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
June 20, 2014

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 began at 8:15 a.m. on Friday, June 20, 2014, in Building 31, Conference Room 6, on the NIH Campus in Bethesda, Maryland.

Dr. Anderson noted that Drs. Ana M. Cuervo and James E. Schwob were unable to attend the day's meeting, and Dr. Nancy L. Haigwood and Mr. Jeffrey A. Kaufman were participating via teleconference. The attendees are identified below.

Following introductions and announcements from Dr. Franziska B. Grieder, Executive Secretary for the NIH Council of Councils, Dr. Anderson reviewed the day's agenda.

A. Attendance

1) Council Members

Council Members Present

Chair: James M. Anderson, M.D., Ph.D., Director, DPCPSI, OD, NIH
Executive Secretary: Franziska B. Grieder, D.V.M., Ph.D., Director, Office of Research Infrastructure Programs (ORIP), DPCPSI, OD, NIH
Philip O. Alderson, M.D., Saint Louis University, St. Louis, MO
Marlene Belfort, Ph.D., University of Albany, Albany, NY
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 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
Judy E. Garber, M.D., M.P.H., Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA
Lila Gierasch, Ph.D., University of Massachusetts, Amherst, MA
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

King K. Holmes, M.D., Ph.D., University of Washington, Seattle, WA
Jeffrey A. Kaufman, M.B.A., Adenoid Cystic Carcinoma Research Foundation, Needham, MA
Norma Sue Kenyon, Ph.D., Wallace H. Coulter Center for Translational Research, University of Miami School of Medicine, Miami, FL
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
Terry Magnuson, Ph.D., University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC
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
Robert F. Murphy, Ph.D., Carnegie Mellon University, Pittsburgh, PA
Norbert J. Pelc, Sc.D., Stanford University, Stanford, CA
Gilbert C. White, II, M.D., Blood Research Institute, Blood Center of Wisconsin, Milwaukee, WI

Council Members Absent

Ana M. Cuervo, M.D., Ph.D., Albert Einstein College of Medicine, Bronx, NY
James E. Schwob, M.D., Ph.D., Tufts University School of Medicine, Boston, MA

2) Liaisons

Janine A. Clayton, M.D., Director, Office of Research on Women's Health, DPCPSI, OD
Paolo Miotti, M.D., Office of AIDS Research (OAR), DPCPSI, OD (representing OAR Director Jack Whitescarver, Ph.D.)
David Murray, Ph.D., Director, Office of Disease Prevention, DPCPSI, OD
William Riley, Ph.D., Acting Director, Office of Behavioral and Social Sciences Research, DPCPSI, OD
Elizabeth L. Wilder, Ph.D., Director, Office of Strategic Coordination, DPCPSI, OD

3) Presenters

Francis S. Collins, M.D., Ph.D., Director, NIH
John D. Harding, Ph.D., Program Director, Division of Comparative Medicine, ORIP, DPCPSI, OD
John Postlethwait, Ph.D., Professor of Biology, Institute of Neuroscience, University of Oregon

4) 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

Dr. Grieder reviewed the following:

- Council members are Special Government Employees during Council meetings and therefore are subject to the rules of conduct 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 members and presenters, but time for comments from other meeting attendees is limited. The public may submit comments in writing; instructions are available in the Federal Register notice for the meeting, which was published on May 13, 2014.

C. Future Meeting Dates

The next Council meeting will be held on September 5, 2014. Council meetings in 2015 will be held on January 30, June 19, and September 1.

II. DPCPSI UPDATE

A. DPCPSI Overview

Dr. Anderson provided an introduction to the newly created Office of Administrative Management and Communications (OAMC). Previously, each of the DPCPSI offices had its own administrative structure. OAMC provides consolidated administrative and communication support to DPCPSI offices. The new Director of OAMC is Ms. Ruby N. Akomeah, who began her career at the NIH in 1986, and assumed progressively greater responsibilities and leadership roles. In her most recent position, she served as the Chief for the Office of Management and Policy Analysis at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

Dr. Anderson introduced other new members of the DPCPSI senior staff:

- Dr. William Riley, on detail from the National Cancer Institute (NCI), is serving as the Acting Director of the Office of Behavioral and Social Sciences Research (OBSSR) during the search for a new Director. Dr. Robert M. Kaplan, the former Director of OBSSR, has assumed a position as the Chief Science Officer at the Agency for Healthcare Research and Quality.

- Dr. G. Stephane Philogene, who has served in a leadership role at OBSSR since 2002, is the new OBSSR Deputy Director.

- Dr. Michael Chang, who began his NIH career in 1992 as an intramural investigator and later served as a program director at the NIH National Center for Research Resources, focusing on non-mammalian models, was appointed as the new Deputy Director of ORIP.

- Dr. Stephanie Murphy is the new Director of ORIP's Division of Comparative Medicine (DCM). Previously Professor of Anesthesiology and Perioperative Medicine at the Oregon Health & Science University, her research career has focused on sex differences and the role of sex steroids in stroke outcomes in animal models.

Dr. Anderson reported that DPCPSI conducted a Scientific Retreat during the week previous to this meeting. The goals of the Retreat were to identify common programs on which the DPCPSI Directors and NIH's Institutes and Centers (ICs) could collaborate and develop processes for coordinating and prioritizing research areas across the ICs. At the Retreat, the DPCPSI Office Directors updated the participants on their scientific initiatives and highlighted opportunities for collaboration. Working groups met in breakout sessions to discuss the objectives that the Division is seeking to accomplish through its mission and identify barriers to achieving those goals. Results from the Retreat included reaching a

consensus that DPCPSI should provide leadership in portfolio analysis to coordinate activities across the ICs. It was recognized that there is a need for opportunities to change directions as science develops. The participants discussed the balance between facilitating and leading research. They also shared best practices for setting priorities, planning, and coordinating with the ICs. Dr. Anderson indicated that in 2015, he will provide the Council with an update on the results from the Retreat. DPCPSI plans to hold additional scientific retreats on an annual basis.

Dr. Anderson concluded his overview by providing updates on three Common Fund programs:

- The Four-Dimensional (4D)-Nucleome is a new program founded on the premise that to understand gene regulation and expression, research must move beyond the linear genome and epigenetic control of the genome. The goals of the program are to develop tools to explore the organization of the genome and map its three-dimensional architecture. The program also will examine temporal aspects of gene regulation and expression (i.e., the fourth dimension).

- The initiative on Glycoscience was developed in recognition that glycans are central to many biological events, particularly those that are extracellular, but they are difficult to study with current tools and technologies. The initiative's goals are to develop laboratory tools that a typical investigator could use to sequence and synthesize glycans, as well as provide access to a database of glycan sequences and reagents.

- The Science of Behavior Change concept is predicated on the idea that there are underlying mechanisms that are common to all behavioral change. If these underlying mechanisms are targeted, clinicians might be able to change a variety of behaviors. The concept is at the stage of identifying transformative deliverables, and a workshop on the topic is scheduled for fall 2014.

B. Portfolio Analysis Updates

Dr. George Santangelo, Director, Office of Portfolio Analysis (OPA), DPCPSI, provided an overview of one of the primary components of OPA's mission: coordinating portfolio analysis activities across the NIH. He focused on the use of content analysis to characterize portfolios and identify potential overlaps. OPA's portfolio analysis coordinating activities include training NIH staff and helping to develop a science of portfolio analysis. OPA shares best practices through outreach, including a blog, symposia and workshops, a robust training program, and consultation with NIH staff in building tools. In developing the science of portfolio analysis, OPA creates new tools and modifies existing ones for NIH use. OPA is building a portfolio analysis community that includes experts from Federal agencies, academia, and the private sector. The philosophy of OPA is to promote accurate interpretations by using "clean," high-quality data, and recognition of the need for measurement to inform effective management decisions.

Content analysis can be used to improve management and strategic planning, demonstrate that inappropriate overlap is minimal, and improve understanding of the alignment of portfolio investments with the current literature. The need for computational assistance for analyzing the biomedical literature is illustrated by the growth of publications in the PubMed database, which now contains more than 23 million publications. IN-SPIRE™ is a computational content analysis tool that can be used to analyze documents ranging from scientific literature to grant applications. OPA offers training programs to NIH staff in its use, as well as training in basic portfolio analysis and network analysis (i.e., the construction of cooperative or citation networks). All OPA analysts have completed advanced IN-SPIRE™ training, and OPA offers introductory, intermediate, and advanced IN-SPIRE™ classes for NIH staff. OPA also has partnered with the Pacific Northwest National Laboratory (PNNL), which developed IN-SPIRE™, to adapt the tool for NIH use.

Dr. Santangelo explained the application of IN-SPIRE™ to content analysis for the NIH. IN-SPIRE™ extracts text from documents, typically from the title, abstract, and specific aims; identifies major terms; and maps each document in a space defined by similarity of major terms. Text processing involves removing "stop words," and using algorithms to create profiles of major terms. Stop words are those that are too common to be useful in creating a profile that is specific to a document. IN-SPIRE™ contains analytical and visualization features to interpret the data. Documents can be visualized in "galaxy view," in which similar documents form clusters grouped by the similarity of major terms. The "theme view" provides a three-dimensional representation of clusters in which the heights of peaks represent the number of documents. OPA is collaborating with PNNL to produce outputs in terms of funding amounts, which can be more valuable in portfolio analysis than the number of projects when there is a large amount of variation in the size of awards.

Using IN-SPIRE™, OPA has conducted an analysis of potential funding overlap at the NIH. For seven of the largest ICs, OPA performed an IN-SPIRE™ comparison for 30,000 R01 grant applications, including actively funded and unfunded proposals, from FY 2012. Almost all of the comparisons between ICs showed distinct distributions, although a few clusters were more equally distributed. OPA conducted a *post hoc* analysis of a selection of 316 projects that were classified as potentially belonging to two different ICs. In a blind, independent evaluation, subject matter experts from the ICs were asked to code the 316 projects, and approximately 80 percent were correctly coded by both experts. The analysis demonstrated that IN-SPIRE™ is an informative tool for program policy staff to use in evaluating overlap, providing both a global overview and the ability to flag projects and evaluate them in detail.

OPA will continue to share databases, tools, and best practices in analyzing portfolios, as well as develop and adapt new tools. OPA is creating a library of case studies, frequently asked questions, and manuals on its website. In addition, new tools are continuing to be developed by OPA for the next generation of content analysis.

Discussion Highlights

- The specific aims of documents also could be included in the IN-SPIRE™ text processing.
- IN-SPIRE™ could be used to collect data on the aspects of diversity (e.g., geographic, gender, racial) of funded and unfunded applications.
- NCI staff comprises the largest segment of OPA trainees. In general, the distribution of staff trained by OPA is reflective of total staffing among the ICs.
- In text processing using IN-SPIRE™, words specific to the mission of particular ICs (e.g., heart, lung, blood), which might be hypothesized to skew document mapping toward an IC regardless of the document's topic, were not removed. In addition to individual words, however, IN-SPIRE™ uses phrases and distances between words in building major terms.
- OPA will make the data on overlap in the NIH portfolio publically available.
- The goal of OPA's training is to enable decision makers to analyze data themselves and make use of the information. For example, two ICs that are funding similar grants were made aware of areas of overlap, and now they are collaborating.
- The NIH is using the portfolio analysis data to respond to Congress regarding stewardship of funding and demonstrate the absence of duplicative portfolios and grants.

III. Aquatic/Zebrafish Models

A. Aquatic/Zebrafish Model Resources: Introduction

Dr. John D. Harding, Program Director, DCM, ORIP, DPCPSI, described the aquatic model resources funded by DCM. Two important missions of DCM are to (1) provide biomedical researchers with high-quality, disease-free animals and specialized research facilities for a variety of model organisms; and (2) help the NIH develop strategies to make animal models more useful for basic and applied research.

Aquatic model resources and research projects funded by the DCM for its zebrafish portfolio encompasses the following areas: resources, particularly the Zebrafish International Resource Center (ZIRC), the centerpiece of the DCM zebrafish portfolio; physiology, including the zebrafish anatomy resources; husbandry, including disease control; transcriptomics; screening, including modeling of human genome-wide association study (GWAS) hits; and regenerative medicine. DCM also offers resources for other aquatic species.

Dr. Harding surveyed the services and function of the ZIRC. The ZIRC, located at the University of Oregon, provides a central repository of mutant, transgenic, and wild-type lines, as well as research materials; acquires, maintains, and redistributes resources; re-derives animals that are free of infectious disease; provides zebrafish health services; and develops standards and provides resources to improve fish biosafety, husbandry, and health. Its resources include 19,400 fish lines, the maintenance and distribution of which are its central function; expressed-sequence tags (ESTs)/cDNAs; and monoclonal antibodies. Services include resource acquisition (5,800 lines in the previous calendar year) and information dissemination.

In 2013, DCM sponsored a workshop on zebrafish and translational research. The purpose of the workshop was to provide information on the current status of technologies using zebrafish that will impact translational research, and provide recommendations to the NIH for new initiatives. The workshop participants were distinguished and diverse, including extramural and intramural leaders in the field. A summary of the science presented at the workshop is included in a final report (http://dpcpsi.nih.gov/sites/default/files/orip/document/zebrafish_workshop_final_report_orip_website.pdf). The participants developed the following recommendations:

- Fund centers for chemical screening and for confirmation of human GWAS hits.
- Develop new tools that will enhance utility for translational research.
- Involve scientists in communication and training.

Dr. Harding concluded by acknowledging Dr. Michael Chang's long-term efforts in guiding the aquatic/zebrafish model program at DCM.

B. A Zebrafish Model for the FA/BRCA Pathway and Connecting Fish Medical Models to Human Health

Dr. John Postlethwait, Professor of Biology, Institute of Neuroscience, University of Oregon, provided highlights from research using the zebrafish model and an explanation of an approach to connect the zebrafish model with human biology. Dr. Postlethwait stated that fish have served as useful models for a variety of human medical conditions, including cleft palate, osteopenia, and polycystic ovary syndrome. They also can be used as models for environmental health. Sticklebacks, which are endemic to the coastal waters of the United States, are exposed to perchlorate and can be used to assess the potential environmental effects of perchlorate poisoning on reproductive health.

The zebrafish model has proven particularly useful. Zebrafish have been used to screen for substances that cause an increase in hematopoietic tissue, leading to Phase 1 trials of prostaglandin as a hematopoietic stem cell expander. A model of tuberculosis in zebrafish was used to understand drug tolerance and discover an inhibitor that cures latent tuberculosis infections in zebrafish as well as mice. A new gene, PDZD7, was identified in zebrafish as causing Usher syndrome, which is a major cause of hereditary deaf-blindness in humans. PDZD7 was added to genetic screening for patients suspected of having Usher syndrome.

Zebrafish are a good biomedical model for several reasons. Zebrafish embryos develop outside of the mother, making them accessible to researchers. Zebrafish also allow for forward mutagenesis. Fish can be mutagenized and hundreds of mutant lines screened to find the developmental interruptions of interest, providing models for human diseases. Zebrafish enable researchers to visualize differences in stereotypic development by comparing mutant and wild-type individuals, which has led to discoveries about skeletal development. Importantly, NIH support of ZIRC (through DCM) and the Zebrafish Model Organism Database (ZFIN) propels the science of zebrafish models forward.

Dr. Postlethwait and his colleagues have used zebrafish to study Fanconi anemia. Fanconi anemia is the most common inherited bone marrow failure disease. It is characterized by interstrand DNA crosslinks, which normally are repaired by a system that requires Fanconi anemia proteins. Mutations in 16 genes, a number of which interact with the BRCA series of proteins, cause the Fanconi anemia phenotype. The molecular and genetic nature of the disease is well known, but there is no effective cure other than a bone marrow transplant from a sibling donor. Transplanted patients are rescued from bone marrow failure but develop lethal squamous cell carcinomas of the head and neck as young adults. Zebrafish models for the disease have been developed to screen for small molecule therapeutics. One mutant line was treated with a library of compounds from the NIH's clinical collection to identify compounds that rescued the phenotype. The most promising compound was warfarin (i.e., Coumadin®). The researchers determined that warfarin rescued the mutants via a vitamin-K dependent mechanism. Currently, the researchers are investigating which of the proteins that are carboxylated by vitamin K is the relevant target for Fanconi anemia.

To connect the zebrafish genome to human biology, it is necessary to understand the phylogenetic relationship between zebrafish and humans. Because of genome duplication at different points in vertebrate evolution, teleost fish such as zebrafish have similar biology to gar, which diverged from teleost fish prior to a genome duplication event. Although dissimilar in biology, the gar genome is more similar to the human than the teleost genome. The researchers hypothesized that human and zebrafish could be linked through the gar by comparing the conserved non-coding elements (CNEs) of the genome, which do not code for RNA but are assumed to be conserved because they perform a regulatory function. The researchers looked for shared CNEs among different vertebrates. Shared CNEs were evident among human, mouse, and chicken; between zebrafish and human, they found no apparent similarities for many genes. There are similarities between gar and zebrafish, however, and between gar and human for many genes that show no similarity directly between zebrafish and human. These shared CNEs identified using the gar genome as an intermediate can be tested for regulatory function, and once their functions are identified, they can be used to compare zebrafish and human biology. By comparing various teleost fish on a genome-wide scale, duplication of the teleost genome has the potential to help assign or rule out potential functions for CNEs, and to determine which CNEs are important for human health. Many human disease GWAS hits are in non-coding regions located in or near CNEs, and the gar and zebrafish data could help assign functions to them.

Discussion Highlights

- Warfarin treatment has not yet been checked to see if it repairs double strand breaks in germ cells. Warfarin treatment during the time when sex is determined, however, did rescue the germ cell phenotype that is essential for female development and is based on repair of DNA breaks by homologous recombination in meiosis.

- Whether warfarin rescues mouse and other mammalian models with Fanconi anemia has not been tested.

- The gar is not a replacement model for the zebrafish. It is not as easy to manipulate and is too large to use as a model organism. Its main value is as a link between zebrafish model and human biology.

- Most of the work on zebrafish is performed with outbred populations. Inbred populations become very weak and tend to be exclusively female.

- The Council members agreed that Dr. Postlethwait's research provides an excellent example of the relevancy of model organism biology that would have broad appeal. It was suggested that Dr. Postlethwait record a TED-type talk for the Foundation for the NIH to promote the NIH's mission.

IV. NIH UPDATE

Dr. Francis S. Collins, Director, NIH, welcomed the Council members and thanked them for providing their advice. Dr. Collins indicated that he would provide updates to the members on issues relating to the stewardship of the NIH, focusing on key areas of interest to the Council, and looked forward to engaging the members in discussion. Currently, biomedical science offers unparalleled opportunities, but the challenge of constrained resources has never been as severe. Accordingly, the NIH leadership is ensuring the most effective use of resources to meet the needs and expectations of the public, Congress, and the scientific community.

Congressional interest in biomedical research is strong, reflecting the dramatic progress being made in scientific research. Evidence that investments in the NIH have improved human health and stimulated the economy is overwhelmingly compelling. The momentum lost in the recent decade, however, threatens the most important resource in research: the researchers themselves, and particularly those early in their careers. Maintaining American competitiveness in biomedical research relative to other nations is an issue of importance to Congress.

Congressional hearings in 2014 have offered the opportunity to address members of the House and Senate regarding the importance of investing in biomedical research. Alzheimer's disease, which places a growing personal and economic burden on the Nation as the population ages, was the subject of a special Congressional hearing. Budget hearings in the House and Senate provided the NIH leadership with the opportunity to inform Congress about current initiatives and the promising future of biomedical research. The Senate Appropriations Committee convened a hearing on innovation in science, at which Dr. Collins and leaders from other Federal research agencies had an opportunity to testify about new developments in science and their concerns arising from decreased Federal commitment to scientific research. In addition, the House Energy and Commerce Committee is sponsoring roundtable discussions among a broad community of stakeholders, including representatives from academia, government, private industry, and patient advocacy, to brainstorm strategies and opportunities for legislative support to translate basic science into clinical benefit.

Dr. Collins observed that financial support for biomedical research has been losing momentum in recent years. There was a doubling of investment in the NIH budget between 1998 and 2003, but since then, with the exception of the infusion of funds from the American Recovery and Reinvestment Act of 2009, the NIH's purchasing power has declined. If the NIH budget had grown steadily at the rate that prevailed prior to 1998, it would be $10 billion more robust than current levels. To make long-range plans, the NIH needs to be able to rely on a steady budget trajectory. The American Cures Act promises such a commitment of resources, proposing a 5 percent increase above inflation for appropriations to support biomedical research to be maintained for several years.

Dr. Collins recognized that the exciting potential for advances in science was evident at the 10th Anniversary Celebration of the Common Fund. Dr. Elizabeth L. Wilder, Director, Office of Strategic Coordination (OSC), DPCPSI, and her staff, did an excellent job organizing the Anniversary Symposium. Presentations from the Anniversary Symposium demonstrated the new technologies, ideas, and innovations to which the Common Fund contributed. The lessons learned in the Common Fund's first 10 years, as well as plans for the coming decade, are described in Drs. Collins, Wilder, and Zerhouni's *Science* article that appeared in press on June 19, 2014.

Dr. Collins updated the Council members on the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative. The BRAIN Initiative is focused primarily on technology development, with the goal of increasing the understanding of neural circuits. Neuroscience is well developed at the scales of whole-brain imaging and understanding individual neurons, but there is limited understanding of the processes between the two scales, and the BRAIN Initiative seeks to bridge this gap. In the spring of 2013, the BRAIN Working Group, an Advisory Committee to the Director, was charged with developing a vision statement for the BRAIN Initiative. The Working Group developed an Interim Report with spending priorities for FY 2014, and in the spring of 2014, the BRAIN Working Group presented the NIH with BRAIN 2025: A Scientific Vision. The scientific plan for the BRAIN Initiative divided the program into two parts. The first 5 years, beginning in FY 2016, will emphasize technology development and the second will emphasize discovery-driven science that would use the new technologies. In BRAIN 2025, the Working Group identified high-priority research areas. The BRAIN Working Group also developed a set of principles, including considering the ethical implications of neuroscience research, which would apply to all aspects of research under the Initiative. BRAIN 2025 is available online at the BRAIN website (http://www.nih.gov/science/brain/2025/).

In addition, the BRAIN Working Group provided the NIH with estimates for the investment that the Initiative would require, considering the costs to implement individual goals, the numbers and types of grants that would be supported, and the cost of similar ongoing projects. The base levels of funding are $40 million for FY 2014 and $100 million for FY 2015. The BRAIN Initiative will support three different types of activities: neurotechnology, neuroscience, and infrastructure development. The Working Group predicted that funding for activities under the BRAIN Initiative would need to increase steadily during the initial phase, plateauing at $500 million annually in FY 2021. In total, the BRAIN Initiative is projected to require an investment of $4.5 billion by FY 2025 to achieve all of its priorities. Dr. Collins indicated that current spending on neuroscience is $5.5 billion annually. The Initiative will realize this investment by providing a foundation for understanding the brain that will have dramatic long-term implications for diseases such as autism, schizophrenia, epilepsy, traumatic brain injury, Alzheimer's disease, and Parkinson's disease. Dr. Collins recognized the historic nature of the BRAIN Initiative, comparing it in boldness with the Human Genome Project and indicating that it too will require recruitment of researchers from outside of their specialties. He noted that other nations, particularly in Europe, are interested in brain research, and the NIH plans to work closely with these nations to synergize with their approaches.

The Accelerating Medicines Partnership (AMP) is a new NIH program that capitalizes on discoveries about the pathways that are involved in human disease and seeks to develop them into ideas that could

lead to the next generation of drug targets. A study in 2011 showed that the failure rates for drug development are very high, particularly in Phase 2 and Phase 3 clinical trials. Most commonly, the failure is attributable to a lack of efficacy, indicating that the process by which targets are being identified is inadequate. During the past 3 years, the NIH and pharmaceutical companies have been meeting regularly to decide how to address this problem, resulting in the formation of the AMP in February 2014. Ten major pharmaceutical companies and 11 nonprofit organizations have partnered with the NIH and the U.S. Food and Drug Administration to form the AMP. The AMP is structured as a 5-year project, with a major evaluation planned at 2 years.

The AMP will focus on three areas of particular need and opportunity: Alzheimer's disease; type 2 diabetes; and the autoimmune disorders, lupus and rheumatoid arthritis. Costs, which are estimated at $230 million over 5 years, will be shared equally between the public and private sectors, but all data produced will remain in the public domain. For Alzheimer's disease, the AMP will focus on developing a well-validated set of biomarkers for clinical trials; for type 2 diabetes, the effort will focus on using genetic risk factors, epigenomic information, and complex phenotype information to select the most likely potential drug targets; and for autoimmune disorders, the emphasis will be on the single cell biology of relevant immune cells.

In his final update, Dr. Collins outlined the NIH's evolving priorities for AIDS research. The story of advances in the treatment of AIDS is dramatic: 25 years ago, AIDS was invariably fatal, but today, a patient diagnosed in his or her twenties with access to retroviral therapies can expect an almost normal lifespan. These therapies do not represent a cure, however, requiring lifelong treatment that is expensive and can have toxic side effects. In addition, despite efforts to diminish transmission rates, there still are 50,000 new cases diagnosed each year in the United States.

The NIH's priorities have evolved over time as a result of the improved ability to treat patients who are HIV-positive. Opportunistic infections are less of a concern; prevention strategies are being emphasized over epidemiology; and increasingly, the use of therapeutics as preventative measures is prioritized. Funding has shifted to research on a cure rather than simply treatment. In addition, there is increased momentum and optimism regarding developing an effective vaccine. OAR establishes AIDS research priorities in its annual strategic plan. To assist the NIH in evaluating its priorities, an OAR Advisory Council (OARAC) was formed in November 2013 and charged with developing a blueprint for future AIDS research in the coming 3 to 5 years. Guidance was sought to identify the highest priority research areas in prevention, treatment, and co-morbidities, as well as in the cross-cutting areas of basic science, training, and information dissemination. The OARAC established a Working Group comprised of eminent experts and community representatives, which recently presented its report to the OARAC. The report highlighted a wide variety of areas on which priority might be placed and was well received by the Advisory Council. Next steps will include OPA conducting a portfolio analysis of current spending and comparing it to the priority areas identified by the Working Group for further consideration by the Advisory Committee to the Director. Dr. Collins concluded his remarks by encouraging the Council members to keep abreast of events and issues at the NIH by reading his blog at directorsblog.nih.gov and following him on Twitter at @NIHDirector.

Discussion Highlights

- Abuse of prescription drugs is a major public health problem in the United States. The NIH is investing in research on opioid antidotes. The NIH also is investigating formulations of opioids that are resistant to abuse. In addition, behavioral research on abuse is ongoing. The BRAIN Initiative also will provide a foundation for exploring new prevention and treatment options through a better understanding of the neuroscience of opioid addiction.

- NIH funding decisions are merit-based. In general, the most competitive applications are submitted by researchers at the institutions with the most significant resources, which are located predominantly on the East and West Coasts. The NIH has sought to broaden the geographical distribution of research funding, however, through its Institutional Development Award (IDeA) program.

- The NIH remains committed to the support of basic biomedical research. There is a perception that the NIH is funding more translational research, but the balance of funding between basic and applied science has remained consistent over the past 10 to 15 years. As the understanding of disease processes has evolved, however, some of the most exciting basic research involves connections between basic science and disease.

- Recent legislation was introduced in Congress advocating for greater support for kidney disease treatment research. Kidney disease has overwhelming consequences for patients, the medical system, and the U.S. economy. In addition to research sponsored by the NIDDK, the NIH is considering diabetic nephropathy as a potential focus for drug development for type 2 diabetes under the AMP program.

- The AMP will be a true public-private partnership. The Foundation for the NIH will provide financial and scientific project management for the program.

- The current success rate for NIH grants is at a historic low of 16 percent. To retain more early- and mid-career researchers, the NIH is considering increasing funding for programs modeled on the NIH Director's Pioneer Award program, making more awards available to mid-career, as well as some early-career, applicants. To diversify the distribution of NIH funding, recipients of these awards might be restricted from applying for R01 grants. In addition, the NIH's Broadening Experiences in Scientific Training (BEST) initiative is designed to increase exposure of trainees to multiple career paths.

- Although not emphasized in the OARAC report, there are growing disparities in HIV/AIDS mortality, including in rural versus urban mortality rates, which the NIH recognizes and which OAR has highlighted in its annual trans-NIH plans for HIV-related research.

V. 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

[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.

the review of 542 NIH Director's Transformative Research Awards and ORIP applications with first-year direct costs requested of $379,905,714.00.

VI. Common Fund: Discussion of Proposed Concepts

Dr. Wilder reviewed the Common Fund strategic planning process, which occurs in two phases. The concept clearance stage occurs early in the planning process before refinement through portfolio analysis, which includes consideration of the concept in the context of existing NIH programs. Thirteen concepts resulted from solicitations of the IC Directors and their staffs. In the interest of increased transparency, OSC decided not to screen the concepts presented to the Council, as it had done in the past. Instead, OSC provided all of the proposed concepts to the Council, and members had pre-voted electronically for clearing each, indicating the following responses: "yes," "no," or "maybe."

Three concepts were cleared by the Council in the pre-meeting vote: A Structural Basis for RNA Therapy, Integrative Geroscience Project, and Next-Generation Cell Engineering. Based on the Council's suggestion, the concept Research to Facilitate Aging in Place will be considered for combining with the Integrative Geroscience Project. OSC will ask the Health Care Systems Research Collaboratory program to consider combining the Multiple Chronic Conditions concept with its ongoing Multiple Chronic Conditions initiative. Dr. Wilder indicated that the eight concepts that she would present today were those that had not been pre-cleared or considered for combining with other programs.

Dr. Wilder reminded the Council members of the criteria for Common Fund programs, which should be transformative, catalytic, synergistic, cross-cutting, and unique. The potential of a concept for having a transformative effect in the near-term (i.e., within 10 years) is key. Concepts also must have the potential for a catalytic effect within 5 to 10 years as a result of adoption by the research community. They must be synergistic and cross-cutting, promote the missions of individual ICs, and be relevant across ICs. To avoid duplication of effort, concepts also must be unique.

Discussion Highlights

- The Council members should use their general knowledge about the research process, rather than expertise in a particular area, to recognize the potential for a transformative effect when voting whether or not to clear a concept.

- The Council will have an opportunity to discuss revisions to the Common Fund planning process in detail at an upcoming meeting.

- The clearance process was developed in recognition of the need for the NIH to focus resources on developing only those concepts that meet Common Fund criteria.

- At the January 2015 meeting, the Council will have the opportunity to provide additional input on cleared concepts, which will have been refined. The Council will continue to influence the progression of concepts in the planning process through discussion of updates to the Council on Phase 2 Common Fund planning.

The following concepts were considered for FY 2016 programs.

A. Enabling Exploration of the Eukaryotic Epitranscriptome

The chemical modifications that can befall RNA molecules, referred to as the "epitranscriptome," affect healthy and diseased biological processes. The proposed concept would aim to develop user-friendly tools

and technologies to better understand the role of the epitranscriptome in human health. It would support: generating tools and technologies to monitor and manipulate eukaryotic RNA modifications; surveying and discovering known and previously unknown RNA modifications; exploring their biogenesis and mechanistic functions; generating a Mammalian Epitranscriptome Catalog; developing computational strategies to predict the presence of modifications; and developing small-molecule modulators as probes and potential therapies.

Discussion Highlights

- If the concept moves forward, it should be broadened to include all modifications of RNA.
- The concept has considerable potential for overlap with the concept that investigates the structural basis for RNA therapy, which was pre-approved. The NIH should consider synergies between the two concepts.

Vote

A motion to clear the concept was forwarded and seconded. The motion passed (22 votes for, 1 against), and the concept was cleared.

B. Fibrotic Diseases: Causes, Consequences, Prevention, and Treatment

Fibrotic diseases represent a major cause of morbidity and mortality worldwide. The biology and pathophysiological progression of fibrotic diseases, however, are poorly understood. A potential program would include initiatives to determine which interventions reverse risk factors for specific diseases, improve understanding of the pathogenesis of fibrosis, and engineer tissue to develop artificial organs. Such a program would help to develop validated approaches to reduce the incidence and mortality attributable to the broad range of fibrotic diseases.

Discussion Highlights

- Fibrosis is associated with many diseases. It is unclear whether the mechanism is disease-specific, or whether it is an end-stage effect associated with a common underlying mechanism for multiple organs.
- As written, the concept is very broad. Specific goals are not defined, and there does not seem to be a particular opportunity for transformative progress in this field.
- A recent development is the finding that fibrosis is reversible. This presents the potential for new therapies. Understanding the biological basis of fibrosis might have far-reaching consequences.
- The goals of the network-based taxonomy are similar to those of this concept but more generalized. Establishing the network first might inform the exploration of different fibrotic phenotypes and outcomes.
- The NIH might consider using a typical request for applications (RFA) grant mechanism rather than the Common Fund to support the program.

Vote

A motion to clear the concept was forwarded and seconded. The motion failed (6 votes for, 14 against, 2 abstentions), and the concept was not cleared.

C. Mobile Health Technologies for Medical Diagnostics in NIH Mission Areas

The high computing power and inherent connectivity of low-cost mobile devices represent great opportunities for mobile health, especially in resource-limited settings. Potential applications include screening, early detection, risk assessment, exposure analysis, diagnosis, and treatment monitoring. To date, however, very few devices that are regulated as medical diagnostic devices have been developed that can monitor health vital signs in the field and capture physiologic measurements. One successful device is LUCAS (Lensless, Ultrawide-field Cell monitoring Array platform based on Shadow imaging), a holographic microscope that can be attached to a cell phone camera and used in a field setting. The initiative would support teams with expertise in diverse disciplines to develop and test devices and implement their clinical use. This program has the potential to change management and care practices; reduce the cost of health care; and significantly improve access to medical diagnostic devices for disease screening, detection and diagnosis, and monitoring, especially in low-resource areas.

Discussion Highlights

- The concept has the potential to have a large impact on public health.
- The NIH might consider pairing the concept with another initiative such as the concept on Research to Facilitate Aging in Place.
- The concept is limited because it does not include external partners. This initiative might be better suited to support under the Small Business Innovation Research (SBIR) program. Other Council members suggested securing collaborative funding from external partners through the Foundation for the NIH.
- Efforts to develop applications for mobile health already are being executed external to the NIH, including by graduate students in public health, as well as by NIH-funded centers, obviating the need for more NIH funding. Other Council members suggested that there is a need for controlled clinical trials to prove the efficacy of applications, which would be appropriate for the NIH to sponsor. In addition, the NIH might select different targets for its applications than would a commercial enterprise.
- The concept needs to articulate more clearly the challenges and goals of developing sensors, providing examples of what might be achievable for a complex disease.
- There was concern that the concept was premature, attempting to develop mobile diagnostics before effective diagnostics have been developed for use in the clinic.

Vote

A motion to clear the concept was forwarded and seconded. The motion passed (11 votes for, 10 against), and the concept was cleared.

D. The Network-based Taxonomy of Disease

Molecular pathways represent an opportunity to understand disease in a new way. The proposed program would integrate research on the molecular bases of diseases with clinical data, and break the boundaries that have been created by research centered on single organs and diseases. It would start by using existing clinical and molecular data and tools to identify potential intermediate, preclinical, and subclinical phenotypes, and develop high-throughput technologies to measure and characterize phenotypes. In its second phase, the program would support multiple centers for the generation of new data and validation

of predictions regarding intermediate and subclinical phenotypes made in the earlier phase, and support a knowledge base center to integrate all of the data generated from the centers. Creating a new disease taxonomy has the potential to enable early diagnosis, more accurate prognosis, and discovery of new therapeutic targets, as well as aid in drug repurposing efforts.

Discussion Highlights

- The NIH should consider merging this concept with the concept on targeting shared molecular etiologies underlying multiple diseases. Both concepts will require collecting similar data, although for different purposes: fundamental understanding versus the development of new therapeutics.

- This proposed program has the potential to form the foundation for the next generation of precision medicine.

- More detail is needed regarding the approach to collecting clinical data. Care should be taken that data used from secondary sources (e.g., published journal articles, databases) is of high quality.

Vote

A motion to clear the concept was forwarded and seconded. The motion passed unanimously, and the concept was cleared.

E. New Technologies to Accelerate Therapeutic Synthesis

There is a need for technologies and methodologies that will accelerate synthesis and formulation of drugs. Proposed initiatives for a program to accelerate synthesis of therapeutics include: development of practical synthetic methodologies to accelerate drug manufacture and lower manufacturing costs; optimization of engineering design of new technologies to allow easy and low-cost implementation; and development of low-cost synthetic processes for manufacture of off-patent drugs and new formulations, as well as creation of an open access database of synthetic processes and formulations, for drugs to treat neglected tropical diseases. New practical synthetic methodologies and low-cost manufacturing technologies would lower the cost of drug development and medical care.

Discussion Highlights

- There is a strong need for new therapeutics to treat neglected tropical diseases.

- The concept appears to be too broad and open-ended. The diseases on which it will focus are not specified.

- The concept does not address potential challenges.

- There was disagreement regarding whether the concept would represent excessive replication of current efforts by pharmaceutical companies. Council members commented that this initiative might be well suited for collaboration with pharmaceutical companies, which do not devote resources to developing new synthetic methods. Other members suggested that companies are exploring new methods.

- The concept would lower drug costs only in developing nations, not in the United States.

Vote

A motion not to clear the concept was forwarded and seconded. The motion passed (20 votes for, 0 against, and 1 abstention), and the concept was not cleared.

F. SaME Therapeutics: Targeting Shared Molecular Etiologies Underlying Multiple Diseases

The Council recommended combining the concept with the Network-based Taxonomy of Disease concept, which was cleared.

G. SPARC: Stimulating Peripheral Activity to Relieve Conditions

Electrical stimulation of nerves has shown promise in treating many diseases and conditions. A better understanding of neural circuits would allow the development of new electrode designs, stimulation protocols, and minimally invasive surgical procedures that will improve existing therapies and provide the opportunity to develop new therapeutic applications. The proposed program would start by mapping the neural circuits for five organ systems. It would support initiatives for anatomic and functional mapping in the five organ systems; developing next-generation tools for visceral nerves; exploring the use of existing, approved devices to address new, small-market indications; and assembling data from all SPARC projects into a coordinated data resource. If successful, the program would catalyze development of new and more efficacious therapies using neuromodulation of end-organ system function, improve the ability to identify likely responders to neuromodulation, and expand the number of organ systems amenable to neuromodulation.

Discussion Highlights

- The five organ systems were not identified in the concept. They will be identified in the second phase of the project.
- If the brain is chosen as one of the organ systems, the NIH should consider including electrical stimulation of the brain in the project.
- The NIH should include the investigation of pain management through neuronal stimulation in the program.
- The project would focus on organ regulation. It is supported strongly by multiple ICs.
- The concept is high-risk but has the potential to produce high rewards. Important potential applications include the treatment of gastroparesis and spinal cord injuries.

Vote

A motion to clear the concept was forwarded and seconded. The motion passed (15 votes for, 1 against, and 4 abstentions), and the concept was cleared.

H. Using Pharmacogenomics to Improve Opioid Pain Management

Opioid analgesics are used widely to treat pain. There are large individual differences, however, in the efficacy and adverse side effects associated with opioid treatment. Identifying the genetic factors controlling individual responses would allow the personalization of pain management with opioids. A program on opioid pharmacogenomics would support assessing treatment efficacy of different types of opioid analgesics for chronic pain, assessing adverse side effects of opioid analgesia, measuring the

pharmacokinetics and pharmacodynamics of prescription opioids, and identifying gene variants associated with the efficacy of treatment and occurrence of adverse effects. In addition, such a program would involve physician training courses on opioid pain management, and integration of the pharmacogenomics of opioid pain management into the curricula of medical and nursing programs. The program has the potential to enable clinicians to prescribe opioids to those who will benefit and reduce unwarranted side effects.

Discussion Highlights

- There was support for the goal of the concept of identifying gene variants associated with treatment efficacy and the severity of side effects. Some gene variants already have been identified. The concept could be broadened to explore the ways in which variants function to produce differences in response.

- The goal of assessing side effects was characterized as worthwhile but poorly developed.

- The concept should be broadened to using pharmacogenomics to address chronic pain and pain management in general. If the concept is limited to opioids, it would be more appropriate to use IC-targeted RFAs rather than the Common Fund for support.

- The emphasis on training is premature. There is no description of the process to proceed from identifying genetic variants to developing content for training. For example, much is known about the genetic variants affecting warfarin response, but there is no consensus about how that information should be used in the clinic.

Vote

A motion not to clear the concept was forwarded and seconded. The motion passed (18 votes for, 2 against), and the concept was not cleared.

VII. Update on the Common Fund Planning and Management Evaluation Report

Dr. K.C. Kent Lloyd, University of California, Davis, and Dr. Janice E. Clements, The Johns Hopkins University School of Medicine, summarized the findings contained in the Common Fund Planning and Management Evaluation Report, prepared by the Common Fund Evaluation Working Group (CFEWG). The CFEWG was comprised of Drs. Lloyd and Clements, as well as Dr. Steven T. DeKosky, University of Virginia, Charlottesville; Dr. Marisa Bartolomei, University of Pennsylvania; Dr. Martin Friedlander, The Scripps Research Institute; and Dr. Sam Gerritz, Bristol-Myers Squibb. The Working Group was charged with assessing the processes used to manage the Common Fund by answering the following questions:

- Are planning processes optimal for identifying program areas that meet the Common Fund criteria?

- Are management and oversight processes optimal for achieving program goals?

To execute its charge, the CFEWG met frequently, both via teleconference and in person. Its members conducted an extensive review of Common Fund documents; surveyed and interviewed IC Directors and others connected with all aspects of Common Fund planning and management; analyzed the data; and drafted a final report to the Council that summarized the results of the analyses and outlined recommendations.

Dr. Lloyd began by summarizing the process by which recommendations were developed for the strategic planning process. Through surveys and interviews, the CFEWG gathered information about the strategic planning process, including the best methods to engage the broader scientific community, whether the format and content of the concepts allows effective review by the Council, the effectiveness of the Phase 2 process in developing clear goals and milestones, the process for planning intramural-only programs, and the appropriateness of the levels of input from IC Directors and the Council in guiding Phase 2 proposal development.

Dr. Lloyd highlighted the CFEWG's primary findings regarding the Common Fund strategic planning process. Importantly, the CFEWG found that the Common Fund was an effective use of the NIH's resources. The Working Group also learned that the Common Fund has increased the likelihood of collaborative and high-impact trans-NIH programs and activities; there is general satisfaction with the current process for soliciting ideas from the ICs; and Common Fund programs are more successful when they are specific and focused and have goals that are articulated clearly after a well-conducted portfolio analysis. Some suggestions were provided by the CFEWG: there is a need to actively engage more ICs and be more creative in identifying Common Fund-relevant concepts; decision making requires more transparency, input, and active and informed engagement and involvement by all stakeholders; a more extended schedule might increase the effectiveness of strategic planning; more consistency, clarity, and transparency in the decision-making and prioritization processes are needed for selecting concepts for Council clearance; and there is a need to define more clearly how rapid responses become an "emergency concept" and differ from other "high-priority" concepts.

The overall conclusion formed by the CFEWG from its analyses was that the strategic planning process was sound overall but might benefit from adjustment. In its recommendations, the CFEWG attempted not to be prescriptive but to provide broad suggestions for which the NIH might develop specific solutions. The CFEWG offered the following 21 recommendations for the strategic planning process:

Phase 1 Planning

1. Enhance efforts to educate and inform the scientific community about the purpose and goal of the Common Fund.

2. Revise the solicitation process in Phase 1 planning to broaden the diversity and scope of input without overburdening the process with ideas that are irrelevant and inappropriate.

3. Evaluate what has worked well, and what has not, in the process for soliciting ideas and concepts internally from ICs and externally from participants at expert meetings, and improve the process where possible.

4. Clearly articulate the purpose and goal of the Common Fund to participants in expert meetings to maximize the relevance of ideas generated.

5. Enhance and refine the existing Phase 1 planning processes to maximize the effectiveness of gathering input from external and internal sources during the allotted 9 months, including developing different approaches and mechanisms for external meetings of experts (i.e., address the importance of seeking external input early in the planning process).

6. Draft guidelines that formalize the process for articulating and developing ideas so that they are presented in a "Common Fund-able" way.

7. Establish other approaches, including a Common Fund pilot project process, which could enhance flexibility in the Common Fund strategic planning process for determining which ideas warrant additional investment.

8. Establish mechanisms that allow more flexibility for managing the development of concepts and refining concepts into program proposals.

Rapid Planning for Urgent Needs

9. Define criteria and establish a standard operating procedure for rapid responses to emergency challenges and opportunities that are consistent with the Common Fund purpose and goal, and justify Common Fund investment.

Council of Councils Review

10. Review and revise procedures by which the Council reviews and assesses concepts for clearance, including developing and articulating guidelines for the criteria used to eliminate or modify ideas before being sent to the Council for clearance (e.g., develop a primer for Council members on assessing whether or not a concept addresses Common Fund criteria).

Phase 2 Planning

11. Establish and articulate the process by which cleared concepts develop and progress into Common Fund programs.

12. Ensure that sufficient time and resources are available for comprehensive and consistent portfolio analyses.

13. Clearly define and clarify the roles and responsibilities of OSC and Working Group members in Phase 2.

14. Create more opportunities for IC Directors and the Council to provide sufficient feedback on concepts that are being developed in Phase 2.

15. Ensure sufficient representation on the Council or a subcommittee of the Council to enable all ICs to participate in Phase 2.

16. Ensure greater transparency and clarity surrounding the process by which programs exit Phase 2 as funded Common Fund programs.

17. Streamline and clarify the steps for selecting Phase 2 ideas and developing them into program proposals.

Intramural-only Common Fund Programs

18. Develop a concrete framework for when a program is suitable for an intramural-only program, including further clarifications regarding the criteria.

Communication and Input

19. Develop a mechanism to increase IC Directors' input to the OD in decision making on Common Fund programs.

20. Improve communication and working relationships between OSC and IC staff developing Common Fund programs.

21. Communicate as early as possible the availability of funds to support new Common Fund programs.

Dr. Clements summarized the process by which recommendations were developed for the management process. Through surveys and interviews, the CFEWG gathered information about the management process, including the clarity of program expectations, the helpfulness of management and oversight processes in meeting goals, the flexibility of management processes in adapting to the scientific landscape, the management process for intramural-only programs, and the ability of the Working Group structure to meet management and oversight needs.

Dr. Clements provided a brief overview of the CFEWG findings regarding the Common Fund management process. In general feedback, nearly all survey respondents agreed that the scientific mission of an individual IC benefits from working with other ICs, and a majority of participants agreed that Common Fund programs have increased the likelihood of collaborative, high-impact trans-NIH programs and activities. In addition, participants observed that when the funding opportunity announcements (FOAs) had clearly articulated goals and milestones, the likelihood of meeting these targets was higher. Specifically, respondents observed that the Epigenomics and Human Microbiome programs were examples of Common Fund programs that were highly successful; a majority of survey respondents agreed that although initially after its formation OSC was less involved, currently OSC staff provide timely guidance during FOA development; respondents noted that most OSC staff members have extensive experience in communicating and providing guidance to Working Groups; many respondents thought the current Working Group structure is effective in meeting the scientific goals of the Common Fund program; and a majority believed that the current Working Group structure effectively manages Common Fund programs.

Some less positive survey findings about the management process were that Common Fund goals and responsibilities of principal investigators (PIs) were not uniformly made clear to Common Fund grantees; progress of Common Fund programs is intended to be documented in Annual Progress Reports, which in addition to scientific progress, also report issues that the Working Groups encountered, changes in the scientific environment, and plans for the upcoming fiscal year, but some Working Group interviewees were unclear about expectations for the specific content in the Annual Progress Reports; and some Common Fund program staff are unclear about the expectations of OSC Program Directors regarding interactions with OSC. In addition, in meetings with IC Directors, the CFEWG learned that many IC Directors reported feeling more detached from the decision-making process in recent years, possibly because of the lack of a joint meeting to solicit ideas, which contributed to a decreased enthusiasm for the Common Fund; IC Directors who are leading or very involved in a Common Fund program closely monitor the progress of the program against its milestones; IC Directors stated that they received almost no information if their IC was not directly involved; and detailed information on the management process of intramural research program-only programs could not be identified, and it was unclear how or why a particular process was chosen and pursued.

The CFEWG had the following 19 recommendations for the management process:

Key Recommendations for FOAs and Kick-off Meeting

1. Provide a comprehensive template for essential elements in Common Fund program FOAs.

2. Include information in the FOAs about how the Common Fund is funded.

3. State goals and milestones explicitly in FOAs and kick-off meetings.

4. A kick-off meeting for all new Common Fund programs should be held with funded PIs, NIH staff, Steering Committee members, and external Scientific Advisory Committee members. The program's overall organization should be described in the Common Fund Handbook to inform participants about the program. Dr. Clements noted that kick-off meetings were found to be very important for setting up programs for success.

Key Recommendations for Common Fund Working Groups and OSC Program Directors

5. OSC Program Directors should educate Working Groups about the need for and use of Annual Progress Reports. Many reports never receive feedback.

6. Define the working relationships and interactions between OSC Program Directors and Common Fund Working Groups.

7. Establish clear mechanisms for communications between Common Fund PIs and their respective Working Groups.

8. Encourage all Working Group members to use the Common Fund Handbook as a guide for program management.

9. Provide an orientation on Working Group structure for new Common Fund programs. Accumulated knowledge is being lost when programs are completed, and there is no mechanism for passing on experience to new Working Groups.

10. Gather and disseminate Common Fund "best practices" for the benefit of all Working Groups.

11. Identify Common Fund mentors who have successfully managed Common Fund programs to guide new Common Fund Working Groups.

Recommendations for Evaluation of Common Fund Programs

12. Clearly define evaluation plans at the outset of Common Fund programs (e.g., include them in FOAs, educate PIs, communicate them in kick-off meetings).

13. Conduct evaluation reviews prior to the end of the first phase of a Common Fund program.

14. OSC should conduct annual Common Fund program management reviews to provide feedback to Working Groups on the management of the Common Fund program and whether the goals and milestones are being achieved. Dr. Clements stated that these should be performed in addition to scientific reviews.

Recommendation for Intramural-only Common Fund Programs

15. Justify the need for intramural-only Common Fund programs, and establish clear processes for all aspects of intramural-only Common Fund program management.

Key Recommendations for Communication and Input

16. Explore ways to leverage the benefit of trans-NIH cooperative relationships developed through Common Fund Working Groups to improve interaction between ICs.

17. Provide regular updates on Common Fund programs to IC Directors (e.g., through Technology, Entertainment, Design [TED] talks, other mechanisms to inform the intramural and extramural research communities).

18. Provide regular updates on Common Fund programs to the NIH community.

19. Improve communication about Common Fund programs by IC Directors.

Dr. Clements commented that the Common Fund Handbook was very valuable, but many do not use it effectively. Its use should be promoted by OSC staff to PIs and others.

Discussion Highlights

- The Common Fund Planning and Management Evaluation Report will be shared with Dr. Collins, OSC, and the ICs, and discussed, possibly at the annual NIH leadership meeting. The NIH then will respond to each of the Council's recommendations.

- Many of the recommendations are a reflection of the rapid growth of the Common Fund, which requires developing new planning and management processes.

- Implementing some of the recommendations, such as increasing evaluation, is likely to require allocation of additional resources.

- The NIH should consider tracking the transition of Common Fund programs to stewardship under the extramural research programs of a single IC. The 10-year limit for funding, which applies to all Common Fund programs with the exception of investigator-initiated programs such as the Pioneer Awards, is part of the enabling legislation for the Common Fund. This will be a particular concern for some of the larger programs such as the Human Microbiome.

- One of the Report's recommendations for strategic planning was that Working Groups should include multiple ICs. There was no formal recommendation that proposals be supported by multiple ICs, however, it should be recognized that proposals supported by more ICs will be stronger and more likely to be cleared.

- In the past, OSC has screened the concepts before submitting them for clearance by the Council but did not this year in the interest of increased transparency. Implementation of the Report's recommendations will require a balance between the need for transparency and the need to ensure that concepts presented to the Council are robust.

- It would be helpful for the Council's clearance process to know which ICs support a given proposal, providing greater context.

- There are significant differences among the IC Directors regarding the extent of their knowledge about Common Fund programs and their level of interest.

- The CFEWG did not offer any recommendations about the size of the Common Fund because that was not part of its charge.

Vote

A motion to add a recommendation stipulating that if needed, OSC be allocated additional resources to pursue implementation of the Report's recommendations was forwarded and seconded.

A motion to approve the recommendations regarding Common Fund planning and management was forwarded and seconded. The motion passed unanimously, and the recommendations were approved.

VIII. CLOSING REMARKS

Dr. Anderson thanked the Council members and speakers for their contributions at this meeting. The next Council meeting will be held on September 5, 2014.

IX. ADJOURNMENT

Dr. Anderson adjourned the meeting at 4:05 p.m. on June 20, 2014.

X. 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, DPCPSI, OD, NIH

7-21-14
Date

Franziska B. Grieder, D.V.M., Ph.D.
Executive Secretary, NIH Council of Councils
Director, ORIP, DPCPSI, OD, NIH

7.21.2014
Date