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

September 20-21, 2006

I. CALL TO ORDER

Dr. Griffin Rodgers, Acting Director, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), called to order the 172nd National Diabetes and Digestive and Kidney Diseases (NDDK) Advisory Council meeting at 8:35 a.m., Wednesday, September 20, 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
Dr. Roberto Coquis
Dr. Raymond DuBois
Dr. Robert Eckel
Dr. Jeffrey Flier
Dr. James Freston
Dr. William Henrich
Dr. David Klurfeld (Ex Officio)
Dr. Mitchell Lazar
Dr. Rudolph Leibel
Dr. Juanita Merchant
Dr. Brian Monahan (Ex Officio)
Dr. David Perlmutter
Dr. Jerry Palmer (Ex Officio)
Ms. Margery Perry
Ms. Lisa Richardson
Dr. Linda Sherman
Dr. Darracott Vaughan

Also present:

Dr. Griffin Rodgers, Acting Director, NIDDK, and Chairperson, NDDK Advisory Council
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, Center for Scientific Review (CSR) Scientific Review Administrators, and other members of the public. Guests were present only during the open sessions of the meeting.

Attendees included the following:

Abraham, Kristin – NIDDK
Akolkar, Beena - NIDDK
Amir, Syed - CSR
Appel, Michael - NIDDK
Arreaza-Rubin, Guillermo – NIDDK
Barnard, Michele - NIDDK
Begum, Najma - CSR
Bishop, Terry – NIDDK
Blondel, Oliver – NIDDK
Beckley, Carey – NIDDK
Bourque, Sharon - NIDDK
Calvo, Francisco – NIDDK
Castle, Arthur - NIDDK
Chamberlain, Joan – NIDDK
Chang, Debuene - NIDDK
Connaughton, John - NIDDK
Curry, Jennifer – NIDDK
Densmore, Christine - NIDDK
DeSanti, Andrea – Fisher Bio. Inc.
Donohue, Patrick – NIDDK
Doo, Edward - NIDDK
Eggerman, Thomas – NIDDK
Eggers, Paul - NIDDK
Everhart, James - NIDDK
Farishian, Richard – NIDDK
Feld, Carol – NIDDK
Ferguson, Frances - NIDDK
Fonville, Olaf - NIDDK
Fradkin, Judith – NIDDK
Gansheroff, Lisa - NIDDK
Goter-Robinson, Carol - NIDDK
Groves, Reed – CSR
Guo, Xiaodu - NIDDK
Haft, Carol - NIDDK
Hamilton, Frank – NIDDK
Hanlon, Mary - NIDDK
Harris, Kimberly - NIDDK
Harris, Mary – NIDDK
Harrison, Barbara – NIDDK
Hoff, Eleanor – NIDDK
Howard, Stuart - NIDDK
Hunter, Helen – NIDDK
Hunter, Joyce – NIDDK
Hunter, Christine – NIDDK
James, Stephen – NIDDK
Jerkins, Ann - CSR
Jones, Teresa – NIDDK
Karp, Bobert - NIDDK
Ketchum, Christian - NIDDK
Kim, Sooja - CSR
Kranzfelder, Kathy - NIDDK
Krishnan, Krish - CSR
Laughlin, Maren – NIDDK
Leschek, Ellen – NIDDK
Linder, Barbara – NIDDK
Malik, Karl – NIDDK
Malozowski, Saul – NIDDK
Manouelian, Denise – NIDDK
Margolis, Ronald – NIDDK
Martinez, Winnie - NIDDK
Matsumoto, Dan – NIDDK
May, Michael (Ken) – NIDDK
McDermott, Julie – NIDDK
McKeon, Catherine - NIDDK
Miles, Carolyn – NIDDK
Miller, David - NIDDK
Miller, Megan - NIDDK
Mineo, David – NIDDK
Moen, Laura – NIDDK
Moxey-Mims, Marva – NIDDK
Mullins, Christopher - NIDDK
Musto, Neal – NIDDK
Patel, D.G. – NIDDK
Perry-Jones, Aretina – NIDDK
Pope, Sharon - NIDDK
Rasooly, Rebekah – NIDDK
Roberts, Tibor – NIDDK
Robuck, Patricia – NIDDK
Rodrigues, Michelle - SRI
Rosenberg, Mary Kay – NIDDK
Rushing, Paul – NIDDK
Sahai, Atul - NIDDK
Sankaran, Lakshmanan - NIDDK
Sato, Sheryl – NIDDK
Sechi, Salvatore - NIDDK
Serrano, Jose – NIDDK
Sheard, Nancy - CSR
Singer, Elizabeth - NIDDK
Smith, Phillip – NIDDK
Stanfield, Brent – NIDDK

Smith, Tyrone – NIDDK
Star, Robert – NIDDK
Staten, Myrlen – NIDDK
Tietz, Dietmar – NIDDK
Torrance, Rebecca - NIDDK
Vinson, Terra - CSR
Wellner, Robert - NIDDK
Williams, Garman – NIDDK
Wright, Anne - NIDDK
Wright, Daniel – NIDDK
Wright, Elizabeth – NIDDK
Xie, Yining - NIDDK
Yanovski, Susan – NIDDK
Zellers, Charles - NIDDK

C. ANNOUNCEMENTS

Dr. Griffin Rodgers, Acting Director NIDDK

New Members: Dr. Rodgers began the meeting by introducing and welcoming two new members to the NDDK Council, both of whom will serve on the Digestive Diseases and Nutrition Subcouncil.

- *Dr. James Freston, MD, Ph.D.* is Professor of Medicine Emeritus and Boehringer Ingelheim Chair of Clinical Pharmacology at the University of Connecticut School of Medicine. He is also Chair of the Foundation for Digestive and Health Nutrition and Director of the Capital Regional Medical Reserves Corp. Dr. Freston is a gastroenterologist with expertise in clinical pharmacology. He has served in a variety of leadership positions and is the most recent past-President of the American Gastroenterological Association.

  Ms. Lisa Richardson is a research advocate for ucerative colitis and is the past National Chairperson of the Board of Directors for the Crohn's Disease and Colitis Foundation of America (CCFA). Overall, Ms. Richardson has been active with the CCFA for over 17 years and has been extremely active in supporting research to prevent and cure Crohn's Disease and ulcerative colitis, and also improving the quality of life for childern and adults affected by these diseases through both educational and support services.

Retiring Members: Dr. Rodgers then recognized five members who were to retire from the NDDK Council after the September 2006 meeting. Retiring members include Drs. Robert Alpern, Raymond DuBois, Robert Eckel, Linda Sherman and Darracott Vaughn. Dr. Rodgers extended thanks to the members on behalf of NIDDK for their service and advice and also for their dedication to promoting human health, which has been clearly demonstrated by the time and effort the members committed in serving on Council.

NIDDK Leadership Changes: Dr. Rodgers announced some changes in leadership at NIDDK.

- *Dr. Josephine Briggs*, Director, Division of Kidney, Urologic, and Hematologic Diseases (KUH) has left NIDDK to become a senior scientific officer at the Howard Hughes Medical Institute. Dr. Rodgers commented on the the passion Dr. Brigges exibited about her work throughout her nine-years at NIDDK. Among her acheivements during her tenure at NIDDK Dr. Briggs helped establish the National Kidney Disease Education Program which is designed to make effective therapies for kidney disease more broadly recognized and used. Dr.

Rodgers related that Dr. Briggs was a very effective spokesperson for KUH programs and recruited top scientists to guide the Division's education and research programs. Dr. Rodgers also related some of Dr. Briggs' successes in trans-NIH activites including her work on the NIH Roadmap and her leadership roles in NIH's Rapid Access to Interventional Development (RAID) program and on the trans-NIH Zebrafish Committee.

Dr. Robert Star has been appointed as Acting-Director of KUH until a permanent replacement is selected. Dr. Rodgers commented that Dr. Star, a nephrologist, is a dedicated physician-scientist who has been a senior scientific advisor in the KUH Division since 1999. In addition, Dr. Star has been a senior advisor for clinical research in the NIH Office of Science Policy and was engaged in many levels of the NIH Roadmap initiative, especially the Re-engineering of Clinical Research Enterprise component.

Mr. David Mineo, NIDDK's Grants Management Officer (GMO) announced his retirement effective October 2006. Mr. Mineo joined NIDDK as GMO in 2001 after being recruited from the University of Georgia where he was Director of Sponsored Programs. Overall, Mr. Mineo has 33 years of federal service. Prior to leaving the government to join the University of Georgia he was the GMO at the National Institute of Environmental Health Sciences. In total Mr. Mineo worked at six NIH institutes and centers over his career. Dr. Rodgers commented that Mr. Mineo and is one of the most highly regarded managers at NIH and because of this he has regularly been called upon for special duties. For example he was tapped to be Acting Director of the trans-NIH Division of Extramural Activities Support when the organization was first implemented. More recently he served as Acting Director of NIDDK's Consolidated Acquisition Center when that organization was first implemented as a result of restructuring of the NIH contracts function. While Mr. Mineo is retiring from federal service he will not be retiring per se, but rather will be joining the Academic Medical Centers practice at Bearing Point as a senior manager.

NIDDK Staff Member Retirement: Dr. Rodgers noted the retirement of Dr. Ned Feder on September 1, 2006. Dr. Feder served at NIH for 41-years, both as a scientist and more recently as a science administrator. He spent the last 15-years in NIDDK's Review Branch where he served as a Scientific Review Administrator.

New NIDDK Staff: Dr. Rodgers recognized several new NIDDK staff members:

- *Dr. Elizabeth Wright* joined NIDDK as a Senior Scientific Advisor and Program Director for Biostatistics. This is a newly created position within the Office of the Director designed to enhance NIDDK's extramural and intramural activities. The position requires expertise in trial design, statistical methods, data analysis and data coordinating center function. Dr. Wright earned a Ph.D. in statistics and has over 30 years experience as a senior statistician. She has served as principle investigator of a data coordinating center for NIH-sponsored multi-center clinical trials. Dr. Wright has worked at George Washington University in Washington DC and more recently worked at the New England Research Institute in Boston.

Dr. Christine Hunter has joined NIDDK's Division of Diabetes, Endocrinology and Metabolic Diseases (DEM) and will be in charge of developing the division's behavioral research portfolio, as well as providing psychological and behavioral expertise for those clinical trials implementing behavioral interventions. Dr. Hunter earned a Ph.D. in clinical psychology from the University of Memphis in 1997 and then served in the United States Air Force on the Armed Force Surgeon General's staff. During that time she completed a fellowship and achieved board certification in clinical health psychology. Dr. Hunter's primary interest and expertise are focused on weight loss, the prevention of weight gain, tobacco use cessation, and reduction of problem alcohol use. She's also had experience in health behavioral changes as a clinician, as a researcher, and as a population-based program manager.

The Grants Management Branch (GMB) also recruited several new staff members including:

- *Maurice Lee*, a recent graduate of the OPM Presidential Management Fellows Program.
- *Lieutenant Helen Hunter*, a member of the Commissioned Corps, who recently joined GMB from the DHHS Office of Minority Health.
- *Ms. Christine Coraz*, a recent graduate of DHHS Emergent Leaders Program.
- *Mr. Edward (Gene) McGeehan*, recently joined GMB from the Agency for Healthcare Research and Quality (AHRQ). Mr. McGeehan was previously a grants specialist at NHLBI.

II. CONSIDERATION OF SUMMARY MINUTES OF THE 171st COUNCIL MEETING

A motion was made, and unanimously passed by voice vote, to approve the summary minutes of the 171st NDDK Advisory Council (May, 2006) as submitted.

III. FUTURE COUNCIL DATES

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

February 21, 2007

May 30-31, 2007

September 19-20, 2007

February 20-21, 2008

May 21-22, 2008

September 24-25, 2008

IV. ANNOUNCEMENTS

Dr. Brent Stanfield, Director, Division of Extramural Activities

A. CONFIDENTIALITY AND CONFLICT OF INTEREST

Dr. Stanfield 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.

B. OTHER ANNOUNCEMENTS

Working Group on Extramural-Intramural Collaborations In Patient-Related Obesity Research

Dr. Stanfield reported that in early 2005 the NIDDK Advisory Council established a temporary Working Group to facilitate extramural-intramural collaborations in patient-related obesity research. The Working Group's specific focus has been on collaborations to utilize the new facilities in the trans-NIH Obesity Clinical Research Center being built in the Clinical Research Center. The Working Group roster includes four present or past members of the NIDDK Advisory Council, each of whom is an expert in obesity research. These Council members include Dr. Robert Eckel, Dr. Jeffrey Flier, Dr. Rudolf Leibel, and Dr. Allan Walker. The group is presently chaired by Dr. Griffin Rodgers.

Based on a series of meetings with NIH intramural scientists and tours of the Obesity Clinical Research Center, the Working Group developed a number of principles to support extramural-intramural collaborations. These principles now will be conveyed to a trans-NIH forum, thus completing the work of the NIDDK Advisory Council Working Group.

Dr. Stanfield stated that the NIDDK Advisory Council will be kept abreast of developments in this area and thanked the members of the Working Group for their contributions.

Loan Repayment Program

This year there were a total of 264 applications to the NIDDK Loan Repayment Program. NIDDK was able to make 72 awards totaling nearly $4 million.

V. REPORT FROM THE NIDDK ACTING DIRECTOR

Dr. Griffin Rodgers, Acting Director, NIDDK

Budget Update

Dr. Rodgers reported that the President's proposed budget for NIH for FY 2007 was $28.6 billion—essentially the same as the FY 2006 appropriation. This proposal includes an increase of $110 million for development of projects related to biodefense. To offset this increase in biodefense project spending the proposal slates individual institutes to receive budget decreases between 0.5% and 0.8%. The President's request for NIDDK is $1.69 billion in FY 2007, representing a decrease of approximately 0.6% compared to FY 2006. While the House and Senate have both completed appropriation subcommittee meetings, neither has a final action from the full chamber. The House proposal is precisely the same as the President's recommendation. The Senate level for NIDDK, however, is $1.7 billion, an increase of approximately $13 million above the President's request, which represents a 0.2% increase above the institute's FY 2006 appropriation. Full action by both chambers will be followed by conference committee action and subsequent adjustments for final appropriations. Dr. Rodgers then mentioned that the dynamics of the election year make a resolution for 2007 more difficult than usual and because of this it is nearly certain that NIH will operate at least part of the year under a continuing resolution.

Dr. Rodgers then reported that during the budget hearing process this year there was some report language from both the House and Senate. This report language recognized a wide range of NIDDK programs including the Action Plan for Liver Disease Research and the National Diabetes Education Program. The reports also made special requests for reports in the field of glomerular disease and hematology research. Other language for NIDDK includes a request for a comprehensive report on current obesity research and an accounting of the activity of the NIH Obesity Research Task Force.

Regarding NIDDK's budget status for FY 2007:

- Dr. Rodgers commended program staff for collaborating only on a small number of necessary initiatives which will help maintain a reasonable payline for research project grants.
- Dr. Rodgers also reported that unless there is a substantial change in the NIDDK appropriations total, the institute will adopt the President's policy requiring a one percent cut in non-competing research project grants.
- National Research Service Award program awardees are slated to receive no stipend increases and no other increases for tuition or training in FY 2007.

From NIDDK's research career mechanism (K awards) $1.35 million will be used to support 15 of the new K99/R00 Pathways to Independence Awards pending the receipt of meritorious applications.
In FY 2007 NIDDK will be contributing $2.9 million to a trans-NIH gene and environment health initiative.
NIDDK's contribution to the NIH Roadmap in FY 2007 will rise from $15.2 million to $20.5 million.

Dr. Rodgers concluded his budget remarks by stating that in the process of formulating the NIH budget for FY 2008 there were a number of programs selected from NIDDK that will be represented as initiatives in the final budget proposal. While Dr. Rodgers was not at liberty to discuss these programs or the budget envelope he assured Council that the process of selecting initiatives to put forward was extremely competitive and NIDDK did very well.

Advances and Emerging Opportunities in Type 1 Diabetes Research: A Strategic Plan

Dr. Rodgers announced that in August 2006 *Advances and Emerging Opportunities in Type 1 Diabetes Research: A Strategic Plan* was published. The plan was developed under the auspices of the statutory Diabetes Mellitus Interagency Coordinating Committee with broad input from a number of scientific researchers external to NIH as well as lay persons representing patient interests. There are two versions of the Strategic Plan available at http://www.T1Diabetes.nih.gov/plan. Version I is tailored to patients and the public. Version II is for the scientific community. A third publication includes a summary and recommendations.

Redesign of the NIDDK Website

Dr. Rodgers announced that the NIDDK has completed phase I of a three-phase redesign of its website. NIDDK is striving to make its web-based publications as user friendly and useful as possible. Highlighting research training, funding opportunities for NIDDK's investigator community, and health information have been major focuses of the redesign. In the two remaining phases of redesign NIDDK looks to incorporate new technologies to facilitate delivery of information and to further modernize and improve the artwork and layout of the website.

VI. UPDATE: LOOK AHEAD

Dr. Rena Wing, Chair, Look AHEAD Trial, Professor of Psychiatry and Human Behavior, Brown Medical School, Director, Weight Control and Diabetes Center, Miriam Hospital

Overview

Dr. Wing began her presentation by explaining that Look AHEAD is a multicenter, randomized clinical trial examining the long-term effects of an intensive lifestyle

intervention program on cardiovascular morbidity and mortality in overweight or obese persons with Type II diabetes. The study is funded primarily by the NIDDK with several co-sponsors.

Dr. Wing commented that weight loss is strongly recommended for overweight patients with diabetes because short-term studies—typically following outcomes for less than a year—have documented that weight loss will improve their lipids, blood pressure, insulin sensitivity, and glycemic control. However, there are few data on the long-term benefits of weight loss in these individuals. There have been no randomized trials to determine whether there are long-term positive or negative health consequences to intentional weight loss in overweight patients with diabetes. This is due in a large part to the difficulty of producing weight loss and then maintaining the loss. The reason that this is such an important topic is that observational studies suggest that weight loss, and potentially weight loss and then weight regain, or weight cycling, may actually be associated not with positive improvements in diabetes control, morbidity and mortality, but actually may exacerbate morbidity and mortality.

Look AHEAD was designed as a randomized clinical trial to evaluate the health effects of interventions designed to produce weight loss in 5,145 individuals with Type II diabetes, recruited from 16 clinical centers across the United States. The individuals were randomly assigned to either an intensive lifestyle intervention or diabetes support and education, which is the control group. The primary hypothesis of the trial is that the incidence rate of a composite outcome measure that includes cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke would be reduced over the 11.5 years of follow-up in the lifestyle intervention group compared to the diabetes support and education control group.

The trial also looks at many other outcomes including all cause mortality, cardiovascular disease risk factors, costs and cost effectiveness, diabetes control and complications, general health, hospitalizations, quality of life, and psychological outcomes. Dr. Wing also reported that there are several ancillary studies connected with Look AHEAD and these ancillary studies will allow more focused investigation of other specific changes for subgroups of the population. For example, one ancillary study will investigate sleep apnea in these patients.

Intervention and Control Groups

Dr. Wing explained that the lifestyle intervention was designed to be intensive with the hope that excellent weight losses could be achieved in the intervention group. Lifestyle intervention patients were seen weekly for the first six months in a combination of group meetings and individual sessions. The goal for all individuals in the intervention group was a weight loss of ten-percent of body weight and study-wide the goal was an average weight loss of seven-percent amongst intervention patients.

Those patients in the intervention group weighing less than 250-pounds were advised to eat either 1200 to 1500 calories per day. Those patients weighing more than 250 pounds

were advised to consume 1500 to 1800 calories per day. The study recommended that 30-percent of patients' calories come from fat. To help individuals lose weight meal replacement products such as SlimFast and Glucerna were suggested based on several studies indicating that adding meal replacement products to the diet improves initial weight loss results. Structured menu plans were also provided to patients based on data suggesting that this would also promote weight loss.

Physical activity recommended for the intervention group was similar in intensity to brisk walking and for most participants the activity was walking. Participants were encouraged to gradually increase their exercise until they were doing 175 minutes per week of physical activity. Pedometers were also distributed to patients to encourage walking 10,000 steps per day.

Dr. Wing reported that the diabetes support and education or control group was seen three or four times per year. The meetings were primarily to promote retention within the study. Covered at the meetings were health education topics including diet and exercise. The diabetes support and education group also received one session per year of social support.

Baseline Characteristics

Dr. Wing reported that amongst approximately 5,000 participants in the study roughly 60% are women and 37% of participants are from minority groups. The average age of participants is 58.6-years. Sixteen-percent of participants are insulin users. Fifteen percent of participants had a prior history of a cardiovascular event.

To be eligible for the intervention individuals had to have a Body Mass Index (BMI) greater than 25 or greater than 27 if the patient was an insulin user. Mean BMI at the beginning of the study was approximately 36.

One-Year Results

Dr. Wing presented the one-year results for changes in weight, fitness, and cardiovascular risk factors in the lifestyle compared to the control group. A manuscript describing these results is currently under review.

Ancillary Studies

Because there were many things that could not be funded within the trial, ancillary studies that do not require the entire cohort were funded separately. For example, additional studies involving more intensive measures on cohorts to look at the effects of the study's weight loss intervention on sleep apnea, sexual dysfunction, and urinary incontinence, are being performed. An ancillary study has also been funded to perform some genetic analyses and the study is storing samples for other genetic analyses.

VII. ADVISIORY COUNCIL FORUM – PART 1

Supporting New Investigators

Dr. Rebekah Rasooly, Deputy Director and Genetics and Genomics Program Director, Division of Kidney, Urologic, and Hematologic Diseases, NIDDK

Dr. Rasooly began her presentation by thanking her NIDDK colleagues who served on the New Investigator Committee, which she chaired, for their work considering how the Institute might better support New Investigators. New Investigator Committee members included Drs. Mary Horlick, Jim Hyde, and Phil Smith. Dr. Rasooly also recognized NIDDK employees Jonathan Dine, Will Williams, Teresa Lindquist, and Beth Paterson for their assistance in data development and verification.

Background and Considerations

Dr. Rasooly reported that the committee began its work by considering the primary sources of funding for new principal investigators (NIs) within the NIDDK extramural program. Analysis demonstrated that new investigators are supported primarily through two mechanisms. The first is career awards or "K" awards, which are mentored salary awards. The second is the R01 grant. Overall, approximately 75% of dollars awarded to NIs come from K or R01 awards. Funding trends show that recently R21 grants to new investigators have been increasing, but still constitute a relatively small fraction of the support NIDDK gives to NIs. Further analysis demonstrated that NIs receive approximately 20% of new competing dollars each year.

Dr. Rasooly presented data demonstrating that while NIDDK gives NI R01 applications a two percentile-point advantage when they are considered for funding and also gives NI applications extra consideration for special emphasis funding, in many years they still do not have the same success rate as experienced investigators in obtaining R01 grants. In addition, Dr. Rasooly reported that while NI R01 applications scoring in the "outstanding" range keep pace proportionally with experienced investigator applications, the proportion of NI R01 applications that score in the "excellent" to "good" range falls off considerably compared to R01 applications from experienced investigators. Furthermore, NI R01 applications are unscored much more frequently than experienced investigator R01 applications.

Regarding applications for the R21 mechanism, Dr. Rasooly reported that approximately half of R21 applications are submitted by NIs—proportionally much higher than what is observed in applications for the R01 mechanism. However, the NI success rate for the R21 is much lower than for experienced investigators and this is even with the special consideration given to NIs. Indeed, approximately 40% of NI R21 awards were made with special emphasis funding and even with this, NIs are not achieving that same success levels as established investigators. Furthermore, Dr. Rasooly emphasized that the R21 is not the path to an R01 that some may have hoped. For both NIs and experienced investigators, only relatively small fractions were able to convert the R21 to an R01 in a reasonable period of time.

Dr. Rasooly commented that it is fairly clear that NIs face a number of challenges in getting their applications funded including being new to the research community, having limited preliminary data, and inexperience in grant writing and formulating research plans. There is no dispute that experience helps.

Dr. Rasooly then made the point that NIDDK values retention of investigators starting their research careers. As a society and as an Institute, she noted, we make a huge investment in training NIs and they probably have new ideas and should be given an opportunity to prove themselves.

New Investigator Committee Recommendations

Dr. Rasooly related that the New Investigator Committee considered as a first working principle that the R01 is the appropriate starter grant and a key to launching an independent career. In contrast, the R21 has too little time and money associated with it. Indeed, the data suggest that obtaining an R21 does little for those applying for a subsequent R01. A second working principle is that NIs cannot be considered established until they are awarded their first renewal and some attention needs to be focused on this transition.

Dr. Rasooly then reported that these two principles led the group to some very specific recommendations. First, NIDDK should give formal administrative review to all NI R01 applications falling within ten points of the payline and also give similar consideration to all first-time renewals of NI R01s. Those NI applications falling outside the payline which show merit might be considered for special emphasis funding or alternatively may be considered for some interim funding using the R56 mechanism to give a small amount of money to NIs to collect pilot data. Put another way, NIDDK should look at NI R01 applications or first renewals of NI R01s and make an affirmative decision one way or another about supporting, in some way, those applications scoring within ten points of the payline. Second, NIDDK should discourage NIs from applying for R21 grants. One way of discouraging NIs from applying for R21s is to retract any preferential treatment of NI applications for R21 awards. It is the committee's hope that implementing this recommendation would reduce the effort NIs focus on R21s and redirect their focus towards the R01 mechanism. Third, NIDDK should enhance the pool of funding for pilot awards. By doing this NIDDK could offer NIs who submit a promising R01 application that did not make the payline, a small one- or two-year award to help them collect preliminary data and/or spend a little more time developing a better revised application. Fourth, the group felt that, in difficult budget times, in order to support as many NIs as possible it may make sense to cap R01s for NIs at a slightly lower cost level. The rationale for this is that NIs setting up a lab should typically have some start-up funds from their institutions and NI fixed costs are relatively lower because, for example, they will not normally have a large established staff. Finally, the committee recommended that NIDDK should provide services for NIs in terms of publicizing our policies and encouraging mentoring. NIDDK has regular meetings for its K awardees that are run by training staff and these could be expanded to include R01 NIs. Program and training staff could also work with review colleagues to ensure that NIs have an opportunity to observe

study sections, perhaps visiting once as a guest reviewer. The institute should also point NIs toward various sources of guidance for career development, grantsmanship and other skills that NIs need to move their careers forward.

Dr. Rasooly then concluded by stating that New Investigator Committee recommends the K and R01 mechanisms as most appropriate for supporting NIs. The committee recognizes that it is difficult to obtain a first R01 even with various types of assistance that the institute is presently offering. To move toward the goal of better supporting NIs the committee recommends enhancing interim funding and career development opportunities for NIs.

Comments by Assigned Discussants

Dr. Sherman commented that she solicited input from colleagues and they agreed that the R01 is the best mechanism to launch a career. However, the problem for NIs is getting enough data together to be competitive. Some NIs receive a nice start up package including several years of salary and other resources and these investigators may be in a better position to compete for an R01. Other investigators need a stepping stone, which the R21 has been. Dr. Sherman indicated that what is needed is flexibility because there are many different scenarios for NI. Dr. Sherman continues that she was not familiar with the R56 mechanism but if it could replace the R21 in terms of being a flexible, short term source of money so NIs can gather data that this would be good news. Dr. Sherman then indicated that something that may help the competitiveness of NI applications is the possibility of allotting time within study sections to review NI R01 applications together. Dr. Sherman suggested that is often difficult for reviewers to change their mindset and appreciate the merits of NI applications when they are reviewed in the context of R01 applications from experienced investigators.

Dr. Abkowitz stated that she felt strongly that the R21 mechanism is not the right mechanism for NIs and her reaction is bolstered by the data indicating that an R21 grant was not especially effective in moving an NI to R01 support. Dr. Abkowitz indicated that she did consider the R21 an appropriate mechanism for innovative science, creative ideas, and novel hypotheses and that preserving the mechanism with a clear focus during hard times was important for NIDDK. Rather than mix the focus of the R21 Dr. Abkowitz indicated support for the committee's recommendation to use the R56 to address the needs of NIs. Dr. Abkowitz did express concern that capping NI R01s may be viewed by some NIs as a penalty that may result in some NIs applying to other institutes but she conceded that this may be offset if the institute made five-year NI R01 awards. Dr. Abkowitz also commented that she thought the committee's consideration of the first competitive renewal by NIs as extraordinarily insightful. While funding may take place in three- to five-year cycles science does not always follow this timeline perfectly and while a NI R01 grantee may be finishing up their studies at the end of the grant period they may not have had time to collect all the preliminary data that they need to support an application for the next five years of solid work.

Dr. Dubois agreed that the R21 mechanism is not an ideal way to fund NIs. Dr. Dubois stated that it is easy to put the onus of the NI problem on NIH but NIs are often not putting in competitive applications and suggested this may be resolved in part by institutions doing a better job mentoring and nurturing their NIs so that they submit more competitive applications.

Council Questions and Discussion

If you considered all of the NI grants ten points above the payline what would the amount of money be if you funded all of those on an R56? What would happen if you compared this amount of money spent on NI R21s? Dr. Rasooly indicated that the New Investigator Committee recognized that funds are limited. It turns out that in a financial analysis of the extreme case where all R21s to NIs are eliminated and all scored NI R01 applications are given an R56, there would still be a little money left over. Dr. Rasooly emphasized that these are extreme scenarios mentioned only to demonstrate that the institute can recoup the money to support the New Investigator Committee's recommendations in a way that won't eat into the payline, which she agreed would be untenable in these hard times.

A NI R01 awards fixed cap presumes that one size fits all. Some NIs may be real stars with exciting ideas and such a cap may ensure a slow start. Does this bring NIDDK back to problems associated with the R29 mechanism? Dr. Carol Haft responded that the point is well taken and an absolute cap was not being considered. The award would depend on the research being proposed. For example, a clinical study might have patient care needs that would change the cost of the award. On the other hand, everyone wants to be the exception and this will not work either if we are going to support more NIs in hard times. Dr. Phil Smith commented if we fund more NIs it increases the odds that we will capture the good ones and continue them. The Institute wants to make sure we can fund a good number of NIs without cutting into the payline—a tension that we have to balance.

The guidelines from the New Investigator Committee indicated that "Each NI R01 application within ten points of the payline should receive formal administrative consideration". The statement is not that these applications "will" receive formal consideration. The same is true for the language regarding formal consideration of first renewals. This should be address so that the requirements of administrative review for NI applications scoring within 10 points of the payline are codified in a way that the review actually happens.

Do we need to be more explicit on some level regarding whether the potential advantage to NIs comes exclusively post-review by staff as opposed to something that goes on in the study section? Dr. Stanfield commented that we can control what NIDDK staff does after review. We cannot control what happens in the study section. CSR's policy is that each NI application will be identified and reviewed in the context of the career stage of the applicant. For example, it would not be appropriate to expect copious preliminary data in a NI application, but appropriate training is a valid consideration. The extent that study

sections do this is quite variable. To attempt to change this would require a broad NIH discussion.

VIII. SCIENTIFIC PRESENTATION

***Dr. Nancy Andrews, Dean for Basic Sciences and Graduate Studies and Leland Fikes Professor of Pediatrics, Harvard medical School*—"Tipping Iron Balance"**

Dr. Andrews gave a presentation focusing on the disease hemochromatosis and modifier genes that affect iron balance (see attached).

Andrews.pdf

IX. REPORT FROM NIH DIRECTOR

***Dr. Elias Zerhouni, Director, National Institutes of Health*—"NIH in the Post Doubling Era: Realities and Strategies for the Future"**

Dr. Zerhouni gave a presentation on the dynamics that have created substantially more demand for NIH funding than present budget realities can accommodate and NIH strategies for balancing and managing competing needs (see attached).

Zerhouni.pdf

X. ADVISORY COUNCIL FORUM – PART 2

NIDDK's Use of the R21 Grant Mechanism

Dr. Carol Renfrew Haft, Senior Advisor for Cell Biology and Associate Director for Grants Administration, Division of Diabetes, Endocrinology and Metabolic Diseases, NIDDK

Dr. Haft began by reminding Council that her presentation was a follow-up to a presentation by Dr. Chris Ketchum at the May 2006 meeting. In that presentation Dr. Ketchum reported that NIDDK's R21 program had grown seven-fold since it was introduced in 2000, a rate that considerably outpaced the growth of the program for most other NIH institutes. Reviewing the data, Dr. Haft established that the vast majority of growth in the NIDDK R21 program was in response to Program Announcements (PAs) and not specific Requests for Applications (RFAs) that had some pool of money set-aside to pay a certain number of grants. Indeed, Dr. Haft reported that NIDDK presently had approximately 30 different PAs soliciting R21 applications. This raises the question, regarding what NIDDK is trying to accomplish with its R21 mechanism. Dr. Haft pointed out that NIDDK's lack of clarity regarding the focus of the program creates confusion among applicants, among staff advising applicants, and review panels reviewing R21 applications assigned to NIDDK. Dr. Haft also pointed out NIDDK had

increased the number of R21 awards substantially over time and this increase may have been driven, in part, simply by the number of R21 applications NIDDK received.

In response to a request by Council for further consideration of these issues, Dr. Haft reported that NIDDK charged a committee that she chaired to define the mission of the NIDDK R21 program. The committee was also charged with recommending 1) the proportion of the budget that would be appropriately used to support the NIDDK R21 program given any refocusing that is recommended and 2) ways NIDDK could help ensure that staff and the research community are informed of any changes regarding how NIDDK will use the R21 mechanism in the future.

Dr. Haft recounted that the committee in general agreed that the R21 mechanism should not be all things to all people. The committee agreed that the primary focus of the mechanism should be highly innovative, potentially paradigm shifting, high pay-off types of studies. Other areas that are appropriately supported by the R21 include tool development and some high-impact discovery projects, and also pilot clinical studies and trials.

Dr. Haft reported that the committee strongly recommended against using the R21 as "mini R01s". The committee also recommended that new investigators should be strongly discouraged from applying for R21 grants except under unique circumstances—e.g., if a new investigator has a magnificent tool that they are ready develop. To fill the gap that this new policy may create, new investigators would be encouraged to apply for R01 grants and the R56 mechanism and special emphasis funds would be used help promising applicants as recommended by the New Investigator Committee (see Advisory Council Forum—Part 1).

Regarding the 30 currently active NIDDK R21 PAs, Dr. Haft conveyed that the committee proposed sun-setting all NIDDK basic science R21 PAs after the October-November 1 receipt date. These PAs would be replaced by NIDDK joining the NIH general R21 PA in time for the February 1 receipt date. Dr. Haft commented that this PA is ideal because it captures very nicely the mission goals the committee recommended for basic science research projects supported by the R21 mechanism. In addition, NIH is trying to unify the way the R21 mechanism is being handled, especially to relieve some of the stress on the referral and review system created by disparate approaches to the R21 program amongst institutes. Besides NIDDK, NIGMS, NCCAM, NCMHD, and NCI are the only institutes that have not opted to join the general PA to date. With NIDDK joining the general NIH R21 PA it is hoped that confusion within review panels will be reduced further and reviewers will be better able to focus on the appropriate criteria for R21s applications submitted to the general NIH PA. This will not only support NIDDK's mission but also the missions of the other institutes that have joined the general PA. R21 applications submitted under a PA to be sunset that are either under consideration presently or have been received (e.g., for February and May Council) will be considered. If an investigator is not successful, he/she would have to determine if the amended application is appropriate to submit under the general PA. By taking this approach it is hoped that NIDDK will begin the process of educating researchers about how the R21

program will be focused in the future while maintaining the applications that are currently being processed.

Dr. Haft related that categories of PAs that the committee agreed should not be sunset include R21s for 1) pilot clinical studies and clinical trials and 2) secondary data analysis. These areas do not contribute large numbers of applications or grants and staff feels that they are important areas to maintain and that the R21 mechanism serves these areas well.

Regarding the size of the R21 program, Dr. Haft reported that the committee considered it important to designate a set pool of money for R21 grants and not allow the number of applications scoring within a given range drive the number of R21 grants funded—and thus the budget for the program. A pool of money would be designated and decisions to fund applications would be dependent on a number of criteria including program goals, programmatic priorities, and score of the application. Not all applications within a score range would be automatically funded. Furthermore, new investigators would not receive special consideration for R21s.

Dr. Haft concluded by reporting that the R21 Committee considered it essential to use the NIDDK website to inform the research community about the mission of the R21 program. The committee recommended developing a new R21 webpage that informs researchers about the focus of the program and also includes information about the success rate realities for R21 and R01 applicants to help dispel misinformation about the relative ease of receiving an award for an R21 compared to an R01. The website would also inform the research community about special considerations being given to R01 applications from new investigators.

Comments by Assigned Discussants

Dr. Alpern indicated that he thought the committee's plan was excellent. He commented that refocusing NIs away from R21s is an especially good idea because the mechanism should not be used to generate preliminary data for standard R01 applications. He warned however that the issue of whether or not R21 grants are easier to get than an R01 is not answered because R21 applications may have been self selected by researchers as proposals that would not do well in R01 competitions. Reviewers may be more enthusiastic about a two-year proposal than a five-year proposal if they have concerns. Dr. Alpern then commented that it is important for NIH to be clear in its language regarding the R21 program that "high risk" is not confused with "high impact". NIH is willing to accept risk for potentially high impact research, but high risk in and of itself has no merit.

Dr. Flier indicated that the discussions regarding the R21 mechanism over the past two Council rounds raised a number of issues that he was previously little aware of and the way staff had recommended resolution to the issues has been generally very well done. Dr. Flier commented that he was very impressed with the analysis and recommendations resulting from the analysis and any comments that he might have would be very small modifications around the edges. Dr. Flier commented that he agreed with the New

Investigator Committee's recommendation that NIs should not be prohibited from applying for an R21. He further agreed that new investigators should be provided with information indicating why the R21 may not be the best mechanism for them. If an NI has an appropriate R21 project, they should be given full consideration but no advantage. Dr. Flier then mentioned his concern about review of R21 applications. He commented on the need for a mechanism that awards a limited number of grants to pursue potentially high impact projects that are not absolutely sure things but are sufficiently exciting that serious reviewers agree that the science is worth pursuing despite some risk. The question is how to change the mindset of study sections, which are often extremely risk-averse, to change their way of thinking?

Dr. Eckel thanked the New Investigator Committee for its work, agreed that the R21 program has historically not accomplished what it was set out to do, and commended the committee on reaching outstanding conclusions. Dr. Eckel then commented that the R21 program has a basic science focus and using it for pilot clinical trials and clinical studies and also for secondary data analyses may not be the best use of the mechanism. A separate mechanism may better serve these areas. Dr. Eckel also commented that new investigators should be discouraged more firmly from applying for R21 grants than the committee has recommended. Given the nature of a two-year award, Dr. Eckel felt the chances for a new investigator being appropriate for an R21 grant is low. Dr. Eckel concluded that overall, the Committees recommendations are generally right on target.

Council Questions and Discussion

In the past, what proportion of R21 awards were focused on basic vs. clinical research? Dr. Haft responded that she did not have these data available to her at this time and that such an analysis would take a thorough grant by grant analysis. Dr. Haft indicated that it was her impression that a large proportion of R21 grants that are awarded are for basic science projects. However, there are specific R21 program announcements soliciting applications for pilot clinical trials and clinical studies and NIDDK planned to retain these.

Study sections often have a hard time of getting out of an R01 review mindset even when other types of applications are grouped and reviewed together. Perhaps reducing the length of the application and number of figures for an R21 would limit reviewer expectations and help correct this problem? Dr. Stanfield commented that changing page limits on grant applications is beyond NIDDK's purview. Dr. Smith then commented that the present R21 application has a 15 page limit, which is a lot but different from the R01 application. Dr. Smith also noted that he is participating on an NIH committee that is considering abbreviating the length of the R01 application.

One of the recommendations of the New Investigator Committee is to continue to use the R21 for feasibility studies of clinical research and clinical trials. These proposals may require very special groups of reviewers to consider the proposals properly. Dr. Stanfield indicated he was aware of this concern in general and reported that NIDDK has successfully negotiated with the Center for Scientific Review (CSR) to place applications

coming from clinical pilot and feasibility study program announcements into special individual review panels and not into regular standing study sections. Dr. Stanfield also conveyed that NIDDK program directors have reported that they have been engaged in helping select reviewers for these panels and that CSR is generally working well with NIDDK staff.

XI. UPDATE ON REPOSITORIES AND CONCEPT CLEARANCE FOR RENEWAL OF NIDDK CENTRAL REPOSITORY CONTRACTS

Dr. Rebekah Rasooly, Deputy Director and Genetics and Genomics Program Director, Division of Kidney, Urologic, and Hematologic Diseases, NIDDK

Dr. Rasooly began by recounting that NIDDK's repositories were established three years ago using the contract mechanism. There are three repositories. The first is a biosample repository, which is in essence a big room full of freezers that stores samples. The second repository is a database archive that also serves as a de facto coordinating center for all three repositories. The third repository is a genetics repository at Rutgers University that immortalizes cell lines, prepares DNA, and does other kinds of specialized genetics activity in support of NIDDK's large-scale multi-site clinical trials.

The scope of the repositories project is large and requires considerable financial ($22 million over five years) and staff time commitment. Dr. Rasooly mentioned that her point person role with the repositories is supported by colleagues in all three programmatic divisions and contracts staff, as well as a new full-time repository specialist.

Dr. Rasooly commented that having central storage for samples from multi-site studies does a number of good things for the Institute from a research perspective. Samples are stored under uniform conditions, access to the samples is simplified for all sorts of future studies, and databases will be maintained in a live and accessible format without being dependent on Data Coordinating Center maintenance.

Currently there are nearly 500,000 samples being stored at the two repositories. Dr. Rasooly reported that study coordinators like having a central repository. Mailing the samples does not cost the study anything and shipping materials and tubes in special configurations are provided at various times depending on the study's needs. Studies do not lose control of their samples—the repositories do not take the materials from the study, they just store the materials. Major HIPAA issues are simplified because the repositories do not accept any protected health information. In addition, the repositories can offer consultation on activities including how to collect, prepare and store samples. Dr. Rasooly commented that each study is treated as if they are the only study that the repository is handling inasmuch as there has been enormous customization and personalization of services depending on what the study needs.

Dr. Rasooly then mentioned that NIDDK has informed other Institutes at NIH and also advocacy groups sponsoring research that by application NIDDK would consider

allowing them to contribute samples and data to the repository, provided a cost recovery agreement can be struck and other kinds of criteria can be met.

Although more than 25 studies are contributing to the repositories, only some have passed the proprietary period and are therefore being made available to outside researchers. Presently there are approximately 8 datasets that are available for distribution and three large studies for which there are sample sets currently available and which are being distributed. Dr. Rasooly explained that there are guidelines for researchers to apply for access to data and samples. Data requests go through relatively streamlined review with the goal of making data available or deny the request within two- to three-weeks. Decisions regarding sample requests are more difficult and it takes approximately six weeks to turn them over. For renewable samples the bar is set relatively low for release. Requests for non-renewable samples are scrutinized much more carefully. Presently there are approximately 70 to 100 people who have agreed to serve as data request reviewers. There is a permanent group for reviewing requests for access to samples and this group is getting larger so the burden on any one reviewer is not too great. To date there have been ten requests for access to data and only one of these applications has been denied because an IRB was lacking and there was no possibility of getting an IRB. There have been seven requests for samples and data and three of these have been denied.

The repositories have an external steering committee that meets once per year. The last meeting of the advisory committee was May 2006 and the topic of renewing the repository contracts was discussed. The contracts end in July 2008 and because the contracts process is so lengthy now is the time to begin planning renewal. The advisors have recommended proceeding with a full and open competition for the contracts, soliciting bidders from across the country. The advisory committee also recommended that input be received from across the community in developing statements of work to ensure that the new contracts or contract renewals meet NIDDK's needs. Dr. Rasooly concluded her presentation by asking for Council's endorsement of the external advisory committee's recommendations.

Council Questions and Discussion

Is there any stipulation for reciprocity from individuals who use either data or materials to deposit back the information to the repository? Dr. Rasooly explained that any time data are generated from samples there is an obligation to reposit the data within a year of generating it. In contrast, there is no mechanism for accepting new analyses on existing datasets and therefore there is no requirement to submit these data.

What are the rules regarding industry access to samples? Have issues such as publication rights been considered? Does the Institute have any capacity to mandate review of publications to ensure acknowledgements are appropriate and data are complete? Dr. Rasooly answered that a distribution agreement must be signed before samples are released and these agreements mandate that the source of the samples and data are acknowledged. Regarding review of data, Dr. Rasooly indicated that data are

going to be interpreted and from time to time individuals who are doing the interpretation will make mistakes.

Is there some type of evaluation process that assesses the cost and benefits of retaining samples? At what point is a decision made that samples are no longer useful? Dr. Rasooly indicated that this is one of the largest concerns of everyone involved with the repository—that you keep building the repository bigger and bigger but are you making it more useful? Dr. Rasooly indicated that she welcomed any thoughts on this matter. The only metrics that would be available currently are requests for access, use, and publications but all this is very thin at this point. Dr. Lazar commented that once the repositories become more mature, goals and metrics should be established and then a later review should be undertaken to ascertain how well the repositories are meeting the goals. Dr. Rodgers also commented that this is an opportunity for NIDDK to use its website and other resources to advertise the availability of these data and samples and what the access policies are.

After asking if there were any further comments Dr. Rodgers indicated that he would entertain a motion to move forward with contract renewal. A motion was made and was carried unanimously by voice vote.

XII. UPDATE: CORP WORKING GROUP

Dr. Sue Yanovski, Co-Director, Office of Obesity Research, NIDDK; Director, Obesity and Eating Disorders Program, Division of Digestive Diseases and Nutrition, NIDDK

Dr. Yanovski began by explaining that the NIDDK Clinical Obesity Research Panel (CORP) is the successor of the National Task Force on Prevention and Treatment of Obesity, which was in existence from 1991 through June 2003. CORP is composed of leading obesity clinicians and researchers and is charged with providing information to the NIDDK Advisory Council on important clinical research needs, including the relative priority and cost of these needs. CORP also serves in a role in overseeing NIDDK's Weight Control Information Network.

Organizationally, CORP is placed under the auspices of the NIDDK Advisory Council and a member of the council serves as a liaison representative to CORP. Presently, the council liaison member is Dr. Bob Eckel.

Dr. Yanovski explained that in 2006 CORP held two meetings in conjunction with the February and September Advisory Council meetings. At its February meeting CORP discussed new initiative concepts, ongoing initiatives, and planned workshops. The September meetings are focused on a single topic and this September the meeting focused on bariatric surgery. The forum included presentations on long-term data on Swedish obese subjects, a study on adolescent bariatric surgery, an update on NIDDK's longitudinal assessment of bariatric surgery which is being conducted as a cooperative agreement, and a talk on hypoglycemia associated with bariatric surgery.

Dr. Yanovski concluded by indicating that she would welcome Council member's input on workshops or initiatives that CORP might develop in the clinical obesity area.

There were no questions or comments from Council regarding this update.

XIII. UPDATE: NIDDK INTRAMURAL PROGRAM

Dr. Marvin Gershengorn, Intramural Program Scientific Director, NIDDK

Dr. Gershengorn explained that giving a brief update on NIDDK's intramural research program is challenging because the program includes 120 independent principal investigators and 60 additional doctoral level scientists.

Focusing first on the Intramural Program budget, Dr. Gershengorn commented that just as the Extramural Program is experiencing hard times so is the Intramural Program. For example, Dr. Gershengorn explained that in the middle of this year the Intramural Program had to reduce laboratory operating budgets by one percent. This was not easy to do because research and plans had been already made. Furthermore, given recent fiscal realities, the 2007 fiscal year was scrutinized very carefully and a decision was made to reduce the number of scientific staff within the Intramural Program. Based on Board of Scientific Councilor reviews and programmatic considerations three laboratories were shut down. In better times reductions would have been achieved through normal attrition (e.g., exits and retirements) but a more proactive approach was viewed as necessary in order to provide sufficient support for programmatic areas considered to be most important over the next few years.

Dr. Gershengorn then discussed extramural-intramural program interactions. He commented that one interaction that has been extremely successful is the Beta Cell Biology Consortium (BCBC). The mission of the BCBC is to facilitate interdisciplinary approaches that will advance our understanding of pancreatic islet development and function with the long-term goal of developing a cell-based therapy for insulin delivery. The scientific goals for the BCBC are to understand the 1) developmental pathways required to produce a fully functional pancreatic islet (beta cell development), 2) mechanisms of beta cell regeneration in adult animals and human islets (beta cell regeneration), and 3) nature of stem or progenitor cells during normal pancreatic development in adult pancreatic islet (stem cell biology). Dr. Gershengorn commented that what he admires most about this consortium is that it has brought together senior investigators from around the world, who are willing to work in an interactive way and share their ideas and findings prior to publication. The BCBC is extremely broad based and includes scientists from the NIDDK intramural program and other scientists from across the United States, Europe and Israel.

Dr. Gershengorn explained that the BCBC meets at least twice per year, with one full retreat where each laboratory has an opportunity to present their most recent research. The meetings provide opportunities for collaborations to be formed and continued. The BCBC has now operated for five years and is presently operating in its first year of four

years of competitive renewal funding (first competitive renewal). Dr. Gershengorn stressed however that the intramural and extramural components are kept completely separate and Intramural Program laboratories that participate in the BCBC operate solely from intramural funds.

Dr. Gershengorn then focused his discussion on the NIDDK Intramural Program response to the Blue Ribbon Panel report that was released approximately two years ago. The Blue Ribbon Panel acknowledged that NIDDK's Intramural Program had an outstanding basic laboratory research program that was very deep. The report highlighted what the program might do to balance the Intramural Programs basic and clinical research efforts. To this end the panel recommended developing an infrastructure that better supports clinical research and to identify a unique clinical research opportunity that NIDDK could move forward on.

Regarding the Intramural Program's response to the recommendation to develop an infrastructure that better supports clinical research, Dr. Gershengorn reported the creation of a clinical research office headed by Terri Wakefield, a registered nurse, who has extensive knowledge of clinical research operations on the NIH campus. The office has also enlisted support of a biostatistician, Libby Wright and is in the process of hiring a second biostatistician to support clinical investigators. The office supports a number of other clinical research associated activities including:

- Coordinating patient recruitment, scheduling, and travel services
- Collecting, processing and cataloging samples in a systematic way with a laboratory staffed with two technicians. The laboratory will also establish assays needed for factors that are not available or not available with high enough quality commercially.
- Regulatory guidance support for investigators

Dr. Gershengorn then commented that one of the areas where the intramural clinical program especially needed support was in the area of bioinformatics. To better support the intramural clinical program a new online database system is being developed that will capture and integrate demographic, physical exam, medications, laboratory tests, etc. and will also generate reports that will be useful for clinical research analysis. This system is being developed in parallel with a more general system that is being set up in the Clinical Research Center and should be functional in March 2007.

Next, Dr. Gershengorn discussed the NIDDK Intramural Program obesity initiative, developed in response to the Blue Ribbon Panel's recommendation that the Intramural Program pursue a unique clinical research opportunity. Dr. Gershengorn explained that the Intramural Program is working to establish a world-class phenotyping center for obese patients. This obesity research initiative involves a number of NIH institutes but NIDDK is the lead institute. The Clinical Obesity Research Initiative Center will be housed in the Mark Hatfield Clinical Center on the main NIH campus. The Center will include a designated patient care unit that has ten private in-patient research beds, an exercise testing laboratory, and a communal dining room. The communal dining room will be next to a computerized food vending distribution center. Patients will be able to

eat whatever they wish but every calorie taken out of the vending machine will be accounted for. There will also be an experimental dining room where researchers can observe patients placed on specific diets and asked to eat in specific ways and a video conference center to enhance interactions with obesity researchers at the NIDDK center in Phoenix and extramural investigators as well. A second component will be a phenotyping unit that is two floors up from the patient care unit. The unit will include three rapid response "respiratory" or "metabolic" chambers, a laboratory that will be able to do body composition testing, and a large-bore MRI, which is housed in the Department of Radiology.

Dr. Gershengorn reported that a major aspect still being worked out regarding the Clinical Obesity Research Initiative Center is developing a mechanism and policy to foster collaborative interactions between the Intramural Program and the extramural community so that investigators from around the country can take advantage of this new resource and participate in studies. Dr. Gershengorn reported that the Intramural Program is working with NIDDK's former Division of Extramural Activities Director, Dr. Robert Hammond, to develop a mechanism, appropriate policies, and a system to review and prioritize proposals. Dr. Gershengorn commented that the present thinking is that the most efficient and effective way to have extramural investigators use the facility is not as if the facility were a service center where patients or subjects are sent but to develop true collaborations between extramural and one or more intramural scientists.

Dr. Gershengorn then asked for any comments or questions.

Council Questions and Discussion

What is the ethnic mix of investigators participating in the program? Are there senior investigators form minority groups or at least junior investigators who can get training and get minority patients involved? Dr. Gershengorn reminded council that Dr. Anne Sumner is an intramural researcher who is studying an African American population. Dr. Gershengorn also commented that the intramural program also is working to recruit a very senior underrepresented minority investigator who would have appointments with NIDDK, NHGRI, and NHLBI. If this recruitment is not successful Dr. Gershengorn indicated that the intramural program will be looking at some junior people as well.

Could you give us an example of how an intramural-extramural collaboration might look that uses the metabolic chamber? While nothing has been implemented, Dr. Gershengorn indicated that there are two models being considered. In one model a service center would be created and patients would be sent to the facility with a prescription and all testing would be performed. Dr. Gershengorn indicated that he was not sanguine that this model would work well. In a model Dr. Gershengorn indicated is more likely to be successful intramural and extramural investigators would collaborate on a clinical protocol and subjects would be invited to and studied at NIH. To enhance these interactions, the extramural scientists would spend some time at NIH.

What is the timetable for completing the metabolic chambers at the Clinical Center? Dr. Gershengorn indicated that the metabolic chambers should be online within the next six to eight months.

The NIDDK Advisory Council Working Group on Extramural-Intramural Collaboration in the NIH Clinical Research Center's Obesity Research Center was hoping to update Council on its activities. What is the status of that group's work? The group has developed a proposal that was brought to the Obesity Task Force. The Obesity Task Force had some concerns about moving ahead too quickly. At this time the revised plan is to have a workshop sometime in the spring of 2007 where approximately 50 extramural investigators will be invited to participate and help consider the practical aspects of how to implement extramural-intramural collaborations and perhaps more importantly determine the priorities for the questions that should be addressed with these collaborations.

XIV. CONSIDERATION OF REVIEW OF GRANT APPLICTIONS

A total of 595 grant applications, requesting support of $127,371,756 were reviewed for consideration at the September 20 and 21, 2006 meeting. Funding for these 595 applications was recommended at the Scientific Review Group recommended level. Prior to the Advisory Council meeting, an additional 922 applications requesting $206,028,371 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 September 20 and 21, 2006 meeting.

XV. ADJOURNMENT

Dr. Rodgers thanked the Council members for their attendance and efforts. There being no other business, the 172nd meeting of the NIDDK Advisory Council was adjourned at 11:40 a.m., September 21, 2006.

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.
Acting Director, National Institute of Diabetes and Digestive and Kidney Diseases,
Chairman, National Diabetes and Digestive and Kidney Diseases Advisory Council