National Arthritis and
Musculoskeletal and
Skin Diseases Advisory Council

MINUTES OF MEETING

February 1, 2011

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL ARTHRITIS AND MUSCULOSKELETAL
AND SKIN DISEASES ADVISORY COUNCIL

MINUTES OF THE 73rd MEETING

February 1, 2011
8:30 a.m. to 3:00 p.m.

I. CALL TO ORDER

The 73rd meeting of the National Arthritis and Musculoskeletal and Skin Diseases Advisory Council was held on February 1, 2011, at the National Institutes of Health (NIH) Campus, Building 31, Conference Room 6. The meeting was chaired by Dr. Stephen Katz, Director, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS).

Attendance

Council members present:

Dr. Lynda F. Bonewald
Dr. S. Wright Caughman
Dr. Leslie J. Crofford (via teleconference)
Ms. Karen B. Evans
Dr. David Eyre
Dr. Linda Griffith
Dr. John Klippel
Dr. Henry M. Kronenberg
Dr. Ted Mala
Dr. Regis O'Keefe
Dr. Alice Pentland
Ms. Jean R. Pickford
Mr. Bradley R. Stephenson, J.D.
Dr. H. Lee Sweeney
Dr. Julio L. Vergara

Staff and Guests

The following NIAMS staff and guests attended:

Staff

Ms. Mary Aninzo
Dr. Carl Baker
Dr. Michael Bloom
Dr. Amanda Boyce
Mr. Gahan Breithaupt
Dr. Branden Brough
Ms. Justine Buschman
Dr. Robert Carter
Dr. Faye Chen
Dr. Ricardo Cibotti
Ms. Barbara Cohn
Ms. Stephanie Craver
Ms. Theresa Do
Dr. Jonelle Drugan
Mr. Erik Edgerton
Ms. Sharon Fair
Ms. Barbara Footer
Dr. Nancy Garrick
Ms. Gerda Gallop-Goodman
Ms. Kaitaia Huynh
Ms. Katie Joffee
Mr. Andrew Jones
Dr. Stephen I. Katz
Ms. Shahnaz Khan
Dr. Gayle Lester
Dr. Helen Lin
Dr. Kan Ma
Dr. Marie Mancini
Dr. Kathryn Marron
Dr. Joan McGowan
Ms. Leslie McIntire
Dr. Laura K. Moen
Dr. Ramesh Nayak
Dr. Glen Nuckolls
Dr. John O'Shea
Dr. James Panagis
Ms. Wilma Peterman-Cross
Dr. Charles Rafferty
Ms. Natalie Reyes
Ms. Trish Reynolds

Dr. Louise Rosenbaum
Ms. Kate Saylor
Dr. Susana Serrate-Sztein
Dr. William Sharrock
Dr. Richard Siegel
Ms. Sheila Simmons
Ms. Allisen Stewart
Ms. Robyn Strachan
Ms. Yen Thach
Dr. Bernadette Tyree
Dr. Fei Wang
Dr. Xibin Wang
Dr. Yan Wang
Dr. James Witter

Guests

Dr. Jeremy Berg, Director, National Institute of General Medical Sciences, NIH
Mr. Michael Bykowski, Consolidated Solutions and Innovations
Dr. Priscilla Chen, Center for Scientific Review, NIH
Ms. Ann Elderkin, American Society for Bone and Mineral Research
Dr. Joy Gibson, Center for Scientific Review, NIH
Dr. John Holden, Department of Veterans Affairs
Dr. Richard Ingraham, Center for Scientific Review, NIH
Dr. Lyric Jorgenson, Office of the Director, NIH
Dr. Rajiv Kumar, Center for Scientific Review, NIH
Ms. Jennifer McBride, Arthritis Foundation
Ms. Jackie Nelson, CureCMD
Dr. Amy Patterson, Office of the Director, NIH
Ms. Meg Pilarcik, Scleroderma Foundation
Dr. Sally Rockey, Office of the Director, NIH
Dr. Anne Rutkowski, CureCMD
Ms. Teresa Wilson, PPD Inc.
Ms. Charlene York, CureCMD

II. CONSIDERATION OF MINUTES

A motion was made, seconded, and passed to accept with no changes the minutes of the 72nd NIAMS Advisory Council meeting, held on September 28, 2010.

III. FUTURE COUNCIL MEETING DATES

Future Council meetings are currently planned for the following dates:

June 14, 2011
September 27, 2011
January 31, 2012
June 5, 2012
September 11, 2012

IV. DIRECTOR'S REPORT AND DISCUSSION

Dr. Katz welcomed Council members, NIAMS staff, and guests. He invited attendees to review the NIAMS ShortTakes online, which includes more details on many of the topics covered in his Director's Report. He noted that his "Director's Column" focuses on the Institute's 25th anniversary, which will feature a scientific session on June 13, 2011, that will focus on scientific advances made possible with NIAMS support, highlight how these advances have improved the lives of patients, and address future directions for NIAMS research. A dinner featuring a guest speaker will take place following these activities. Council members were invited to attend the anniversary celebration, which will occur on the day before the June 14, 2011, Council meeting.

Council member Dr. Leslie Crofford, Chief of the Division of Rheumatology within the Department of Internal Medicine at the University of Kentucky, participated in the meeting via teleconference. Council members Dr. Harry Dietz (Victor A. McKusick Professor of Medicine and Genetics at McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medicine) and Ms. Anne Kunkel (Education Coordinator, University of Kansas Medical Center) were unable to attend this Council meeting.

Dr. Katz introduced four *ad hoc* Council members:

- Dr. Lynda Bonewald, the Lefkowitz Professor in the Department of Oral Biology in the School of Dentistry at the University of Missouri-Kansas City. Dr. Bonewald's research led her to initiate a new area of examining osteocyte biology, which may be responsible for sensing mechanical stress and signaling osteoblasts to form new bone and osteoclasts to resorb bone. She is the future President of the American Society for Bone and Mineral Research.

- Dr. David Eyre, Professor in the Department of Orthopaedic and Sports Medicine at the University of Washington School of Medicine. Dr. Eyre's discoveries led to the development of a rapid and inexpensive urine test used to identify those at risk for bone loss and to monitor the effectiveness of treatments for the disorder.

- Dr. Ted Mala, Director of the Traditional Healing Clinic at the Southcentral Foundation, Alaska. Dr. Mala's experience includes serving on the Council of Public Representatives of the NIH. Dr. Mala continues to be involved in programs across the NIH, including the NIAMS Multicultural Outreach Initiative.

- Dr. Alice Pentland, the James H. Sterner Professor and Chair of the Department of Dermatology at the University of Rochester School of Medicine and Dentistry. Dr.

Pentland's research has led to considerable increases in the knowledge base regarding basic photobiology and skin cancer. Dr. Pentland is a past President of the Society for Investigative Dermatology.

Dr. Katz acknowledged and congratulated Mr. Gahan Breithaupt, NIAMS Associate Director for Management and Operations, who was recently awarded a 2010 Presidential Rank Award for meritorious executive service. Mr. Breithaupt was the only NIH recipient of the award in 2010. Dr. Katz also noted that 20 NIH-supported researchers, including NIAMS grantee Dr. Edward Botchwey of the University of Virginia, recently received the Presidential Early Career Award for Scientists and Engineers (PECASE)—the nation's highest honor for scientists and engineers at the outset of their professional careers. Dr. Botchwey received the award in recognition of his innovative work to promote the growth of mature vascular networks to repair damaged musculoskeletal tissues. Dr. Botchwey is a close collaborator and mentee of former Council member Dr. Cato Laurencin, a prominent orthopaedic surgeon and bioengineer.

Personnel Changes at the NIH/NIAMS

At the NIH level, there is an ongoing search for a new Director of the National Heart, Lung, and Blood Institute. Dr. Katz co-chairs this search committee and invited Council members to suggest any appropriate candidates. The NIH also is preparing to recruit a new Director for the National Institute of General Medical Sciences (NIGMS). Dr. Jeremy Berg, who has served as NIGMS Director since 2003, announced that he will step down from this position in June 2011 to become the Associate Senior Vice Chancellor for Science Strategy and Planning for the Schools of the Health Sciences at the University of Pittsburgh. Upon his departure from the NIGMS, an Acting Director will be named if the search for a new Director is ongoing. Dr. Katz noted that later during this meeting, Dr. Berg would be presenting findings on changes to the NIH peer review system to the Council.

The NIH is also searching for a new Director for the National Institute of Dental and Craniofacial Research (NIDCR). Former NIDCR Director Dr. Larry Tabak moved from this position to become the NIH Principal Deputy Director. Dr. Katz is a member of the search committee that is considering candidates for this position. In the NIH Office of the Director, Dr. Barry Kramer, Associate Director for Disease Prevention and Director of the Office of Disease Prevention retired after 24 years of federal service. The NIH is recruiting to fill Dr. Kramer's position.

At the NIAMS level, the Institute is seeking a physician-scientist to serve as its new Clinical Director. Dr. Daniel Kastner, who formerly held this position, has moved to the National Human Genome Research Institute (NHGRI). NIAMS Deputy Director Dr. Robert Carter is chairing this search committee. Dr. Katz announced that after 40 years of federal service, Dr. Paul Plotz will retire at the end of this month. Dr. Plotz served as the NIAMS Acting Deputy Director before Dr. Carter accepted the permanent Deputy Director position. Dr. Katz commented that the NIH and the patients and families who have benefited from his work are immensely grateful for the insights his studies have provided into the basic mechanisms of inflammatory muscle diseases and his efforts to develop treatments for people who have Pompe disease. Also at the Institute level, Dr. Nancy Garrick has been recruited from the National Institute of Mental Health

and is the new Deputy Director of the NIAMS Office of Communications and Public Liaison.

Update on Budget and Congressional Activities

Dr. Katz reported that in fiscal year 2010 (FY 2010), the NIAMS funded 301 new and competing continuation applications for a success rate of 21.4 percent, slightly higher than last year's rate of 19.9 percent. The overall NIH success rate for FY 2010 is estimated at 20.6 percent.

As is the case with most of the federal government, the NIAMS is operating under a Continuing Resolution for the first part of FY 2011. The Continuing Resolution, which expires on March 4, 2011, provides funding to the NIH at the annualized rate of $31 billion. This translates into approximately $539 million for the NIAMS, which is essentially level with the Institute's FY 2010 budget. Dr. Katz explained that specific funding policies will not be known until an appropriations bill is passed. The Institute has posted a conservative interim funding plan on its Web site. For new investigators, the NIAMS is funding through the 12th percentile. For all other R01s, the Institute is funding through the 8th percentile.

Dr. Katz indicated that he would provide an update on the President's proposed FY 2012 budget, which has not yet been unveiled, at the June Council meeting. Agencies across the federal government are bracing for budget challenges in the coming years. Dr. Katz invited Council members to join him in a discussion at the conclusion of his Director's Report about how to fulfill the NIAMS mission in times of fiscal constraints.

Highlights of Selected Recent Scientific Advances

- Dr. Mark Shlomchik and his team at Yale University, along with collaborators at other institutions, found that deleting dendritic cells from lupus-prone mice significantly reduces disease activity, indicating the critical role of dendritic cells in lupus progression. The investigators concluded that dendritic cells are essential for the invasion of target organs by inflammatory cells, including T cells, and responsible for localized tissue damage (*Immunity*. 2010 Dec 14;33(6):967-78. PMID: 21167752).

- Scientists in the NIAMS Intramural Research Program (IRP) led by NIAMS Scientific Director Dr. John O'Shea have redefined the roles of several cytokines (proteins that influence the behavior of cells) involved in the generation of immune cells implicated in severe autoimmune diseases. The study in mice showed that development of Th17 immune cells can occur without the presence of transforming growth factor (TGF)-beta, a mediator thought to be required for Th17 cell development. The study demonstrates that the interaction of three inflammatory cytokines—interleukin-6 (IL-6), IL-1-beta and IL-23—is responsible for the creation of Th17 cells that are more active in promoting autoimmunity than Th17 cells generated with IL-6, IL-1-beta and TGF-beta (*Nature*. 2010 Oct 21;467(7318):967-71. PMID: 20962846).

- Also from the NIAMS IRP, Dr. Richard Siegel and colleagues have identified a promising potential target for treating the rare inherited inflammatory condition TNF receptor-associated periodic syndrome (TRAPS). By blocking molecules called the reactive oxygen

species that are produced by the mitochondria, Dr. Siegel and his team were able to reduce inflammation in cells (*J Exp Med.* 2011 Jan 11. Epub ahead of print. PMID: 21282379).

- Dr. Andrew Luster and his colleagues at Massachusetts General Hospital and other institutions have been delineating the chemokine-induced recruitment process for neutrophils into joints in a mouse model of rheumatoid arthritis. They have found that neutrophils can produce IL-1-beta, a key inflammatory molecular mediator, which, in turn, induces the synthesis of neutrophil-activating chemokines from many different types of cells in the inflamed joints. Together, these findings suggest that neutrophils can amplify their own recruitment to the joint to promote inflammation, and that individual chemokines may participate in the recruitment of neutrophils during different phases of the disease (*Immunity*. 2010 Aug 27;33(2):266-78. PMID: 20727790).

- Dr. Paul Khavari and colleagues at Stanford University delivered a normal, functional type VII collagen gene into recessive dystrophic epidermolysis bullosa (RDEB) patient skin cells, called keratinocytes, with a viral vector. The modified keratinocytes were grown into sheets in culture, then grafted onto the skin of mice that have a condition similar to human RDEB. The grafted cells were able to produce normal, functional type VII collagen for up to 12 months, and the type VII collagen was incorporated correctly into the skin and anchoring fibrils (*Hum Gene Ther.* 2010 Oct;21(10):1299-310. PMID: 20497034).

- A group of researchers, led by Dr. Jerry Mendell at Ohio State University, is testing the safety and duration of expression of alpha-sarcoglycan gene delivery to a small foot muscle in six patients with type-2 limb-girdle muscular dystrophy. Building on results from the first three patients, the researchers enrolled three additional patients who underwent muscle biopsy six months after gene transfer. Data from this second cohort suggests that alpha sarcoglycan expression can be sustained in limb-girdle patients for at least 6 months after delivery using an AAV vector containing genetic elements that restrict expression to muscle cells (*Ann Neurol*. 2010 Nov;68(5):629-38. PMID: 21031578).

- Dr. Justin Fallon of Brown University recently demonstrated that treatment with biglycan protein restores the muscle function of a mouse model of Duchenne muscular dystrophy by improving utrophin's ability to stabilize cell membranes. The National Institute of Neurological Disorders and Stroke and the NIAMS are supporting additional studies toward developing a U.S. Food and Drug Administration (FDA) Investigational New Drug application for biglycan-based therapeutics. If successful, the project would lead to clinical trials for people who have Duchenne or Becker muscular dystrophy (*Proc Natl Acad Sci USA*. 2011 Jan 11;108(2):762-7. Epub 2010 Dec 27. PMID: 21187385).

- Dr. Bjorn Olsen and his team at Harvard University, along with colleagues at the University of Pennsylvania, discovered that vascular endothelial cells, which line the inside of blood vessels, are one of the main sources of ossified tissues in fibrodysplasia ossificans progressiva (FOP). Under the influence of inflammation, which usually accompanies an injury or infection, these endothelial cells leave their locations in blood vessels to become stem cells. As stem cells, they can develop into new cell types, such as cartilage, bone, or fat. The researchers showed that they could induce this conversion in cell culture, by first

coaxing endothelial cells to become stem cells and then guiding the newly formed stem cells to develop into bone cells. Additional experiments confirmed that ALK2, the gene mutated in FOP patients, plays an essential role in the endothelial-cell-to-stem-cell transition (*Nat Med.* Published online 21 Nov 2010 doi:10.1038/nm.2252 PMID: 21102460).

- In a recent paper, Dr. Xu Cao's research team from the Johns Hopkins University reported an explanation for how alendronate blunts parathyroid hormone's bone-building activity. It inhibits the release of the active form of the protein TGF-beta-1, which in turn decreases the recruitment of mesenchymal stem cells to the bone remodeling sites where they would turn into osteoblasts and produce new bone. Based on these findings, the researchers suggest that use of parathyroid hormone before antiresorptive therapy could be more effective than the reverse sequence. Moreover, the improved understanding of the mechanisms underlying bone turnover may also help to provide a rationale for future osteoporosis therapies (*Cell Stem Cell*. 2010 Nov 5;7(5):571-80. PMID: 21040899).

- People who have severe vertebral deformities due to osteoporosis have an increased likelihood of additional painful, debilitating fractures and should be treated aggressively. However, the correlation between milder defects and the development of osteoporosis is less clear. Dr. Sundeep Khosla at the University of Rochester recently published work showing that many women who have only mild vertebral deformities actually have early osteoporotic spine fractures (*J Bone Miner Res*. 2010 Sep;25(9):1922-30. PMID: 20533526).

- A research team led by Dr. Scott Rodeo at the Hospital for Special Surgery studied the effect of mechanical loading on healing following anterior cruciate ligament reconstruction surgery in rats. They compared healing following mechanical loading early in the healing process, mechanical loading that began after the resolution of acute inflammation due to surgery, and complete immobilization of the knee. They observed that mechanical loading is beneficial and improves the properties of the repair tissue once the rats had recovered from the surgical trauma. These results may have important implications for post-operative physical therapy for people who require ACL reconstruction (*J Bone Joint Surg Am.* 2010 Oct 20;92(14):2387-401. PMID: 20962189).

NIH/NIAMS Activities and Plans for the Future

Dr. Katz noted that Council member Dr. Regis O'Keefe, Chair of the Department of Orthopaedics and Rehabilitation at the University of Rochester Medical Center, represents the National Arthritis and Musculoskeletal and Skin Diseases (NAMS) Advisory Council on the NIH Council of Councils. Later in this meeting, Dr. O'Keefe provided an update on the NIH Council of Councils, which last met on November 8, 2010. The NIH Council of Councils includes approximately 30 individuals selected from NIH Institutes and Centers (IC) advisory councils and has oversight of the NIH Common Fund. The NIH Reform Act of 2006 called for the institution of the NIH Council of Councils. The Act also authorized the NIH Scientific Management Review Board (SMRB) to advise Department of Health and Human Services (HHS) and NIH officials on issues pertaining to NIH's structure and organization. On November 15, the NIH SMRB recommended to NIH Director Dr. Francis Collins that NIH create a new Institute focusing on substance use, abuse, and addiction research. This new

Institute would integrate the relevant research portfolios from the National Institute on Drug Abuse, the National Institute on Alcohol Abuse and Alcoholism, and other NIH ICs. At Dr. Collins' request, Dr. Katz is working with NIH Principal Deputy Director Dr. Larry Tabak to convene a task force of experts from within the NIH to look carefully across all of NIH's 27 ICs to determine where substance use, abuse, and addiction research programs currently exist, and make recommendations about what programs should be moved into the proposed new Institute. A detailed reorganization plan will be presented for Dr. Collins's consideration in the spring of 2011.

The SMRB also has been studying how the NIH could better support translational medicine and therapeutics development. The SMRB Translational Medicine and Therapeutics (TMAT) Working Group submitted its recommendations to Dr. Collins in December 2010. Dr. Amy Patterson, NIH's Associate Director for Science Policy, provided an update to the Council on these findings and next steps later in the meeting.

Dr. Katz reminded Council members that part of the Patient Protection and Affordable Care Act of 2010 required the establishment of the Patient-Centered Outcomes Research Institute (PCORI). This non-profit organization's purpose is to assist patients, clinicians, purchasers, and policy-makers to make informed health decisions, by carrying out research projects that provide quality, relevant evidence on how diseases, disorders, and other health conditions can effectively and appropriately be prevented, diagnosed, treated, monitored, or managed. As a member of the PCORI Board of Governors, Dr. Collins will ensure that the NIH plays an appropriate role in the Nation's comparative effectiveness research agenda.

At the last Council meeting, Dr. Katz provided a brief update on NIH's policy regarding research using human embryonic stem cells. At that time, the U.S. Court of Appeals for the District of Columbia had granted a temporary stay to block the injunction that had stopped federal funding for this type of research. This stay allowed NIH-funded researchers to restart their work, and the NIH is continuing to consider new lines for inclusion in its Human Embryonic Stem Cell Registry.

Later in this meeting, Dr. Sally Rockey, NIH Deputy Director for Extramural Research, presented NIH plans to develop a model for a sustainable and diverse U.S. biomedical research workforce. Dr. Katz commented that this is an era of burgeoning possibilities for biomedical and behavioral science. Harnessing these opportunities to benefit public health lies with new investigators, who are preparing to take the mantle of the future in U.S. biomedical research.

Dr. Katz emphasized that the Institute is committed to continuing to support clinical research, even during these tight budget times. For the past two years, the NIAMS has been engaged with Council members and the research community about steps it can take to enhance its clinical research portfolio. As part of this new process, the NIAMS will strongly encourage investigators to apply for a clinical trial planning grant in advance of support for the full clinical trial, beginning with its FY 2012 awards. The Institute will also receive input from the Council's Clinical Trial Working Group as well as a NIAMS clinical trials study section.

In October and November 2010, the NIAMS held a series of roundtables as a part of its long-range planning process. Every year, Institute leadership identifies four or five areas on which to focus during these sessions—some are program-specific, and some are cross-cutting. The NIAMS is interested in hearing about scientific opportunities, needs, and gaps from the perspective of the extramural research community. This year, Council members Dr. John Klippel (President and CEO of the Arthritis Foundation) and Mr. Bradley Stephenson (Attorney at Law, PLLC, and member of the Muscular Dystrophy Association National Task Force on Public Awareness) participated in a roundtable meeting on the mechanisms of exercise-induced health. Additional topics of discussion at the roundtables included research needs related to itch, the preclinical disease phase of autoimmune skin and rheumatic diseases, and psychosocial and behavioral therapies for musculoskeletal and rheumatic disease outcomes. Over the long term, these roundtable discussions help shape the Institute's thinking about areas of importance in its basic, translational, and clinical portfolios. Summaries of these deliberations are posted on the NIAMS Web site.

Dr. Katz then described highlights of NIAMS information dissemination efforts. At the request of the NIAMS Coalition, nine Congressional staff from eight different House and Senate offices toured NIAMS laboratories in October. Intramural researchers described their research to the staff members, many of whom had not been to the NIH before. Drs. Katz, Carter, O'Shea, and NIAMS Deputy Scientific Director, Dr. Juan Rivera, also met with the group and provided a more global picture of the Institute and its mission.

Many of those who received two-year grants under the American Recovery and Reinvestment Act (ARRA) will begin preparing manuscripts for publication. Dr. Katz emphasized the importance of explaining how this infusion of funding is benefiting the American public. He repeated a request made at previous Council meetings, asking Council members and their colleagues to inform the Institute of how scientists are using ARRA funds to create or preserve jobs, to keep laboratories running, and to advance research. The NIAMS remains extremely interested in hearing success stories related to its ARRA awards.

The NIAMS also is expanding the reach and speed of its dissemination efforts through Twitter. The Office of Communications and Public Liaison will post weekly "tweets" that link to stories, publications, and other content on the NIAMS web site. The Institute recently updated its web site to include a centralized page from which visitors can access videos, images, and audio publications. The new multimedia page includes the NIAMS Image Gallery, an online searchable database of NIAMS photos and illustrations, and audio publications in both English and Spanish. The NIAMS also launched a new set of "Kids Pages," where young people can find relevant science-based health information about bones, joints, muscles, and skin. Dr. Katz thanked Dr. Janet Austin, Director of the NIAMS Office of Communications and Public Liaison, and her team for leading these communication efforts.

Dr. Katz closed his Director's Report by asking Council members for feedback on how the NIAMS can support research during the challenging budget times it currently faces.

Discussion

Council members had questions about the projected R01 payline if the Institute has a budget at the same level as last year's. Dr. Katz reminded Council members that the success of applications that are not within the payline also factors into this equation, and that he anticipates an R01 payline of better than the 8th percentile. There is great uncertainty in this area, however, and only three or four ICs have posted their paylines. Council members noted that there is significant concern among their colleagues that paylines are falling into the single digits at many NIH ICs while at the same time investigators are not allowed to submit their grants more than twice. Key projects may not be funded, and it is difficult to manage grants from both the NIH's and the investigators' perspectives.

There were also questions about the pressures of the budget on the IRP. Dr. Katz commented that the pressures are the same. He explained that he and Dr. O'Shea would be discussing the IRP budget later that day with NIAMS budget staff. They will discuss possibilities such as a 5 percent budget decrease and a flat budget. There are certain items that will be maintained, such as research management and services, which involve salaries and support for the research administration.

Dr. Katz explained that the NIAMS remains committed to investigator-initiated research. There have not been many Requests for Applications (RFAs) from the NIAMS recently, in part because the Institute feels that the investigator community is driving the exciting research in areas of interest to the NIAMS.

In response to a question about the new NIH National Center for Advancing Translational Sciences and the roles that the various NIH ICs will play, Dr. Katz noted that Dr. Patterson is leading this activity and would be discussing these issues in her presentation. He commented that the Center is meant to facilitate the activities ongoing within the ICs rather than creating a new IC for conducting this type of research.

V. ANALYSIS OF THE PEER REVIEW SYSTEM

Dr. Berg, who co-chaired a group reviewing the NIH peer review process, explained that in the new NIH scoring system, each reviewer provides an initial overall impact score on a 1 (best) to 9 (worst) integer scale. These scores are refined during discussion and all members of the study section vote to provide scores. The impact score is averaged, and this average is provided to one decimal place and multiplied by 10 (e.g., scores on an application of 3, 4, 3, 5, and 4 average out to 3.8 and an impact score of 38).

Each reviewer also now provides five criterion scores: (1) significance, (2) investigator, (3) innovation, (4) approach, and (5) environment, again on a 1 (best) to 9 (worst) integer scale. These scores are not explicitly discussed during the study section meetings and are provided to the applicants in the summary statement as individual, unaveraged scores. Dr. Berg noted that the overall impact score is not intended to be algorithmically related to criterion scores; rather, the criterion scores are intended to provide information to IC advisory councils, program staff,

and the applicants about how the reviewers felt about the application. One reason for not linking the criterion scores algorithmically to the impact score was that the weights of these different factors vary from reviewer to reviewer and from application to application. The criterion scores provide data that can be analyzed more effectively to review the peer review system.

The first analysis was carried out on scores from 2009 and involved scores (including all criterion scores) for 360 NIGMS primary R01 applications. For the analysis, the criterion scores were extracted and averaged. In terms of the correlations between the overall impact and criterion scores, the results were 0.74 for approach, 0.63 for significance, 0.54 for innovation, 0.49 for investigator, and 0.37 for environment (reviewers were informed that the criterion and impact scores would not be algorithmically related). Dr. Berg presented plots showing the correlation between impact scores and each of the criterion scores.

Having these implicit criterion scores provides an additional approach for the NIH to examine applications with particular characteristics. To illustrate this, Dr. Berg discussed a set of applications that scored worse than average in terms of innovation but had high overall impact scores. One of the applications, which focused on resource development, indicated in its summary statement that it was not an innovative project. Two additional applications in this group were relatively strong A2 applications that were applying standard methods to important problems; in these two cases, the impact scores appeared to have been relatively inflated compared with the criterion scores by the study section to convince NIH decisionmakers of the merit of these applications.

Similarly, there were applications that had very strong innovation scores but lower relative impact scores. Dr. Berg described six of these applications, two of which came from new investigators, for which concerns about the approach and significance adversely affected the overall impact scores.

Dr. Berg noted that the availability of these criterion scores, particularly when used across an entire portfolio, provide program staff with additional information that can be used to highlight particular applications and help guide funding decisions. To help determine whether the results of this analysis were unique to the NIGMS or reflective of the entire NIH, an analysis across the NIH was conducted. In comparing averages of each of the five criterion scores between the NIGMS and the NIAMS, no significant differences were found, nor were any found between the NIGMS and other NIH ICs.

Dr. Katz asked how the criterion scores for the NIGMS compared with those for the National Institute of Biomedical Imaging and Bioengineering (NIBIB), given that the NIBIB funds many projects related to technological innovation. Dr. Berg indicated that the innovation score for the NIBIB was almost at the average for other NIH ICs (0.62 for the NIBIB compared with 0.63 for the entire NIH). He cautioned that the innovation criterion score should not be interpreted as a perfect measure of innovation for a given project. There is still debate about the meaning of innovation and how best to evaluate it when judging research applications. Council member Dr. Linda Griffith, Professor of Teaching Innovation in the Biological Process Engineering Center at Massachusetts Institute of Technology commented that one topic for discussion among her community is how well technologies are being framed by good questions and integrated into IC

missions. Some feel that the NIBIB should also be viewed as working on engineering approaches, not just technologies, that can be used as frameworks for addressing research needs, and it is difficult to envision how some of the NIBIB's work connects to the missions of other NIH ICs. This topic may be discussed at a future Council meeting.

Dr. Berg noted that there have been only very small changes in the criterion scores over time. Between 2009 and 2011, there was a slight tendency across the NIH for the criterion score correlations to increase as study sections became more familiar with the revised scoring system. A principal components analysis was conducted to determine which combination of single factors would best predict variance in the scores. In the NIGMS data, one component accounted for slightly more than 70 percent of the variance approach.

In concluding his remarks, Dr. Berg summarized that individual criterion scores provide additional information that can be analyzed to understand NIH peer review system behavior and, potentially, to support funding decisions. By the measures used, average peer review system behavior appears to be remarkably robust across ICs, over time, and with changes in application format.

Discussion

Council member Dr. Henry Kronenberg, Chief of the Endocrine Unit at Massachusetts General Hospital and Professor of Medicine at Harvard Medical School, commented that the criterion score "investigator" may be misnamed in its intent. Study sections can be hesitant to give a low score to "investigator" because they do not want the score to be interpreted as representing their feeling toward the investigator as an individual. If the term "track record" were used in place of "investigator" for this score, it may be more effective. Dr. Berg noted that this issue arose in discussions when changes to the NIH peer review system were made. An investigator's track record or past performance is as good a predictor of future performance as any other measure. The challenge is to not systematically put new investigators and early stage investigators at a disadvantage.

Dr. Berg explained that there is information being captured by the individual criterion scores. With that information available, IC Program Directors can use this information to help pull out applications that appear to be unusual in terms of innovation, where the overall impact score does not match well with the individual criterion scores, etc.

Dr. O'Keefe asked about how ICs are making sure that the best research gets funded. He asked if Dr. Berg had a sense of how well study sections can distinguish between the top 10 percent of applications and the top 25 or 50 percent of applications. Dr. Berg noted that one additional analysis his group is conducting involves examining 774 NIGMS competing applications that were funded in 2006 and their publication records, citation records, etc., and determining whether any of these measures correlate with priority scores. The correlation coefficients are substantial—Dr. Berg commented that the NIH peer review system does measure future productivity effectively. He also noted that in this analysis, each quartile of the funded applications was statistically different from the others based on measures used in the analysis.

Council member Dr. S. Wright Caughman, Professor in the Department of Dermatology at Emory University School of Medicine, asked if applications that were close to the payline but not funded by the NIGMS were examined in relative terms of their productivity, assuming some of them received funding from other sources. Dr. Berg indicated that this has not been studied yet. He noted that there is not much difference in terms of scores between grants at the 20th percentile and those at the 21st percentile. At some point, however, there is a sharp boundary between highly productive projects and those that are not productive.

Council member Dr. Julio Vergara, Distinguished Professor in the Department of Physiology at the University of California, Los Angeles School of Medicine, noted that the criterion score approach appeared to be critically important and had the highest correlation to impact score. He asked if shortening the applications has impaired the analysis by Dr. Berg and colleagues. Dr. Berg responded that this is unclear as of now, but their work should provide an answer to this question in the future. The issues to consider when making a funding decision include the importance of a project, if it works, how likely it is to work, and what the likelihood is that new and useful information will be gained from the project.

Dr. Katz commented that the meaning of the term "productivity" as it relates to funded research can be unclear. The number of papers published from a project is not necessarily reflective of overall productivity.

Dr. Susana Serrate-Sztein, Director of the NIAMS Division of Skin and Rheumatic Diseases, asked about "significance" as a criterion score. She noted that when NIAMS staff reviews summary statements, a great deal of variability is seen in how the applicants approach the question of significance. In some cases, the concept is confused with burden of disease, disease prevalence, or disease mortality. Dr. Berg indicated that "significance" has a broad meaning.

VI. RECOMMENDATIONS OF THE NIH SCIENTIFIC MANAGEMENT REVIEW BOARD: ADVANCING TRANSLATIONAL MEDICINE AND THERAPEUTICS

Dr. Patterson focused her presentation on recent SMRB recommendations regarding translational medicine and therapeutics (TMAT) development, driven in large part by the changing drug development landscape and NIH's role in advancing translational research. She explained that despite greater investments in research and development by the pharmaceutical industry, FDA approvals of new molecular entities have declined. Very few candidate compounds prove to be safe and effective, and there are growing pressures on the pharmaceutical industry as it searches for ways to increase the number and quality of cost-effective new medicines without continuing unsustainable research and development risks and costs.

Dr. Patterson explained that the drug development paradigm has shifted from a silo approach to a highly collaborative model that distributes risk. There is a need for innovative models for research and development partnerships that transcend sectors and international boundaries, involving the pharmaceutical and biotechnology industries as well as academia and government. Training and incentives for investigators who pursue careers in clinical and translational research are needed. She noted that the "valley of death" (the period of transitioning risky, early stage

research into promising compounds) has been a wasteland for many drug companies, and as the NIH becomes more involved in this area, it faces the challenge of defining its role in helping investigators successfully navigate this landscape. There are particular challenges associated with preclinical and early phase clinical trials in an open access environment. Complicating these matters are the diverse needs and expectations of patients, Congress, academic researchers, industry, and the general public. These issues are at the forefront of NIH's thought process, and it has asked the SMRB to define the NIH role in this arena.

When he started as NIH Director, Dr. Collins outlined five opportunities for research. Two of them have particular applicability to therapeutics development: (1) translating basic science discoveries into new and better treatments, and (2) putting science to work for the benefit of health care reform. Dr. Patterson noted that NIH ICs have a number of programs designed to build the bridge between research and therapeutics development.

Dr. Collins has indicated the need for the NIH to begin to systematically engineer this bridge in a focused way. In addition, a provision of the Patient Protection and Affordable Care Act specifically tasks the NIH with playing a key role in the development of "high need cures." On May 19, 2010, Dr. Collins charged the NIH SMRB with:

- Identifying attributes, activities, and functional capabilities of an effective translational medicine program for advancing therapeutics development, and

- Broadly assessing the NIH landscape for extant programs, networks, and centers for inclusion in this program and recommend their optimal organization.

Dr. Patterson reminded the Council that the SMRB was established by the NIH Reform Act of 2006 to advise the NIH Director through reports to Congress regarding the use of certain organizational authorities. These organizational authorities include: (1) establishing or abolishing national research institutes; (2) reorganizing Offices within the NIH Office of the Director (including adding, removing, or transferring the functions of such Offices or establishing or terminating such Offices); and (3) reorganizing Divisions, Centers, or other administrative units within the NIH (including adding, removing, or transferring the function of such units, or establishing or terminating such units). Dr. Katz is a member of the SMRB, which is chaired by Dr. Norman Augustine (former CEO of Lockheed Martin). Four SMRB working groups have been formed to date and include Deliberating Organizational Change and Effectiveness (DOCE); NIH Intramural Research Program (IRP); Substance Use, Abuse, and Addiction (SUAA); and TMAT.

The DOCE Working Group issued a report with the overarching conclusion that: "The only defensible rationale for organizational change at NIH is to improve the agency's ability to fulfill its mission." The report sets out a series of guiding principles, logical steps, and underpinning attributes. Within the context of this report, the SMRB began deliberating on what the NIH could do to better position itself to play a more focused and effective role in therapeutics development.

The SMRB TMAT Working Group addressed this issue through a deliberative process that included consultation with diverse groups and sectors (e.g., patient advocacy groups, leaders of academic health centers, Clinical and Translational Science Award [CTSA] recipients, venture capitalists, industry specialists, non-profit organizations, NIH IC staff). The TMAT Working Group indicated that there is a need for change, in so far as the NIH could do more to capitalize on emerging scientific opportunities. The Working Group also recommended that the NIH address the evolving landscape of therapeutics development, recognize synergy in leveraging resources effectively, and authorize the Cures Acceleration Network (CAN). The TMAT Working Group also concluded that this is an opportune moment to expand and augment NIH's efforts in advancing translational medicine and developing new therapeutics (including but not limited to drugs, biologics, and devices) and diagnostics. Toward that end, the Working Group noted that it will be critical that the NIH pursue a deliberate and rational approach that effectively leverages existing efforts, supports promising areas of research, and enhances synergy between public and private sectors.

The TMAT Working Group also made the following recommendations:

- Support and strengthen TMAT research.
- Provide a central locus for information on and access to resources, tools, and expertise related to TMAT.
- Serve as a catalyst and convener for collaborative TMAT interactions and partnerships.
- Expand the pre-competitive space.
- Support training for translational research investigators.
- Enhance communication with and among all stakeholders regarding TMAT.

The SMRB examined the current NIH landscape and identified a number of programs that map naturally to the drug development pipeline. These include the Molecular Libraries Program (MLP), Therapeutics for Rare and Neglected Diseases (TRND) Program, NIH Rapid Access to Interventional Development (RAID) Program, the NIH-FDA Regulatory Science Initiative, the CTSA Program, and the NIH Clinical Center.

After considering these programs, the SMRB proposed that the NIH establish a new Center to:

- Develop and provide research infrastructure for advancing translational medicine and therapeutics development
- Foster new and innovative strategies for TMAT research by advancing a process engineering approach to developing therapeutics, including strengthening and streamlining the process itself

- Serve as a catalyst, resource, and convener for collaborative TMAT interactions and partnerships, capitalizing on the relative strengths of the extra- and intramural communities, private sector, government, and academia, to promote quick-win, fast-fail paradigms and further develop the pre-competitive space.

The SMRB concluded that this new Center should include the MLP, TRND, CTSAs, CAN, and the NIH-FDA Regulatory Science Initiative. The SMRB also indicated that the bulk of this new Center's activities should focus on providing and supporting resources, training, and tools to enable TMAT research. As necessary, the new Center should house targeted activities to perform its functions. Importantly, the SMRB noted that the functions and activities of any new Center should not duplicate, consume, or undermine the successful activities already underway within NIH ICs.

The SMRB also emphasized that the new Center should be evaluated periodically to determine whether it is meeting its goals and address any untoward consequences. Given the lengthy timelines, high-risk nature, and difficulty associated with TMAT research, interim metrics will be critical to enabling short-term evaluation and making necessary adjustments. The SMRB underscored the need to consider the inclusion of other relevant NIH programs and to analyze previous NIH experience in implementing TMAT development programs, including lessons learned and failures.

Dr. Patterson explained that although the SMRB recommended the inclusion of CTSAs in the new Center, it did not make a recommendation on what should be done with the rest of the National Center for Research Resources (NCRR), which housed the CTSAs. The SMRB did note that many of the NCRR's resources are germane to the resource function of the new Center, and that the NIH may consider the incorporation of these relevant components.

On December 7, 2010, the SMRB recommended, by majority vote, that a new TMAT Center be created at the NIH. The SMRB endorsed and supported NIH's commitment to undertake a more extensive and detailed analysis through a transparent process to evaluate the impact of the new Center on other relevant extant programs at the NIH (including the NCRR). The NIH has accepted and concurred with the SMRB recommendations and has formed groups to consider the structure of this new Center, consider the role of the NCRR and its programs, and recommend potential models of partnership with the external community. On February 23, 2011, the NIH will report its progress and findings to the SMRB. The NIH also will provide a detailed plan for the proposed Center to HHS Secretary Kathleen Sebelius in mid-2011. Interested parties can provide feedback to the NIH via the web site http://feedback.nih/gov/.

Discussion

In discussion, Dr. Katz noted that there is a need to control expectations from this TMAT endeavor. This issue has been discussed in open meetings of the TMAT Working Group, and it is important to temper undue expectations for the rapidity with which advances will be made. Dr. Patterson agreed, noting that in acknowledging the tremendous opportunities for therapeutics development, there needs to be an effort to ensure that the public and Congress are cognizant of the long timeline and difficulties that are inherent in the process.

Dr. Griffith commented that many in her community are curious about whether the new Center will include both small molecules and biologics. The way the Center is structured, it appears that it may favor small molecule development, because they are more amenable to high-throughput technologies. There is also interest in whether encouragement will be given to combination therapies and therapeutics that may fall into the gaps of what pharmaceutical companies typically pursue. Dr. Patterson emphasized that the NIH is still in the deliberative mode regarding the new Center and clarified that by using the term "therapeutics," she is including biologics, devices, drugs, and other types of interventions including diagnostics and preventive approaches.

Dr. Katz explained that the new Center will not be redundant with the activities of other ICs. Rather, it is meant to facilitate and accelerate these activities.

Dr. Kronenberg expressed enthusiasm for the new Center, noting that movement of the CTSAs from the NCRR makes good sense but also is potentially confusing. The CTSAs have a much broader mission than the new Center, in terms of clinical research.

Dr. Serrate-Sztein commented that one of the largest obstacles facing the new Center is assisting the community with regulatory issues related to developing new therapeutics. Dr. Patterson extended an open invitation to the Council to contact her with specific issues the new Center should address in this area. Last year, the NIH launched a new partnership with the FDA that involves the heads of FDA Centers and NIH IC Directors, with the goal of finding a path that allows the FDA to carry out its mission while overcoming the regulatory hurdles that slow down research.

VII. NIH SUPPORT OF BIOMEDICAL RESEARCH

Dr. Rockey explained that the NIH is embarking on a workforce analysis—Dr. Collins has charged the Advisory Committee to the Director with modeling the workforce for the future (e.g., the size of the workforce, how it should be constructed, how the NIH should support it, what type of training is needed, etc.). As background, Dr. Rockey's group prepared information on the current state of the workforce at the NIH and how it is supporting the biomedical research enterprise.

Dr. Rockey presented a slide showing the total NIH budget authority for FY 2009 and illustrating that research project grants (RPGs) represent by far the largest part of the NIH research portfolio, followed by research and development contracts, intramural research, research Centers, etc. She then explained that while the NIH budget has grown slightly since 2003, actual spending power has decreased. The number of research grants funded by the NIH increased in the years following the doubling of the NIH budget but has plateaued in recent years. After the budget doubled, there was an echo effect in which the number of applications to the NIH grew substantially—this also has flattened in recent years. The success rate dropped from approximately 30 percent to 20 percent because of the large number of applications received following the doubling of the budget. It is likely that the overall NIH success rate will hover at around 20 percent in the coming years.

The average size of grants has grown in recent years, corresponding to the increasing cost of research. The average NIH R01 equivalent grant is approximately $400,000. The percentage of women receiving R01 equivalent grants has increased. Currently, approximately 30 percent of these awards are given to women. Dr. Rockey commented that despite this progress, there is much work to do in order to reach a point at which the workforce resembles the overall U.S. population. African American Principal Investigators (PIs) represent only 1.3 percent of NIH RPG PIs. This percentage has remained essentially unchanged in the last 25 years. Diversifying the workforce remains a significant challenge.

The average age for receiving a first R01 equivalent has been slowly increasing. The average age for M.D.s receiving their first R01 equivalent is 43. The average age for Ph.D.s receiving their first R01 equivalent is just over 41. To address the pool of new investigators, in 2007 the NIH began setting goals for the number of new investigators and their success rate. Dr. Rockey reported that the NIH has been successful in increasing the number and percentage of successful new investigators in its programs.

Dr. Rockey explained that medical schools receive more than 50 percent of NIH grant support funds, and overall, NIH grant support by type of organization has remained stable over the last 25 years. At the top five NIH-funded higher education institutions (all of which have medical schools), between 33.5 percent and 88.9 percent of the research and development budget came from the NIH. NIH funds make up approximately 2 percent of the research and development budgets for those higher education institutions at the 50^{th} percentile of NIH funding.

In reviewing the average number of applications per institution per year, Dr. Rockey noted that medical schools submit by far the highest number of applications, an average of about 250 applications per year (other types of institutions average approximately 10-25 applications per year). Interestingly, the number of applications per investigator per year has remained fairly stable, at between 1.4-1.6 (the data presented by Dr. Rockey did not include ARRA awards). Although there are some investigators who have a large number of NIH grants, on average, each NIH-funded PI has about 1.4 NIH grants.

Dr. Rockey presented a slide showing the distribution of FY 2009 RPG funding across institutions, noting that 10 percent of the organizations that the NIH funds receive 80 percent of the funding. Approximately 60 organizations receive roughly 50 percent of NIH RPG funds. Overall, the NIH funds approximately 3,000 organizations each year, including small businesses. Policy changes that affect organizations receiving substantial NIH funding (i.e., primarily medical schools) will affect the workforce. Dr. Rockey also noted that about 20 percent of NIH-funded PIs receive 50 percent of NIH RPG funds. Of the investigators in this top 20 percent, many have up to four grants.

The number of biomedical science Ph.D. researchers holding tenure or who are tenure-track decreased from 45 percent in 1980 to just over 25 percent in 2006. Roughly 70 percent of NIH-supported scientists are Ph.D.s. M.D.s represent just under 20 percent of NIH-supported scientists, and M.D.-Ph.D.s represent approximately 10 percent. The group of M.D.-Ph.D.s has increased somewhat in recent years—Dr. Rockey commented that growth in this area is encouraging, based on NIH's emphasis on clinician scientists.

Data from several sources suggests that 30-50 percent of faculty salaries are derived from soft funds. Dr. Rockey clarified that in this sense, soft funds represent money that is not obtained directly from an investigator's home institution (e.g., through a grant). This percentage varies based on whether the faculty is at a public or private institution, at a medical school, and whether the faculty has clinical or non-clinical status.

Dr. Rockey explained that the NIH supports career stages from the time a researcher is a graduate student or in medical school. She listed a number of NIH mechanisms designed for specific stages of a researcher's career and noted that the undergraduate population may represent an unmet need in this regard. She explained that many students are receiving degrees and training from community colleges, which tend to include very diverse populations of students. Finding ways to move students with a strong interest in science from two-year community college programs to four-year colleges and then undergraduate programs may help improve the diversity of the workforce. Currently, there are very few NIH mechanisms that support community colleges. The NIH also does not have a mission in grades K-12, when a strong interest in science often takes root.

Dr. Rockey concluded her presentation by discussing the results of an NIH study to determine when researchers fell out of the workforce. Interestingly, it was found that PIs on RPGs leave the NIH funding system for a period of five years or more at relatively constant rate between the ages of 35 and 68. Additional investigations will be carried out to determine the reasons researchers drop out of the NIH funding system. She noted that a number of listening sessions will be held around the country to discuss workforce issues and invited Council members to submit comments.

Discussion

Dr. Mala asked if there was any incentive for the 20 percent of NIH-funded PIs who receive roughly 50 percent of RPG funds to include underrepresented or minority populations. He added that Native Americans represent 0.2 percent of PIs who are awarded RPGs. He also asked if there were any programs at the NIH for senior researchers to help bring along researchers from underserved populations. Dr. Katz noted that the NIAMS has a supplement program for this purpose that has been extremely successful. Dr. Rockey added that at the NIH level, the Diversity Supplement Program allows an NIH-funded PI to bring in a researcher from an underserved population to help work on the grant. This has been tremendously important in terms of training opportunities, but has not translated into increased numbers of new PIs from underrepresented populations. Dr. Griffith added that diverse populations often are attracted to newer fields of study, such as biological engineering. Newer disciplines could represent an opportunity for including diverse populations at the undergraduate level.

Dr. Kronenberg asked about the average time an individual stays in research, suggesting that he had heard it that it ranges between five and eight years. Dr. Rockey indicated that the time is likely above eight years, and that the Federal government as a whole is trying to find more effective ways to track individuals as they move out of federal funding systems (e.g., whether they drop out of research entirely, move to industry, etc.).

In response to a question about grant renewals, Dr. Rockey explained that new investigators have the same success rate as established investigators coming in for their first renewal. Overall at the NIH, renewals have a much higher success rate than do first-time applications, largely because the investigators are more established, they have data supporting their project, and the NIH has a vested interested in seeing good science continue.

Dr. Bonewald asked about the criteria being used with regard to research training for NIH-supported graduate students. Dr. Rockey noted that this is a significant issue for graduate students and postdoctoral students participating on research grants, and something that the NIH may look into in the future to ensure that these individuals are not disconnected from the research enterprise. Dr. Rockey also commented that in the past foreign nationals who received training in the United States typically remained in this country. There has been a shift, largely due to the availability of new opportunities in their home countries, such that many of these individuals are returning to their country of origin after completing their training. This will have a significant effect on the workforce.

VIII. COUNCIL OF COUNCILS MEETING

Dr. O'Keefe attended the November 8, 2010, meeting of the NIH Council of Councils and provided the NIAMS Advisory Council with an update. The meeting featured a presentation on the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) by DPCPSI Director Dr. James Anderson. Created by the NIH Reform Act of 2006, DPCPSI's mission is to:

- Identify emerging scientific opportunities, rising public health challenges, and scientific knowledge gaps that merit further research.
- Develop and apply resources (databases, analytic tools, and methodologies) in support of portfolio analyses and priority setting.
- Plan and implement trans-NIH initiatives supported by the Common Fund.
- Plan, support, and provide technical assistance in the development of program evaluations.
- Coordinate research related to AIDS, behavioral and social sciences, women's health, and disease prevention.

Within the DPCPSI, the NIH Council of Councils advises the NIH Director on DPCPSI policies and activities. The Council of Councils advises on research responsive to emerging scientific opportunities, public health challenges, and knowledge gaps. It also conducts concept reviews for proposed initiatives to be supported through the Common Fund and carries out second-level review of the Transformative R01 Grant Program that is supported by the Common Fund.

Dr. O'Keefe presented a slide showing the organizational structure of DPCPSI, noting that the DPCPSI Office most relevant to the NIH Council of Councils is the DPCPSI Office of Strategic

Coordination (OSC). The OSC: (1) works with staff and leadership across the NIH to identify and promote NIH-wide scientific opportunities supported by the NIH Common Fund, including the former NIH Roadmap for Medical Research Programs; (2) coordinates a strategic planning process that engages the broad community of stakeholders to identify emerging opportunities and priorities; and (3) manages the Common Fund, making funds available to the ICs that implement the programs.

Dr. O'Keefe reminded Council members that the goals of the NIH Common Fund are to accelerate basic research discoveries and speed translation into clinical practice, address roadblocks that slow the pace of biomedical research to improve health, develop new ways to fund innovative and potentially transformative research, and develop programs that no single IC would fund that are relevant to much or all of the NIH.

The November 8 Council of Councils meeting also included an update on Common Fund initiatives and a presentation on the lifecycle of Common Fund programs by Dr. Elizabeth Wilder, OSC Deputy Director. Dr. O'Keefe described the lifecycle of Common Fund programs (which generally last five to 10 years), starting with the identification of needs and opportunities and moving through refinement of concepts into specific initiatives, concept clearance, program implementation, modification as necessary to benefit science, and a decision as to whether continued Common Fund support is necessary. The NIH Council of Councils is involved in the stages related to concept clearance, program implementation, and modification as necessary to benefit science.

Dr. O'Keefe mentioned the NIH Epigenetics Program, the NIH Human Microbiome Program, and initiatives related to health economics as examples of Common Fund programs that were shaped in large part by the NIH Council of Councils. He also noted that in response to NIH Council of Councils input, initiatives such as the Molecular Libraries and Imaging Program transitioned from the Common Fund while maintaining utility.

Dr. O'Keefe discussed the National Nanotechnology Initiative (NNI), an NIH Common Fund program designed to detect disease before health has deteriorated using tissue engineering to repair or replace body parts. This cross-cutting initiative has bearing on a number of ICs. The NNI is novel and open to risk, multidisciplinary, and focused on translational studies.

Discussion

Dr. Katz thanked Dr. O'Keefe for representing the NIAMS on the NIH Council of Councils. He explained that the NIH Common Fund represents approximately 1.7 percent of the total NIH budget. A challenge that needs to be addressed centrally at the NIH is that there are monies within the common fund that are supposed to be turned over every five to 10 years, but there are programs (e.g., Pioneer Awards, New Innovator Awards) that are in place, presumably to stay.

IX. COUNCIL OPERATIONS

NIAMS Advisory Council Executive Secretary Dr. Laura K. Moen, Director of the NIAMS Division of Extramural Research Activities, explained that each year, the NIH asks Institutes to revisit their Advisory Council operating procedures with the members of their respective councils. Council members are asked to renew the understanding that exists between the advisory council and the Institute.

Council members were provided with the operating procedures for the NAMS Advisory Council. Dr. Moen explained that there have been no major changes in the operating procedures between this year and previous years. Council members were asked to vote on acceptance of these operating procedures.

A motion was made, seconded, and passed to approve the operating procedures of the NAMS Advisory Council. Council members voted unanimously to renew the operating procedures.

X. BIENNIAL INCLUSION REPORT

Ms. Shahnaz Khan explained that the concept that women and minorities should be represented in biomedical and behavioral research began more than 25 years ago. In 1993, this policy became mandated by Congress through the NIH Revitalization Act. Since that time, the NIH has made revisions to the policy to clarify its definition of clinical research, the racial and ethnic categories, and the roles and responsibilities of NIH staff and the extramural research community. The last major update to this policy was in 2001.

There are several ways that the NIH and NIAMS monitor adherence to this policy. During peer review, the Scientific Review Officers instruct the reviewers to evaluate the inclusion plans. Once a study has been funded with an acceptable plan, the Program Director ensures that the investigator is complying with the proposed plan for including women and minorities through their review of the inclusion and enrollment tables that are submitted with the annual progress report. Every two years, the Office of Research on Women's Health on behalf of the NIH Director reports to Congress on the number of women and minorities that have enrolled in NIH-funded clinical research. A statement from each IC's advisory council is provided to confirm compliance with the NIH policy.

The written *Biennial Inclusion Report* was shared with NIAMS Advisory Council members and includes a description of the Institute's efforts to monitor compliance with the law and the number of women and minorities that were involved in NIAMS-sponsored clinical research during the past two years. The Council must certify that the NIAMS has complied with the provisions of the law. Overall aggregate data has demonstrated that the Institute continues to see similar trends in enrollment as in previous years and has representation of all minority groups and women in its clinical research. Dr. Katz commented that the NIAMS is an Institute of women and minorities, given the fact that many of the diseases of interest to the NIAMS disproportionately affect women and minorities.

Council members voted unanimously to approve the NIAMS *Biennial Inclusion Report* and the Institute's commitment to including women and minorities in its research.

XI. CONSIDERATION OF APPLICATIONS

The Council reviewed a total of 813 applications in closed session requesting $1,159,983,349 and recommended 813 for $1,159,983,349.

XII. PORTFOLIO ANALYSIS

This portion of the meeting occurred during closed session.

XIII. ADJOURNMENT

The 73rd National Arthritis and Musculoskeletal and Skin Diseases Advisory Council Meeting was adjourned at 3:00 p.m. Proceedings of the public portion of this meeting are recorded in this summary.

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

Laura K. Moen, Ph.D.
Executive Secretary, National Arthritis and Musculoskeletal and Skin Diseases Advisory Council

Director, Division of Extramural Research Activities, National Institute of Arthritis and Musculoskeletal and Skin Diseases

Stephen I. Katz, M.D., Ph.D.
Chairman, National Arthritis and Musculoskeletal and Skin Diseases Advisory Council

Director, National Institute of Arthritis and Musculoskeletal and Skin Diseases