Meeting Minutes
Department of Health and Human Services
Public Health Service
National Diabetes and Digestive and Kidney Diseases
Advisory Council
May 30-31, 2002

I. CALL TO ORDER

NIDDK Director Dr. Allen Spiegel called to order the 159th National Diabetes and Digestive and Kidney Diseases Advisory Council meeting on May 30, at 8:32 a.m. in Conference Room 6, Building 31C, the NIH campus, Bethesda, MD.

Dr. Spiegel made a series of announcements. Dr. Joseph Spence, who was an *ex officio* Advisory Council member representing the USDA, has been reassigned to the Department of Homeland Security. Dr. Earl Harrison will now represent the USDA, and will join the Digestive Diseases and Nutrition Subcommittee of Council. Dr. Richard Goodman, an NIDDK Council member, has been elected to the National Academy of Sciences along with Dr. Bruce Spiegelman, an NIDDK grantee, and Dr. Adriaan Bax, an NIDDK intramural scientist. Dr. Marva Moxey-Mims is the new Pediatric Nephrology Program Director, Division of Kidney, Urologic and Hematologic Diseases. Rochelle Blaustein, J.D., is the new Technology Development Coordinator, Office of Technology Development, NIDDK. Ms. Barbara Merchant, NIDDK Executive Officer, has received the NIH Director's Award for Mentoring.

A. ATTENDANCE – COUNCIL MEMBERS PRESENT

Mr. David Baldridge
Dr. Edward J. Benz, Jr.
Ms. Mary E. Clark
Dr. Richard H. Goodman
Dr. Jeffrey I. Gordon
Hon. Levan Gordon
Dr. Edward W. Holmes
Dr. C. Ronald Kahn
Dr. James W. Kikendall (*Ex officio*)
Dr. Earl Harrison (*Ex Officio*)
Dr. Sum P. Lee.
Dr. John McConnell
Ms. Nancy J. Norton.
Dr. Daniel Porte, Jr. (*Ex Officio*)
Dr. Sandra Puczynski
Dr. Vicki Ratner
Dr. Robert W. Schrier
Dr. W. Allan Walker.
Dr. Rena Wing

Also present:

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

Council members absent:
Dr. Jose Caro
Dr. Carolyn Kelly

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:

Beena Alkolkar, NIDDK;
Syed Amir, CSR;
David Badman, NIDDK;
Michele Barnard, NIDDK;
Terry R. Bishop, NIDDK;
Rochelle Blaustein, NIDDK;
Sharon Bourque, NIDDK;
Josephine Briggs, NIDDK;
Francisco Calvo, NIDDK;
Joan Chamberlain, NIDDK;
Dolph Chianchiano, National Kidney Foundation;
Michelle Cisselle, NIDDK;
Laura Cole, NIDDK;
John Connaughton, NIDDK;
Catherine Cowie, NIDDK;
Florence Danshes, NIDDK;
Jane DeMouy, NIDDK;
Tony Demsey, OD;
Louise Dickerson, ASI;
Linda Edgeman, NIDDK;
Michael Edwards, NIDDK:
Samuel Edwards, CSR;
Thomas Eggerman, NIDDK;
Gayla Elder-Leak, NIDDK;
Jody Evans, NIDDK;
James Everhart, NIDDK;
Richard Farishian, NIDDK;
Robert Fay, NIDDK;
Ned Feder, CSR;
Carol Feld, NIDDK;
Olaf L. Fonville, NIDDK;
Judith Fradkin, NIDDK;
Randi Freudlich, NIDDK;
Joanne Gallivan, NIDDK;
Lisa Gansheroff, NIDDK;
Janet Gregory, NIDDK;
Carol Renfrew Haft, NIDDK:
Barbara Harrison, NIDDK;
Trude Hillard, NIDDK;
Gladys H. Hirschman, NIDDK;
Eleanor Hoff, NIDDK;
Jay Hoofnagle, NIDDK;
Thomas H. Hostetter, NIDDK;
Ann Karen Howard, NIDDK;
Stuart Howards, NIDDK;
Van S. Hubbard, NIDDK;
Donna Huggins, NIDDK;
James Hyde, NIDDK;
Donna James, NIDDK;
Stephen James, NIDDK;
Ann Jerkins, CSR;
Robert Karp, NIDDK:
Mary Beth Kester, NIDDK;
Mushtaq Khan, CSR;
Sooja Kim, CSR;
Katie Kindher, JDRF;
Kathy Kranzfelder, NIDDK;
Krish Krishnan, CSR:
Robert Kuczmarski, NIDDK;
Todd Le, NIDDK;
Maxine Lesniak, CSR;
Marion Liebert, AUA;
Barbara Linder, NIDDK;
Helen Ling, NIDDK;
Billie Mackey, NIDDK;
Saul Malozowski, NIDDK:
Denise Manouelian, NIDDK;
Ronald Margolis, NIDDK;
Michael Martin, CSR;
Winnie Martinez, NIDDK;
Dan Matsumoto, NIDDK;
Michael K. May, NIDDK;
Catherine McKeon, NIDDK;
Barbara Merchant, NIDDK;
Catherine Meyers, NIDDK;
Carolyn Miles, CSR;
David Mineo, NIDDK;
Marva Moxey-Mims, NIDDK;
Christopher Mullins, NIDDK;
Neal Musto, NIDDK;
Leroy Nyberg, NIDDK;
Elizabeth Paterson, NIDDK;
Judith Podskalny, NIDDK;
Sharon Pope, NIDDK;
Rebekah Rasooly, NIDDK;
Patricia Robuck, NIDDK;
Lakshmanan Sankaran, NIDDK;
Sheryl M. Sato, NIDDK;
M. James Scherbenske, NIDDK;
Salvatore Sechi, NIDDK;
Jose Serrano, NIDDK;
Kathleen Shino, NIDDK;
Michelle Shorter, NIDDK;
Philip Smith, NIDDK;
Joan Starr, NIDDK;
Mehrdad Tondravi, NIDDK;
George Tucker, NIDDK;
Renetta Turner, NIDDK;
Ana Velez, NIDDK;
Dorothy West, NIDDK;
Susan Yanovski, NIDDK;

Charles Zellers, NIDDK.

II. CONSIDERATION OF THE SUMMARY MINUTES OF THE 158th COUNCIL MEETING

The summary minutes of the 158th Council meeting were approved unanimously.

III. FUTURE COUNCIL DATES

September 18-19, 2002
February 19-20, 2003
June 11-12, 2003
September 24-25, 2003
February 4-5, 2004
May 26-27, 2004
September 22-23, 2004

IV. ANNOUNCEMENTS: CONFIDENTIALITY AND CONFLICT OF INTEREST STATEMENT

Dr. Hammond

Dr. Robert Hammond called to the attention of the Council members the procedures to ensure confidentiality and to avoid conflicts-of-interest. He discussed the scope and applicability of these procedures and requested Council compliance. Members were asked to sign and return a conflict-of-interest statement. Dr. Hammond reminded Council members that they need to leave the room when individual applications from their institutions are discussed in order to avoid an actual or perceived conflict-of-interest. They do not need to do so for *en bloc* actions. Under new procedures, Council members from multi-site campuses do not need to leave the room when applications from sites separate from their own specific site are discussed. Material furnished to Council members for purposes of peer review discussion during the closed portion of the meeting is considered privileged information. Moreover, the outcome of discussions during closed session may be disclosed only by NIDDK staff and only under appropriate circumstances. Council members should not respond to any direct communications they receive from applicants; they should refer applicants to NIDDK staff.

V. REPORT FROM THE DIRECTOR

Dr. Spiegel

Dr. Spiegel stated that the NIH welcomes a new, permanent Director, Dr. Elias Zerhouni, who was formerly Executive Vice Dean of Johns Hopkins University School of Medicine, Chair of the Russell H. Morgan Department of Radiology and Radiological Science, and Martin Donner Professor of Radiology and Professor of Biomedical Engineering at Hopkins. President George W. Bush nominated Dr. Zerhouni at a White House ceremony on March 26, 2002. The Senate

rapidly confirmed the nomination, following a hearing chaired by Senator Kennedy on April 30, 2002. The NIDDK is looking forward to Dr. Zerhouni's leadership in a time of vast scientific opportunity, momentum and challenge. Prior to Dr. Zerhouni's appointment, Dr. Ruth Kirschstein served as Acting NIH Director for well over 2 years. Dr. Kirschstein has been widely commended by the Congress, the NIH Institute and Center Directors, the research community and numerous volunteer health organizations for her exemplary service in that capacity. The NIDDK joins in extending its appreciation to Dr. Kirschstein.

The NIH is also in the process of filling several other leadership positions, including all of the neuroscience institutes (NINDS, NIMH, NIAAA, and NIDA). Dr. Spiegel noted that he and Dr. Michael Gottesman, the NIH Deputy Director for Intramural Research, are co-chairing the search for a new Director for the National Institute of General Medical Sciences (NIGMS). Dr. Roderic Pettigrew, formerly of the Emory Medical School, has just been appointed Director of the newly established National Institute of Biomedical Imaging and Bioengineering (NIBIB). While at Emory, Dr. Pettigrew was a Professor of Radiology, Medicine (Cardiology) and Bioengineering, as well as the Director of the Emory Center for Magnetic Resonance Research. The NIDDK hopes to collaborate with NIBIB in several areas, such as a shared program interest in the use of non-invasive means to detect iron in the heart and other organs.

With respect to budget cycles, Dr. Spiegel reminded the Council that the NIDDK is always dealing with three budget years at one time. The Institute is currently implementing the FY 2002 budget, while concomitantly planning for FY 2003 and even, in a very preliminary way, for FY 2004. Dr. Zerhouni has clearly identified at least two major budget challenges as the new NIH Director: (1) accounting for the productive use of the generous funding the NIH has been given during the 5-year period of budget doubling, and (2) articulating in a compelling way the research needs and opportunities that can be pursued with sustained growth. In response to a Council member's question, Dr. Spiegel noted that Dr. Zerhouni will be discussing these challenges at a budget retreat with the Institute and Center Directors, the focus of which will be the transition from FY 2003, the last year of the budget doubling, to FY 2004, the first year post-doubling. As editorials in *Science* and elsewhere have pointed out, it will be critical for NIH to make a smooth transition between the doubling and post-doubling periods, especially with respect to signals to new investigators, who could become discouraged by a budget downturn. We must also find the most efficient budgetary ways to exploit the incredible opportunities arising from recent technological advances and the remarkable new knowledge gained from the Human Genome Project.

Regarding the FY 2003 budget, NIH witnesses recently testified on behalf of the President’s request before the House and Senate Labor/HHS appropriations subcommittees. Harking back to a Council member's question from the previous meeting, Dr. Spiegel noted that the plans are largely set for use of the $1.7 billion for biodefense included in the FY 2003 NIH budget request, based on advisory panels that NIAID convened. Much of the targeted funding will support infrastructure development, and the NIDDK will therefore not be participating directly in these efforts. However, looking forward to potential FY 2004 opportunities for collaborative

biodefense initiatives, Dr. Steve James, Deputy Director of the Division of Digestive Diseases and Nutrition, is developing some relevant concepts in food safety and food-borne illness. It is possible that there may also be opportunities for collaborative intramural initiatives, possibly related to structural biology studies of toxins.

In addition to hearings specifically on the FY 2003 President's budget, the House appropriations subcommittee also held a series of "theme" hearings, as it did last year. On March 14, 2002, Dr. Spiegel testified on a theme panel along with the Directors of NIAID, NCI, NINDS and NIA concerning how basic research moves "From the Bench to the Bedside and Beyond." This was generally viewed as a positive hearing, in which there was an opportunity not only for each Director to put forth important accomplishments and challenges pertaining to his or her Institute, but also opportunities for synergy among the respective Institutes. There are many other indications that the NIH remains of high interest to the Congress. For example, several Institutes presented vignettes of NIH research to public audiences at two bi-partisan health forums requested by the Chair and Ranking Minority Member of the Labor/HHS Appropriations Subcommittee, Representatives Ralph Regula (R-OH) and David Obey (D-WI), respectively. Dr. Spiegel represented the NIDDK at the Ohio forum, while the Deputy Director, Dr. Griffin Rodgers, spoke at the Wisconsin forum. Dr. Spiegel also had the opportunity to make a requested research presentation to Senator Kennedy, Chair of the NIH Senate authorizing committee, along with Dr. Anthony Fauci, Director of NIAID, and Dr. Francis Collins, Director of NHGRI.

The "bench to bedside" theme is of recurrent interest to the Congress and to patient-oriented advocacy groups. Patient groups understandably want to know when the fruits of the Human Genome Project and other NIH investments will be translated into clinical advances that have an impact on improving health. In response, the NIH can indeed provide excellent examples, including not only the impressive results of major clinical trials, but also incremental steps. However, the challenge remains for the NIDDK and the Council to frame innovative ideas for more rapidly advancing "translational" research so that discoveries in the laboratory can be propelled more quickly into the clinical arena.

Dr. Spiegel noted several ways in which the NIDDK is facilitating translational research. One is the use of its strategic planning process to spur the translation of new knowledge about stem-cell biology, developmental biology, and genomics. Other approaches are the establishment of biotechnology centers to aid distribution of microarray technology to NIDDK grantees, the creation of genetics consortia to speed the search for disease-causing genes, and the establishment of a repository to ensure that clinical data and other clinical research resources from NIDDK-funded clinical trials are intelligible and available to the broad investigative community. Looking toward the future, perhaps the NIDDK should also explore the use of research training approaches to further translational efforts. The Institute supports an extensive array of Ph.D.s in its research training mechanisms, but there is a shortage of M.D. trainees for patient-oriented research. Therefore, there may be opportunities for the NIDDK to target Ph.D.s as a source for disease-oriented translational training. The Institute might also develop

mechanisms to enhance the planning and implementation of pre-clinical research and early-stage clinical trials. The NIDDK could also leverage its investments and attain economies of scale by encouraging ancillary studies within existing clinical trials in which Institute resources have already enabled the assembly of large patient cohorts and databases.

Several Council members commented:

- As phenotyping and genotyping permit patient populations to be more rigorously stratified, the era of the large clinical trial may be past. Rather, a new player may become the dominant force: the academic medical center that can conduct small clinical trials targeted to well-defined patient populations. This would require medical schools to become quite adept at performing clinical trials, as well as the existence of a nationwide connection of core resources, such as genome centers, that are able to receive specimens and process them rapidly and economically.
- Perhaps it is more appropriate to use the term "hypothesis testing in man," rather than "clinical trials," as a way to orient translational research. Sometimes, but not always, this research will take the form of a trial; however, in some cases, there are many important questions about pathogenesis of disease that need to be answered before a trial is undertaken. It was noted that sometimes a fundamental clinical observation, which is not made in the context of a trial, leads to an important clinical discovery. Another member stressed that NIH has the unique ability to ask the biological questions that are embedded within the framework of a randomized clinical trial. Thus, when planning a trial, NIH staff should ask whether, with just a marginal additional investment, new knowledge could be generated about the biology of the disease. Dr. Spiegel noted that, in a sense, this is the purpose of ancillary studies. For example, the NIDDK has included in its viral hepatitis C trial some mechanistic studies, such as sequencing of viral genomes, to gain insights into differences in responsiveness to interferon among patient groups. Dr. Spiegel noted that stratification of patients is important with respect to hepatotoxicity and other issues in order to determine the comparative efficacy of interventions. There are concerns about the efficacy of current pharmacogenomic methods for doing this; however, the NIDDK can strive to establish well-characterized groups of patients, and, if efficient to do so, it can perform pilot studies, such as the 3-year pilot envisioned for the new hepatotoxicity network being undertaken by the Division of Digestive Diseases and Nutrition.
- Improvements are needed in the ability of investigators to assimilate longitudinal clinical information, and perhaps the field of bioinformatics should be extended to clinical or medical informatics. Investigators need the ability to access unstructured clinical information, organize it coherently and match it with phenotypic data. Many institutions do not have efficient electronic medical systems.
- With respect to "people power," there is a need to expand the pool of individuals who have the training and interest to conduct an ancillary study or an independent clinical, physiological or pathophysiological study. It may be beneficial to find additional ways to integrate basic and clinical research training experiences for investigators, as is done in highly successful M.D.-Ph.D. programs. Didactic courses to train Ph.D.s in medical issues can be helpful in this regard.

Dr. Spiegel thanked the Council members for their initial feedback. He strongly encouraged them to consider the various approaches he described and to "brainstorm" other suggestions for innovative ways to enhance translational research. He would appreciate it if some of the outgoing members of the Council would be amenable to presenting their visions of future research at the next Council meeting, with emphasis on translational research. The tentative suggestions were Dr. Robert Schrier for the kidney field; Dr. John McConnell for urology; Dr. Ronald Kahn for diabetes/endocrinology; and Dr. Jeff Gordon for gastroenterology.

VI. NIDDK EXTRAMURAL RESEARCH BUDGET GROWTH
Dr. Robert Hammond

In response to several inquiries from Council members, Dr. Hammond stated that the NIDDK has assembled some data on 10-year trends in its extramural research budget and the effects on grant numbers and size. As noted in tables distributed to the Council, the budget for research project grants increased from approximately half a billion dollars in 1991 to over $1.1 billion in 2001, the most recent year for which complete data are available on awards. There are marked percentage increases beginning in FY 1999, the first year public policy makers committed to doubling the NIH budget over a 5-year period. The upswing from single-digit to double-digit percentage increases in FY 1999 and subsequent years contributed significantly to the 119 percent growth in the total budget for NIDDK research project grants, including SBIR/STTR grants, from 1991 through 2001.

The budget category of "research project grants" includes grants of diverse purpose and size: R01 grants, program project grants, planning grants, R21 grants, and cooperative agreements. Excluding SBIR/STTR grants, the number of research project grants increased from 2,036 to over 2,700 from 1991 through 2001, or 35 percent. The comparable percentage growth in funding and average grant size was 110 percent and 55 percent, respectively. For the same time period, an analysis of the subset of R01 grants, most of which were unsolicited, shows that the number grew from 1,509 to 2,220, or 47 percent. The comparable percentage growth in funding and average grant size was 127 percent and 54 percent, respectively.

Management strategies and practices influence these data, especially with respect to average grant size. For example, NIDDK management has established funding caps for some types of applications: applications for program projects and applications submitted under RFAs usually have dollar caps, as do planning grants. Reductions in grant size also occur in peer review, as well as in programmatic decisions made by NIDDK. Over the years, NIDDK management has applied a banded series of programmatic reductions, with the most meritorious applications subjected to the least reductions. The most severe reductions occurred in 1992, with cuts of 25 percent on both new grants (type 1) and competing continuation grants (type 2).

For most of the 10-year period, the banding for competing continuation grants (type 2) was tied

to the size of the prevailing award. Thus, a growth limit was determined based on the amount of the prevailing award (type 5), plus a given percent increase on that base. However, staff found that the competing renewal applications were disadvantaged by this practice. Investigators were not able to take advantage of emerging scientific opportunities because they were locked to the existing budgets, whereas a new applicant could submit an application for any budget amount. For FY 2002, NIDDK has adopted the same banding for competing renewal applications as for new applications and expects that programmatic reductions for both types of grants will be approximately 12 percent.

In discussion, Council members raised several questions: *With regard to the increased number of grants, has the number of funded investigators actually increased, or is the increase in grants explained by the fact that more investigators are holding multiple grants?* Dr. Hammond responded that the number of investigators with more than two grants is quite small. Dr. Spiegel noted that an analysis of multiple grant holders would be one way to approach the question posed. *Given the dearth of physician-scientists, coupled with the 5-year budget doubling, has NIH put an appropriate proportion of funding into awards to attract physicians to research careers?* Dr. Spiegel noted that most research training awards in an Institute like NIDDK are almost exclusively for post-doctoral fellowships, the parameters of which are set at the NIH level. Based in part on a report of the National Academy of Sciences, the NIH made a decision to increase stipends on those awards. Only about one-third of post-doctoral fellows are supported directly on NIH research training grants; many are supported on R01 grants. The NIDDK can provide these data, both in terms of numbers and funding amounts. With respect to research career awards (K awards), there has been substantial growth because of the creation of new mechanisms, including the K23 and K24, which began in 1999. *Do the data on average size of awards include indirect costs?* Dr. Spiegel replied in the affirmative. He also pointed out that the NIH holds its intramural program to a ceiling of 11.3 percent of the total budget, and this program also must absorb indirect costs. In NIDDK, the intramural program represents 10 percent of overall budget, and NIDDK extramural administrative costs represent approximately 3.5 percent.

VII. EXTRAMURAL LOAN REPAYMENT PROGRAM
Dr. Robert Hammond

Although the NIH has had an intramural loan repayment program for over a decade, this year is the first time it has had a broad extramural loan repayment program. As reported at the last Council meeting, the NIH is proceeding with implementation of two new extramural loan repayment programs. The first, the loan repayment program for clinical research, was authorized by the Public Health Improvement Act of 2000. The second, for pediatric research, was authorized by the Children's Health Act of 2000. As noted in the briefing paper prepared for the Council, information regarding eligibility requirements and benefits for these programs may be obtained at the NIH Loan Repayment Website at http://www.lrp.nih.gov.

The purpose of both of these programs is the recruitment and retention of highly qualified health

professionals as clinical investigators and pediatric researchers, respectively. To help defray the costs of their medical educations, successful applicants under these programs can receive up to $35,000 annually plus a Federal tax offset, up to a total of $100,000 over 2 years. Only U.S. citizens or permanent residents are eligible to apply. Applicants must hold one or more of the degrees listed in the eligibility criteria. For FY 2002, eligible applicants need to be the recipient of an NIH qualifying grant. However, in FY 2003, this eligibility requirement will be broadened to include applicants who have 2 years of institutional support through any non-profit source. To qualify for the program, the amount of educational loan debt must be equal to or in excess of 20 percent of annual income or compensation. These awards are contracts, under which recipients must engage in qualified clinical or pediatric research for at least 2 years in exchange for the funds they receive to help them repay their educational loans. There is no other type of payback or service requirement. Each applicant must self-select one or the other track, either clinical or pediatric research.

At the February 2002 receipt date, the NIH received 691 applications, of which 487 were clinical and 204 pediatric. From these, 65 were referred to NIDDK, of which 36 were clinical and 29 pediatric. Following peer review, the initial breakout of awards was 23 clinical, and 18 pediatric, representing an estimated commitment of approximately $2 million in NIDDK funds at a success rate over 60 percent for each of the tracks. However, it is probable that the final NIDDK funding level may change, depending upon negotiations with other Institutes, which may wish to fund some awards initially unfunded by the NIDDK.

Review of the applications referred to NIDDK was conducted via mail ballot and conference call by 21 external reviewers, including five pediatricians, convened as a special emphasis panel by the Institute's Review Branch. Review criteria were standard across the NIH. Post review, an NIDDK Working Group considered the career stage of the applicant and the need to maintain balance among NIDDK program areas. NIDDK senior management had previously determined that, in keeping with the intent of the program, an effort should be made to give special consideration to applicants who had already made some commitment toward a research career, such as recipients of K awards, and who thus have a high probability of remaining in research. Although the number of applications and awards are quite small in some NIDDK programs, such as urology, hematology, and nutrition/obesity, it is likely that, because eligibility for this program is tied to a currently funded grant, individuals in these fields may have applied to the Institutes and Centers from which they receive their primary grant support. For example, the NCI is a major source of urology research funding; the NHLBI is a key source of funding for clinical hematology research; and many NIH components fund clinical research on nutrition and obesity.

Council members had several comments and questions: A Council member noted the importance of creating a feedback loop so that medical schools will see the average indebtedness of these awardees. This would be useful to medical schools, which debate the amount of funds to put into need-based *versus* merit-based scholarships and the impact of rising tuition costs. In response to a Council member's question about evaluation, Dr. Hammond said that NIH will use

an evaluation model focused on long-term outcomes. This model was established for the intramural loan repayment program and is now being applied to perform an analysis of that program from 1999 to the present. For the short-term, evaluation will focus on assessing the effectiveness of the application and award processes, and the characteristics of the awardees. With regard to the latter, the NIDDK will have more details for Council members at the next meeting. Dr. Spiegel underscored the difficulties in capturing data from individuals long after they have exited an NIH-funded program. The greatest opportunity for collecting data on these awardees will be during the 2 years of the contract, when it can be ascertained whether or not they are still performing qualified and effective research. However, it may be possible to use other means, such as an exit interview, to determine the awardee's plans and how the loan repayment program has influenced his or her career choices. In response to a question, Dr. Spiegel stated that the two pieces of enabling legislation do not contain a specific sunset date. There is a small group of Institute Directors, including Dr. Spiegel, who are involved in planning and implementing the program, and a small group of extramural staff, including Dr. Hammond, who are addressing evaluation issues.

VIII. TRANSITION OF EXTRAMURAL SCIENTISTS TO INDEPENDENT RESEARCH CAREERS

A. UPDATE ON NEW AWARD MECHANISMS FOR RESEARCH CAREER DEVELOPMENT: K01, K23, K24, K30

Dr. Judith Podskalny

In addition to the long-standing K08 award with which the Council is familiar, the NIDDK is supporting several other mechanisms to facilitate research career development:

< *K01 Mentored Research Scientist Award* - used to transition non-clinical investigators from a fellowship to a successful R01. The NIDDK has reached a relatively steady-state of 60 applications annually. The overall portfolio is currently 59 basic scientists supported by this mechanism. Of the first cohort of ten individuals who received these three-year awards in 1999 and are now completing the program, five have applied for and one has received R01 funding thus far. This program has been re-announced with the option of applying for up to five years of support.

In an effort to promote the training and the careers of physician scientists engaged in patient-orient research, the NIH in 1999 launched three new programs: the K23, the K24, and the K30.

< *K23 Mentored Patient-Oriented Research Career Development Award* - used for early-career clinical scientists, with terms and conditions similar to the K08. The NIH is currently supporting approximately 500 K23 awards, meeting the projected five year goal in only three years and attesting to the need for and popularity of this program. The NIDDK currently supports 33 K23s and receives about 30 applications annually. Furthermore, these are in

addition to, NOT in place of, K08 applications. The number of K08 applications assigned to the NIDDK has remained relatively constant over the same time period.

< *K24 Mid-Career Investigator Award in Patient-Oriented Research* - used to support mid-career individuals for 25 to 50 percent effort, thus allowing them the protected time needed to pursue their patient-oriented research and serve as mentors for upcoming physician scientists. The NIH is currently supporting 214 awards, of which the NIDDK funds 29. The target number of K24s when the program reaches steady state after five years will be 300-400. The current number is meeting this target.

< *K30 Clinical Research Curriculum Awards* - used to develop curricula to train clinical scientists in patient-oriented research. There are currently 55 NIH-funded sites, with most programs awarding a Master's level degree.

To integrate these programs, the NIDDK encourages K24 investigators to serve as mentors for K23 applicants. Currently, six K23 recipients have a mentor funded by a K24, but many are working in laboratories where they receive mentoring from investigators who hold an R01. The NIDDK training program staff also encourage K23 applicants to take advantage of K30 curricula at their institutions. In NIDDK, 26 of the 33 investigators who hold K23 awards are at institutions that have a K30 award and 16 of these individuals are participating in the K30 program.

A major NIDDK meeting in April 2003 will provide information intended to aid investigators in their research career transitions. In addition, the NIDDK has a unique program that permits its K08 awardees to apply for an R03 to be awarded concurrently with the fourth and fifth year of the K08, providing the successful applicant with additional support and another peer review opportunity to increase grantsmanship skills. This works well for the institution that will receive full indirect cost rates, and it allows the successful applicant to work independently, without a mentor, thus demonstrating his/her independence. The preliminary data from the work supported by the R03, and the K08, can then form the basis for an R01 application.

The Council discussed ways to promote the research careers of minority investigators. Dr. Podskalny noted that the NIDDK is forming a network of its minority research investigators to aid sharing of information and experiences. The NIDDK has also crafted, with other Institutes, a Master's program in clinical research at a minority-serving institution. In addition, the NIDDK has a new initiative with tribal colleges and universities to create a diabetes-focused science education program at the elementary, middle school and high school levels. The principal support for minority investigators at the NIH is provided through the Minority Access to Research Careers Program and the Minority Biomedical Research Supplements–both of which are administered by the National Institute of General Medical Sciences.

Also in discussion, the following points were made:
<With respect to tracking the future research careers of K awardees, data on the first batch of

R03 applications from the K23 recipients are expected to be available next year.

< Renewability of K30s is currently being addressed by NIH.

< The NIDDK has not tried networking K24 awardees with K23 awardees who might or might not be in the same institution, but this might be beneficial.

< K awards are reviewed through the NIDDK Review Branch.

< Success rates for K awards are much higher than for R01 grants. If new investigators are not funded on their first application, they may be lost to research forever; therefore, it is extremely important to facilitate their first attempt to secure an R01 grant.

< For NIDDK, the funding of new R01 investigators is a priority, as reflected by the inclusion of new investigators as one of the categories for Special Emphasis funding.

< Many young surgeons who are interested in pursuing patient-oriented research cannot commit the required percentage of their time for a K23 award, especially given the salary limitations of this award.

B. SCIENTISTS IN THE PIPELINE
Dr. Robert Hammond

Dr. Hammond reported on a limited analysis of two long-standing K award mechanisms: the K08 Mentored Clinical Investigator Award and the now defunct K11 Physician-Scientist award. This analysis is not comprehensive, but was undertaken to shed some light on the issue of whether these types of grants have been useful in enabling recipients to compete successfully for regular research grants later. In 1992, a "snapshot" year, 136 individuals received support through these types of awards. Of these, 91 applied for at least one research project grant within the subsequent 10-year period. Of those who applied, 70 successfully obtained funding.

In response to questioning, Dr. Hammond said that no comparative group was included in the analysis, such as a control cohort of R01 applicants who did not hold K08 awards. Dr. Podskalny noted that, in her experience, approximately 70 percent of K awardees apply for an R01 grant. Also, about 70 percent of all R01 grant applicants eventually succeed in obtaining funding, often through the revision/reapplication process. With respect to correlations between successful R01 funding and degree held, Dr. Spiegel noted that analyses to date show that M.D.-Ph.D.s have excellent success, but that the success of M.D.s relative to Ph.D.s has been declining over the years.

Dr. Hammond pointed out that there are no clear trends in the breakout of the long-term K08 and K11 data among major NIDDK subprogram areas; the numbers are really too small to draw conclusions. It was also noted that these data do not reflect all NIDDK career development activity, as they do not include data on the recently introduced mechanisms covered in Dr. Podskalny's presentation. A Council member suggested that--although it is difficult to make manpower projections, and we do not have data on the universe of investigators in particular fields--it would nonetheless be beneficial for NIDDK to have pipeline targets in specific fields for which career development seems less robust, such as nutrition and obesity. Setting such targets would help ensure a sufficient cadre of future investigators in those areas. Dr. Spiegel

responded that it might be worthwhile to do another, more-inclusive analysis of the total K award data relative to total RPG support. He suggested that several Council members, including Dr. Ron Kahn, Dr. Allan Walker, and Dr. Bob Schrier, might wish to follow-up on this with NIDDK staff.

IX. MEDICAL THERAPY OF PROSTATIC SYMPTOMS (MTOPS)

Dr. John McConnell

Dr. John McConnell presented the major findings of the NIDDK's recently-completed clinical trial, "Medical Therapy of Prostatic Symptoms (MTOPS)." By way of background, Dr. McConnell noted that an estimated nine million men suffer from symptoms of benign enlargement of the prostate gland, known as benign prostatic hyperplasia, or BPH. Most usually need treatment at some time. Over the years, researchers have tried to find a way to shrink or at least stop the growth of the prostate without surgery. The Food and Drug Administration has approved four drugs to relieve common symptoms associated with an enlarged prostate. One drug, the 5 alpha-reductase inhibitor finasteride (marketed under the name Proscar), inhibits production of the hormone dihydrotestosterone, which is involved with prostate enlargement. Its use can actually shrink the prostate in some men. Another drug, the alpha-1 receptor blocker doxazosin (marketed as Cardura), acts by relaxing the smooth muscle of the prostate and bladder neck to improve urine flow and to reduce bladder outlet obstruction. Doxazosin was first developed to treat high blood pressure.

The MTOPS was a multi-center clinical trial that evaluated the long-term effects of doxazosin and finasteride, and whether treatment with the combination of the two drugs was more effective than either drug alone in preventing the clinical progression of BPH. Clinical progression was defined primarily as a significant worsening of symptoms, recurrent urinary tract infection, urinary retention, incontinence, or the need for invasive therapy such as surgery.

Physicians at 17 medical centers treated 3,047 men age 50 and older for an average of 4.5 years. The men all had symptomatic BPH and were evenly divided into four groups that took either finasteride (5 mg daily), doxazosin (4 mg or 8 mg daily), both drugs, or a placebo. The study showed that using finasteride and doxazosin in combination was more effective than either drug alone to relieve symptoms and prevent BPH progression among men with symptomatic BPH. The two-drug regimen reduced the risk of BPH progression by 67 percent–an extraordinarily positive result for a clinical trial–compared to 39 percent for doxazosin alone, and 34 percent for finasteride alone. The study also demonstrated clearly which patients are at increased risk of progression and are most likely to benefit from treatment.

Combination therapy not only provides better, long-lasting and safe symptom relief, but because finasteride reduces prostate size, patients have fewer episodes of urinary retention and invasive treatments. No patient in any of the drug treatment groups developed kidney problems from BPH, a very significant and clinically important finding. The MTOPS results are expected to produce major improvements in medical practice in the treatment of BPH.

X. SCIENTIFIC PRESENTATION

BEHAVIOR CHANGE AND THE DIABETES PREVENTION PROGRAM (DPP) PAST, PRESENT, AND FUTURE

Dr. Rena Wing

The intensive lifestyle intervention arm of NIDDK's recently completed Diabetes Prevention Program (DPP) clinical trial yielded remarkable findings about how diet and physical activity can reduce the risk of developing type 2 diabetes in individuals who are prone to the disease. Trial participants who lost 7 percent or more of their body weight and who performed at least 150 minutes of physical activity per week reduced their chance of developing diabetes by 58 percent over an average 2.8 year follow-up period. Rigorous, systematic, and controlled testing of the weight loss-physical activity hypothesis through the DPP provided definitive proof that prevention of type 2 diabetes is possible through lifestyle changes.

Perhaps the most important factor contributing to the success of the intensive lifestyle intervention was a history of several decades of investment in programmatic basic behavioral intervention research, and the translation of that research. It was this strong research foundation that enabled DPP investigators to design an effective weight-loss program. The intensive lifestyle intervention was based on prior observational studies suggesting that modest changes in weight or physical activity might reduce the risk of developing type 2 diabetes. Clinical trial data also existed that suggested modest changes in weight and physical activity could be produced.

To achieve the weight loss goal, participants were instructed to reduce their dietary fat intake to less than 25 percent of total calories. Because the combination of diet and exercise was known to be particularly effective for long-term maintenance of weight loss, the intervention included a defined physical activity component. Participants were encouraged to exercise at least three days per week, with at least 10 minutes per session, with a goal of at least 150 minutes per week.

A key feature of the lifestyle intervention was the use of frequent contact and ongoing intervention. Research had shown that positive reinforcers, contingency contracts, and particularly frequent and intensive contact can help individuals maintain their behavior changes.

With the completion of the DPP, Dr. Wing is turning her attention to ways to implement the lessons of the intensive lifestyle intervention to prevent type 2 diabetes. She believes that to apply the results of the DPP to the general population, it is important to disseminate the DPP message effectively to a large number of people, and she is looking at the Internet as one means of doing this.

Dr. Wing also noted that the DPP results suggest certain areas of particular importance for future research. Perhaps the highest priority is to understand how to help individuals maintain their

weight loss long-term, or maintain other aspects of behavior change. Some of Dr. Wing's own research on the maintenance of weight loss indicates that low-calorie diets and, more importantly, low-fat diets are critical to maintaining weight loss long-term. Also important is a relatively high level of physical activity, up to 2,800 calories per week. Dr. Wing stressed, however, that new and innovative approaches to improving long-term maintenance of weight loss must be developed.

XI. ADJOURN FOR LUNCH

Dr. Spiegel thanked all the presenters and then adjourned the open session of the full Council meeting at 12:27 p.m. on Thursday, May 30, 2002.

XII. SUBCOMMITTEE MEETINGS

At approximately 1:30 p.m., separate meetings were convened of the Diabetes, Endocrinology and Metabolic Diseases; the Digestive Diseases and Nutrition; and the Kidney, Urologic and Hematologic Diseases.

Subcommittee meetings reconvened on May 31 at approximately 8:00 a.m. and continued until approximately 9:45 a.m.

XIII. REPORTS OF SUBCOMMITTEES: CONSIDERATION OF APPLICATIONS (CLOSED SESSION)

At 9:56 a.m. on Friday, May 31, 2002, Dr. Spiegel reconvened the open session of the full Council.

XIV. CENTER FOR SCIENTIFIC REVIEW (CSR): STATUS OF REORGANIZATION ACTIVITIES

Dr. Michael Martin

Dr. Michael Martin reported on reorganization activities within the NIH Center for Scientific Review (CSR), subsequent to a report submitted by the "Panel on Scientific Boundaries for Review." The Chair of this panel was Dr. Bruce Alberts, President of the National Academy of Sciences, and the membership included NIDDK Council member Dr. Ed Holmes. The initial report, as well as a range of follow-up documents, can be accessed at the CSR homepage: http://www.csr.nih.gov/review/reorgact.asp

The expert panel recommended the establishment of 24 Initial Review Groups (IRGs) largely

oriented to organ systems or diseases, in the context of the biological question being addressed. Seven IRGs had already been reorganized. For the remaining 17, the CSR established 11 "Steering Committee and Study Section Boundary Teams" of 20 to 35 individuals to create guidelines for the study sections, propose suitable names, and prepare functional descriptions, including statements of intersecting areas of interest. Each of these teams was comprised primarily of external scientific experts, along with some NIH program staff. The hematology team launched this process with a meeting in February 2001. In April 2002, team meetings addressed three other areas of high interest to the NIDDK: digestive sciences; endocrinology, metabolism, nutrition and reproductive sciences; and renal and urological sciences. Recommendations from the various teams are posted for a 12-week period of public comment. There is a large broadcast to professional societies, to reviewers who serve on CSR study sections, and to the NIH community at large. For any team's recommendations, the fewest comments CSR has received is 40 and the most is 400. After the close of the comment period, CSR consolidates the comments and posts them on the website. The CSR is also doing some "mock" testing to assess how well the proposed guidelines match what is actually being reviewed, and whether or not the sizes of the suggested study sections are appropriate. The major next steps for the CSR are to identify and resolve areas of "shared interest"--paying close attention to how both the team recommendations and public comments address this issue. Final reorganization decisions will be made by Dr. Elvira Ehrenfeld, Director of CSR. Implementing change will require about a year from the date that a decision is made to establish a new study section. This time will permit the investigative community to acclimate to the reorganization.

In questioning from a Council member regarding the effects on the size of study sections, Dr. Martin responded that there has been a deliberate attempt to move into organ-system-oriented study sections the basic science applications that have such an orientation. When queried as to how malignant diseases of organs would be handled, Dr. Martin noted that the guidelines call for placing malignancy-related research in the oncological sciences. However, recognizing that there is a transition from normal growth processes to neoplasia, it would be natural for research on the transition from dysplasia to neoplasia to be at the organ-system level. A Council member noted that it would be useful to see whether the reorganization has an impact on the balance of funding among fields and that this could probably be assessed retrospectively.

Dr. Spiegel urged Council members, as liaisons to their respective communities, to access the CSR website for more detailed information on the reorganization, and to promote community input to CSR.

XV. REPORT FROM THE NIDDK INTRAMURAL RESEARCH PROGRAM

Dr. Marvin Gershengorn

Dr. Gershengorn presented a vignette of the Division of Intramural Research. This Division consists of 90 tenured scientists, 51 staff scientists who are Ph.D. or M.D. level fellows, and 25 tenure-track scientists who will have an opportunity to earn tenure during a 6-year period.

Nineteen of the 20 laboratories and branches are located in Bethesda, with a very important branch in Phoenix, Arizona. Peer review is conducted by an external Board of Scientific Counselors, which meets two or three times annually to review three or four laboratories on an approximate 4-year rotational schedule.

Several examples of ongoing research illustrate the wide span of NIDDK's intramural efforts from basic studies to patient-oriented research.

Examples from the Laboratory of Molecular Biology include:

< Development of a cell-free system capable of carrying out all the steps of recombination that generate antibody diversity;

< Identification of the protein CTCF as necessary and sufficient to block the effects of a distal enhancer on a gene promoter;

< Identification of a novel protein that blocks the self-destructive auto-integration of retroviral DNA;

< Elucidation of the catalytic mechanism of the multiple chemical steps of phage Mu recombination by using stereochemical methods;

< Development of fluorescence-based tools for the real-time study of higher-order protein-DNA complex assembly mechanisms.

< Application of x-ray crystallography techniques to gain new insights into transcription factors and the HIV integrase; enzyme kinetic interactions and protein-protein interactions; protein components of signal transduction pathways; restriction endonucleases and enzymes that act on DNA; and integral membrane proteins.

Examples from the Laboratory of Chemical Physics include:

< Development of methods to solve a major problem in solution NMR, that is, to determine the relative orientation of domains or subunits in multi-subunit proteins and to identify DNA binding in DNA protein complexes;

< Development of novel solid state nuclear magnetic resonance methods to determine a sufficient number of distance and angular constraints to build the first experimentally-based structure of the amyloid fibrils that are formed in Alzheimer's disease.

< Performance of the first sub-nanosecond resolved protein crystallographic experiment to observe the complete atomic structure of myoglobin;

< Development of methods to investigate the early events in protein folding;

< Development of new vibrational infrared imaging microscopy techniques;

Turning to patient-oriented research, Dr. Gershengorn highlighted several examples. The Phoenix Epidemiology and Clinical Research Branch continues to generate important insights into type 2 diabetes and obesity in the Pima Indians. Researchers have found that insulin resistance and a relatively lower acute insulin response to glucose are both predictive of subsequent development of type 2 diabetes, independent of any effects of obesity. They have also demonstrated that several markers of chronic inflammation predict subsequent development of diabetes, and that one of these, adiponectin, also predicts a decline in insulin sensitivity. Other researchers in the Branch have presented the first experimental evidence that a reduced rate of energy expenditure is a risk for weight gain and were the first group to map brain responses to both hunger and satiety.

Also of particular clinical note is that the first islet transplant patient of the Transplantation and Autoimmunity Branch has now been insulin-independent since February of 2001, having suffered with brittle type 1 diabetes since 1950. This Branch is also studying whether immunomodulatory therapies can ameliorate the autoimmune destruction of insulin-producing beta cells, which underlies type 1 diabetes. Two novel approaches are using antibodies directed against cell-surface markers. In complementary research, the Diabetes Branch has a new focus on the endocrine pancreas. Several researchers are studying *in vitro* growth and developmental factors that induce differentiation of human pancreatic precursor cells into hormone-producing cells of the pancreatic islets. This Branch also features award-winning studies of glucose transport in both adipose tissue and skeletal muscle.

In discussion, a Council member expressed interest in the attributes of intramural research that differentiate it from extramural academic research programs. Dr. Gershengorn responded that there are certain types of higher-risk research that can be performed more readily intramurally than extramurally. The intramural program also has leading experts in certain methodologies that are not usually pursued extramurally, such as the examples he provided from the Laboratory of Chemical Physics. In some computational biology areas, the intramural program not only develops new approaches, but also can serve as a central repository to aid investigators.
Dr. Spiegel also made note of the excellence of the intramural program, with three Nobel prizes over the years given directly to intramural investigators, and the election of intramural scientists to the National Academy of Sciences. Dr. Spiegel also made note of the unique Branch in Phoenix, and the efforts of NIDDK's Deputy Director, Dr. Griffin Rodgers, to spearhead new community intervention efforts there with respect to increased physical activity among Pima children, and increased attention to diabetic foot disease.

XVI. REPORTS FROM NIDDK EXTRAMURAL DIVISIONS

A. Division of Digestive Diseases and Nutrition
Dr. Jay Hoofnagle

With regard to the funding of grants in this Council round, Dr. Hoofnagle noted that--of 129 scored applications--the Division had a total of 71 grants within the pay line, including 56 R01s and two MERIT award extensions. Three P01s, five R21s and five R03s will also be funded. Over half of the grants funded are initial applications. By contrast, a few years ago, over 70 percent of the grants being funded were revisions. Eighteen percent of the grants funded in this Council round were considered clinical research. These include grants on obesity prevention, hepatotoxicity, hepatitis C, functional bowel syndrome, and other topics.

The Division will be making awards under three RFAs this Council round. One of these initiatives is to develop a cohort study on adult-to-adult living donor liver transplantation--a procedure whose use has increased rapidly since the first such transplant in 1997. The study will include a data coordinating center and six-to-seven transplant centers. Another RFA to be funded will develop a clinical research consortium on biliary atresia, consisting of a data coordinating center and at least seven other participating centers. This consortium is the result of several years of planning with the pediatric liver disease community. Finally, as a result of funding a third RFA, the Division will establish an inflammatory bowel disease (IBD) genetics research consortium, which will include a data coordinating center, along with five centers that will accrue patients and carry out genetic research.

Upcoming meetings will include a consensus development conference on management of hepatitis C, and meetings on obesity prevention, small bowel transplantation, hepatitis C and renal disease, hepatitis C in prisons, and inflammatory bowel disease.

Dr. Susan Yanovski, Director of the NIDDK's Obesity and Eating Disorders Program, recently co-authored a review article on the pharmacology and treatment of obesity in *The New England Journal of Medicine*.

B. Division of Diabetes, Endocrinology, and Metabolic Diseases
Dr. Judith Fradkin

At its March 2002 meeting, the Diabetes Mellitus Interagency Coordinating Committee agreed to adopt the term “pre-diabetes” to encompass both impaired fasting glucose and impaired glucose tolerance. The April issue of *Diabetes Care* published new guidelines--jointly issued by the NIDDK and the American Diabetes Association–which include recommendations for identification of patients with pre-diabetes by screening with either a fasting blood glucose or oral glucose tolerance test. Individuals over age 45 and overweight, as well as younger people who are overweight with additional risk factors such as family history or ethnicity, should be screened for pre-diabetes. For those with pre-diabetes, lifestyle modification is the first choice for reducing the risk of developing full-blown diabetes. The importance of lifestyle modification is also being stressed in a new campaign of the National Diabetes Education Program to translate

the lifestyle message of the DPP to all the populations that may benefit.

The May 15, 2002 issue of *The Journal of the American Medical Association* focused exclusively on diabetes and included a number of papers, many of which were supported by NIDDK. One particularly important paper was from the Epidemiology of Diabetes and Its Complications (EDIC), a follow-up of the Diabetes Control and Complications Trial (DCCT) population. EDIC found that, 7 years after the end of the DCCT, individuals who received intensive therapy during the trial continued to have a dramatically lower risk of complications than those who had been on conventional treatment. These observations demonstrate not only that intensive management of blood glucose levels is extremely effective in reducing the painful, debilitating, and costly complications of diabetes, but also that the benefits of intensive therapy persist for years. This finding raises interesting questions about the mechanism of this metabolic memory and how the continued differential in risk of complications develops. The individuals in the EDIC study have been well-phenotyped and a tremendous amount of metabolic data is available. To capitalize on this resource, the NIDDK will begin a study to look at urologic complications in this population. The 20th Anniversary of EDIC will be celebrated in 2003 with a special symposium on microvascular complications.

Results of the Diabetes Prevention Trial for Type 1 Diabetes (DPT-1) were recently published in *The New England Journal of Medicine*. Although administration of parenteral insulin did not prevent type 1 diabetes in an at-risk population, the accompanying editorial called it a landmark study because of its success in predicting diabetes risk and the many valuable insights it provided. Over 80,000 people were screened to enroll 339 patients in the study--about 250 people screened for every patient enrolled. This study has shown that it is possible to accurately identify individuals at 50 percent risk of developing type 1 diabetes over a 5-year period. Screening tests for immunologic assessment of these at-risk individuals are now more refined and researchers are well-positioned to conduct similar studies for prevention of type 1 diabetes as new potential immunomodulatory agents become available.

The same issue of *The New England Journal of Medicine* included a report of a pilot trial of a modified murine monoclonal anti CD3 antibody that has shown some promise in preserving beta cell function in new onset type 1 diabetes. To further evaluate this preliminary but exciting result, the NIH plans to do a larger study in about 80 new onset type 1 diabetes patients through the Immune Tolerance Network, spearheaded by the NIAID and co-sponsored by the NIDDK. If results are positive, this agent may be tested in a large-scale intervention study through the newly-formed Type 1 Diabetes TrialNet. This TrialNet initiative was one of many discussed at a May 16, 2002, special advisory panel meeting to assess the use of special congressional funding provided specifically for research on the prevention and cure of type 1 diabetes.

C. Division of Kidney, Urologic, and Hematologic Diseases
Dr. Josephine Briggs

The Division has undertaken new efforts to enhance support for research trainees through

mentorship and meetings; an initial highly successful workshop led by Dr. Terry Bishop focused on grant application preparation and was highlighted by a mock study section review. A program led by Dr. Robert Star focuses on training clinical investigators in urology and nephrology, and an Interagency Coordinating Committee led by Dr. Stuart Howards focuses on training programs for surgical investigators in urology. Complementary efforts are promoting coordination and networking among renal investigators. The Division is also working to encourage more R01-funded clinical studies.

The Division has recruited three new staff members: Dr. Christopher Mullins, a cell and molecular biologist, Dr. Catherine Meyers, a renal immunologist and Dr. Rebekah Rasooly, a geneticist. Dr. Briggs recognized the work of Dr. Rasooly in leading the effort to develop a trans-NIDDK data and tissue repository in order to make optimal use of clinical resources available through NIDDK-funded clinical trials.

Two major clinical trials funded by the Division have yielded important results. The first trial, MTOPS, was the subject of the scientific presentation the previous day (see summary of Dr. McConnell's presentation). The second trial, HEMO, was a study of standard *versus* intensive dialysis in over 2,000 patients with kidney disease. The trial found no additional benefit of high-dose dialysis and confirmed that the current dialysis regimen is optimal.

Several ongoing or upcoming projects of note include: (1) a longitudinal cohort study of persons with chronic renal disease; (2) a trial of the ability of folic acid and B vitamins to lower homocysteine levels in patients undergoing kidney transplants; (3) a study of minimally invasive surgical therapies for benign prostatic hyperplasia; (4) a trial of saw palmetto in the treatment of prostate disease to be jointly undertaken with the National Center for Complementary and Alternative Medicine; and (5) a planned trial network for studies of polycystic kidney disease and focal segmental glomerular sclerosis in children.

Division staff are giving increased thought to some strategies for stimulating investigator-initiated portfolios, a topic that was mentioned in the last Council meeting. Staff are attempting to strengthen outreach in fields such as cell biology and structural biology. Staff are also working with renal investigators on a plan for improving trial site networking. They believe that in some cases it would be beneficial for new clinical trials to do some cross-recruiting.

D. Division of Extramural Activities
Dr. Robert Hammond

Dr. Hammond noted the list of RFAs under which applications are scheduled to be reviewed in the summer of 2002 and presented to Council for second-level peer review in September. Many of these are important RFAs, which are targeted for funding in FY 2002. Dr. Spiegel noted that nine of the 20 RFAs on the Council's listing are being funded, in whole or in part, with special funds for type 1 diabetes research that are outside of the regular NIH/NIDDK appropriations process.

The NIDDK is continuing to adopt innovative electronic approaches for increasing the efficiency

of Council review. In a closed session of one of the subcouncils, members are using materials provided to them on compact disk, as opposed to the traditional printed versions of these materials. Moreover, the NIDDK homepage has been redesigned to make Council information more readily visible and accessible. This information includes the Council roster and an orientation book for new Council members.

With respect to *en bloc* concurrence, Dr. Hammond stated that there were 148 applications that have gone through early concurrence, with 78 awards made to that point in time. The early concurrence procedure aids grantees in planning their research and aids program staff in planning their workloads. Currently, the early-concurrence process is only being applied to R01 grants and to R03 (small) grants. However, NIDDK staff now has the capability of applying early concurrence to additional mechanisms if Council concurs.

XVII. ADJOURNMENT

Dr. Spiegel thanked the Council members for their attendance and advice. There being no further business, Dr. Spiegel adjourned the 159th meeting of the NIDDK Advisory Council on Friday, May 31, at 11:35 a.m.

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

Allen M. Spiegel, M.D.
Director, National Institute of Diabetes and Digestive and Kidney Diseases
Chairman, National Diabetes and Digestive and Kidney Diseases Advisory Council