Meeting Minutes

Department of Health and Human Services

National Institutes of Health

National Diabetes and Digestive and Kidney Diseases Advisory Council

I. CALL TO ORDER

Dr. Griffin P. Rodgers, Director, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) called to order the 179th meeting of the National Diabetes and Digestive and Kidney Diseases Advisory Council at 8:30 a.m., Wednesday, February 18, 2009, in Conference Room 10, Bldg. 31, NIH, Bethesda, Maryland.

A. ATTENDANCE – COUNCIL MEMBERS PRESENT

Dr. Nancy Andrews
Ms. LaVarne Burton
Dr. Charles Elson, III
Dr. Robert Flanigan
Dr. James Freston
Dr. Christopher Glass
Dr. David Klurfeld
Dr. Mitch Lazar
Dr. Mark Magnuson
Dr. Juanita Merchant
Dr. William Mitch
Dr. Brian Monahan
Dr. Jerry Palmer
Dr. David Perlmutter
Ms. Margery Perry
Ms. Lisa Richardson
Dr. Anthony Schaeffer
Mr. James Schlicht
Dr. John Sedor
Dr. Patrick Tso

Also present:

Dr. Griffin P. Rodgers, Director, NIDDK, and Chairperson, NIDDK Advisory Council

Dr. Brent Stanfield, Executive Secretary, NIDDK Advisory Council

B. NIDDK STAFF AND GUESTS

In addition to Council members, others in attendance included NIDDK staff members, Center for Scientific Review (CSR) Scientific Review Officers, and other NIH staff members. Guests were present during the open session of the meeting. Attendees included the following:

Abankwah, Dora – NIDDK
Agodoa, Lawrence – NIDDK
Akolkar, Beena – NDDK
Appel, Michael – NIDDK
Bell, B. – Social Scientific Systems
Barnard, Michele – NIDDK

Bethea, Gina – NIDDK
Bishop, Terry – NIDDK
Blondel, Olivier – NIDDK
Calvo, Frank – NIDDK
Carrington, Jill – NIDDK
Cash, Lisa - CSR
Castle, Arthur – NIDDK
Chamberlain, Joan – NIDDK
Chang, Debuene – NIDDK
Chen, Kong – NIDDK
Chianchiano, Dolph – National Kidney Foundation
Chon Lee, Angie – NIDDK
Christiansen, Dane – Digestive Disease National Coalition
Clemens, Quentin – University of Michigan
Connaughton, John – NIDDK
Cowie, Catherine – NIDDK
DeSanti, Andrea – Social Scientific Systems
Donohue, Patrick – NIDDK
Doo, Edward – NIDDK
Edwards, Michael – NIDDK
Eggerman, Thomas – NIDDK
Eggers, Paul – NIDDK
Evans, Mary – NIDDK
Everhart, James – NIDDK
Ferguson, Frances – NIDDK
Feld, Carol – The Hill Group
Fonville, Olaf – NIDDK
Fradkin, Judith - NIDDK
Gallivan, Joanne – NIDDK
Gansheroff, Lisa – NIDDK
Garfield, Sanford – NIDDK
Greene, Lucy – NIDDK
Gutierrez-Lugo, Elizabeth - NIDDK
Haft Renfrew, Carol – NIDDK
Hamilton, Frank – NIDDK
Hanlon, Mary – NIDDK
Hansen, Rick – Digicon Corp
Harris, Kimberly – NIDDK
Harris, Mary – NIDDK
Hilliard, Trude – NIDDK
Hoff, Eleanor – NIDDK
Hoofnagle, Jay – NIDDK
Horlick, Mary – NIDDK
Hoshizaki, Deborah – NIDDK
Hubbard, Van – NIDDK
Hunter, Christine – NIDDK
Hyde, James – NIDDK
Jerkins, Ann - CSR
James, Stephen – NIDDK
Jones, Teresa – NIDDK
Karp, Robert – NIDDK
Ketchum, Christian – NIDDK
Kim, Sooja - CSR
Kuczmarski, Robert – NIDDK
Khan, Mahfuzul - CSR
Kusek, John – NIDDK
Laughlin, Maren – NIDDK
Linehan, Amanda - NIDDK
Magra, Amy - NIDDK
Malik, Karl – NIDDK
Malozowski, Saul – NIDDK
Mascone, Lisa – NIDDK
Manouelian, Denise – NIDDK
Margolis, Ronald – NIDDK
May, Michael (Ken) – NIDDK
McGowan, Melissa – NIDDK
McKeon, Catherine – NIDDK
Meyers, Catherine – NIDDK
Miles, Carolyn – NIDDK
Miller, David – NIDDK
Miller, Megan – NIDDK
Moxey-Mims, Marva – NIDDK
Mullins, Christopher – NIDDK
Narva, Andrew – NIDDK
Newman, Eileen – NIDDK
Nyberg, Leroy – NIDDK
Ngwu, Ezuma – NIDDK
Patel, D. G. – NIDDK
Perry-Jones, Aretina – NIDDK
Pike, Robert – NIDDK
Podskalny, Judith – NIDDK
Rankin, Tracey – NIDDK
Rasooly, Rebekah – NIDDK
Richter, Holly – University of Alabama at Birmingham
Roberts, Tibor – NIDDK
Robinson, Terra – NIDDK
Rosenberg, Mary Kay- NIDDK

Rushing, Paul - NIDDK
Sagan, Rebekah – NIDDK
Sahai, Atul - NIDDK
Salomon, Karen – NIDDK
Sankaran, Lakshmanan – NIDDK
Sato, Sheryl – NIDDK
Savage, Peter – NIDDK
Sawhney, Ravi – NIDDK
Sechi, Salvatore – NIDDK
Seeff, Leonard – NIDDK
Serrano, Jose – NIDDK
Sheard, Nancy – CSR
Smedberg, Paul – American Society of Nephrology
Smith, Philip – NIDDK
Spain, Lisa – NIDDK
Staten, Myrlene – NIDDK
Star, Robert - NIDDK
Stone, Arthur – NIDDK
Tatham, Thomas – NIDDK
Torrance, Rebecca – NIDDK
Wallace, Julie – NIDDK
Wellner, Robert – NIDDK
Willard, Alan - NINDS
Williams, Will – NIDDK
Woynarowska, Barbara – NIDDK
Wright, Elizabeth – NIDDK
Xie, Yining – NIDDK
Yanovski, Susan - NIDDK
Zellers, Charles - NIDDK

C. ANNOUNCEMENTS

Dr. Rodgers thanked the Council members for their participation and made the following announcements.

Council Members

Dr. Rodgers welcomed the following four new members to the Advisory Council and extended his appreciation to them for their willingness to serve on the Council.

- *Dr. Christopher Glass—Appointed to the Subcouncil for the Division of Diabetes, Endocrinology and Metabolic Diseases:* A Professor of Medicine and Cellular and Molecular Medicine at the School of Medicine, University of California, San Diego, Dr. Glass' research interests focus on the regulation of macrophage gene expression. His laboratory uses molecular and biochemical approaches to elucidate the mechanisms of action of transcription factors that mediate the biological effects of retinoic acid, vitamin D and other hormone-like molecules during macrophage development and terminal differentiation. These approaches are also used by his laboratory to investigate mechanisms of transcriptional control of macrophage-specific genes that have been implicated in the pathogenesis of atherosclerosis and other diseases. Dr. Glass earned both his M.D. and Ph.D. degrees from the University of California, San Diego. His research has been funded by NIH since 1991 and he has published over 125 original articles. He has also authored 50 invited articles and book chapters. He has served as a member and as chair of the NIH Endocrinology Study Section, and has also chaired or co-chaired a number of Gordon and Keystone conferences.

- *Ms. LaVarne Burton—Appointed to the Subcouncil for the Division of Kidney, Urologic, and Hematologic Diseases.* Ms. Burton is President and Chief Executive Officer of the American Kidney Fund (AKF), an organization that educates patients and the public about kidney disease. AKF also provides direct

financial assistance to kidney patients experiencing economic hardship to help them maintain health insurance and related health care service. In her role with the Foundation, Ms. Burton has focused on the prevention of kidney disease via the creative Minority Intervention and Kidney Education (or MIKE) program. This program provides free kidney screenings and follow-up services to members of minority populations who are most at risk for kidney disease. Ms. Burton has previously served as a consultant on health care and pharmacy-benefits industry issues, and has worked at the Department of Health and Human Services and on the House of Representatives Budget Committee. She is on the Board of Advisors for Women Business Leaders in the U.S. Health Care Industry Foundation, and is a Fellow of the National Academy of Public Administration.

- *Robert Flanigan, M.D.—Appointed to the Subcouncil for the Division of Kidney, Urologic, and Hematologic Diseases.* Dr. Flanigan serves as the Department Chairperson and a Professor of Urology at Loyola University. A practicing physician active in multiple community health education and outreach activities, Dr. Flanigan also currently holds the position of Secretary for the American Urological Association. A board-certified urologist, Dr. Flanigan graduated from the Case Western Reserve University School of Medicine and also completed his residency there. His research interest is focused on clinical urology, especially urological oncology.

- *John Sedor, M.D. —Appointed to the Subcouncil for the Division of Kidney, Urologic, and Hematologic Diseases.* Dr. Sedor is Professor of Medicine and Physiology at Case Western Reserve University and serves there as the Vice President for Research on the MetroHealth System Campus. Dr. Sedor has been the recipient of numerous awards and NIDDK grants. He serves as Director of an NIDDK O'Brien Renal Research Center at Case Western Reserve, and as a participating investigator in the Family Investigation of Nephropathy of Diabetes (FIND) Consortium. In addition, he has quite often participated in NIDDK and NIH Study Sections since 1989. Dr. Sedor's research interests span basic and clinical nephrology, with a particular focus on understanding genetic mechanisms of progressive kidney disease, including diabetic nephropathy.

Current NIDDK Advisory Council members *Drs. Juanita Merchant* and *David Perlmutter* and former Council member *Dr. Jeffery Gordon* were among the new members and foreign associates announced by the Institute of Medicine in conjunction with its 38th annual meeting. The NIDDK has an outstanding Council and is very proud of its current and former members. Election to the IOM is considered one of the highest honors in the fields of health and medicine and recognizes individuals who have demonstrated outstanding professional achievement and commitment to service.

NIH Grantees

Dr. Rodgers made the following announcements regarding NIH grantees:

Dr. Michael J. MacCoss: An Assistant Professor of Genome Sciences, University of Washington, Seattle, Dr. MacCoss received a Presidential Early Career Award for Scientists and Engineers. The Presidential Award is the highest honor bestowed by the U.S. government to outstanding scientists and engineers beginning their independent careers. Each year the White House confers the awards—which honor and support the awardees—based on recommendations from eleven participating federal agencies. Dr. MacCoss was one of the 12 NIH-nominated Presidential Awardees honored at a ceremony on December 18, 2008 on the NIH Campus, the day before the White House ceremony. Dr. MacCoss received his award for the development and application of mass spectrometry and stable isotope-based technologies for the high-throughput measurement of dynamic changes in the proteome and for his mentorship of graduate students and postdoctoral fellows.

Dr. Timothy Ley: A Professor in the Department of Medicine and the Department of Genetics, Washington University School of Medicine, St. Louis, Dr. Ley received the 2008 American Society for Hematology Mentor Award (Basic Science). The award recognizes and rewards outstanding role models in the hematology community. Dr. Ley's nomination recognizes his personal integrity, scientific rigor, commitment to his trainees, and his advocacy of scientific education. Dr. Ley has been an NIDDK grantee since 1987 and presently has support from both NIDDK and the National Cancer Institute.

NIDDK Staff Members

Dr. Rodgers made the following announcements:

Lieutenant Rebekah Sagan: **Following a two-year tour as a Special Assistant to the Surgeon General, Lieutenant Sagan is joining the Division of Digestive Diseases and Nutrition as a Health Research Administrator. She earned an undergraduate degree in kinesthesiology and exercise leadership from James Madison University and a Masters in Public Health from the University of South Carolina. Dr. Sagan recently received the "Reserve Officers Association's VADM C. Everett Koop Outstanding PHS Junior Officer of the Year Award." This major award recognizes her "outstanding leadership, commitment, and dedication to public health while assigned to the Office of the Surgeon General."**

Ms. Traci Melvin: Joining the NIDDK, Ms. Melvin will serve as the Deputy Ethics Counsel. She served previously in the Office of the Director, NIH Ethics Office, where, as Deputy Director of the NIH Ethics Office, she planned and had oversight responsibility for work of the office. She has a Bachelor's Degree in Management from Howard University, Washington, D.C., and a Master's Degree from Johns Hopkins University, Baltimore, Maryland. Ms. Melvin began her career at NIH after graduation from Howard University. Previous to her position at the Office of the Director, NIH

Ethics Office, she worked with the National Cancer Institute and the National Institute of General Medical Sciences.
Dr. Patricia Robuck: Serving as Director, Clinical Trials Program, Division of Digestive Diseases and Nutrition, Dr. Robuck was recognized recently by the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. Dr. Robuck was the first recipient of the organization's Pediatric Research Advocacy Award in recognition of her ongoing support for research to address the numerous conditions affecting the liver and gastrointestinal tract in children.

Publications

Dr. Rodgers noted the following publications:

DMICC: Coordinating the Federal Investment in Diabetes Programs To Improve the Health of Americans: The is booklet highlights the accomplishments of the statutory Diabetes Mellitus Interagency Coordinating Committee, which is chaired by Dr. Judy Fradkin, Director, Division of Diabetes, Endocrinology and Metabolism, NIDDK. The Committee has 35 members representing diverse agencies within the Department of Health and Human Services, the Department of Defense, the Department of Agriculture, and the Veterans Health Administration. The booklet is designed primarily to increase the presence and knowledge of the DMICC beyond federal agencies. Dr. Fradkin provided leadership to this project--with many contributions from Members of the Committee and from the NIDDK Office of Scientific Program and Policy Analysis.

Recent Advances & Emerging Opportunities: This booklet highlights some of the exciting NIDDK-supported research advances from the past year. It also includes "stories of discovery," which trace research progress in specific areas over a longer period of time. Profiles of patients who are benefiting from NIDDK-supported research are featured. Scientific presentations made to the Advisory Council during 2008 are summarized, including presentations given by Council members Dr. Tso and Dr. Perlmutter. The cover graphic illustrates how the NIDDK is using a "bedside to bench to bedside" approach to support research that has led to the identification of numerous genes associated with diseases within the NIDDK mission. The Institute is now building on those findings to understand the role of those genes in health and disease, with the ultimate goal of improving the health of people. The NIDDK Office of Scientific Program and Policy Analysis led the development of this booklet, with substantial input from the NIDDK Divisions.

Two important and inter-related NIH reports focusing on digestive diseases have recently been released. The NIDDK provided leadership and support for these efforts.

- *The Burden of Digestive Diseases in the United States:* This report builds on two previous analyses to update knowledge of the state of digestive diseases across the nation. Its development was overseen by Dr. Jay Everhart, Chief, Epidemiology and Clinical Trials Branch, Division of Digestive Diseases and Nutrition.
- *Opportunities and Challenges in Digestive Diseases Research: Recommendations of the National Commission on Digestive Diseases:* This long-range research

Both of these reports will help to guide the NIH and other research partners in pursuing promising research opportunities to ultimately improve the lives of those affected by digestive diseases.

Review Branch

The NIDDK Review Branch was commended by Dr. Rodgers for its excellent work during the past year. In 2008, the Review Branch conducted reviews of over 1,000 applications, most of which were either complex or needed special consideration or handling. These applications included R01s received in response to specific PARs or RFAs; multicenter clinical trials; program projects; core center applications; cooperative agreement applications; institutional and individual training applications; loan repayment applications (clinical and pediatric); and research and development contract proposals. The reviews required the coordination of nearly 2,000 reviewers and included expertise that cut across an extremely large body of science. Moreover, the Review Branch assumed additional work this last year in reviewing fellowship applications for which it instituted a streamlined process. The work of the NIDDK's Review Branch in 2008 was consistently performed in a professional manner; included recruitment of some stellar reviewers; and provided the Institute with information essential to the NIDDK mission.

II. CONSIDERATION OF SUMMARY MINUTES OF THE 178th COUNCIL MEETING

Following a motion, the Council unanimously approved by voice vote the summary minutes of the 178th Council meeting.

III. REPORT ON INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH

Following a motion, the Council approved the NIDDK's 2009 Biennial Advisory Council Report on Inclusion of Women and Minorities in Clinical Research. This report is required by the NIH Revitalization Act of 1993, P.L. 103-43.

IV. FUTURE COUNCIL DATES

Dr. Rodgers called the attention of the Council to future meeting dates.

2009

May 13 (Wednesday)

September 9 (Wednesday)

2010

February 24-25 (Wednesday and Thursday)

May 12-13 (Wednesday and Thursday)

September 22-23 (Wednesday and Thursday)

2011

February 16-17, 2011 (Wednesday and Thursday)

May 11-12, 2011 (Wednesday and Thursday)

September 7-8, 2011 (Wednesday and Thursday)

The expectation is that most meetings in 2010 and 2011 will be a single day: Wednesday. However, the NIDDK asks Council members to hold both days to ensure flexibility should a situation arise where a longer meeting is required.

V. ANNOUNCEMENTS

Dr. Stanfield

Confidentiality

Council members were reminded that material furnished for review purposes and discussion during the closed portion of the meeting is considered confidential. The content of discussions taking place during the closed session may be disclosed only by the staff and only under appropriate circumstances. Any communication from investigators to Council members regarding actions on an application must be referred to the Institute. Any attempts by Council members to handle questions from applicants could create difficult or embarrassing situations for the members, the Institute, and/or the investigators.

Conflict of Interest

Dr. Stanfield emphasized that advisors and consultants serving as members of public advisory committees, such as the NIDDK Advisory Council, may not participate in situations in which any violation of conflict of interest laws and regulations may occur. Responsible NIDDK staff shall assist each Council member to help ensure that he or she does not participate in, and is not present during review of applications or projects

in which, to the member's knowledge, any of the following has a financial interest: the member, or his or her spouse, minor child, partner (including close professional associates), or an organization with which the member is connected.
To ensure that a member does not participate in the discussion of, nor vote on, an application in which he/she is in conflict, a written certification is required. A statement is provided for the signature of the member, and this statement becomes a part of the meeting file. Dr. Stanfield drew the Council's attention to a statement within each member's folder regarding conflict of interest issues in review of applications. Each Council member was asked to read it carefully, and to sign and return it to NIDDK before departing the meeting.
At Council meetings when applications are reviewed in groups without discussion, that is, "en bloc" action, all Council members may be present and may participate. The vote of an individual member in such instances does not apply to applications for which the member might be in conflict.

Dr. Stanfield addressed multi-campus institutions of higher education as follows: An employee may participate in any particular matter affecting one campus of a multi-campus institution of higher education, if the employee's financial interest is solely employment in a position at a separate campus of the same multi-campus institution, and the employee has no multi-campus responsibilities.

VI. ANNUAL APPROVAL OF THE COUNCIL OPERATING PROCEDURES

Dr. Stanfield

Following a motion, the Council approved the Council Operating Procedures and En Bloc Early Concurrence Procedures, which were consolidated into one document.

Due to the recent enactment of the American Recovery and Reinvestment Act NIDDK may soon need to move forward on some spending initiatives. A motion was made and passed by voice vote to enable NIDDK, between now and the next meeting of Council, to utilize the en bloc early concurrence procedures and subcommittee for any needed Council clearance of such initiatives.

VII. NIH PEER REVIEW UPDATE

Dr. Alan Willard
Chief, Scientific Review Branch
National Institute of Neurological Disorders and Stroke

Dr. Rodgers introduced Dr. Alan Willard, who, in addition to his regular duties, is serving nearly full-time as an integrator and program manager for several teams responsible for finalizing the development and implementation of concepts for changes in the NIH peer review system. Dr. Rodgers noted that the NIH has been involved in this dynamic process for two years, and that the Council has received periodic updates. The process has involved diagnosis of some of the specific challenges associated with the

peer review system, and enhancements to help overcome them. It has been a deliberative and collaborative approach, which engaged both NIH staff and many members of the extramural research community to help ensure that a range of perspectives was considered. Dr. Rodgers thanked Dr. Willard for his contributions to shepherding these efforts.

Dr. Willard began with a brief overview of the NIH Peer Review Enhancement process, which was begun by former NIH Director, Elias Zerhouni. NIH recognized that the peer review system had been in place for over 50 years, had served the community well, and had received wide respect and emulation around the world. Nevertheless, there was also recognition that the system had been developed at a time when the NIH scientific enterprise was far less complex than it is today. The process was put in place before the burgeoning of the investigative community, the advent of sophisticated new technologies, and the trend toward more team science--with an emphasis on multidisciplinary and collaborative research. The question therefore arose as to whether the NIH peer review system was optimal for fueling today's scientific enterprise or whether it should or could be enhanced. Among the issues that needed to be addressed were ways to identify and encourage new and early-stage investigators; to ease the peer review burden on the research enterprise; and to streamline the time from research application to award, which could take anywhere from nine months to a year and a half. The overriding goal established by Dr. Zerhouni was to fund the best science, by the best scientists, with the least amount of administrative burden.

An initial diagnostic phase was led by Dr. Jeremy Berg, Director, National Institute of General Medical Sciences, and Dr. Larry Tabak, Director, National Institute of Dental and Craniofacial Research. Input and suggestions were gathered in a number of ways, including through a Request for Information, several surveys, and townhall-style meetings both at NIH and around the country. Analyses were also conducted of existing long-term data. As a result, over 5,000 comments were gathered and analyzed as the basis for recommendations made to the NIH Director in February 2008. The second phase focused on design of an implementation plan, which was presented to Dr. Zerhouni in the summer of 2008, including key recommended actions. By September 2008, the third phase was launched to implement a subset of selected recommendations through the activities of four working groups. Dr. Willard noted that his role was to help coordinate the efforts of these four groups, whose goals were to: (1) engage the best reviewers; (2) improve the quality and transparency of review; (3) ensure balanced and fair review across scientific fields and career states; and (4) provide for continuous review of peer review. An NIH web site provides up-to-date information regarding the current status of these efforts and their timelines, as well as providing frequently asked questions, communications resources, and an email pop-up box for individuals to submit questions. The URL for accessing this site is:
http://enhancing-peer-review.nih.gov/index.html
A link to this site can also be found on the main NIH web site: www.NIH.gov

Dr. Willard described several changes in the peer review system--some already in place and others yet to be implemented. One procedural goal is to implement major changes at

the start of the fiscal year on October 1--when most Institutes and Centers set their paylines for the new fiscal year. Ideally, all applications in a given fiscal year should be subject to the same general funding parameters and review procedures. With respect to FY 2010 funding, R01 applications were received in February 2009; will be reviewed by study sections in the spring; and will be considered at the fall Council meetings. Two policy changes already in place will affect these applications. The first is a new policy regarding resubmissions and the second change relates to the NIH goal to improve support for early-stage investigators.

Under the first policy change, grant applications can be revised and resubmitted only once, rather than twice. This change is consistent with the goal of funding meritorious projects as early as possible so that investigators can begin to move their research ideas forward rapidly. The initial application, first revision, and second revision have been designated A-0, A-1, and A-2 applications, respectively. The new policy eliminates the possibility of A-2 revisions. From the Peer Review Enhancement process, it became clear that a large number of meritorious applications from excellent scientific teams were being revised and resubmitted to address very minor considerations. Moreover, the initial peer review scores of these applications were sufficiently meritorious that they would have been funded in previous years without the need for revision. Hence, a great deal of time and effort was being expended on a protracted review process that did not materially improve the scientific work eventually funded, but that significantly delayed its funding. The new policy that permits only one amendment per application became effective January 25, 2009--the first receipt date for FY 2010. In addition to R01 grant applications, the policy will affect some of the large, complex applications for program project grants and center grants that were submitted at that time. It will also apply to competing renewal applications due in March 2009.

Under the second new policy in place, the NIH is encouraging new investigators--including early-stage investigators who are starting their independent careers--to apply for R01 grants as opposed to other grant mechanisms. The NIH definition of "new investigator" is someone who has never competed for major, independent research support, such as an R01 grant. The definition of "early-stage investigator" refers to the subset of new investigators who received their terminal research degree or completed their clinical research training less than 10 years prior to their grant application. A widely held view in the research community is that many investigators have their best and most creative ideas early in their careers. Yet, analyses performed during the Peer Review Enhancement process showed that too many new investigators and early-stage investigators seem to be applying for small, short grants, such as R03s and R21s, instead of applying for R01 grants, which provide the duration and level of support needed to launch an independent career. The new policy, published in the fall of 2008, states that the NIH will support R01 applications from new investigators at success rates comparable to those of new applications from established investigators. It is hoped that early-stage investigators will constitute a majority of those new-investigator applicants. To enable NIH to identify early-stage investigators, individuals will need to access their NIH Commons Account and input data concerning when they received their degrees or completed their clinical residencies. It will be possible to use the NIH Commons

Account to apply for an exception to the ten-year rule for reasons such as medical issues or military service. Based on the information provided, the NIH will determine whether or not investigators are eligible for the designation of "early-stage investigator." In addition, when logically feasible, study sections will try to cluster R01 applications from new and early-stage investigators so that they can be reviewed as a group.

Dr. Willard next described changes whose implementation will occur shortly for applications submitted in or after February 2009—whether new applications or competing renewals. The first impending change is the use of a new peer review scoring system. Previous studies of the NIH peer review system have noted that the current scoring system is not compatible with the scope of human abilities to categorize items into groups and to clearly differentiate among them. The NIH is therefore introducing a new two-digit, integer-based scoring system of 10-90 to replace the current scale that goes from 100 to 500 in tenths of a point. (A subsequent Notice in the *NIH Guide* described the core criteria: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-025.html)

The new scoring system will likely result in more applications receiving similar scores, but that will appropriately reflect the real-world, in which there are relatively modest differences among applications of similar scientific merit. Another scoring change will involve core criteria that apply to all applications of a certain type. For example, for R01 grants, the five core criteria are significance, investigator, innovation, approach, and environment. For other categories of applications, such as Small Business Innovation Research grants and Career Development Awards, there are different core criteria. Templates will require reviewers to give more structured critiques. For each core criterion, reviewers will be asked provide bullets regarding an application's strengths and weaknesses. General comments or advice unrelated to the scoring of an application can also be provided, but in a separate box. The goals of the scoring changes are to improve the quality of the information that both applicants and NIH staff receive about applications and to help them understand more fully the reasons underlying the assigned impact/priority scores. These changes will respond to applicants' concerns that past critiques have not helped them fully understand the reviewers' assessment of their proposed research. Greater transparency and clarity will help to convey the essential reasons for the ratings given.

In March 2009, baseline surveys will be sent to applicants, reviewers, NIH staff, and institutional officials. A series of questions will be posed about the level of understanding and satisfaction with the system. The information gained will be used as a basis for comparison for studies that will be performed after a series of peer review changes have been implemented. This process is one of the ways that NIH will meet its goal of having continuous review of peer review. The goal is not only to do no harm, but also to enhance the system.

There are several other peer review changes that will be undertaken at a later point. For example, applications will be restructured to shorten the "Research Plans" section. NIH expects to reduce the length of R01 applications by half—from 25 pages to 12 pages—

and to align them with the new core criteria. Investigators will be expected to address the criteria very specifically in their applications. One of the most important considerations for determining the overall score is the "impact" of the proposed research. Impact includes the significance of the research question being addressed and the scope of the scientific discipline and/or diseases that will be positively affected by the research, if it is successful. Another consideration regarding impact is an assessment of the likelihood of success, given the proposed technical approach, the team of investigators, and the research environment in which the research will be conducted. Investigators will therefore need to include this type of information in their applications.

Council Questions and Discussion

Is the overall score the arithmetic mean of the individual scores on the core criteria? Dr. Willard stressed that no arithmetic formula will be applied. Applications may be rated well or poorly on individual core criteria. However, the overall impact/priority score will reflect the judgment of the reviewers in terms of the mix of importance of the research proposal and the likelihood of its success.

Will the scores on the individual core criteria be available to investigators whose applications are scored by not discussed by the study section? Dr. Willard replied in the affirmative. It has frustrated investigators that, in the past, only about half of the applications have been discussed by study sections. Moreover, the researchers with undiscussed applications have felt that they have not received appropriate feedback. With the scoring changes, investigators whose applications are not discussed will definitely receive their scores on the core criteria. Thus, they should be better informed about whether they should invest their time in revising and resubmitting their applications.

Would scores change as a result of any discussions by the study sections? No. Dr. Willard said that study section discussions will not alter the criteria scores that have been given.

Elimination of the A-2 revision and resubmission process will not eliminate a funding queue (or backup) unless funding is increased or the number of investigators is limited or declines. Dr. Willard noted that there will be a "wash-out" period for the A-2s. Those investigators who are still eligible for the A-2 process will have until January 2011 to submit their second revisions for potential funding in Fiscal Year 2012. It is correct that, if the amount of available funds remains level and the number of number of applications remains constant or increases, then a funding queue will occur. However, the process for handling the applications will have been improved.

Have the changes been pilot tested with study section members and, if so, have they been receptive? Dr. Willard noted that, as with all groups, there are differences among study section members in their responses to the changes being made. The NIH recognizes that implementing the changes will be challenging, and staff members have been working diligently to have as smooth a transition as possible. The Scientific Review Officers have

been alerting standing study section members of the changes at their regular meetings. A variety of educational materials, both handouts and brief videos, has been developed to explain the new system and its goals. The NIH has also had meetings with a number of study sections to test and refine the instructions for using the new scoring system. Some study section members who have just completed reviews using the old scoring system have been asked to think about how they would have applied the new system to the same grants. One very important aspect of the new system is that it resets the percentile basis. Over the years, NIH has received increasing numbers of excellent applications that could not be funded at the point of initial submission due largely to existing payline cutoffs. As a result, the number of resubmissions increased, which tended to move scores and percentiles upward. Not long ago, a priority score of 150 might have placed an application in the 4th or 5th percentile. Recently, such a score might equate with the 15th or 20th percentile in many study sections. Under the new system, only ten percent of the applications will be in the top 10th percentile—starting in May 2009. This change provides an opportunity to recalibrate.

What is being done about recruiting and retaining reviewers? Dr. Willard commented on several approaches being taken, such as providing greater flexibility in tours of duty. Instead of serving three times a year for four years, study section members will have the opportunity to serve twice a year for six years. Another benefit offered to study section members is flexibility regarding when they can submit their own grant applications. Alternatives to face-to-face meetings are also being explored so that study section members can avoid travel issues. Development of high-quality video conference centers would be a great aid, but the technology is still evolving. Other upgrades of information technology are under discussion. The shortening of the grant application should also reduce the burden on reviewers. During the time that NIH is working to streamline the process, it will still need reviewers who are willing to share their good judgment and breadth of vision, and to provide their best advice about the overall quality of applications.

VIII. DIRECTOR'S REPORT
Dr. Griffin P. Rodgers

American Recovery and Reinvestment Act

On February 17, 2009, the President signed into law the American Recovery and Reinvestment Act (ARRA)—commonly called the economic stimulus package. The law provides the NIH with a total of $10.4 billion over two years to help stimulate the U.S. economy through the support and advancement of scientific research. The Recovery Act provides one-time-only additional funding spread over the two-year period ending in September 2010. The funds are to be administered through a special account in order to monitor the speed of their award and their effects on the U.S. economy. There are no current expectations that funds provided to NIH under the Recovery Act will be added to the base of the NIH budget.

The importance of NIH as an engine of economic stimulus was described by the Acting NIH Director, Dr. Raynard Kington, in his November 2008 testimony before the House Subcommittee on Energy and Commerce. Dr. Kington did not request additional funding for the NIH, but gave the Committee members important information about the broad reach of biomedical funding throughout the nation. For example, NIH grants support an estimated 300,000 jobs in the U.S. It is estimated that every $250,000 NIH grant supports seven jobs. Moreover, NIH funding drives thousands of inventions, patent applications, and awarded patents. NIH-funded research has contributed to one in every six new drugs approved by the FDA in the last 25 years. Dr. Kington also highlighted the NIH role in emerging technologies and fields, such as genomics, proteomics, nanotechnology, and systems biology. The funds provided to NIH under the Recovery Act are being used in several ways.

An estimated $8.2 billion will be used to support scientific research priorities.

- The Office of the NIH Director will use about $800 million of this amount to address a range of "Challenge Areas" that focus on specific knowledge gaps, scientific opportunities, new technologies, data generation, or research methods. It has been determined that these areas would benefit from an infusion of funds to rapidly advance the science in significant ways. Within each broad Challenge Area, the NIH Institutes, Centers, and Offices have specified particular Challenge topics that are important to their respective missions. The Office of the NIH Director will issue a funding announcement with an April receipt date for Challenge Grant applications. Each applicant can request up to $500,000 in total costs per year, for a maximum of two years.
- The Institutes and Centers and the NIH Common Fund will use a total of about $7.4 billion to support additional research across the NIH mission. While the guidelines for using these funds are under development, it is likely that the funds may be used to support research concepts in grants that have already been peer-reviewed, short-term bridge awards through the R56 mechanism, and the augmentation of research centers, ongoing clinical studies, and consortia. Again, awards are for a maximum two-year duration, so some restructuring of project scope may be necessary. The requirement for rapid initiation of Recovery Act projects will make it difficult to match a new proposal currently under development with the Act's timeframe. NIDDK research funds provided by the Recovery Act will be approximately $230 million per year for two years--for a total of about $460 million. Unlike regularly appropriated funds, the Recovery Act funds do not carry specific requirements for supporting AIDs research or for awards through the Small Business Innovation Research Program or the Small Business Technology Transfer Program. However, no grant mechanisms are excluded from use of these funds, and research and development contracts are also eligible. No awards can be made to foreign research institutions. Council members were asked to consider various approaches for Recovery Act investments and provide their advice to NIDDK during Subcouncil meetings.

The NIH will expend approximately $400 million of Recovery Act funds over a two-year period for comparative effectiveness research. The NIDDK estimates that its share of

these funds would be approximately $12.5 million in each of those years. The Congressional Budget Office defines comparative effectiveness research as rigorous evaluation of the impact of different options that are available for treating a given condition for a particular set of patients. Such studies may compare similar treatments, such as different drug regimens, or may assess very different approaches such as surgery and drug therapy. The analysis may focus only on the relative medical benefit and risk of each option, or it may also weigh both the costs and benefits of these options. The Recovery Act also provides funding for comparative effectiveness research to the Agency for Healthcare Research and Quality, and it is possible that the NIH will be invited to collaborate in the use of those funds.

With regard to infrastructure support, the Recovery Act provides $1 billion to the National Center for Research Resources (NCRR) to support extramural construction, repairs, and alterations in support of all NIH funded research institutions, and another $300 million for shared instrumentation and other capital equipment to support all NIH activities. This latter effort will not conflict with NIDDK's intention to use its regularly appropriated funds to help replace equipment at its research centers. The NIDDK will move forward with consideration of requests for the purchase of pieces of equipment costing under $100,000 at these centers, and funds awarded will not be counted against the funds the NCRR will administer for infrastructural programs under the Recovery Act. The NIH will also use approximately $500 million in Recovery Act funds for high-priority repair, construction and improvement projects within the NIH intramural program.

Many of the operational details of NIH funding under Recovery Act will be forthcoming. The NIDDK will keep the Council informed of developments.

2009 Appropriation

Dr. Rodgers reported that final action was still pending on the regular FY 2009 appropriations bill for the Department of Health and Human Services. Therefore, since the start of FY 2009 on October 1, 2008, the NIH has operated on a Continuing Resolution. The funding level of the Continuing Resolution was set below the President's proposed budget. If a final budget accord is reached, it is possible, but not certain, that the FY 2009 budget for the NIH may provide some increment over the FY 2008 operating level.

At the same time that the NIH is managing its FY 2009 resources and its role in the Recovery Act, preparations are under way for the FY 2010 appropriations process. Due to national economic issues, the transition to a new Administration, and other factors, the FY 2010 budget proposal is still under development. The NIDDK will continue to share budget information with the Council as soon as it is available.

Council Questions and Discussion

Will any consideration be given to extending the grants of current study section members in light of the changes in the peer review process coupled with the new research activity to be funded under the Recovery Act? Dr. Rodgers replied that NIDDK does not yet have those types of details, but will look into the issue and inform the Council.

Given the large influx in Recovery Act funds that must be spent over two years, are there any administrative mechanisms by which the NIDDK could defer the expenditure of some of its regularly appropriated funds to later years? Dr. Rodgers replied that the issue had been discussed with members of the Department and the Congress, and that no deferral of expenditures to later years will be possible.

How will peer review be handled for projects funded under the Recovery Act? Dr. Stanfield commented that Challenge Grants will definitely be reviewed by the NIH Center for Scientific Review. If NIDDK issues its own RFAs, then responsive proposals would most likely be reviewed by NIDDK-convened review panels. Competitive supplements will be reviewed in the same venue of the parent application. Administrative supplements could be reviewed by NIDDK staff. Because of the two-year time frame for expending the Recovery Act funds, it will be important to look at all review options and have as much flexibility as possible in making timely awards. Dr. Rodgers noted that the guidance will be forthcoming on many of these details. The NIH leadership has already held a series of meetings with Institute and Center Directors regarding how best to optimize the use of these funds, and discussions are continuing. A very capable team of NIH staff members is moving forward to resolve implementation issues.

Is it possible that Recovery Act funds for supporting instrumentation and technology could be used to support staff and service contracts in addition to necessary renovations? Dr. Stanfield replied that the use of funds for any project must be within the initial scope of the application that was peer reviewed. There may be some possibility of using Recovery Act funds to quicken the pace of a project if so doing is within the peer-reviewed scope. However, if there is another component of the study that goes beyond the peer-reviewed scope of the original project, that component would need to be peer-reviewed in order to be eligible for Recovery Act funds.

How will the use of Recovery Act funds be made transparent as possible? Dr. Rodgers commented that a government-wide website will provide a precise delineation of the number of jobs created or retained as a result of the stimulus package. The numbers of individuals who are hired to support shared instrumentation and other NIH efforts under the Recovery Act would be specifically listed. The NIH is determining how best to capture and input this information to that website.
http://www.recovery.gov/

Is it possible to use Recovery Act funds to support recent applications for research projects and research centers that were peer reviewed well, but were just beyond the NIDDK payline? Such scientifically meritorious projects would be "shovel-ready," but probably were not proposed for a maximum of two-year funding. Dr. Stanfield replied

that all Recovery Act funds must be expended by the NIH by September 30, 2010. Dr. Rodgers noted that NIH would like to explore possibilities with investigators whose previously unfunded applications for research projects were highly meritorious and very close to the payline, and who could benefit from bridge funding through the R56 mechanism. To date, there has not been a discussion about using Recovery Act funds for new awards for research centers or related mechanisms. However, it is possible that Recovery Act funds may be available for equipment and potential supplements for existing research centers. Guidance will be forthcoming.

Does the two-year time frame for expending the Recovery Act funds change the factors that are taken into consideration for making awards? Will the time constraint change priority-setting and lead to reordering of the payline? Dr. Rodgers replied that the NIDDK makes its paylines widely known once it has a budget, and that the Institute follows its paylines closely. However, funding of applications beyond the payline can arise from determinations made by the Divisions with the concurrence of the Council. The NIH can only use Recovery Act funds for scientifically meritorious activities that can reasonably be accomplished with the specified two-year period. Therefore, the two-year requirement will probably have to be factored into NIDDK's priority setting process. Research efforts that might be rapidly accomplished include those that are technology-oriented. On the other hand, funding a clinical trial may be difficult with Recovery Act funds due to the long-term nature of clinical trials relative to the short time line imposed on expenditure of Recovery Act funds. Therefore, a previously peer-reviewed R01 grant application for a clinical trial that was just beyond the NIDDK payline may not fare as well with respect to consideration for the special Recovery Act funds *versus* a project to develop a new animal model of disease or similar research objective that presumably could be reasonably accomplished within the time constraints of the Act.

While the infusion of Recovery Act funds is greatly welcomed by the NIH research community, are there "lessons learned" about the unintended consequences of the 5-year doubling of the NIH budget that should be considered when using these new Recovery Act funds? Could the NIDDK staff summarize for discussion with the Council some of the previous "lessons learned"? Dr. Rodgers agreed that the NIH budget doubling demonstrated the difficulties in responding "real-time" to large infusions of funds. For example, the demand placed on the budget by increasing numbers applications following the announcement of the NIH budget doubling continued well beyond the time during which the additional funds were available. The result was a sort of reverse supply-and-demand situation--with success rates dropping with the end of the budget-doubling period. Even with the two-year timeframe of the Recovery Act, the NIH can probably expect that increased demand on the system will continue beyond September 2010, as it did following the budget doubling. When Recovery Act funds terminate, the NIH might face the same challenge of falling success rates and other budget-system issues in 2011 and 2012, unless the budgetary base were to increase substantially.

What, if anything, can be done to mitigate the likely competitive advantage that Recovery Act recipients will have for funding in 2012? Will they have an edge over other researchers whose scientifically meritorious work could not be accomplished within the

time constraints of the Recovery Act? Dr. Rodgers expressed his hope that NIDDK Recovery Act funds would be used to pursue scientific opportunities that will expand and move forward scientific fields of importance to the entire Institute and its many grantees. Some projects funded under the Recovery Act will undoubtedly lead to subsequent grant applications, some of which may be accommodated by future changes in the NIDDK budgetary base. The NIDDK will look to guidance from the Council in making these sorts of calculations and developing models that will aid decision-making. Although the NIDDK budget has remained relatively stable since 2003, the NIDDK—with the Council's assistance—has been able to increase its paylines over the last three years.

How will the Challenge Grants be administered and will the NIDDK have input into that process? Dr. Rodgers replied that the Challenge Grants will be under the direction of the Office of the NIH Director. As noted, the Institutes and Centers have had major input to development of this program by identifying topics for the funding announcement to the investigative community. If there are NIDDK-relevant applications for Challenge Grants that cannot be accommodated within the funds targeted at the NIH level, then the NIDDK would have the opportunity to step in and fund those projects.

Is there any way that research institutions could mitigate or offset the fact that the Recovery Act will only provide funds for job creation or retention for a maximum of only two years? Institutions would be much more likely to hire research staff if there were a way to retain them for longer than a year or two. Dr. Rodgers replied that there will be reporting requirements that research institutions will need to meet regarding how Recovery Act funds are being used. Consistent with the law, and within the scope of those reporting requirements, investigators will likely use every option available to them to maximize the research enterprise.

Can Recovery Act funds be used to address hiring freezes that some research institutions have placed on searches for junior faculty? Is there any possibility of establishing a special grant mechanism to help those individuals either stay in their current positions or be supported in some kind of transition state so they don't become lost to the research enterprise? Dr. Rodgers encouraged the Council members to discuss this and other ideas in their Subcouncil meetings. If the NIDDK cannot act on such ideas directly, it will convey them to the Office of the Director, NIH.

Are any of the NIH Recovery Act funds specifically available for research training programs? Dr. Rodgers noted that he does not believe that NIH funds under the Recovery Act would be specifically focused on research training. However, there are opportunities for administrative supplements that might conceivably be used to target some aspects of research training or research career development.

Reporting requirements of the Recovery Act could be a means by which advocacy groups can reinforce the economic benefits of NIH-funded research. Dr. Rodgers agreed with the comment and thanked the many scientific societies and patient advocacy groups that help explain NIH research efforts to the public and to policy makers.

IX. ADVISORY COUNCIL FORUM: CATALYZING TEAM SCIENCE
Dr. Ron Margolis, Senior Advisor in Molecular Biology and Associate Director for Grants Administration within the Division of Diabetes, Endocrinology and Metabolic Diseases, NIDDK

Dr. Rodgers introduced Dr. Margolis, whose presentation focused on ways the NIDDK might encourage and support large-scale, highly innovative research in the scientific areas related to the Institute's mission.

Dr. Margolis pointed out the trend toward the development of large, collaborative science projects—highlighted by the Human Genome project and all of the "omics" projects that followed it. In many cases, these projects have involved high-throughput technologies, the rapid accrual of enormous amounts of data, and the subsequent application of informatics approaches to analyze the data as a basis for generating and testing new hypotheses. The trend toward large, team science projects was recognized in 2003-2004 by two Institute of Medicine reports and an NIH symposium. These events made clear that some scientific questions require extensive input from individuals, many of whom are drawn from multiple, different disciplines. These types of collaborative approaches complement rather than supplant investigator-initiated research. Within this context, a group of staff members from across the NIDDK Divisions examined the ways that the Institute supports collaborative research with a view toward preparing a report to the Council and seeking its advice. Participants in this analysis included Drs. Jill Carrington, Carol Haft, Deborah Hoshizaki, Bob Karp, Karl Malik, and Rebekah Rasooly.

Research Grant Mechanisms Used To Support Collaborative Research

The NIDDK seeks to encourage the best ideas relevant to its mission by supporting the formation of collaborative, multidisciplinary teams to exploit the strength of the team-based approach in order to produce paradigm-shiftng advances in knowledge. The NIDDK supports such team science through three major approaches:

1. Investigator-Initiated Research Project Grants with More Than One Principal Investigator (PI) or Project Director (PD): Regular research project grants known as R01 grants have historically had a single Principal Investigator (PI) who led the work of his or her group. Recently, however, the NIH established a new model in which the leadership for an investigator-initiated R01grant can be shared among Principal Investigators (PIs) or Project Directors (PDs). These so-called multi-PI or multi-PD R01 grants involve a collaborative effort by two or more individual investigators with joint responsibility and credit for the research.

When a multi-PI or multi-PD R01 application has a budget that approaches or exceeds $500,000 in direct costs for any year, it requires pre-approval by NIDDK prior to acceptance. These grants fall within the research project grant (RPG) component of the NIDDK budget, which accounts for 60 percent of the Institute's grant funding. Because the multi-PI or multi-PD R01 grant is a new approach, limited data are available about its use.

2. Investigator-Initiated Program Project Grants (P01 Grants): The long-standing mechanism for NIDDK support of collaborative research is the program project grant or P01 grant. This mechanism is used to encourage broad-based, multidisciplinary or multifaceted research programs developed around a major objective or central theme. Applications must be structured to include at least three R01-like projects, as well as one or more cores integrated with the projects. Importantly, there must be a central theme that draws the projects together. P01 grants typically involve investigators from the same institution, and often, from the same department. Synergies are expected to arise from interactions between and among researchers and the cores. Through these P01s, opportunities often arise for research training and for the career development of young investigators, as well as R01 spinoffs. The maximum dollar request for new NIDDK program project applications remains subject to a limit of $5 million in direct costs over 5 years.The absolute budget cap on direct costs for competing continuation applications remains $6.25 million.

There is no limit on the life cycle of P01 grants, which can recompete indefinitely; yet, many seem to come to a natural end. There were 49 P01 grants across the three NIDDK extramural Divisions at the end of FY 2008, and nearly two-thirds of those that received funds in that fiscal year were in their first or second period of award. This observation suggests recognition on the part of both investigators and peer-reviewers that the peer review process may not be receptive to P01s because they are large-budget grants that involve risk-taking. The NIDDK investment in P01s has been relatively modest and stable. From 2003-2007, P01s accounted for less than 6 percent of the NIDDK's research project grant (RPG) budget. This proportional investment was relatively modest compared to many other NIH components. In Fiscal Year 2008, P01s accounted for 6.6 percent of NIDDK's total grant funding.

3. Research Resource Grants (R24 Grants): The R24 grant is a new mechanism that is being pilot tested by the NIDDK Division of Diabetes, Endocrinology and Metabolic Diseases. The Division's Subcouncil approved the first Program Announcement for this award in Fiscal Year 2007. The Division recognized that, while other mechanisms (such as multi-PI R01s, P01s, and research centers) can foster certain kinds of collaborations, their structures cannot always readily accommodate interdisciplinary team science that synergizes around a single set of unified aims and goals. To provide a flexible mechanism to achieve this objective, the Division launched the Collaborative Interdisciplinary Research Program, which focuses on single, large, and scientifically complex problems relevant to its mission. For example, the goal of one project was to develop chemical modifiers of insulin signaling, particularly with regard to inflammation, and to determine how they affect the development of type 2 diabetes. Team members brought expertise from the fields of molecular, chemical and computational biology.

Through the R24 mechanism, collaborative interdisciplinary or trans-disciplinary teams may pursue basic, or integrated basic and clinical studies that have a potential to move forward the NIH agenda on translation. The research must be conducted by

interdisciplinary teams, and multiple PIs or PDs are possible. Unlike the P01 grants, there is no specific structure imposed on R24 grants as to numbers of projects or the presence of cores; instead, the applicants can define their needs for resource development and use. The NIDDK encourages diverse expertise so that the investigators will pursue scientific risk-taking and will synergistically apply their many different perspectives and cutting-edge resources. Each applicant is asked to describe how the proposed project's goals are relevant to the Division's mission; the complex central problem being addressed; the roles that will be played by each collaborator in tacking that problem; and how project outcomes are expected to have a major impact on the field. Applications may request budgets equal to or greater than $500,000 in direct costs per year for up to 5 years, but require pre-approval by NIDDK staff before submission. These projects compete directly with P01 applications for funds available in the Division's budget for investigator-initiated collaborative science.

Evaluating the Impact of Collaborative Research

The NIDDK is very interested in ways to assess the impact of collaborative research. Because the P01 is the long-standing mechanism for this type of research, its analysis provides some insights. The NIDDK has noted that the peer review process for its portfolio of P01s has given the best marks to those applications that offer a very tight integration of the component projects--with a very clear use of cores to benefit the projects--but with a scope that is relatively conservative and R01-like. Peer review also favors P01s that conform well to the guidelines with respect to the structure of the projects and cores. The NIDDK staff has observed that, although risk-taking is encouraged by the P01 mechanism, it seems to be discouraged by the peer review process. It may be possible that P01 investigators themselves are more conservative in the applications they submit because they realize that risk-taking will engender more peer-review scrutiny and criticism. The peer review system seems to impose turn-over in P01 grants. In addition, teams evolve over time—with changes in interests, emphases, and technologies. In some cases, the team members themselves put their P01 grants to rest to go their separate ways. However, some P01 grants seem to reinvent themselves with new members and ideas that enable them to continue to survive many cycles of peer review.

In peer review, productivity is usually assessed in terms of numbers of publications generated by a grant. There is sometimes a view that publications should be in "high impact" journals, but a particular field may require publications in journals relevant to the field, as opposed to broader-based journals. Quality is difficult to gauge, but across the NIDDK portfolio of P01 grants, it appears generally high.

Seeking Council Advice

The NIDDK believe that team science can address significant research challenges, but that outreach efforts by program staff are important to help identify scientific opportunities and even potential teams. It will be essential for NIDDK to monitor the outcomes of team science in order to validate the concept. The NIDDK would also like to work on peer-review related roadblocks to risk-taking. To this end, the NIDDK has formulated four questions for Council discussion and advice.

- *What emerging scientific questions might require a team approach?* What disciplines and approaches should be targeted? How can program staff proactively identify ideas and teams?
- *How can real or perceived roadblocks be overcome?* These may include unfamiliarity with the collaborative research mechanisms, resistance to risk-taking imposed at peer review; the exploratory nature of some studies; and the high level of energy needed to form and activate a diverse team.
- *What should the interdisciplinary team of the future look like?* What is the experience of Council members in assembling a team? What are the incentives/disincentives to team participation?
- *What metrics should be applied for evaluation?*

Council Questions and Discussion

The Council members offered generally positive comments on interdisciplinary research efforts. Several members have been PIs on P01 grants, with first-hand experience with the challenges of constructing teams, integrating research concepts, and securing funding for collaborative research endeavors.

Why is it that the RFA for the pilot study of the R24 mechanism solicited research projects with strong preliminary data, with criteria that were more selective than for an R01 project? Isn't a goal of the R24 to propel less-developed areas of investigation? Dr. Margolis replied that the R24 program has two tracks—one for a fully formed team with strong preliminary data and a second for a start-up team that needs to be seeded to develop data. The program provides a four or five year award to fully formed teams *versus* a smaller sized, one-year award for start-up teams.

Will investigators invest the enormous amount of time and energy needed to put together a team for an R24 grant application that is resource-driven (e.g., development of new chemicals), rather than hypothesis-driven, and that can only run for five years or possibly be renewed once? Dr. Margolis responded that the NIDDK expects the investigative team to apply their various viewpoints, gained from different disciplines, to formulate and test hypotheses that can be moved forward. Part of the research can be discovery-based, but it can also be hypothesis-testing. The NIDDK is mainly looking for the development of a good idea.

The greater flexibility provided by the R24 over the P01 will potentially attract more investigators to collaborative research; however, the question that they will be asking is: What will be the success rates for the R24 applications? Dr. Margolis noted that the

NIDDK does not want to supplant the P01 grant, which it considers valuable. However, there may be additional, more flexible ways that can also support team science. In the two years since the R24 announcement was issued, the NIDDK received 10 R24 applications and funded five of them to varying degrees. The success rate for P01s is also high. However, both types of applications benefit from extensive pre-screening by NIDDK staff for relevance to the NIDDK mission and the suitability of the proposed research mechanism to the scientific concept being proposed.

How will the changes in the NIH peer review system apply to P01 and R24 applications? Dr. Stanfield replied that the implementation teams for the NIH Peer Review Enhancement process have been largely focused on the R01 grant. Details have not yet been forthcoming as to the way that some changes--such as the shortening of the grant application--will affect other, more complex, mechanisms. Presumably, the core review criteria for other mechanisms will be similar to those used for R01 grants, but the Institutes and Centers may have some opportunity for fine-tuning.

How will NIH address the inherently difficult review problems posed by applications involving interdisciplinary teams? Will there be sufficiently broad expertise on review panels who will appreciate the value of team science? Will there be recognition in the review process that the shape of the interdisciplinary teams of the future will depend on the scientific problem being addressed—that each different problem will need a differently configured interdisciplinary team? Dr. Margolis noted that the NIDDK staff members are eager to work with the NIDDK Review Branch to address those questions.

What can be done to emphasize the important contributions of team members on collaborative grants for purposes of career advancement within academic research institutions? A Council member noted that co-authorship of papers by two or more of members of a research team are given considerable positive weight in the peer review process, but the same co-authorship can cause junior investigators to lose credit toward promotion within academic research institutions. Essentially, co-authorship is a plus for grantsmanship, but a negative for promotion. It was suggested that the peer review process might include, as part of its metrics, good evidence that a paper indeed benefited from synergistic interactions, even if only one member of the team is an author. Dr. Margolis noted that this issue had been addressed at an NIH symposium on catalyzing team science. The participating deans and university presidents agreed that team science is valuable, but that it would not affect the policies governing appointments, promotion, and tenure at their institutions. Therefore, a cultural change is needed within these institutions to deal with team science based on the recognition that a contributor to a research team is a contributor to the institution. Another Council member offered her view that a slow evolution toward cultural change is occurring in some institutions. At her institution, an effort is made to ask about and assess the specific contributions each team member has made to a paper, and particularly, the contributions of the individual under consideration for promotion. Dr. Margolis commented that some journals are doing essentially the same thing by listing at the end of published articles the roles of each member of the research team.

How can bioinformatics be more fully integrated into team science so that it is recognized by research institutions as a vital component of innovations and breakthroughs? Universities and medical schools have difficulty deciding whether bioinformatists are members of cores, faculty, or independent researchers. Would it be possible to have a "bioinformatics component" of team science that would be considered a separate project--both to recognize its importance in the post-Genome era and to address promotion issues for team scientists who are bioinformatists? Dr. Margolis agreed that bioinformatics, as a relatively new field, has yet to receive the recognition it deserves. By drawing individuals from different disciplines together, interdisciplinary teams will help to melt down silos regarding the role of the bioinformatist and will promote interactions between experts in computational biology, chemistry, and other fields.

What can be done to promote the synergistic functionality of teams, as well as diversity of expertise? A Council member noted that the terms "interdisciplinary" and "multidisciplinary" can sometimes work against putting together a high-functioning team. Moreover, investigators who have somewhat diverse interests but who already know each other may be more effective at team science than a multidisciplinary group comprised of totally new people. Pilot funds can play an essential role in assembling robust teams. Such funds can provide the motivation for developing a P01 application that is more than just a cluster of R01-like projects that can be disassembled and resubmitted as R01s if the P01 is not competitive for funding. Team science requires a mindset that will strive to integrate the projects so that they work synergistically. Extraordinary effort is required to weave concepts, projects, and human efforts together. In this regard, the administrative cores of P01s play a huge supportive role, yet these components seem to receive little attention during peer review and are often the targets for budget cuts.

Can interdisciplinary research programs be used to boost the apparent decline of interest in academic and scientific careers? Also, could they be integrated in a meaningful way with training programs and programs for younger investigators so that they could see the excitement generated by team science? Dr. Margolis noted that senior investigators who are developing science teams may want to include individuals who have received NIDDK research training awards (T32s) and career development awards (Ks).

What are the reasons that some Institutes and Centers are increasing the proportion of their budgets directed to P01s while some are decreasing it? Dr. Margolis replied that the reasons for these changes are varied. He is aware that two smaller Institutes made conscious decisions to discontinue use of the P01 mechanism. They concluded that the large amount of funds required for P01s could be used to increase the number of smaller projects that could be supported. The NIDDK has been fortunate to be able to continue to its support for investigator-initiated team science projects as a complement to its other research mechanisms.

Are there any data to support the view that peer review issues are limiting many NIDDK P01s to one or two rounds of competitive funding? Is there a failure of teams to reapply for a third round of funding or is there something wrong with their third-round or

subsequent applications? Dr. Margolis said that the NIDDK staff analysis included a sampling of P01s from each Division. This information led to observations and trend analyses, but not to any type of comprehensive hard data. One observation was that peer review issues were effectively limiting the lifecyles of the P01s. Factors could include the changing boundaries of science, changes in the investigative team, or a loss of momentum due to a drop in productivity or because questions initially driving the research have been solved or become moot. A combination of factors may be at work.

Could the concept of collaborative research be extended to include fields in addition to science —such as law, business, and engineering? It was noted that addressing issues such as the cost of health care and the impact on society may need very far-reaching perspectives.

Regarding evaluation, what has been the impact of discontinuing site visits as part of the review process? Has it made a difference in the way the P01s have been evaluated? The synergy expected of P01s is a characteristic that is perhaps best evaluated through site visits. Also, it is important for the research community to challenge itself to explore different metrics for evaluation. While publications are significant, the translation of research discoveries into clinical benefits that touch patients is a critically important research outcome. Dr. Margolis responded that, in his view, site visits did have an impact on peer review. Now, however, assessments are performed based solely on the paper application. That is one of the reasons that it is important for NIH staff to work with investigators prior to the submission of their applications, so that they can receive the best advice. The NIDDK Review Branch also gives investigators the opportunity to provide a late update to their applications; however, it does not substitute for the face-to-face interactions of a site visit.

With respect to the R24 grant, how can NIDDK staff help investigators form teams from different institutions to explore ideas such as the reversal of diabetes through gastric bypass surgery? Dr. Margolis noted that the R24 announcement contains a link directly to NIDDK's description of programs, with names of contacts. The announcement also encourages potential individiuals to contact NIDDK staff as soon as they have a compelling research idea--before they start developing their applications. The NIDDK staff also discusses approaches with individuals at various scientific meetings. However, the NIDDK recognizes that it is difficult to make multidisciplinary connections across institutional lines.

Should NIH try to overcome the skepticism for risk-taking that is embedded in the peer review process, and if so, how can this be done? Dr. Margolis discussed the separation between program and review functions. At the NIH Center for Scientific Review, that separation is absolute. In NIDDK, the clear separation is maintained, but there are opportunities for information sharing. For example, NIDDK recently had the first review of the R24 seeding applications. The Review Branch arranged for a pre-review conference call between program staff and a number of reviewers to discuss the mechanism and the importance of risk-taking to the goals that NIDDK wants to achieve. Where possible, those sorts of interchanges could be encouraged.

Dr. Rodgers closed the forum by thanking Dr. Margolis, the other NIDDK staff who participated in the analysis, the Council discussants, and the other Council members. He noted the overall positive response of the Council to NIDDK programs that promote interdisciplinary team science. Collaborative and multi-disciplinary team science can often complement research by individual investigators and can make transformative contributions to knowledge of biological systems. The discussion at the Council Forum will assist the NIDDK in further exploring this approach, including issues such as the review process for grants that involve risk-taking and the use of appropriate metrics in evaluating team science.

X. SCIENTIFIC PRESENTATION: Muscle Wasting in Catabolic Diseases

Dr. William Mitch

Dr. Rodgers introduced the presentation by Council member, Dr. William Mitch, the Gordon A. Cain Professor of Medicine and Chief of Nephrology at Baylor College of Medicine. Dr. Mitch earned his M.D. degree from Harvard Medical School, did his residency at Brigham and Women's Hospital in Boston, and then was a resident fellow at Johns Hopkins. Dr. Mitch's clinical interests include acute and chronic kidney failure. He is recognized around the world as an expert on the care of patients with hypertension and chronic kidney disease, using dietary methods to protect the kidney. Dr. Mitch's research has been supported by NIH since 1979. He is presently a Principal Investigator on three NIDDK grants including a MERIT award and a P50 grant, and he has authored nearly 250 publications.

XI. CONSIDERATION OF REVIEW OF GRANT APPLICATONS

A total of 1,129 grant applications, requesting support of $289,163,768 were reviewed for consideration at the February 18, 2009 meeting. Funding for these 1,129 applications was recommended at the Scientific Review Group recommended level. Prior to the Advisory Council meeting, an additional 1,216 applications requesting $336,058,524 received second-level review through expedited concurrence. All of the expedited concurrence applications were recommended for funding at the Scientific Review Group recommended level. The expedited concurrence actions were reported to the full Advisory Council at the February 18, 2009 meeting.

XII. ADJOURNMENT

Dr. Rodgers thanked the Council members for their attendance and valuable discussion. There being no other business, the 179th meeting of the NIDDK Advisory Council was adjourned at 4:30 p.m.

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

Griffin P. Rodgers, M.D., M.A.C.P.
Director, National Institute of Diabetes and Digestive and Kidney Diseases
Chairman, National Diabetes and Digestive and Kidney Diseases Advisory Council