENWALD, PH.D., Simbex, iWalk, Thayer School of Engineering, Lebanon, NH
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
JEAN MCSWEENEY, PH.D., R.N., F.A.H.A., F.A.A.N., University of Arkansas Medical Sciences, Little Rock, AR
ROBERT F. MURPHY, PH.D., Carnegie Mellon University, Pittsburgh, PA
JOYCE A. MITCHELL, PH.D., University of Utah, Salt Lake City, UT
REGIS O'KEEFE, M.D., PH.D., University of Rochester School of Medicine and Dentistry, Rochester, NY
REGINA RABINOVICH, M.D., Global Health Consultant, Seattle, WA
DAVID VALLE, M.D., Johns Hopkins University School of Medicine, Baltimore, MD
GARY L. WESTBROOK, M.D., Oregon Health and Science University, Portland, Oregon
TERRIE FOX WETLE, PH.D., Brown University Medical School, Providence, RI
LUTHER WILLIAMS, PH.D., Tuskegee University, Tuskegee, AL

2) Liaisons

JANINE A. CLAYTON, M.D., Director, Office of Research on Women's Health, DPCPSI, OD
PAUL M. COATES, PH.D., Acting Director, Office of Disease Prevention, 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., Acting Director, Office of Research Infrastructure Programs, DPCPSI, OD
ROBERT M. KAPLAN, PH.D., Director, Office of Behavioral and Social Sciences Research, DPCPSI, OD
ELIZABETH L. WILDER, PH.D., Deputy Director, Office of Strategic Coordination, DPCPSI, OD

[1] Dr. Elias attended by teleconference during the closed session.

3) **Ex Officio Member**
LAWRENCE A. TABAK, D.D.S., PH.D., Principal Deputy Director, NIH (absent)

4) **Presenters in Attendance**
CATHY L. BACKINGER, Ph.D., M.P.H., Deputy Director for Research, Office of Science, Center for Tobacco Products, Food and Drug Administration
FRANCIS S. COLLINS, M.D., Ph.D., Director, NIH
JOSEPH L. MANKOWSKI, D.V.M., Ph.D., Department of Molecular and Comparative Pathobiology, Department of Neurology, and Department of Pathology, Johns Hopkins School of Medicine
GEORGE SANTANGELO, Ph.D., Director, Office of Portfolio Analysis, DPCPSI, OD
WILLIAM T. WATSON, D.V.M., M.S., DACLAM, Division of Comparative Medicine, Office of Research Infrastructure Programs, 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 individual Institute or Center (IC) advisory councils. Financial disclosures are used to assess real and perceived conflicts of interests, and Council members must recuse themselves from 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
The next Council meeting will be held January 22, 2013. Other Council meetings in 2013 will be held on May 14, and September 24.

II. DPCPSI UPDATE

Dr. Anderson reminded the Council of the organizational changes to DPCPSI that have occurred since the dissolution of NCRR, and he noted that a Council working group to review the Office of Science Education in ORIP, DPCPSI, will be convened later this year. He then provided an update of DPCPSI activities.

The Office of AIDS Research (OAR) continues to engage and align with international efforts to address HIV/AIDS. Dr. Jack Whitescarver, OAR Director, serves as a co-director on the coordinating committee of the International AIDS Society, and staff from the Office recently participated in an international meeting in France to identify goals in working toward a cure. OAR also planned scientific programs for the International AIDS Conference in Washington, DC, and 19 Institutes and Centers (ICs) participated. OAR is also active in several White House initiatives, as well as an initiative led by the Office of the Vice President to address violence against women. The Office continues to coordinate research with the President's Emergency Plan for AIDS Relief, a plan that was established by President Bush in 2003, and in so doing interacts with countries around the world.

The Office of Research on Women's Health (ORWH) "Building Interdisciplinary Research in Women's Health" program, which is focused on career development for junior faculty, has awarded 14 new grants in 2012, and the Specialized Centers of Research (SCOR) program, which focuses on sex and gender differences in many disease areas, has awarded 11 new grants. ORWH continues to implement its strategic plan, and it has co-funded 13 new awards with participation from eight ICs. ORWH continues to be involved in outreach and development and has recently developed a mobile app that introduces areas of women's health and helps users keep records of their own health concerns.

The Office of Behavioral and Social Sciences Research (OBSSR) continues work to facilitate incorporation of behavioral and social sciences research across NIH to increase understanding of the influence of behavior on disease prevention and outcomes. To that end, OBSSR holds summer training programs, including a meeting to train investigators in incorporating behavioral interventions in randomized clinical trials, an institute on systems science and health, and a training institute for dissemination and implementation research.

The Office of Disease Prevention (ODP) continues its efforts to train the media in understanding and reporting medical research. In addition, ODP will hold a consensus conference in October to explore diagnosis of gestational diabetes. Within ODP, the Office of Dietary Supplements has held a summit on fitness and dietary supplements and a conference on phenylketonuria in August, and it is planning another conference on high levels of folic acid.

Dr. Anderson announced that Dr. David Murray will join NIH/DPCPSI on September 24, 2012, as the NIH Associate Director for Prevention and the Director of ODP. Dr. Murray comes to NIH from the Ohio State University, where he has served as Chair of the

Division of Epidemiology in the College of Public Health. Upon his arrival at NIH, he will begin work on developing a strategic plan for ODP based on feedback from all stakeholders in prevention. Dr. Anderson called for two Council members to volunteer to serve on the planning group for the ODP strategic plan. Dr. Anderson also thanked and commended Dr. Paul Coates for his work as Acting Director of ODP.

Dr. Anderson then turned to the topic of concept review. As discussed during the June Council meeting, the Council is now asked to review and clear concepts for Common Fund projects at a much earlier point in the planning process, before these concepts have been shaped into projects. During the current planning cycle, an initial list of 37 unique topics was presented to the Council, which cleared 26 topics for further development. Further discussion among IC Directors narrowed the list to 12 program ideas. These ideas have been assigned to IC Directors, who will convene work groups to conduct portfolio analyses, hold workshops, and engage in collaborations to identify opportunities and assess where potential projects can have the most impact.

Dr. Anderson updated the Council on Common Fund ideas that have undergone further development. Initiatives to explore extracellular RNA communication and expand the Undiagnosed Diseases Program will roll out in FY 2013. Initiatives planned for FY 2014 include a citizen science program, which will explore ways to involve the community in conducting research and will align with social media and crowdsourcing; an initiative on Deorphanizing the Druggable Genome, which will focus on deciphering the functions of unidentified genes and the potential discovery of new therapeutics; and an initiative focused on a synthetic cohort, which will coordinate clinical trials through the Health Care Systems Research Collaboratory program.

The Office of Strategic Coordination (OSC) also administers the Early Independence Award (EIA), also known as the "skip the postdoc" award. This program has awarded its second round of grants, and OSC is fine-tuning the program based on feedback from and site visits with the first group of awardees. Preliminary assessments suggest that the EIA program is a success, having supported extraordinarily talented scientists. Half of the first class of awardees was listed in *Forbes* "30 under 30" as biomedical investigators to watch. To further enhance the program, OSC is setting up a website to help potential applicants and institutions find each other and ensure applicants' independence. In addition, NIH has extended the application period to 6 months.

The Office of Research Infrastructure Programs (ORIP) has held several workshops to gather information on trans-NIH infrastructure needs. The first, held in May 2012, explored roadblocks that could be addressed by animal models to advance research in human regenerative medicine. A workshop report has been posted on the ORIP website, a manuscript summarizing workshop recommendations is under review for publication in a major journal, and program announcements based on these recommendations are expected. The second—a ninth annual grantee meeting with Comparative Medicine Resource Directors—identified the need for better informatics tools to present resource models and where they are best used, as well as a need to make resources more accessible for the average investigator. A third meeting on September 6 will bring together experts

in personalized animal models to explore ways to develop and use animal models that are more predictive for therapeutic response and toxicities.

Discussion Highlights

- Council members suggested that Common Fund concepts be brought back to the Council once they are more fleshed out. Several members noted that some concepts had insufficient information for them to vote "yes" or "no," and the members expressed concern about considering concepts cleared when they receive a "maybe vote." This was further discussed as the Council reviewed the draft Council Operating Procedures (see below).

- DPCPSI will provide the Council with a "mid-course" update on cleared Common Fund concepts at the January 2013 meeting.

- Although the Council acknowledges the difficulty in defining budgets for potential Common Fund support, some idea of the potential budgetary impact of a proposed project could help with the Council's ability to judge project ideas.

- The comments made by Council members during Common Fund concept clearance proved valuable to the IC Directors as they further narrowed down the list of potential ideas. DPCPSI encourages the Council to make additional comments.

III. COMPARATIVE MEDICINE RESEARCH TRAINING OPPORTUNITIES

A. Overview

In his opening comments, Dr. William Watson of the Division of Comparative Medicine (DCM) noted that all veterinary scientists are trained in comparative medicine since they study multiple species. Veterinary scientists also can develop animal models and conduct studies in a wide spectrum of research areas, and they consider the potential public health impact of diseases they observe in animals. Thus, veterinarians can make a valuable contribution to translational research, and training veterinarians for biomedical research is worthwhile.

DCM supports programs at various stages of the veterinary pathway to research independence. A 12-week summer experience (T35) and a 1-year research experience (T32) aim to introduce veterinary students to research. Because these programs extend students' time in school, they tend to be associated with combined degree programs. DCM also supports a postdoctoral T32 program and a mentored K01 award. In 2012, more than 200 veterinarians participated in postdoctoral training programs, and approximately 150 T35 students participated in summer research programs. DCM is supporting 19 institutional T32 postdoctoral programs, and K01s at 19 different institutions and at some of these institutions, the awardees interact with other DCM-supported resources. Although DCM aims for the majority of trainees to become independent researchers, some trainees have gone on to become veterinary college deans, research administrators, training or DCM resource directors, or research department

chairs. The time it takes a veterinary scientist to achieve research independence is in line with the time it takes for most investigators.

B. Preventing HIV-Induced Cardiac Dysfunction: Novel Insights From the SIV Macaque Model

Johns Hopkins University has a long tradition in comparative medicine, beginning with the 1888 appointment of Dr. William Osler, who had a deep interest in the area. Hopkins established its first macaque colony during the 1920s, and the first training grants for veterinarians in research were established during the 1960s. In the 1970s, Hopkins researchers Opendra Narayan, Arthur Silverstein, and Richard Johnson studied visna virus infection in lambs as a model for demyelination. When the AIDS epidemic emerged in the 1980s, Dr. Narayan, Dr. Janice Clements, and colleagues published an article reporting morphologic and molecular similarities between visna and the virus now known as HIV. Now, in the fourth decade of the global HIV/AIDS epidemic, researchers are still exploring the pathogenesis of HIV, but their animal model has shifted from the lamb visna model to SIV infection in macaques. African macaques have a high viral load but no symptoms. However, when SIV is transferred from these primates to Asian macaques, the Asian macaques develop symptoms similar to those seen with HIV/AIDS.

Dr. Joseph Mankowski, a former Division of Comparative Medicine T32 and K01 trainee who is now an independent researcher at Hopkins, discussed his work on HIV-associated cardiomyopathy. He and his colleagues have developed an SIV cardiomyopathy model in macaques and have used mitral flow Doppler imaging and tissue Doppler imaging to show that these animals exhibit diastolic dysfunction similar to that seen in HIV-infected patients. Although Dr. Mankowski and colleagues have observed increased macrophage activation, it is SIV replication in the myocardium that correlates highly with diastolic dysfunction. Dr. Mankowski and colleagues also have found that addition of SIV or the CCR5 ligand CCL5 to cardiomyocytes decreases their contractility *in vitro* and that treatment with the CCR5 inhibitor maraviroc, which was recently approved by the U.S. Food and Drug Administration for antiretroviral therapy, can prevent that decrease. Consistent with these results, maraviroc protects the heart *in vivo* in the SIV/macaque model.

This work demonstrates the value of animal models in pathogenesis studies, discoveries of molecular mechanisms, diagnostic improvements, and development of novel therapies and preventive approaches. Dr. Mankowski noted that animal models can thus serve as a cornerstone for fostering interdisciplinary translational research. He further acknowledged the value of NIH funding and DCM-supported training opportunities, and he noted that several veterinarians now work in his laboratory with DCM training support.

Discussion Highlights

- The types of studies described by Dr. Mankowksi also can be used to investigate Chagas disease, which is a leading infectious cause of heart disease. About 10% of

dogs and thousands of humans in southern Texas are infected with *Trypanosoma cruzi*, the infectious agent associated with this disease.

- DCM should consider additional ways to formalize relationships among physician and veterinary scientists. Cross-training programs for M.D./D.V.M.s, programs that introduce veterinarians to research at early stages in their careers, additional slots for veterinarians in M.D./Ph.D. programs, and links with the Clinical and Translational Science Awards program are possible mechanisms.

- High-level communication and networking are important to assist investigators in choosing the right animal model for their research question. DCM, DPCPSI, and NIH overall should consider working with the communications industry to make resources more visible. The Linking Animal Models to Human Disease program is one mechanism implemented by DCM and NIH to help investigators select the right animal model or seek alternatives to animal models.

- Ensuring access to animal resources and assistance in getting started with a new model are just as important as increasing visibility. Educational programs at the Jackson Laboratories, Woods Hole, or Cold Spring Harbor can help in this aspect. The Genetics Society of America, which consists of geneticists focused on non-human models, also could be used as a partner in standardizing access.

- Investigators also should consider how the resources they develop fits into an emerging paradigm that is based on new sequencing technologies that allow a deeper inspection of the genome.

- The Knockout Mouse Project Phase 1 (KOMP1), a collaboration involving the United States, Europe, and Canada, has created 8,500 conditional-ready and deletional mutations in mouse embryonic stem cells. Phase 2 of the project, which involves the United States and 14 other countries, will focus on converting these lines into mouse mutants and then conduct broad, high-throughput phenotypic screening across a number of organ systems. In the future, because of the infrastructure, technology, and expertise built under KOMP could develop further to interrogate human mutations and ask how best to model the associated phenotypes for pre-clinical, clinical, and post-clinical studies.

IV. REMARKS BY THE NIH DIRECTOR

Dr. Francis Collins began his remarks by noting the publication in *Nature* of data from the Encyclopedia of DNA Elements (ENCODE) project, which has yielded a large amount of information on the epigenome. Dr. Collins pointed to the ENCODE dataset as one example of exhilarating scientific developments that generate a wide array of information and technology that can be applied from early discovery to clinical trials.

However, even as Dr. Collins expressed a sense of excitement for the state of science, he also noted that NIH continues to be faced with fiscal constraints and must therefore prioritize its decisions. The spending power of NIH has constantly eroded since 2003 and

is now approximately 20% less than what it was in 2003. As a result, NIH is forced to make choices between, and in many cases reject, highly meritorious grant applications, resulting in grant application success rates of less than 20% across ICs. The President has submitted a budget for FY 2013, but what exactly will happen is not clear. It is likely that Congress will pass a continuing resolution to extend current levels for 6 months, but what will happen after that will depend on the outcome of the election and on whether Congress addresses the looming threat of sequestration. The Congressional Budget Office estimates that in the event sequestration occurs, the NIH budget would be cut by 7.8%, which would have a substantial impact on the number of grants NIH can fund. Despite these concerns, Dr. Collins pointed out that the case for supporting NIH is strong, that its contributions to human health and the economy are compelling, and that most people he has spoken with agree that sequestration would be destructive.

Dr. Collins focused the remainder of his remarks on four themes for scientific opportunity in FY 2013.

Investing in Basic Research

Dr. Collins referred to an editorial he had published in *Science* and reiterated that NIH remains committed to basic science, which he cited as a fundamental part of what NIH does. 135 NIH grantees or trainees have gone on to become Nobel Laureates. He also noted that the Common Fund has emerged as a major area for new and exciting initiatives, including many basic science projects ranging from single-cell biology to the microbiome. The Common Fund provides NIH with an opportunity to pursue exciting ideas, and it more than justifies the dollars that have been devoted to it.

Accelerating Discovery Through Technology

Many major scientific advances in technology, such as the use of induced pluripotent stem (iPS) cells, nanotechnology, and imaging technology, have arisen from discoveries at NIH. In addition, NIH advances have allowed DNA and RNA sequencing to be done at high throughput and low cost, enabling a wide range of applications that were not possible before and opening enormous opportunities in basic and applied science. Examples include explorations of the epigenome in many different cell types, sequencing on a reference set of 1,000 to 2,500 genomes from individuals around the world, and the Cancer Genome Atlas, which has now expanded to 25 tumor types.

All these technologies generate massive amounts of information, raising questions about how to store, compute, and share Big Data and placing biomedical research in the same sphere as research in cosmology or weather patterns. An Advisory Committee to the Director (ACD) working group has examined these issues for the past year, and it recommends that NIH:

- Promote data sharing through central and federated catalogues.
- Support the development, implementation, evaluation, maintenance, and dissemination of informatics methods and applications.

- Build capacity by training the workforce in the relevant quantitative sciences.
- Develop an NIH-wide strategic plan for information technology.
- Establish a new position of Chief Scientific Information Officer.
- Provide a serious funding commitment to support these recommendations.

The working group presented its recommendations at the June ACD meeting. Dr. Collins has convened a group of IC directors to review these recommendations, and he and all IC directors will discuss, prioritize, and determine how to implement the recommendations when they meet at a leadership forum in late September.

Advancing Translational Science

Translational science, which will allow scientists to make the most of the deluge of discoveries regarding the molecular causes of diseases, has been pursued for many years by all NIH ICs, particularly the National Cancer Institute (NCI) and the National Heart, Lung, and Blood Institute (NHLBI), with an annual investment of approximately $5 billion. The National Center for Advancing Translational Sciences (NCATS) has been established to address generic problems faced by everyone trying to translate discoveries into therapeutics. For example, NCATS is addressing the high failure rate in this pipeline through a collaboration with the Defense Advanced Research Projects Agency and the U.S. Food and Drug Administration (FDA) to create a biochip that screens for safe, effective drugs. In addition, NCATS is collaborating with several pharmaceutical companies to repurpose abandoned compounds for other medical needs or applications.

Other translational priorities include working toward an AIDS-free generation, as first articulated by Secretary of State Hillary Clinton when she visited NIH. Such a goal can be envisioned thanks to advances in preventing mother-to-child transmission, treatment as prevention, and other approaches, even as the HIV vaccine remains elusive. Another area of focus is Alzheimer's disease, which constitutes an enormous threat to the nation in terms of suffering and costs. The discoveries that the Tau protein can move across neurons, that a drug for T-cell lymphoma can rapidly diminish the quantity of amyloid in mouse models, and that iPS cells derived from inherited versus sporadic Alzheimer's disease have distinct differences are all examples of opportunities to push significant progress on the disease.

New Investigators, New Ideas

Investigators remain NIH's most critical resource, and NIH has therefore undertaken several initiatives to encourage creativity and innovation, many supported by the Common Fund. A new program, the NIH-Lasker Clinical Research Scholars program, provides clinical investigators with support for their independent research programs in the Intramural Program for 5 to 7 years, with the option of continued support even if those investigators want to move their programs elsewhere. NIH also continues its efforts to evaluate applications from new investigators in a separate pool where they compete against each other, enabling success these investigators might not see in an overall competition that includes more experienced investigators.

Two ACD working groups are focused on the research workforce. One working group is exploring why NIH has not succeeded in recruiting a diverse workforce despite its best efforts. At the June ACD meeting, the working group presented its overall recommendations for:

- Improved data collection and evaluation.
- Mentoring and career preparation and retention.
- Institutional support, both at university or academic centers and at NIH.
- Bias research and intervention testing.

The second working group is examining the research workforce as a whole, for example the number of individuals who are trained and the diversity of careers for which they are prepared. This working group also presented its recommendations at the June ACD meeting. Recommendations from both working groups are under review by subgroups of IC Directors and will be discussed further at the leadership forum.

Return on Investment and Global Competitiveness

Dr. Collins closed his remarks by noting a document from the Information Technology and Innovation Foundation, which has outlined the value of biomedical research to a nation's economy and noted areas where the United States is declining on a world stage. NIH funding is the foundation for the nation's competitiveness in biotechnology, drug development, and devices, and the life sciences industry in the United Stated supports 7 million jobs and accounts for $69 billion annually in economic activity. Yet the nation's investment in NIH continues to decline, while other countries, such as the United Kingdom, Germany, Singapore, and China, are increasing their investments. NIH has a webpage called "Impact" describing the economic impact of NIH-supported research. In addition, the Milken Institute will be sponsoring a 3-day event (September 7–9), "A Celebration of Science: Renewing Our Commitment to the Future," to kick-start a renewed commitment to bioscience, to improve the health of America's people and economy, and to aid in informing decision-makers on the value of biomedical research.

Discussion Highlights

Part of NIH's work in addressing the budget includes communicating its story. Dr. Collins noted that when he testifies on Capitol Hill, he hears that the contribution of NIH to the nation's health is not always well understood. Although Dr. Collins is prohibited from lobbying, he encouraged Council members and others to communicate with their representatives about NIH's value.

Dr. Collins is also undertaking other efforts to address budget constraints. He has talked with the heads of international research organizations and with chief scientists at pharmaceutical companies about potential collaborations. The Foundation for the NIH is also instrumental in forming partnerships, and NIH is looking for additional efficiencies in what it does. Dr. Collins noted that while the economic constraints are inspiring more

creativity and invention, NIH is often prevented from investing in compelling ideas at the level and pace they deserve.

Dr. Collins and Council members also noted the following:

- A discussion with Dr. Ruxandra Draghia-Akli, of the European Commission on Research and Innovation-Health, which cited data suggesting that the probability of surviving the current economic downturn is proportional to the amount of investment in science and technology.

- Current trends are reaching a point where the United States will be unable to sustain its critical mass of biomedical scientists. NIH leadership has held several discussions on actions it could take. Dr. Sally Rockey, Deputy Director for Extramural Research, NIH, has a blog, Rock Talk, which explores the numbers and options.

- The pharmaceutical industry is also feeling a squeeze, so any potential relationship will have to present a clear benefit to these companies. However, there are arguments for partnerships in training new scientists, and the heads of research and development at pharmaceutical companies are open to opportunities to collaborate.

V. COUNCIL OPERATING PROCEDURES

Dr. Anderson presented a draft version of the Council Operating Procedures, which are designed to meet the unique mission of this Council while remaining consistent with the overarching principles of NIH-wide advisory council operating policies. The Council will review these procedures in September of each year and make recommendations for revision, where appropriate.

Closed Session Operating Procedures

Dr. Anderson reminded the Council that DPCPSI has two distinct funding activities: ORIP and the Common Fund. The review process used for funding ORIP grants is similar to that used across NIH to fund grants. On the other hand, applications for many Common Fund projects move to individual IC councils for second-level review, as those ICs will be responsible for the projects once they move from the Common Fund. Applications for two Common Fund programs--Transformative Research Awards (TRA) and Early Independence Awards (EIA) come to Council for second-level review.

As is the case for IC Advisory Council second-level review, the primary purpose of the Council of Councils' review is to advise—in this case, the NIH Director and the DPCPSI Director—on the appropriateness of the initial review. The Council can also make recommendations regarding the program balance of the research portfolio and the priority with which NIH should attempt to support certain studies. In addition, the Council reviews applications brought to its attention through staff flags for consideraton for high program priority. Other applications requiring individual attention include those from foreign institutions; with concerns about human subjects or animal welfare and/or gender and minority representation; or with concerns about Biosafety, Biocontainment, and

Security of Select Agents. Letters of appeal and applications from well-funded investigators must also be reviewed by the Council. The Council's recommendations about which applications should be supported are not binding on DPCPSI. The only specific, binding action that Council may take is to designate which applications should not receive support. Such issues are discussed and decided by majority vote of the members appointed to the Council.

Before each meeting, the Council receives an Electronic Council Book that includes results from the initial peer reviews, and members can identify any grants they want to raise for individual discussion. Although early concurrence is not used for the Common Fund-supported TRA and EIA programs, it is available for ORIP-funded programs. In the case of ORIP applications, the Council Executive Secretary assigns each application to two members for early concurrence review. If the two members agree, DPCPSI may fund the application. If the members do not agree, the application is discussed during the closed session of the Council meeting.

Dr. Anderson noted that some IC councils conduct early concurrence *en bloc* and that NIH policy allows for Councils to establish an early concurrence committee consisting of a Chair and a subgroup of members. He invited the Council to consider whether and how this approach might be better than the approach of assigning two reviewers to each application.

Open Session Operating Procedures

The Council advises DPCPSI in program planning, particularly on future plans and directions for scientific research, with an emphasis on public health implications. The Council reviews the objectives, priorities, and accomplishments of DPCPSI programs and conducts concept clearance for Funding Opportunity Announcements to ensure that concepts adequately address ORIP or Common Fund objectives and that approaches will lead to desired outcomes.

Dr. Anderson reminded Council that the process for concept clearance differs between ORIP programs and Common Fund programs. The process for ORIP programs is similar to that used by other IC Councils; staff prepares concept slide presentations, and Council can recommend approval, offer recommendations for modification, defer, or recommend disapproval. For the Common Fund, the Council considers a list of broad concepts and decides whether the concepts are appropriate for Common Fund initiatives. Concepts for which the majority of Council votes "yes" or "maybe" are developed into initiatives through workshops and reviews.

Authorities Delegated to DPCPSI Staff

On a yearly basis, Council delegates some of its responsibilities to DPCPSI staff. These responsibilities include, but are not limited to:

- Interim funding decisions when deferral on a competing continuing application would result in loss of project continuity.

- Restoration of direct costs and/or years deleted during an initial review of applications, in amounts that meet the needs of the project and DPCPSI.
- Procedures for revising Council Operating Procedures.

Discussion Highlights

- Council members expressed concerns about concept clearance for the Common Fund. Although they appreciated the opportunity to provide their input early in the process, they were concerned about concepts being "cleared" with a majority "maybe" vote. Council members called for an opportunity to see those concepts again once they have been developed more fully. However, DPCPSI staff made the point that a two-step clearance process for "maybe" votes could impede efforts during the next phase of planning for those concepts.

- A motion was forwarded and seconded to change the language on page 9, item 3 of the draft Operating Procedures as follows: "Concepts for which the majority of voters vote 'yes' will be deemed cleared. Concepts for which the majority of appointed members vote 'maybe' will not be deemed cleared until additional information is provided to the Council to clear or reject the concept." Council members clarified that additional opportunities for discussion of these concepts could take place either by providing concepts ahead of the June meeting, which would allow Council members to seek more information on sketchy concepts, or by bringing concepts receiving "maybe" votes back to Council for review at the January meeting, after the concepts are fully developed. The motion passed (9 for, 7 opposed, 2 abstentions).

- When amending the operating procedures, DPCPSI should clarify and define "majority vote."

- For their second level review responsibilities, Council members requested access to full applications, particularly for those proposals that require additional scrutiny. They acknowledged that the Council is not intended to re-review applications, but they pointed out that such access provides the information Council needs to make its recommendations. DPCPSI staff were willing to consider opening access to full applications that require additional scrutiny, but they expressed concern about the technical aspects of providing access to all applications.

  A motion was forwarded and seconded for DPCPSI staff to explore the possibility of providing access to all applications for which Council has procedural responsibilities. This edit will be incorporated on pages 2, 3, and 6 (item 3) of the draft Operating Procedures document. The motion passed unanimously.

- Page 2 of the draft Operating Procedures should distinguish policies related to Common Fund initiatives from those related to ORIP.

- Establishment of an early concurrence committee might prove useful in the future and should therefore remain in the Operating Procedures. However, at present, with the

small number of flags and discussions, the Council does not see the need for such a committee. Further discussion was therefore tabled.

- The Council noted differences across ICs in interpretation of NIH policy regarding Special Council Review for well-funded investigators. Some ICs trigger a Special Council Review if even one investigator within a program project or other multi-component grant application passes the funding threshold, whereas others trigger such a review only if all investigators pass that threshold. However, the Council agreed to table that review until September 2013, when it will re-review its Operating Procedures.

- Page 4 of the draft Operating Procedures should clarify the time period members have to raise questions about applications. Early concurrence reviews should not take place until this time period has passed.

- Council members agreed with delegation of certain authorities to DPCPSI staff, but suggested that the procedures be modified such that, at each Council meeting, staff reports on actions taken on the Council's behalf.

- While there is so me ed iting and restruct uring that needs to be done to the draft Operating Procedures, there was agreem ent on the Procedures for th e coming year. An updated version of the Council Operating Procedures reflecting the amendments, editing, and restructuring, will be provided via e-mail to the Council for review. If any major issues remain, a discussion will be held during a Council of Councils' open session.

VI. UPDATE FROM THE WORKING GROUP ON CHIMPANZEES IN NIH-SUPPORTED RESEARCH

Drs. Daniel Geschwind and K.C. Kent Lloyd, Working Group co-chairs, reminded the Council that the Working Group was charged with developing a plan for: implementing recommendations from the Institute of Medicine (IOM); analyzing active, NIH-supported research using chimpanzees; advising on the size and placement of active and inactive populations of NIH-owned or –supported chimpanzees that might be affected by implementation of the IOM recommendations; and developing a review process to consider whether future use of chimpanzees in NIH-supported research is scientifically necessary and consistent with IOM principles. The Working Group has had six meetings, reviewed active projects for conformance with the IOM recommendations, conducted field trips to chimpanzee facilities to see how the chimpanzees are managed, and consulted with experts in relevant areas. The Working Group also has formed subgroups to consider specific recommendations.

The co-chairs reported that the Working Group also has begun to address issues left unresolved by the IOM report. These issues include what to do in the event of emerging diseases and what constitutes an ecologically appropriate environment. In addition, the co-chairs noted an IOM recommendation for the establishment of an independent oversight committee, separate from but built on the Interagency Animal Model

Committee, to assess the extent to which proposals that propose use of NIH-supported chimpanzees in research conform to IOM recommendations and meet specific criteria required for being considered for NIH funding. Such a committee, which will include federal and non-federal representatives, would have more time and relevant expertise than most SRG members necessary to discuss the complexities associated with using chimpanzees in research. Such a review will occur after IC Directors approve a grant for funding but under the condition that the oversight committee recommends that the application is consistent with the IOM criteria. Review at this position in the review process should allow for greater transparency.

Between now and December 2012, the Working Group will hold additional meetings, consult with experts and consider needs for any additional expert input, and review remaining projects. The Working Group aims to present its final recommendations to the Council in January 2013, after which the recommendations will undergo a 60-day public comment period.

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).[2] 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 reviewed 984 applications with total direct costs of $923,493,256.

TOBACCO CONTROL REGULATORY SCIENCE: UNDERSTANDING THE FAMILY SMOKING PREVENTION AND TOBACCO CONTROL ACT

The Family Smoking Prevention and Tobacco Control Act, passed in June 2009, gives the FDA authority over cigarettes, roll-your-own tobacco, and smokeless tobacco products, defined as "any product made or derived from tobacco that is intended for human consumption, including any component part, or accessory of a tobacco product." Although this authority does not yet extend to other tobacco products, such as cigars, pipe tobacco, or hookah/water pipe tobacco, FDA will propose a rule to deem these products subject to FDA authority.

The Act also established the FDA Center for Tobacco Products (CTP), which uses a population-level health regulatory standard to account for both users and non-users of tobacco products. The Center is funded solely from user fees from tobacco company assessments, with an expected budget of $505 million for FY 2013 and capped at $712 million by FY 2019. CTP aims to prevent youth from initiating tobacco use, encourage

[2] 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.

current users to quit, and decrease harms of tobacco product use. The Act grants specific authorities to CTP, such as setting tobacco product standards and restricting advertising promotion. However, it also limits those authorities. For example, CTP cannot require that nicotine levels be reduced to zero, nor can it set clean indoor air policies. Dr. Cathy Backinger, Deputy Director for Research in the Office of Science, CTP, reviewed several CTP accomplishments, including the prohibition of misleading marketing terms and the ban of flavored cigarettes, and she briefly described pathways to market, tobacco product standards, and modified risk tobacco product provisions. She then focused the remainder of her presentation on research opportunities afforded by the Act.

In January 2012, CTP issued a list of 56 research questions in seven topic areas. The FDA is collaborating with NIH, the Centers for Disease Control and Prevention, and the FDA National Center for Toxicological Research, as well as with non-HHS organizations, such as research contractors with relevant expertise. The NIH-FDA partnership has established a science workgroup and will coordinate research collaborations through the NIH Office of Disease Prevention. The NIH-FDA partnership will also support the Tobacco Centers of Regulatory Science program, a P50 mechanism to support multidisciplinary research that will inform the regulatory authority of CTP, as well as intramural and training projects. In addition, FDA has worked with the Center for Scientific Review to align research peer review criteria with FDA's needs. NIH has launched a website with information for researchers interested in these opportunities.

Discussion Highlights

- Research funded through the collaboration between FDA and NIDA can help answer questions about thresholds of nicotine dependence for adults.

- The NIH-FDA partnership should also consider unintended consequences, for example current users smoking more if nicotine levels are reduced.

- At present, the NIH-FDA partnership receives no co-funding or matching funds from NIH.

VIII. PORTFOLIO ANALYSIS

The Office of Portfolio Analysis (OPA) was established in DPCPSI in 2011 to conduct, coordinate, and improve portfolio analysis at NIH and to train NIH staff to promote the effective use of analytical tools. Dr. George Santangelo, OPA Director, highlighted examples of work in four core areas:

- Conduct portfolio analyses of Common Fund initiatives or as requested by senior scientific leadership. OPA emphasizes scientific portfolio analysis, which uses quantitative, data-driven methods and rigorous scientific standards to analyze investments in research. For example, as it analyzed 38 metabolomics centers across the United States, the Office characterized global investment in metabolomics and identified gaps. Information gained from this analysis shaped a new metabolomics

request for applications, which emphasizes coordination and the leveraging of resources among the states.

- Coordinate portfolio analysis activities across NIH. OPA has: built a computer laboratory to tailor existing and new computational tools to NIH needs and to train NIH staff; conducted workshops and symposia to identify gaps and overlaps and foster collaboration; and centralized a web-based repository to disseminate computational tools. OPA also is forming a trans-NIH working group.

- Improve portfolio analysis across NIH. OPA has identified limitations to cross-referencing databases, the need for new computational tools that address NIH-specific needs, and the need for accurate models of NIH output and health impact as issues impeding portfolio analysis. OPA is tracking progress in the new field called "science of science", and identifying new methods and synergies among parallel agencies, academia, and industry. The Office also is improving database management, developing tools in collaboration with the Center for Information Technology, and developing models of NIH processes.

- Train NIH staff to promote the effective use of analytical tools. OPA has conducted *ad hoc* training and plans to begin offering formal courses in October 2012. The Office also has provided numerous consultations with IC staff members, some of which have involved training, and others which have led to collaborations.

Dr. Santangelo highlighted one modeling project, a pilot study of the influence of bibliometric output on the renewal of R01 grants. OPA chose 12 journals in three categories based on impact factor, examined all papers published in those journals during a single year, and looked at all citations of those papers since that year. The Office found a severely skewed plot, suggesting (as predicted by the power law relationship) that the top 20% of papers accounted for 80% of all citations; citations therefore cannot be represented accurately by averages. The analysis also revealed that peer reviewers were influenced more by the *perception* of citation behavior, rather than actual data regarding the number of citations. OPA is now expanding this analysis, though it will require improved connectivity among the relevant databases.

Discussion Highlights

- On the basis of this pilot analysis and various experiences, impact factor is a flawed metric. For example, citations in a single journal can range over several orders of magnitude, and impact factor ignores publications in conference proceedings, which some disciplines, such as computational biology, view as high impact. However, publishers continue to emphasize impact factor, and the fact that it is flawed has not been widely accepted by the scientific community.

- Each literature database has unique coverage. Therefore OPA needs to aggregate them and link them to NIH award and application data to perform a comprehensive analysis of NIH output and impact. However, tools are needed for disambiguation,

and at the present time OPA has no way to compare publications among successful and unsuccessful applications.

- Many computational tools developed by OPA are made available to the scientific community through the NIH Office of Extramural Research. However, some tools are under development and not yet suitable for release.

- Google and Microsoft have systems to track citation counts, but NIH must still solve problems internally, because Google and Microsoft do not have access to the entire corpus of NIH data.

IX. CLOSING REMARKS

Dr. Anderson thanked Council members and speakers for their contributions at this meeting. The next Council meeting will be held on January 22, 2013.

X. ADJOURNMENT

Dr. Anderson adjourned the meeting at 5:07 p.m. on September 5, 2012.

XI. CERTIFICATION

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

10-23-2012

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

10/23/2012

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

Date