DRAFT -

Meeting Minutes
Department of Health and Human Services
National Institutes of Health
National Diabetes and Digestive and Kidney Diseases Advisory Council

February 15-16, 2006

I. CALL TO ORDER

Dr. Allen Spiegel, Director, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), called to order the 170th National Diabetes and Digestive and Kidney Diseases (NDDK) Advisory Council meeting at 8:35 a.m., Wednesday, February 15, 2006 in Conference Room 10 on the 6th Floor C Wing of Building 31, NIH, Bethesda, Maryland.

A. ATTENDANCE – COUNCIL MEMBERS PRESENT

Dr. Janis Abkowitz
Dr. Robert Alpern
Dr. Janice Arnold
Ms. Janet Brown
Dr. Roberto Coquis
Dr. Raymond DuBois
Dr. Robert Eckel
Dr. Jeffrey Flier
Dr. William Henrich
Dr. Rudolph Leibel
Dr. Brian Monahan (*Ex-officio*)
Dr. Jerry Palmer (*Ex-officio*)
Dr. Linda Sherman
Dr. Edwin Vaughan

Also present:

Dr. Allen Spiegel, Director, NIDDK and Chairperson, NDDK Advisory Council
Dr. Griffin Rodgers, Deputy Director, NIDDK
Dr. Brent Stanfield, Executive Secretary, NDDK Advisory Council

B. NIDDK STAFF AND GUESTS

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

Kristin Abraham, NIDDK
Lawrence Agodoa, NIDDK
Beena Akolkar, NIDDK
Syed Amir, CSR
Michael Appel, NIDDK
Guillermo Arreaza-Rubin, NIDDK
Michele Barnard, NIDDK
Olivier Blondel, NIDDK
Clarice Brown (affiliation not known)
Francisco Calvo, NIDDK
Arthur Castle, NIDDK
Joan Chamberlain, NIDDK
Debuene Chang, NIDDK
Christine Densmore, NIDDK
Patrick Donohue, NIDDK
Edward Doo, NIDDK
Michael Edwards, NIDDK
Paul Egger, NIDDK
Jody Evans, NIDDK
James Everhart, NIDDK
Robert Fay, NIDDK
Frances Ferguson, NIDDK
Olaf Fonville, NIDDK
Jeffrey Fox, NIDDK
Judith Fradkin, NIDDK
Joanne Gallivan, NIDDK
Lisa Gansheroff, NIDDK
Christine Gill, NIDDK
Elisa Gladstone, NIDDK
Carol Goter-Robinson, NIDDK
Mary Hanlon, NIDDK
Mary Harris, NIDDK
Barbara Harrison, NIDDK
Andrew Hawkins, Research Policy Alert
Trude Hilliard, NIDDK
Eleanor Hoff, NIDDK
Mary Horlick, NIDDK
Van Hubbard, NIDDK
Joyce Hunter, NIDDK
James Hyde, NIDDK
Stephen James, NIDDK
Teresa Jones, NIDDK
Robert Karp, NIDDK
Christian Ketchum, NIDDK
Sooja Kim, CSR
Kathy Kranzfelder, NIDDK
Robert Kuczmarski, NIDDK
Tina Lancaster, NIDDK
Maren Laughlin, NIDDK
Ellen Lescheck, NIDDK
Barbara Linder DDEM
Helen Ling, NIDDK
Karl Malik, NIDDK
Saul Malozowski, NIDDK
Denise Manouelian, NIDDK
Dan Matsumoto, NIDDK
Michael May, NIDDK
Julie McDermott, NIDDK
Melissa McGowan, NIDDK
Rebecca Menso, NIDDK
Barbara Merchant, NIDDK
Carolyn Miles, NIDDK
David Miller, NIDDK
Laura Moen, NIDDK
Marva Moxey-Mims, NIDDK
Christopher Mullins, NIDDK
Neal Musto, NIDDK
D.G. Patel, NIDDK
Judith Podskalny, NIDDK
Sharon Pope, NIDDK
Rebekah Rasooly, NIDDK
Patricia Robuck, NIDDK
Mary Rosenberg, NIDDK
Norka Ruiz Bravo, OD
Paul Rushing, NIDDK
Atul Sahai, NIDDK
Karen Salomon, NIDDK
Antonio Scarpa, CSR
Leonard Seef, NIDDK
Jose Serrano, NIDDK
Philip Smith, NIDDK
Lisa Spain, NIDDK
Robert Star, NIDDK
Myrlene Staten, NIDDK
Dietmar Tietz, NIDDK
Rebecca Torrance, NIDDK
Chris Vonn Seggern, NIDDK
Rachel Weinstein, NIDDK
Dorothy West, NIDDK
Barbara Woynarowska, NIDDK
Susan Yanovski, NIDDK

C. APPOINTMENTS, ACKNOWLEDGEMENTS, AND AWARDS
Dr. Allen Spiegel, Director NIDDK

New Council Members: Dr. Spiegel introduced the names of new members of the NDDK Advisory Council:

- *Dr. Mitchell Lazar*, Director of the Institute of Diabetes, Obesity and Metabolism at the University of Pennsylvania. Dr. Lazar's research is focused on mechanisms of hormone action. (Division of Diabetes, Endocrinology, and Metabolic Diseases Subcommittee)
- *Dr. Juanita Merchant*, Professor of Internal Medicine and Integrative and Molecular Physiology at the University of Michigan Medical School. Dr. Merchant's research interests concern the molecular mechanisms underlying normal and neoplastic epithelial cell growth in the luminal gastrointestinal tract. (Division of Digestive Diseases and Nutrition Subcommittee)
- *Dr. David Perlmutter*, Physician-in-Chief and Chair of the Department of Pediatrics at University of Pittsburgh Medical Center, Children's Hospital of Pittsburgh. Dr. Perlmutter is an accomplished clinician, educator and researcher, whose investigation of alpha-1 antitrypsin deficiency has earned him distinction as a leading authority on the most common genetic cause of childhood liver disease. (Division of Digestive Diseases and Nutrition Subcommittee)
- *Ms. Margery Perry*, former Chair of Research for the Juvenile Diabetes Research Foundation (JDRF). As Chair of Research for the JDRF Ms. Perry had responsibility for supervising and approving all aspects of the JDRF's research program, and oversaw both the development and implementation of the JDRF's research goals and priorities. (Division of Diabetes, Endocrinology, and Metabolic Diseases Subcommittee)

New "Ex-Officio" Member: Dr. Spiegel introduced a new "ex-officio" member of the advisory council. Dr. Spiegel pointed out that these are individuals from other government agencies and entities:

- *Dr. David Klurfeld*, National Program Leader of Human Nutrition, in the Human Nutrition Research Center at the United States Department of Agriculture (Division of Digestive Diseases and Nutrition Subcommittee)

Member Resignation: Dr. Spiegel announced with regrets that Dr. Ronald Ruecker, a member of the Digestive Diseases and Nutrition Subcommittee has resigned from the advisory council because of other commitments.

Unable to Attend the Meeting: Dr. Spiegel announced that Dr. Josephine Briggs, Director for Kidney, Urologic and Hematologic Diseases is unable to attend the meeting due to travel commitments.

- *Dr. Rebeka Rasooly*, Deputy Director of the Division of Kidney, Urologic and Hematologic Diseases served in place of Dr. Briggs for the meeting.

New NIDDK Staff: Dr. Spiegel introduced one new NIDDK staff member.
Joining the Division Nutrition Research Coordination

- *Ms. Rachel Fisher*, Nutrition Program Analyst, Division Nutrition Research Coordination. Ms. Fisher previously worked as health policy analyst in Health Care, Finance and Policy, which is a Division of Health and Human Services in Massachusetts

Awards to NIDDK Staff: Dr. Spiegel announced an NIDDK staff member received a special award for excellence in minority health, an award created as part of the celebration of the 20th year of the Department of Health and Human Services Office of Minority Health.

- Dr. Lawrence Agodoa received the first Health and Human Services Office of Minority Health Director's Award in recognition of his inspirational leadership and work collaborative with other agencies including the Centers for Disease Control and Prevention and the Indian Health Service, with the singular purpose of improving minority health and eliminating health disparities.

Awards to NIDDK Grantees: Dr. Spiegel announced that one of eight winners of the 2004 National Medal of Science, which is awarded by the White House, is a long-time grantee:

- Dr. Thomas Starzl, a transplant surgeon at the University of Pittsburgh School of Medicine is a former MERIT awardee of NIDDK and had served for several years on the Digestive Diseases Advisory Board. Dr. Starzl was a pioneer of liver transplantation and a variety of other innovative efforts and he continues work on xenotransplantation.

II. CONSIDERATION OF SUMMARY MINUTES OF THE 169th COUNCIL MEETING

A motion was made, and unanimously passed by voice vote, to approve the summary minutes of the 169th NDDK Advisory Council (September, 2005) as submitted.

III. FUTURE COUNCIL DATES

Dr. Spiegel asked Council members to take note of future Council meeting dates as follows:

- May 31, 2006 (single day meeting)
- September 20-21, 2006
- February 21-22, 2007
- May 30-31, 2007
- September 19-20, 2007

IV. ANNOUNCEMENTS

A. CONFIDENTIALITY AND CONFLICT OF INTEREST
Dr. Brent Stanfield, Director, Division of Extramural Activities

Dr. Stanfield shared that Jody Evans, who has worked closely with NIDDK Advisory Council members, has left the Division of Extramural Activities and has joined the NIDDK Executive Office.

Dr. Stanfield then outlined the procedures to guarantee confidentiality and avoid conflicts of interest, discussed the scope and applicability of these procedures, and requested Council compliance. Members were asked to sign and return a conflict-of-interest statement and were reminded that materials furnished are considered privileged information and are to be used only for the purpose of review and discussion during the closed portions of the meeting. The outcome of the closed-session discussions may be disclosed only by staff and only under appropriate circumstances; all communications from investigators to Council members regarding actions on applications must be referred to NIDDK staff.

Furthermore, Council members should recuse themselves when individual applications from their institutions are discussed in order to avoid an actual or perceived conflict of interest. This is unnecessary with *en bloc* votes, for which all members may be present and may participate. Council members from multi-campus institutions of higher education may participate in discussions of any particular matter affecting one campus of that multi-campus institution if their disqualifying financial interest is employment at a separate campus of the same multi-campus institution and is in a position with no multi-campus responsibilities.

V. ANNUAL APPROVAL OF THE COUNCIL OPERATING PROCEDURES
Dr. Brent Stanfield, Director, Division of Extramural Activities, NIDDK

Dr. Stanfield reminded council members that the council exists by law and operates under law, regulations and policies. However, exactly how the council conducts its business is established in operating procedures that must be confirmed by the council every year, during the February meeting. Dr. Stanfield asked if there were any questions regarding the draft operating procedures sent to council members. These new draft procedures were modified only slightly from the procedures adopted the previous year to now include operation of expedited concurrence.

With no questions forthcoming a motion was made to approve the operating procedures and the motion was unanimously passed by voice vote.

VI. REPORT FROM THE NIDDK DEPUTY DIRECTOR

Dr. Griffin Rodgers, Deputy Director, NIDDK

Fiscal Year (FY) 2006 Appropriation and FY 2007 President's Budget Proposal

FY 2006 Appropriation and Impacts

Dr. Rodgers reported Congress had finalized the FY 2006 appropriation for NIH since the last time that council had met. For FY 2006, Congress appropriated $28.6 billion dollars to NIH in total. Of this amount, NIDDK received a budget of approximately $1.7 billion. Compared to FY 2005, in FY 2006 NIDDK recognized a slight cut (about $8.5 million) in its budget—a decrease of approximately 0.5%. Putting NIDDK's budget cut in perspective, it is the same magnitude of cut experiences by essentially all of the other NIH Institutes with the exception of the National Institute of Allergy and Infectious Diseases (NIAID), which received a budget increase for bioterrorism research.

The FY 2006 budget cut has consequences. For non-competing commitments, research project grants for all NIH Institutes will be cut by 2.35% from FY 2006 commitments of record. Also, all future year commitments for FY 2007 and beyond will also be reduced by 2.35%. Competing Research Project Grants will receive no average cost increase over FY 2005 levels. National Research Service Award (NRSA) stipends will increase by 0-4% depending on the level of experience of the fellows and postdoctoral fellows will continue to receive the $500 health benefit increase established in FY 2005.

NIH Roadmap project funding will increase from $235 million in FY 2005 to $329 million in FY 2006. NIDDK's contribution to Roadmap was $10.8 million in FY 2005 and this increases to $15.2 million in FY 2006.

NIDDK continues to use special emphasis discretion to reach out to promising New Investigators.

FY 2007 President's Budget Proposal

Dr. Rodgers reported that the President proposed a budget that was made public earlier this month for FY 2007. For NIH, the President proposes a budget of $28.6 billion dollars—the same amount as for FY 2006. In this budget plan, NIDDK's appropriation will decrease slightly from $1.704 billion to $1.694, a decrease of $11 million or 0.6%. Once again, to put NIDDK's situation in context, Dr. Rodgers mentioned that with the exception of NIAID, the other NIH Institutes and Centers are slated in the President's budget to receive a cut of a similar magnitude.

The President's budget proposes a 1% cut for non-competing Research Project Grants, but where NIDDK is already committed to a programmatic increase for awards, such increase would be honored before that 1% reduction would be taken.

Under the President's budget scenario, NRSA programs would receive no stipend increases for tuition and training-related expenses.

In FY 2007 the NIH Roadmap will enter its fourth year and it is scheduled to increase from $329 million dollars to $443 million dollars for all of NIH. NIDDK's obligation to Roadmap will grow to $20.5 million dollars in FY 2007, from $15.2 million dollars in FY 2006.

Responsible Management in the New Fiscal Environment

Dr. Rodgers pointed out that we must continue in these times to nurture a vibrant and creative workforce, including a sufficient number of New Investigators with new ideas and skills. In the FY 2007 budget NIDDK has set aside $1.35 million dollars to support 15 new Pathways to Independence K99/R00 awards.

The budget environment also mandates that NIDDK limit the number of new and expanded initiatives as we move forward. Three proposed initiatives for FY 2007 include:

Collaborative research between basic and clinical researchers in obesity—NIDDK plans to solicit research application to foster synergistic progress in understanding the underpinnings of overweight and obesity.

HALT-C (Hepatitis C Antiviral Long-Term Treatment against Cirrhosis)—is an ongoing multi-center, randomized controlled study. NIDDK is presently entertaining a "follow-on" to this important study.

New imaging methods for hepatic and renal fibrosis—a common problem associated with studying diseases of the liver and kidney is to monitor the disease progression, particularly how to assess fibrosis that occurs in these organs over time. NIDDK will be entertaining and soliciting proposals for new imaging methods for hepatic and renal fibrosis.

Council Questions and Discussions

Roadmap: How are IC contributions to Roadmap derived? Dr. Spiegel explained that the Roadmap process began as a series of focus groups and sessions. From these sessions three principle components of the Roadmap emerged including New Pathways to Discovery, Research Teams of the Future, and Reengineering the Clinical Research Enterprise and these were refined with extensive consultation with the research community, advocacy groups and the public. The Roadmap was originally envisioned to be larger than what it is now, but through a process of prioritization, deliberation and negotiation with Institute Directors an initial budget was established and consensus was developed for a trajectory for future budgets extending through 2009. The NIH Director has discretionary authority for a finite percentage of the NIH budget and, especially in the first years of the Roadmap, a portion of Roadmap costs came from the NIH Director's discretionary authority. To achieve the full dimension of the Roadmap, there was also a requirement for contributions from the Institutes. Dr. Spiegel emphasized that these

contributions were/are essentially pro forma proportionate to the size of the Institute budgets—"there is no gaming the system, it's a straight proportionality." Dr. Spiegel then addressed how Roadmap funds are distributed. He emphasized that the money is distributed over a fairly large landscape that ranges from large science projects such as the Molecular Libraries screening centers to investigator initiated research including the Director's Pioneer Awards. All of these projects have the goal of either eventually enabling further investigator initiated hypothesis driven research or accelerating translation of research. Finally, Dr. Spiegel addressed the trajectory of Roadmap projects beyond the 2009. He pointed out that some projects would end or if it was deemed appropriate to continue them they would find a home in a specific Institute that was most appropriate. However, the actual details of how this will happen and the budget implications generally have not been clearly established.

Roadmap: Is there a discussion ongoing regarding the value of Roadmap relative to investigator initiated R01 research? Given the current fiscal outlook is there any thought to whether the Roadmap should be shrunk? Dr. Spiegel commented that the only extent to which the Roadmap is being shrunk is to the extent that the FY 2006 NIH budget saw a decrement, with the exception of biodefense, for the first time since 1970. The decrement from Roadmap was a decrement from an upward trajectory that was already planned and there is no plan for retrenchment from that trajectory. Dr. Spiegel argued that there has been a focus on Roadmap "as if that is where all the money is." However, an accounting at the NIH- and NIDDK-level doesn't support this. Dr. Spiegel then emphasized that NIDDK has placed the highest priority during this time of budget austerity on investigator initiated research and payline. To support this, NIDDK has cut to the maximum extent that we feel feasible, various initiatives. At a trans-NIH level, there is consensus that Roadmap should not grow any more than the envelope originally agreed to by the Institute Directors. Indeed, as part of the vision for the new Office of Portfolio Analysis and Strategic Initiatives (OPASI), there is a plan to eventually morph Roadmap into a "common fund," that might grow incrementally to as much as five percent of the NIH budget. However, at a budget retreat of the Institute Directors there was an agreement that so long as the NIH budget is not growing at least in keeping with the BRDPI there could be no growth in the Roadmap/Common Fund envelope. In other words, by agreement, the Roadmap/Common Fund cannot grow beyond what has already been established for Roadmap until such a time as the NIH goes back to robust and significant budget increases that exceed inflation.

Budget and Policy: There have been lots of rumors that NIH may look at the maximum numbers of grants by Principal Investigator or possibly change the size of grants or look at portfolios of investigators rather than looking at each grant separately. Is there any truth to this? Dr. Spiegel indicated that there is a balance at NIH between central policy and flexibility among NIH's Institutes and Centers to execute their mission as they see fit, and this really gets to the heart of the question. For example, regarding some of the budget policies such as size of growth for a non-competitive continuation, there's no variability. That policy is established at the trans-NIH level and is an element that everyone has agreed to. Within other parameters there is variability among Institutes. For example, there is no set policy for the maximum number of grants any PI can have at

NIDDK or at the broader NIH level, but the policies among the NIH Institutes on this matter may differ. Dr. Spiegel pointed out as an aside that the possibility of adopting an NIH wide policy was discussed at a NIH budget retreat approximately a year ago. Consideration of the possibility was data driven and the data showed that during the period of the doubling there was a very small increase in the average number of grants per PI. In doing the math, calculations of the savings for limiting the number of grants to "...pick a number..." the actual saving that would be returned were so marginal that it was not considered worth further consideration.

VII. REPORT FROM THE NIDDK DIRECTOR

Dr. Allen Spiegel, Director NIDDK
Dr. Elias Zerhouni, Director, NIH

Because this was Dr. Spiegel's final Council meeting as Director, NIDDK, Dr. Elias Zerhouni, Director, NIH addressed the Council to recognize Dr. Spiegel and wish him farewell. Dr. Zerhouni's remarks and the discussion that followed are summarized here since this portion of the meeting used the time allotted for the NIDDK Director's Report.

Dr. Zerhouni's Remarks

Dr. Zerhouni began by indicating that he was addressing Council to acknowledge Dr. Spiegel for his service and leadership at NIH for 33 years—especially as head of NIDDK for the past six years. Dr. Zerhouni expressed his sorrow that Dr. Spiegel will be leaving NIH, but also indicated that he is very happy for Dr. Spiegel because the job that he is taking is an outstanding opportunity for him. In addition, Dr. Zerhouni offered that he feels that Dr. Spiegel's acceptance of the position as Dean of Albert Einstein College of Medicine is a historical transition for that school and also for science. Dr. Zerhouni commented that whatever Dr. Spiegel does, "he does extremely well, with grace and with insight and with one of the most insightful, analytical minds I've met in my career."

Dr. Spiegel's Remarks

Dr. Spiegel thanked Dr. Zerhouni for coming to the meeting and acknowledging his tenure as NIDDK Director. He then commented on how important NIH has been to him over the past 33 years—"not the buildings, the labs, the campus, as impressive as those are, but the people of NIH and the goals for which they work every day." Dr. Spiegel finished his comments by stating that he thinks NIDDK will continue to flourish with new leadership, and that it was time for a new and different challenge for him. He added that while he will be working with a different community, a different group of people, the goal of improving the health of the American people remains the same.

Dr. Zerhouni then took question from Council members.

Council Questions and Discussion

Pathways to Independence: What is the vision for the new K to R award? Dr. Zerhouni said that he has been very public about his concern about new investigators. The impact of a flat budget is typically not on bricks and mortar or equipment, but rather it is on people and the most vulnerable layer of people for science and for the future of science are the new investigators who get discouraged. The Pathways to Independence Award is one way of responding to this concern. It will commit NIH to fund 150 to 200 New Investigators per year for the next five years. At the end of the process NIH will have allocated almost $400 million to the program. Dr. Zerhouni indicated that he did not feel that this was sufficient. He suggested that we need to "really" find a way to encourage independence and the entry of new ideas and new areas of science into the mix.

Pathways to Independence vs. Team Science: NIH is trying to foster the independence of junior investigators while simultaneously trying to stimulate team science, for example with the co-PI process. Is this a bit of a mixed message? Dr. Zerhouni indicated that it is important to realize that fostering the independence of junior investigators and stimulating team science is complementary, not opposed. Dr. Zerhouni explained that interdisciplinary teams require strong interdisciplinary minds. The ability to function as a strong member of an interdisciplinary team requires experience as an independent thinker "with your own ideas that you bring to the table." Dr. Zerhouni then refined his point by stating that he felt the process from independence to team science is a continuum. It is initially desirable for investigators to receive independent support so that they can develop expertise and knowledge, which is then complimentary with their participation on a team sometime later. The biomedical research enterprise still requires basic investigations using a single investigator initiated project model. As projects mature a desirable outcome is that they click with other components that can come together.

Escalating Costs of Research: Would you like to comment on the escalating costs of performing research in the context of NIH facing possible budget cuts and competing priorities? Dr. Zerhouni confirmed that the perception regarding the rising cost of performing research is real. The Biomedical Research and Development Price Index (BRDPI) estimates inflationary trends on the cost of performing research from year to year and the dominant component of inflation within the index is people costs. Dr. Zerhouni asserted that inflationary pressure associated with performing research is really driven by the cost of attracting, recruiting, and retaining people in competition with the greater market. He then pointed out that the Department of Health and Human Services (HHS) received a 2.7% across the board cut this year, that NIH is a component of HHS, and to have a flat budget in this context is a substantial accomplishment. NIH must become very aggressive in how we manage our portfolios and make a strong case that you cannot, over time, maintain the vitality of this people dependent enterprise without taking these inflationary factors into account. Dr. Zerhouni stated that a challenge that we currently need to overcome is guilt about the doubling of NIH's budget. If we are not careful the progress that has been made with the doubling will be a distant dream because of inflation, "as a scientific community we need to get together, understand this and make

a case regarding the impact on science over time." There has been a push to support the physical sciences and science education. Dr. Zerhouni emphasized the he supports this effort, but he also made the point that he has publicly stated that this new focus should not come at the expense of the biological sciences.

VIII. NEW INVESTIGATORS

Dr. Ruiz Bravo, Director, Office of Extramural Research, NIH
Dr. Rodgers, Deputy Director, NIDDK

Pathways to Independence

Dr. Ruiz Bravo discussed the new "Pathways to Independence Award." She explained that over time the average age at which investigators receive their first independent research award has been pushed to 44 for M.D.s and M.D./Ph.D.s and 42 for Ph.D.s. A committee was established to consider this problem and develop a list of action items that had the potential to foster and maintain a healthy cohort of new and talented investigators. A focus of this committee was to facilitate the ability of outstanding new investigators to receive their first R01 award earlier in their career via a standardized career transition program and from this focus the "Pathways to Independence Award" was developed.

The new Pathways to Independence Award will utilize the K99-R00 mechanism. Awards will include a total of five years of support and consist of two phases. Phase I will give individuals one to two years of mentored support. The total cost would be $90,000 per award, including eight percent Facilities and Administration costs (indirect costs). Phase II provides up to three years of independent research support, but this support is contingent upon securing an independent research position and administrative review. This administrative review will be important and will consider the institutional commitment made to the new investigator to help ensure that the investigator has appropriate resources to make the transition. This "R" portion of the award includes $249,000 and Facilities and Administrative costs. An important difference between the K99-R00 mechanism and other K mechanisms is that U.S. citizens and non-U.S. citizens are eligible to apply for the K99-R00. Dr. Ruiz Bravo explained that science is a global enterprise and NIH feels it important to open this opportunity to foreign scientists. However, training and work must occur at a U.S. institution.

NIH Institutes and Centers have committed to 150 Pathways to Independence Awards in the first year—assuming of course that budgets permit and sufficient numbers of quality applications are received. Locus of review will be within the Institutes and Centers rather than the Center for Scientific Review because it was decided that the K components of the applications would be best considered by review panels overseen by the Institutes and Centers. Institutes with similar interests may combine review resources and review the applications in a cluster.

Dr. Ruiz Bravo ended her presentation by emphasizing that the Pathway to Independence Award complements ongoing NIH efforts to foster new investigator independence. She mentioned that there are a number of Institutes and Centers that have practices to assist New Investigators. These practices range from giving applications from New Investigators special attention at council, to extending the payline for New Investigator applications, which is something that NIDDK does. Some Institutes also allow New Investigators whose applications score beyond the payline to submit a brief letter responding to critiques for consideration at their council meeting.

Council Questions and Discussions

Will this be a more advanced pool than the fellows who get regular K awards? Dr. Ruiz Bravo explained that applicants may apply for this award with zero time as a postdoc and the idea is to for awardees to be really extraordinary people, "the cream of the crop is what we are expecting for this award."

How does the applicant make the transition from the K99 to the R00? When is a person eligible for the R portion of the award? Dr. Ruiz Bravo explained that there will be an administrative review by NIH staff (for awards made by NIDDK, by NIDDK staff). Dr. Spiegel then added that the expectation is that the awardee will secure an authentic tenure-track assistant professor-type position before the R phase of the award is administratively approved. Programmatic staff will not approve the second phase of the award unless the person has a bona fide, tenure-track, independent position with appropriate institutional support.

What is the K99 portion of the award accomplishing that wasn't being accomplished with the T32 award? Dr. Ruiz Bravo explained that the award is a full package—including a training component followed by initial independent research support. With the T32 there is no expectation that any portion of the award can be administratively reviewed and transferred to a new job (e.g., transition from the K portion to the R portion of the K99-R00). Trainees on a T32 must apply for an R01 to begin an independent research program. Dr. Spiegel then added that another consideration is that the award is not limited to U.S. citizens or permanent residents and therefore, the pool of potential recipients is enormously expanded.

What impact will the K99-R00 award make on NIH's commitments to New Investigators? Dr. Ruiz Bravo explained that approximately a quarter of NIH's research project grant budget is not committed—i.e., available for new awards. Within that uncommitted share, each percentage point represents approximately 75 researchers. The 150 Pathways to Independence Awards that NIH intends to make represents approximately 2% of the uncommitted research project grant budget. Currently, approximately 23% of NIH competing research dollars go to New Investigators. Therefore, in rough figures, addition of 150 new awardees will increase the percentage of competing research project grant dollars committed to New Investigators from 23% to 25%.

What will the K99-R00 applications look like? Training will take place in a lab that may be reflective of the work of the mentor and not the trainee, but the trainee would have to anticipate what her/his new lab will be working on. Dr. Ruiz Bravo stated that the award will be for those extraordinary people who know what they would like to do early on. Dr. Spiegel added that one could imagine a dialog between a mentor and a trainee regarding the aspects of projects that the trainee could take with them. Applicants who have generous mentors may have some advantage. Dr. Spiegel also pointed out that in the course of the K to R transition there does not necessarily need to be a change in institutions. This may have some advantage for some clinical researchers since past experiences show that clinical investigators often have difficulty in moving from their earlier training phase to another institution because of the nature of clinical research—e.g., cohorts of patients, etc.

Before moving to Dr. Rodger's talk Dr. Spiegel indicated that NIDDK intends to support 15 Pathways to Independence Awards. While 15 awards is disproportionate to the size of NIDDK's budget (in context with the budgets of other NIH Institutes and Centers), the number is consistent overall with NIDDK's strong commitment to training and support of New Investigators. Dr. Spiegel indicated that NIDDK, in general, experiences a very robust applicant pool. However, NIDDK will only support 15 awards if there are enough high quality, well-deserving applications.

NIDDK Trends for Training and New Investigators

Dr. Rodgers reported that approximately 7% of NIDDK's $1.7 B budget (slightly over $100 million dollars) is committed to training (F and T series grants) and career (K series grants) awards. The aggregate funding for these awards has increased continuously since 2001 when the aggregate figure was approximately $65 million to the figure slightly over $100 million in 2005. During this period growth was largely in mentored career awards which have increased on average by 4% per year, while the training award budget has grown by an average of 2% per year. At a more granular level, the total numbers of F32 trainees (Postdoctoral Individual National Research Service Award) and costs per year for the F32 program have been fairly stable. In contrast the numbers of T32 (Institutional National Research Service Award) awards rose through 2003 and then decreased slightly, while total costs for the T32 program continued to increase despite the plateau in numbers of trainees. Total costs for T32 trainees is somewhat greater than for F32 trainees perhaps reflecting seniority of T32 trainees and other factors such as health care benefits.

Regarding New Investigators, Dr. Rodgers reported over the past five years the number of awards has been fairly stable, with some year to year variability (with a low of 73 New Investigator Awards in 2001 and a high of 109 in 2003). The percentage of Type 1 R01 grants that are awarded to New Investigators has gradually increased from 19% in fiscal year 2000 to a fairly stable value of approximately 30% in fiscal years 2002 through 2005. Dr. Rodger's reported that this compares favorably with recently reported NIH-wide data.

Dr. Rodger's concluded his presentation by showing data regarding NIDDK's efforts to support promising New Investigators using Special Emphasis discretion. Since fiscal year 2000 approximately 20-25% of awards made to New Investigators were the result of the automatic two percentile advantage given to New Investigator applications and other Special Emphasis consideration.

Council Questions and Discussions

What percentage of T32 awardees and K08 awardees get R01 funding? Dr. Rodgers explained that NIDDK is currently studying this question and asked Dr. Judy Podskalny to elaborate. Dr. Podskalny explained that the question has proven difficult to answer, especially for T32 trainees, because there are hundreds of them each year—many who are physicians who are rotated onto the training grant and prove especially difficult to track over time. For K awardees, each Division does its own tracking and the numbers are a bit more manageable. Approximately, 60-70% of NIDDK K awardees receive some type of research project funding—although these project grants may include not just R01s but also R21s and U01s. Dr. Stanfield then mentioned that tracking the success of trainees is a systems problem that NIH is presently trying to address.

IX. SCIENTIFIC PRESENTATION

***Dr. Raymond DuBois, B.F. Byrd Jr. Professor of Molecular Oncology, Professor of Medicine, Cancer Biology and Cell & Developmental Biology, and Director, Ingram Cancer Center, Vanderbilt University*—"Translational Medicine: COX-2, Prostaglandins, Intestinal Biology and Cancer"**

See attached presentation.

NIDDKdubois06.ppt

X. ADVISIORY COUNCIL FORUM

NIH Peer Review: Continuity and Change

Dr. Antonio Scarpa, Director, Center for Scientific Review, NIH

Dr. Scarpa began by mentioning his strong belief in the importance of peer review. He gave a brief history of the development of peer review, which he stressed was in large part developed 60-70 years ago by NIH, and has been the "heart and soul of NIH" and an important factor in protecting NIH from outside influence.

In a brief overview, Dr. Scarpa related that CSR receives all applications submitted to NIH and reviews 65 to 70 percent of those applications. Over the past three years CSR has absorbed substantial increases in the numbers of applications that it receives and reviews (approaching a doubling). NIDDK applications represent approximately 8% of CSR's workload and this proportion has changed little over the past three years. NIDDK

applications are distributed fairly widely across CSR study sections, but the vast majority of NIDDK applications are reviewed in essentially 30% of CSR study sections. NIDDK applications within CSR study sections score slightly above average with 10% of NIDDK applications scoring within the 10th percentile and slightly more than 20% of NIDDK applications scoring within the 20th percentile.

Dr. Scarpa reported that over the past seven months he has had extensive discussions regarding the problems and challenges that CSR faces with stakeholder groups ranging from NIH program staff, to NIH Advisory Councils, to professional societies and patient advocacy groups. From these discussions he has been working to synthesize the recommendations and ideas into actionable plans. Thus far, the changes that Dr. Scarpa feels are necessary can be broken down into three categories or matrices. One category of change is focused on CSR's internal operations and Dr. Scarpa feels that those changes will be the easiest to execute. A second category of change is more broadly focused inasmuch as these changes will affect all the NIH Institutes and their stakeholders and therefore require wide-scale approval and buy-in before they can be implemented. A final category of possible change asks the question whether we should keep the same system that has served NIH so well for the past 60 years or if we should consider a different system. Whether or not changing systems is at all possible is not clear to Dr. Scarpa, but considering if the current system is the best possible for the times is something that he feels should be discussed.

Regarding internal changes, Dr. Scarpa reported that he has already made some progress and gave examples:

- Dr. Scarpa felt communication within CSR, from CSR to other components of NIH, and from CSR to the extramural scientific community was poor and he is working to make CSR's operations more transparent. For example, once per month CSR sends out Peer Review Notes to notify stakeholders of changes and the reasons underpinning these changes.
- Dr. Scarpa also reported that the there was substantial diversity in many of CSR's key work processes and outputs. For example, the time to release a summary statement was highly variable and now has been standardized to a month or less after the review meeting. Dr. Scarpa has also overseen making the resume of the summary statement more structured so that it will be more helpful to investigators.
- Because workload has increased so substantially, CSR is imposing unscoring of fifty percent or more of applications within study sections so that more time can be focused on those application that have a chance of being considered for funding.
- To be more efficient, CSR is embracing a paperless workplace. Dr. Scarpa reported that while CSR's workload has increased dramatically it budget has been flat. Essentially half of CSR's workspace is presently consumed by paper and with electronic submission some of this space can be recovered and the resources redistributed and focused on additional Scientific Review Administrators.
- To improve streamline and improve referral and review operations Dr. Scarpa reported that CSR is piloting the use of Knowledge Management tools to assign

applications to study sections and to help review staff identify reviewers for applications assigned to study sections.
To help ensure that CSR's Integrated Review Groups (IRGs) keep pace with the changing landscape of science, each month a different IRG will be reviewed (instead of reviewing all IRGs on a 5 year cycle). In this way, since CSR has 24 IRGs, all of CSR's IRGs will be reviewed every two years.

Dr. Scarpa then discussed some of the broader scale challenges that he sees for CSR and some of his ideas to address these challenges. For example:

- NIH currently uses a very complex and "antiquated" process for receipt and review of applications. CSR is currently looking for ways to streamline this process and is using New Investigator applications in some study sections to pilot compressing the review cycle in a way that will give investigators the opportunity to revise and resubmit their application in time for the next review round.
- There are concerns that clinical research applications are disadvantaged in CSR study sections. Dr. Scarpa mentioned that CSR's Special Advisor on Clinical Research, Dr. Theodore Kotchen has collected data that show a very small but consistent difference in review outcomes between basic research and research that involves human subjects (a surrogate for clinical research), where the human subjects research does not do as well in review. These data are not perfect because of the complications of defining clinical research. Dr. Scarpa also mentioned that the reason for this difference is not clear and requires more study.
- Dr. Scarpa contended that NIH has developed a culture where applications proposing safe research do the best in review—at the expense of those proposals presenting more innovative and risky ideas, which are potentially higher impact. Dr Scarpa admitted that he did not have a "silver bullet" for this problem and it may need to be approached in several different ways.
- Attracting the best reviewers to serve on NIH peer review committees is becoming more and more difficult because of increasing demands on their time. To address this problem, CSR has established several pilots of alternative review formats. For example, in one pilot reviewers are sent a computer video camera and software to support video-enhanced teleconferences that can include up to 25 people. In another pilot using "asynchronous electronic discussion" reviewers can post their critiques and then their comments and rebuttals to others comments onto an online message board over the course of several days. This latter format allows place and time flexibility that is key for some expertise especially difficult to recruit for a face to face meeting (e.g., M.D.s who have substantial clinical responsibilities or foreign experts who would have to travel great distances).

Dr. Scarpa then argued that the present peer review system was developed long ago and that technology, scientific culture and fiscal realities have changed. He pointed out that numbers of applications are increasing, more and more reviewers are needed to review these applications, reviewers will commit to service only with reduced workloads (which exacerbates the need for more reviewers), and CSR's operational budget is flat or in decline. All this culminates in a new reality where business as usual—logistically and financially—is no longer possible. This presents the opportunity to consider what a

review system that we would develop today would look like if there were no review system currently in place.

Dr. Scarpa remarked on some examples of policies and processes that he feels are vestiges of a different time and are now detrimental. Dr. Scarpa sees the tradition of three annual receipt dates for applications as unnecessary because the timing of funding is no longer directly linked to Council meetings and inefficient because of the capacity requirements associated with bolus receipt dates as compared with more continuous system. Dr. Scarpa also commented that it may be beneficial to reduce the length of the R01 application and also to eliminate appendices to facilitate electronic receipt and also reduce burden on reviewers. Finally, given the breadth of science considered in modern study sections and the number of reviewers typically required to review the applications assigned to a given study section, it seems that the present system used to score applications may be antiquated. Dr. Scarpa argued that typically only three of the reviewers have read the application in depth and therefore it may not make sense to have the entire committee vote a score for each application. Chemistry once inherent in smaller more cohesive study sections, which made the process of giving each reviewer a vote for each application a sensible approach to assigning a score to applications, may be diminished in more recent times.

Dr. Scarpa concluded his presentation by commenting that NIH has an excellent peer review system. However, changes are needed because the world is changing and CSR has to adapt to those changes.

Council Questions and Discussions

What can NIH do to encourage service, especially among long-time NIH grantees who have never served on study section? What can be done to encourage service by senior reviewers? Dr. Scarpa recognized that these are common concerns and the problems are thorny. It is not possible to force scientists to serve as peer reviewers for many reasons, but a key reason is that people who are pressed into service may do a poor job either because of lack of motivation or out of spite. As an incentive for service, a common suggestion is that NIH extend the grant award period of people who serve on study section. However, this type system may have the appearance of *quid pro quo* and the public might see the incentive as extremely large payment for service. Dr. Scarpa feels that the best way to encourage service is to remove barriers. For example, rather than having members serve for three or four years on narrowly constituted study sections, perhaps a better model would be service on very broad study sections for ten years. These study sections could include 100 members rather than 20, and only 30 or 40 members per review round would be asked to review applications, depending on the application received and the expertise needed. In such a system, reviewers would only be asked to serve once or twice per year and this may encourage service by more senior reviewers. Dr. Scarpa mentioned that presently approximately 6% of CSR reviewers are assistant professors, where just a few years ago only 1% of reviewers were assistant professors. This sets up a paradoxical situation where the age of new investigators is going up but the age of reviewers is going down.

Applications that are 25 pages are too long and contribute to reviewer reluctance to serve and other review problems such as inappropriate focus on detail. Dr. Scarpa agreed that reducing the length of applications would be the closest approximation to a "silver bullet" that NIH has for several current problems associated with its peer review process. For example, while there may not be a linear relationship between length of applications and the number of applications that reviewers can review, it is likely that reviewers would be willing to review a greater number of shorter applications per review round—thereby taking some of the pressure off the need to find increasingly larger numbers of reviewers. Dr. Scarpa also suggested that there are arguments to be made that reducing the page limit might stimulate more creativity because there will be fewer details to pick at. Dr. Scarpa then mentioned that it is often new investigators who feel they need 25 pages for their application and he also mentioned the concern that reducing the length of the application will stimulate more application submissions. He indicated that he feels it unlikely that the latter concern would be realized because it would probably take applicants longer to condense their ideas into a shorter application.

The question of how NIH might move toward a shorter application was then raised. Dr. Spiegel indicated that there are a multitude of venues that such a decision might have to go through. Dr. Spiegel indicated that the Peer Review Advisory Committee (PRAC), which includes NIH and outside members, is probably the most relevant entity. Dr. Spiegel suggested that Dr. Stanfield circulate membership of PRAC and interested members of council could weigh in on this matter with that group.

Has NIH considered testing the idea of organizing study sections more like the way editorial boards are organized where associate editors or board members outsource reviews? Dr. Scarpa indicated that he has raised something along these lines with Dr. Zerhouni. The model is somewhat similar to the National Science Foundation process of peer review and Dr. Scarpa indicated that he felt that such as system could work if there were a core of nominated reviewers who committed themselves to performing a certain number of reviews per year.

XI. CONSIDERATION OF REVIEW OF GRANT APPLICTIONS

A total of 541 grant applications, requesting support of $135,883,632 were reviewed for consideration at the Feb. 15-16, 2006 meeting. Funding for these 541 applications was recommended at the Scientific Review Group recommended level. Prior to the Advisory Council meeting, an additional 799 applications requesting $189,535,394 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 on February 16th.

XII. ADJOURNMENT

Dr. Rodgers thanked the Council members for their attendance and efforts. There being no other business, the 170th meeting of the NIDDK Advisory Council was adjourned at 11:27 a.m., February 16th, 2006.

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

Griffin Rodgers

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