

**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 24, 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, September 24, 2013, in Building 31, 6th Floor, Room 10, on the NIH Campus, Bethesda, Maryland.

Dr. Anderson noted that Drs. Elias, Lively, Lyerly, Murphy, O'Keefe, Rabinovich, and Wetle would be absent from the day's meeting. Dr. Emery Brown participated by teleconference. Dr. Anderson acknowledged that Drs. Elias, Hotez, Lively, Lyerly, O'Keefe, Rabinovich, and Wetle would be rotating off the Council, and he thanked them for their service.

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
SUSAN F. GOEKLER, Ph.D., M.C.H.E.S., Directors of Health Promotion and Education, Washington, DC
RICHARD M. GREENWALD, Ph.D., Simbex, iWalk, Thayer School of Engineering, 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
K.C. KENT LLOYD, D.V.M., PH.D., University of California, Davis, CA
CRAIG J. MCCLAIN, M.D., University of Louisville School of Medicine,
Louisville, KY
JOYCE A. MITCHELL, PH.D., F.A.C.M.G., F.A.C.M.I, University of Utah, Salt
Lake City, UT
JAMES E. SCHWOB, M.D., PH.D., Tufts University School of Medicine, Boston,
MA
GILBERT C. WHITE, II, M.D., Blood Research Institute, BloodCenter of
Wisconsin, Milwaukee, WI

Council Members Absent

JACK A. ELIAS, M.D., Yale University School of Medicine, New Haven, CT
MARK O. LIVELY, PH.D., Wake Forest University School of Medicine, Winston-
Salem, NC
H. KIM LYERLY, M.D., Duke University School of Medicine, Durham, NC
ROBERT F. MURPHY, PH.D., Carnegie Mellon University, Pittsburgh, PA
REGIS O'KEEFE, M.D., PH.D., University of Rochester Medical Center, Rochester,
NY
REGINA RABINOVICH, M.D., Global Health Consultant, Seattle, WA
TERRIE FOX WETLE, PH.D., Brown University Medical School, Providence, RI

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 OAR 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 (ODP),
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

ABRAHAM LEVY, PH.D., Health Scientist Administrator, Office of Research Infrastructure Programs, DPCPSI

KAMIL UGURBIL, PH.D., Professor, Departments of Biochemistry, Radiology, and Medicine, McKnight Presidential Endowed Chair of Radiology, University of Minnesota

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. Kawazoe reviewed the following:

- Council members are Special Government Employees on days of Council meetings and are therefore subject to the rules governing Federal employees.
- Each Council participant 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 interest, 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 in the *Federal Register* notice for the meeting published on September 11, 2013.
- 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 on January 31, 2014. Other Council meetings in 2014 will be held on June 20 and September 5, and Council meetings in 2015 will be held on January 30, June 19, and September 1.

II. DPCPSI UPDATE

A. Office of Disease Prevention Strategic Plan

Dr. David Murray, Associate Director for Prevention, and Director of the Office of Disease Prevention (ODP), DPCPSI, reported that the Office has completed a first draft of a strategic plan for 2014 through 2018. This draft was developed following meetings between Dr. Murray and all Institute and Center (IC) Directors, meetings between senior ODP staff and IC Division Directors, focus groups involving program and review staff, a

request for information (RFI) to obtain public input, and engagement with professional societies and extramural investigators. The draft strategic plan centers on six priorities:

- Systematically monitor NIH investments in prevention research and assess the progress and results of that research. This priority includes the development of a new taxonomy and new tools for portfolio analysis.
- Identify prevention research areas that need additional investment and activity. This will include working with stakeholders and the ICs to identify gaps.
- Promote use of the best available methods in prevention research, and support development of better methods. This will include cataloguing existing resources, encouraging improvement and innovation in methods, and disseminating best practices.
- Promote collaborative prevention research projects and facilitate coordination of such projects across the NIH and with other public and private entities. This priority will include the establishment or promotion of necessary infrastructure and processes and addressing needs relevant to multiple ICs.
- Identify and promote the use of effective, evidence-based interventions and promote the conduct of implementation and dissemination research in prevention. This priority will involve partnerships between ODP and other organizations.
- Increase the visibility of prevention research at NIH and across the country. This will involve increasing communication, collaboration, and the availability of information about prevention research.

The preliminary draft has been approved by Dr. Francis Collins, NIH Director, and ODP will seek public comment through an RFI to be published in October. A final draft of the strategic plan is expected in late fall.

Discussion Highlights

- Opportunities for organizations to work with NIH to build better tools for ongoing education and prevention activities will enhance the effectiveness of existing efforts.
- The Centers for Disease Control and Prevention (CDC) will be an important partner in fulfilling the strategic plan for ODP. The Office already engages extensively with CDC.
- The draft strategic plan includes detailed tasks, subtasks, and timelines, along with measurable benchmarks.
- The infrastructure developed under the ODP strategic plan could serve as a model for other interagency initiatives.
- For many initiatives, ODP will likely play a coordinating role by bringing interested parties together and developing funding opportunity announcements (FOAs) that will cut across ICs.

B. Other DPCPSI Updates

Dr. Anderson reminded the Council that the President's FY 2014 budget calls for a reorganization to improved coordination of Federal programs in science, technology, engineering, and mathematics (STEM) education. This reorganization seeks to remove duplications by terminating 78 programs across nine agencies and by transferring remaining programs to the Department of Education (improving K-12 instruction), the Smithsonian Institute (developing infrastructure and supporting STEM instruction and engagement), and the National Science Foundation (focusing on undergraduate STEM education).

In response to these developments, NIH has paused new grants and contracts in K-12 STEM education for FY 2013. The Science Education Partnership Award (SEPA) program announcement was not reissued, but non-competing continuation SEPA awards were funded, though subject to 5% sequestration. NIH plans to fund all non-competing SEPA awards in FY 2014. The Office of Science Education will be phased down, but the teaching curricula will remain available at <http://science.education.nih.gov>. NIH has met with the three lead agencies to discuss the transition and future collaborations. In light of the reorganization, DPCPSI no longer sees a need for a Council of Councils Working Group on STEM Education, which was established in June 2012.

The new Chimpanzee Research Use Panel (CRUP) was established by the Council on August 14, 2013, to consider requests for the use of chimpanzees in research and ensure that these requests are consistent with Institute of Medicine (IOM) criteria. CRUP will review grants, contracts, and intramural project proposals that are recommended for funding, in the competitive range, or approved by IC Scientific Directors, then report its findings to the Council. The Council will then make recommendations to the NIH Director for approval or disapproval of these applications. The Panel, which will be co-chaired by Council Members Barbara Guthrie, R.N., Ph.D., and Gilbert White, M.D., will include experts in relevant disciplines, as well as a bioethicist and two or more public representatives. Dr. Anderson noted that deliberations are still ongoing to define space density for captive research chimpanzees. The NIH is preparing a Guide Notice to inform investigators about processes, timelines, and studies exempt from CRUP review.

Dr. Anderson closed his update by noting that the Council will be asked to establish a working group to review the processes for managing the Common Fund.

Discussion Highlights

Council members noted concerns, on the part of the SEPA community, that the mission and goals of the program will not be replicated upon transition to the lead agencies. One member pointed out that the community has advocated with Congress, resulting in FY 2014 budgetary language stating that SEPA funds will not be moved from NIH. It is not clear whether that language will be in the final legislation. In response to questions, Dr. Anderson speculated that reinstating programs at NIH would not take long if that were passed. However, he cautioned that at present, NIH is working with the lead agencies to ensure that STEM education activities continue to address NIH's needs.

Other discussion focused on the CRUP:

- Research using stored samples will be exempt from CRUP review, provided they are collected under an approved protocol or were collected before the IOM established its criteria.
- Efforts are underway to centralize information about sample collections NIH has supported.

III. MANAGEMENT OF THE COMMON FUND

A. Update on Common Fund Initiatives and Background on Management

Dr. Elizabeth Wilder, Director of the Office of Strategic Coordination (OSC), provided an overview of the activities and management processes of the Common Fund (CF). This discussion began during the morning open session and continued during the afternoon open session. After reviewing the history of the CF, Dr. Wilder provided an overview of CF management processes, and described three CF programs and how management processes have affected them.

Originally conceived as the NIH Roadmap, the CF serves as a trans-NIH incubator for programs that catalyze research across a wide variety of disease areas. Considerations for programs developed through the NIH Roadmap include the following, which provide the basis for the current criteria used for Common Fund programs.

- Is the initiative truly transforming? Will it dramatically change how or what biomedical research is conducted over the next decade?
- Would the outcomes of the initiative be used by and synergize the work of many ICs?
- Can the NIH afford *not* to do it?
- Will the initiative be compelling to our stakeholders, especially the public?
- Does the initiative position the NIH as unique? Is it doing something no other entity can or will do?

The NIH Roadmap was implemented in 2003, with nine programs focused on new pathways to discovery, research teams of the future, and re-engineering the clinical research enterprise. Initial programs included the Clinical and Translational Science Awards program, the NIH Director's Pioneer Awards, and programs focused on small molecule screening, nanomedicine, interdisciplinary research, structural biology of membrane proteins, proteomic technologies, and bioinformatics and computational biology. Since then, the CF has grown to approximately 30 programs and an annual budget of \$540 million dollars, similar in size to mid-sized IC budgets. Management of the programs involves more than 70 NIH staff contributing at least 50% of their time, with many more contributing anywhere from 10% to 50%. All CF programs are led by two ICs and involve trans-NIH committees.

At first, Roadmap programs were funded by a pool drawn from 1% of each IC's budget. Management and coordination of the programs involved the NIH Director and Deputy Director, IC Directors, and an NIH Roadmap Implementation Coordinating Committee, which included the chairs from the program working groups. The Coordinating Committee provided governance for the overall Roadmap by setting policy and oversight, reviewing fiscal and human resources, facilitating coordination and communication among Roadmap working groups, and providing guidance for evaluation of the overall Roadmap. Guidance and oversight of individual programs were left to the IC Directors leading those programs. Oversight of the Roadmap worked within funding levels projected for FY04 through FY09.

As the programs were implemented and matured, however, they became static, with limited flexibility. The flow of information between OD and the ICs was limited and inconsistent, and although OD needed to evaluate programs as a whole, there was no formal structure in place for evaluation. Each working group self-evaluated their programs. Despite these challenges, the overall consensus was that the Roadmap was off to a good start.

With the NIH Reform Act of 2006, Congress created the CF, funded by a specific appropriation to the NIH Office of the Director (OD), rather than a pool relying on contributions from the ICs. The Act also established DPCPSI to provide OD with an administrative structure for management. As a result of this shift, management of the CF became a partnership between OD and ICs. Activities continued as they had prior to the NIH Reform Act, but the ties between OD and ICs were stronger, with more active communication, at all phases of program development and management. Now the NIH Director and Deputy Director work with the DPCPSI Director to specify program goals and provide guidance at critical points, and OSC works with IC teams to develop management plans, implement initiatives, track budgets, oversee and assess programs, make adjustments as needed, communicate about the programs, and make plans for transition of programs out of the CF. Each CF award is managed by the lead ICs, but OD oversees its budget. This partnership ensures that the relevant NIH expertise is brought to each program, that IC Directors are engaged, that ICs and grantees benefit from the program, and that each program is communicated effectively. Such a partnership is one unique aspect of the CF.

Another unique feature of the CF is its strategic planning process, which involves two phases. The first phase, which involves a large amount of input from stakeholders and the Council of Councils, determines the mission for the next 5 to 10 years by identifying broad scientific areas where the CF can make an impact. The second phase is similar to the strategic planning process undertaken by the ICs and other DPCPSI Offices. During this phase, portfolio analysis is undertaken to refine cleared concepts further into initiatives with specific objectives. IC Directors have an opportunity to review these initiatives and comment on the possible benefit to their missions, and the NIH Director makes the final decision as to which programs move forward. The overall, two-phase process for strategic planning takes about 18 months. Although this appears to be a long time, DPCPSI has found that 18 months is often insufficient to develop an integrated set of initiatives.

Yet another unique aspect of the CF involves the specific timeline for programs. Although the stated time horizon is 5 to 10 years, OSC pushes for timelines closer to 5 years. This aspect of program development involves not only specific definitions, goals, and deliverables, but also consideration of the potential for sustained impact. This type of specificity represents a different way for NIH to stimulate research.

Dr. Wilder discussed three examples of CF programs and how current management processes affect them. One, the Human Microbiome Project (HMP), catalogues the microbes living on and within humans. HMP illustrates a program that provides core fundamental knowledge to investigators working across disease areas. Implementation of this program included support for sequencing centers; demonstration projects to enable investigators to ask how changes in the microbiome affect health status; development of computational tools; data analysis presented in a usable format, and incorporation of ethical, legal, and social considerations. HMP has been successful, in part because of the extensive planning that preceded program implementation, with a clear definition of goals.

A second program is the Patient Reported Outcomes Measurement Information System (PROMIS), which provides clinicians and researchers access to efficient, precise, and valid adult- and child-reported measures of health. This program uses measurement science to create an efficient, state-of-the-art assessment system for self-reported health. PROMIS now includes 40 adult measures and 20 pediatric measures. Its assessment centers have supported more than 100 studies, and the use of PROMIS has contributed to more than 100 peer-reviewed publications. NIH is now working with the U.S. Food and Drug Administration (FDA) to have PROMIS measures used as measures of patient outcomes, and efforts are under way to integrate PROMIS more effectively into other situations. PROMIS is an example of a tool that would not have been developed by a single IC, and its success arises partly from significant outreach efforts and collaborative efforts in tool development.

The third program, Epigenomics, highlights the importance of strategic planning. The original concept was proposed as “epigenetics,” with a goal to explore the epigenetic mechanisms underlying many diseases. Portfolio analysis identified a large amount of funding, primarily by the National Cancer Institute. This finding led to an emphasis on understanding the epigenetic changes underlying non-cancer diseases. However, there also was recognition that genome-wide analysis of epigenetic marks was difficult. OSC and ICs therefore developed a program with a significant technological development component, along with mapping centers to look at a variety of primary human cells, a data coordinating center, an emphasis on *in vivo* epigenomic imaging, and a basic discovery component. When faced with challenges in communicating program outcomes to the community, NIH solicited input from extramural investigators. Based on this feedback, NIH focused on making its data more user-friendly for the scientific community.

Discussion Highlights

- Initially, evaluation for each Roadmap program was intended to be a mid-course assessment for the first 5 years, including decisions about whether to continue the program. Because all the initial evaluations were positive, all nine programs continued.
- The launch of the NIH Roadmap/Common Fund has coincided with the growth of a movement toward systems biology. Although DPCPSI has not made a concerted effort to link with this movement, some CF activities have likely facilitated systems biology.
- As suggested by Council members, criteria for future CF programs could include major, cross-cutting health issues, which could aid in prevention and meet the mission of NIH to have an impact on the nation's health.
- As suggested by Council members, future CF initiatives might need to include additional emphasis on retaining new investigators to address the current workforce crisis. One Council member noted that his institution saw more junior faculty resignations during the previous year than it has ever seen.
- Roadmap/CF programs might have created other bottlenecks that the CF could resolve. For example, many programs have generated large amounts of data, leading NIH and investigators to consider problems associated with Big Data.
- Phase I of the planning process also involves input from IC Directors and staff, in addition to input from other stakeholders and the Council. DPCPSI has experience with several mechanisms to gather input from a broad representation of the scientific community and the public. In the future, however, DPCPSI should consider including specific patient groups.
- Some cases might require an expedited planning process. Two examples are the Gulf Coast Oil Spill Long-Term Follow-Up project and a collaboration between NIH and the Defense Advanced Research Projects Agency to build integrated tissue chips representing a physiological system.
- The planning process focuses on meeting the needs of the scientific research community. Thus, DPCPSI lets science, rather than availability of funds, drive program development. There is consideration of cost, and if needs outweigh available funds, DPCPSI tries to pool its resources with those from other ICs and stakeholders.
- In some cases, decisions might be made not to take a program forward, even after extensive planning. For example, a concept for disruptive proteomic technologies had moved past phase I, but portfolio analysis found a large amount of existing investment in that concept. Thus, it was not pursued as a CF program.

B. Establishment of a Council of Councils Working Group on the NIH Common Fund

With the CF reaching its tenth year, DPCPSI is requesting the Council to evaluate the management of the CF. Specifically, DPCPSI would like to know:

1. Whether CF processes are working optimally to identify programmatic areas where transformation is needed and possible, specify goals and ensure these goals are met, adapt to evolving scientific needs, and assess program outcomes.
2. Whether OD-IC partnerships are adequate to support program management. Specifically, do working groups receive appropriate guidance from OD leadership? Do ICs have the resources needed to manage CF programs? Is communication between ICs and DPCPSI/OSC fluid and effective? Do working groups see OSC as part of the team?

Because such an evaluation is consistent with the Council's role, DPCPSI proposes that the Council establish a working group to assess and advise on the processes to manage the CF, including those used to plan, implement, and oversee programs. The working group will review materials prepared by OSC and conduct interviews and surveys of CF stakeholders. If approved, the working group will receive its charge in October, present findings and recommendations on the planning process (Question 1) at the January 2014 Council meeting, and present its findings and recommendations on CF oversight and governance processes (Question 2) at the June 2014 Council meeting.

Discussion Highlights

- As it considers the planning process, the working group is considering whether this process leads to the best science.
- The working group is not being asked to review the criteria for CF programs.
- At present, with programs only 10 years into addressing fundamental barriers, it might be too soon to assign monetary value to them. As suggested by Council members, however, return on investment, as illustrated by stakeholders' view of program success and traditional measures of scientific productivity, should be part of the evaluation. This return could be compared with the return on investment in traditional research approaches, and it could be done for a subset of CF programs. By considering value, NIH could identify areas with the highest potential for further investment.

Vote

A motion to approve establishment of this working group was forwarded and seconded. The motion passed unanimously.

IV. REMARKS BY THE PRINCIPAL DEPUTY DIRECTOR, NIH

Dr. Lawrence Tabak, Principal Deputy Director, NIH, began his remarks with an update on the NIH budget, which is \$29.1 billion in FY 2013 following sequestration. Dr. Tabak pointed out that many legislators question the need for NIH, in light of the ongoing university research in their districts. However, that very research is funded primarily by NIH; 84% of the NIH budget is spent on extramural research. Dr. Tabak also noted that legislators continue to point to the budget doubling from 1996 through 2003. However, the budget has remained flat since 2003, and in terms of actual buying power, the budget has effectively been “undoubled.” Success rates for grant applications have reached an all-time low, but only partly because the number of applications has increased. In addition, Dr. Tabak noted that research organizations around the world, for example in China, Germany, Japan, and South Korea, have increased their research and development funding dramatically, while such investment continues to decline in the United States.

Dr. Tabak’s remarks then turned to the biomedical research workforce. The number of scientific opportunities has never been greater, and biomedical research is poised to make breakthrough on many fronts. Yet there is concern about whether the current workforce training model will continue to attract and retain the best and brightest biomedical researchers. Launching a traditional, independent research career is increasingly difficult; training periods are long, and early career salaries are low. Yet many investigators continue to train junior researchers “in their own image.” In addition, attempts to diversify the biomedical research workforce have not been successful. There are individual success stories, but institutional and cultural changes are still needed. Many younger individuals are questioning whether there is a future in biomedical research, and many are considering professions with greater stability and financial reward.

The Advisory Council to the Director (ACD) has convened working groups to address these challenges. One working group, which focused on Ph.D. scientists, has recommended enhanced training for multiple career outcomes, a shortened pathway to independent careers, improvements in tracking trainees, and an urgent attention to workforce diversity. In response to these recommendations, NIH is implementing the Broadening Experiences in Scientific Training (BEST) program, which encourages innovative approaches to complement traditional training at NIH-funded institutions. This program requires institutions to conduct rigorous analyses to demonstrate the impact of new approaches, and it includes opportunities to exchange ideas and disseminate proven approaches. NIH also has developed an overarching strategy for improving workforce diversity, including the NIH Building Infrastructure Leading to Diversity (BUILD) program, a National Research Mentoring Network, activities to ensure fairness in peer review, and increased engagement by all NIH leadership.

A second working group has been convened to look at the physician scientist workforce. This working group, which defines “physician” to include “physicians, veterinarians, and dentists,” is charged with analyzing the current composition of the workforce, assessing needs and career opportunities, identifying incentives and barriers, and recommending ways to support a sustainable and diverse clinical research infrastructure. The working group is expected to present its final report to the ACD in June 2014.

Dr. Tabak also noted the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, which aims to address the increasing burden of brain disorders by accelerating new technologies that will produce real-time pictures of neural circuits. An ACD working group is developing a plan for this initiative, with input from experts across sectors and disciplines. The working group presented its interim report in the summer of 2013 and will issue its final report to the ACD in June 2014.

Dr. Tabak closed his remarks by discussing NIH activities to address Big Data. With the myriad –omics data, advances in imaging technologies, and increasing use of electronic medical records, biomedical research has entered the age of Big Data. Like other fields, biomedical research must now find ways to integrate various datasets and enable real-time analysis. Thus biomedical researchers must address problems of locating, accessing, organizing, managing, processing, sharing, and analyzing data. NIH has established a new position, the Associate Director for Data Science, as well as two internal governing and oversight bodies: the Scientific Data Council and the Administrative Data Council. NIH also has implemented a new trans-NIH initiative, Big Data to Knowledge (BD2K), which will facilitate the broad use and sharing of complex datasets; develop and disseminate new analytical methods and software; enhance training of data scientists, computer engineers, and bioinformaticians; and establish Centers of Excellence to address biomedical analytics, computational biology, and medical informatics. BD2K is expected to launch in 2014.

Discussion Highlights

- The scientific community must do more to explain to the non-scientific community what biomedical researchers do and how their work contributes to people's health. NIH-supported biomedical research remains one of the United States' best-kept secrets. Although NIH staff cannot advocate as Federal employees, scientists and professional societies can engage the non-scientific community.
- Institutions supported by the BUILD initiative will be expected to partner with several types of institutions, including research-intensive ones, to create a consortium and promote entry into the research workforce pipeline. Community colleges also should be considered as partners.
- In light of existing budgetary constraints, NIH, extramural community, and academic health centers must engage in serious and candid discussions about issues such as new training models, the percentage of faculty members' salary supported by NIH, and others.
- NIH and professional societies can provide forums to discuss the sea change taking place with implementation of the Affordable Care Act and its downstream effects in terms of jobs and time for research.
- Although the majority of clinical scientists are M.D.s, the working group on physician scientists is charged with considering all clinical scientists, including

veterinarians and dentists, with the understanding that each group has its unique needs.

V. THE SHARED AND HIGH-END INSTRUMENTATION PROGRAM

A. Overview

Dr. Abraham Levy, Health Scientist Administrator in the Division of Construction and Instruments, ORIP, DPCPSI, explained that the Shared Instrumentation (SIG) and High-End Instrumentation (HEI) grant programs provide researchers with the funds to acquire commercially available, state-of-the-art instruments, such as optical microscopes, mass spectrometers, or biomedical imagers, that are too expensive for any one grant. The SIG program announcement is posted annually and provides \$100,000 to \$600,000 for equipment purchases. HEI is posted biennially and provides \$750,000 to \$2 million. These unique programs are critical to the NIH mission as they provide essential instrumentation to maintain the competitive edge of already-funded research,

To be eligible for SIG or HEI grants, applicants must be major user groups of three or more NIH-supported grantees who can specify how the instrument will enhance NIH-funded research projects. The grants are for purchases only. The applicants are required to have appropriate technical expertise to maintain the equipment, a plan to assure equitable use, and institutional commitment to provide the infrastructure needed for the equipment. There are no limitations on the number of applications per institution, and co-funding is not required. Applications are reviewed by the Center for Scientific Review.

With the influx of funds from the America Recovery and Reinvestment Act (ARRA) in 2009, there was a spike in the number of applications between 2009 and 2011. Although the number of applications has declined since the end of ARRA, it is still higher than it was in 2002. The success rate for SIG and HEI applications has declined from 30% in 2009 to 22% now. In FY 2013, the budgets for the SIG and HEI programs totaled \$67.2 million and supported a total of 118 awards.

B. Imaging Human Brain Anatomy, Function, and Connectivity: Advances Achieved through Novel Instrumentation

Dr. Kamil Ugurbil, of the University of Minnesota, described the impact of SIG and HEI grants on functional brain imaging. Functional magnetic resonance imaging (fMRI) was first introduced in 1992 by laboratories at the University of Minnesota and Massachusetts General Hospital (MGH), with a paper describing brain regions that were activated in response to light. This introduction arose in part from investments in a 4 Tesla (T) human-capable MR instrument at the University of Minnesota and a 1.5 T, ultrafast imaging-capable instrument at MGH.

fMRI follows neuronal activity indirectly through associated increases in regional blood flow and decreases in deoxygenated hemoglobin (deoxy-Hb), which is paramagnetic. Dr. Ugurbil and colleagues obtained an SIG/HEI grant to purchase a 9.4T, 31 cm bore system, which allowed them to map blood flow directly by MRI, rather than by following deoxy-Hb, in animal models. By measuring changes in blood flow following stimulation,

Dr. Ugurbil and colleagues found that cerebral blood flow is regulated at the level of cortical columns. With support from the SIG/HEI program, along with support from other funders, Dr. Ugurbil and colleagues were able to refute the prevailing assumption that “the brain waters the entire garden for the sake of a thirsty flower” and show that, in fact, “the brain waters the thirsty flower while it sprinkles generously around it.”

Direct measurement of blood flow for detecting alterations in brain function is not very sensitive, however; researchers still rely on indirect measurement via changes in deoxy-Hb. With SIG/HEI funds, along with support from other funders, Dr. Ugurbil and colleagues could purchase the components needed to construct a 7 Tesla (T), 90 cm bore system. Moving from a 4T to 7T magnet allowed them to detect more activity in the brain, with higher sensitivity and accuracy. Moreover, Dr. Ugurbil and colleagues were able to obtain data noninvasively from the human brain that had been obtainable only by invasive measures in animal models. For example, they were able to show the same kind of organization in the human brain that had been seen by optical imaging in the monkey brain. They also could obtain high-resolution images, both across brain layers and at the surface of each layer. Imaging with the 7T system also allowed Dr. Ugurbil and colleagues to view neuronal activity as people listened to natural sounds. All of these developments would not have been possible without the advanced instrumentation (7T for human MRI) developed by SIG/HEI funds which ushered in previously unavailable new measurement capabilities.

The Human Connectome Project is an NIH-funded consortium aiming to describe the functional and structural connections among gray matter locations in the human brain. Data will be collected from 1,200 sets of twins and non-twin siblings and be made publicly available. To achieve as high a resolution as possible, the Project is employing resting-state fMRI to visualize networks and diffusion-weighted MRI to infer structural connectivity. These techniques are complemented by data from morphological imaging, task fMRI, genotyping, and phenotyping.

To achieve a high spatial resolution over the entire brain, Human Connectome Project investigators needed to maximize the signal-to-noise ratio and acquire data more quickly without sacrificing that ratio. To overcome this challenge, the consortium has built advanced instrumentation in house to enable slice-accelerated, simultaneous multi-slice, multiband imaging. The Project also faces a challenge in standard clinical instrumentation, which still operates at 3T with 40 mT/m gradients. The consortium has built a 3T system equipped with 100 mT/m gradients, which provides additional magnetic gradient fields for diffusion encoding; the consortium is also aiming for a 7T measurements for the connectome data. With this advanced instrumentation, Project investigators were able to achieve 1.25 mm resolution in diffusion weighted imaging and previously unavailable accuracy in visualization of neuronal tracts; most clinical work is hampered by images at 2 mm or courser resolution. In addition, the opportunities afforded by these higher magnetic fields go beyond fMRI and the brain, and unique applications in the organ systems of the torso were also briefly mentioned.

Dr. Ugurbil closed his presentation by noting that his team is now working with a 10.5T system that was supported by ARRA funds. He also emphasized that the SIG/HEI grants

not only enabled the purchase of new instrumentation, but also helped investigators to leverage funds to develop instrumentation further and achieve the kind of science he described.

Discussion Highlights

- The scientific success achieved with the equipment purchased with SIG/HEI funds also requires a multidisciplinary team effort.
- Investigators did not simply buy equipment and push a button to move the field forward. They also bought components to construct new systems, ushering in new systems. The Minnesota team established the first 7T system with SIG/HEI. 7T systems are now available from commercial manufacturers, who are considering such systems for the clinic.
- The data generated by these new technologies provide a rich dataset for multidisciplinary scientists to extract additional knowledge. In addition, Dr. Ugurbil and colleagues are supporting other users with novel sequences developed in their technology driven effort and helping commercial manufacturers develop these pulse sequences as part of their product so as to make it more generally available to the biomedical research and clinical communities.

VI. 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 159 ORIP applications with total direct costs of \$71,207,340.

VII. COUNCIL OF COUNCILS OPERATING PROCEDURES AND VOTE

The Council of Councils operating procedures, which were approved on May 14, 2013, outline procedures used in the open and closed sessions of Council meetings, authorities delegated by the Council to DPCPSI staff, and processes for revising the operating procedures. No changes have been made to the Council operating procedures since they were approved.

Discussion Highlights

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.

- In response to a question, it was noted that the Council can concur with all or part of an applicant's appeal but ultimately, the Council has two options: (1) concur with the applicant's appeal and recommend the application be reviewed, or (2) concur with the Scientific Review Group's recommendation and deny the appeal.

Vote

A motion to approve the Council operating procedures for FY 2014 was forwarded and seconded. The motion passed unanimously.

VIII. REPRODUCIBILITY AND TRANSPARENCY

Dr. Anderson noted that several recent publications have raised concerns about the reproducibility and transparency of research findings. There has been a particular focus on preclinical studies; a high percentage of published animal studies cannot be reproduced by other researchers or the pharmaceutical industry pursuing a potential drug target. Recent assessments have found, for example, that of 157 stroke studies conducted in transgenic animals, only three assessed outcomes blindly, raising issues of potential misinterpretation or bias. They have also found that none of the studies had included a pre-determined statistical power analysis and that reporting of methodological approaches was inconsistent. Moreover, a recent meta-analysis found that among a year's worth of neurological studies, the average power ranges from 8% to 21%. Because the results of preclinical studies are used to design human clinical trials, these findings raise concerns about safety and potential waste.

At NIH, the National Institute of Neurological Disorders and Stroke (NINDS) and the National Cancer Institute (NCI) have taken the lead in addressing issues of reproducibility and transparency. In 2012, NINDS held a workshop on optimizing the predictive value of preclinical research, and NCI held workshops on reproducibility and data standards. IC Directors also discussed the issue, and a working group was formed by Dr. Collins to address it. The working group identified poor training, poor evaluation, and perverse reward incentives—i.e., “publish or perish”—as factors underlying problems with reproducibility and transparency. The group recommended increased community awareness, enhanced formal training, improved evaluation of grant applications, the adoption of more systematic review processes to protect scientific integrity, and increased stability for investigators as principles for addressing the underlying factors. On the basis of these principles, the working group made the following recommendations:

- Encourage ICs to discuss this issue with advisory councils and other stakeholder communities. All ICs and OD Offices will discuss reproducibility and transparency of research findings with their communities and solicit feedback by the end of the 2013 calendar year.
- Integrate modules or courses on experimental design into existing required training courses and award terms and conditions. The Office of Intramural Research is creating and piloting a new module on research integrity, and once this module is tested, the Office of Extramural Research will encourage the adoption of this or equivalent modules by extramural training programs.

- Consider options for evaluating the scientific premise of a grant application. Select ICs will perform pilot evaluations.
- Collaborate with scientific journals and the scientific community to enhance review and improve rigor. NIH will continue outreach to and partnerships with journals to evaluate recently adopted reporting guidelines, and it will evaluate a pilot program testing options for scientists to post online comments on original research studies.
- Adapt the NIH grant application biosketch to allow investigators to place their work into a functional context. Select ICs will conduct pilot evaluations of changes to the biosketch, additional pilot experiments to reduce perverse incentives, and evaluate these experiments.
- Improved guidelines and checklists for reviewers and support of replication/reproducibility studies or centers were also suggested.

Dr. Anderson pointed out that several ICs have ongoing projects that are separate from or complementary to proposed pilot projects. For example, the National Institute of Diabetes and Digestive and Kidney Diseases supports centers that conduct mouse phenotyping in a standardized, high-quality way, and NCI has considered re-instituting the Outstanding Investigator Award to provide more stability and reduce perverse incentives. Dr. Anderson asked Council members to inform their communities that addressing issues of reproducibility and transparency is a high priority at NIH.

Discussion Highlights

- Until 15 or 20 years ago, graduate students were not required to include statistical analyses in their training. However, investigators are increasingly required to include such analyses in their grant proposals. The scientific community has a responsibility to hold all investigators to that standard. This can include requiring statistical analyses during peer review of a manuscript, similar to what is done for grant applications.
- Journal editors also have a responsibility to require authors to provide details about their randomizations, study schemes, methodologies, statistical analyses, and, importantly, negative data. To accommodate word-count limits, methodology descriptions and negative data could be posted on the Web or deposited into a repository to aid other investigators in replicating results.
- The National Center for Biotechnology Information and the Public Library of Science have systems where investigators can comment or blog on published papers. However, there are some risks with allowing comments. To overcome these risks, anonymous comments should not be allowed.
- NIH should consider a training mechanism, for example a slide set, to help study section members understand what should be evaluated.
- Issues of reproducibility can conflict with the recent emphasis on innovation.

- Methodology descriptions should include the limitations of the study sample. In addition, the pre-specified framework for reporting on gender and racial/ethnic diversity in grant applications is not appropriate for every study. Work is under way to improve reporting on enrollment in clinical trials.

IX. CLOSING REMARKS

Dr. Anderson thanked Council members and speakers for their contributions at this meeting and reminded the Council that the Working Group on Common Fund Management would receive its charge in the next month. The next Council meeting will be held on January 31, 2014.

X. ADJOURNMENT

Dr. Anderson adjourned the meeting at 4:38 p.m. on September 24, 2013.

XI. CERTIFICATION

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



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

11-4-2013

Date



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

11/4/2013

Date