DRAFT

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

May 19, 2005

I. CALL TO ORDER

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Director, Dr. Allen M. Spiegel, called to order the 168th National Diabetes and Digestive and Kidney Diseases (NDDK) Advisory Council meeting on May 19, 2005, at 8:30 a.m. in Salons A-C of the Grand Ballroom, Bethesda Marriott, Bethesda, MD.

A. ATTENDANCE – COUNCIL MEMBERS PRESENT

Dr. Janis Abkowitz
Dr. Robert Alpern
Dr. Janice Arnold
Ms. Janet Brown
Ms. Mary Clark
Dr. Roberto Coquis
Dr. Raymond DuBois
Dr. Robert Eckel
Dr. Jeffrey Flier
Dr. Richard Goodman
Dr. Earl Harrison (*Ex officio*)
Dr. William Henrich
Dr. Sum Lee
Dr. Rudolph Leibel
Dr. Brian Monahan *(Ex-officio)*
Ms. Nancy Norton
Dr. Jerry Palmer (*Ex-officio*)
Dr. Linda Sherman
Dr. E. Darracott Vaughan
Dr. W. Allan Walker

Council Member Absent:
Dr. Ronald Ruecker

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

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:

Kristen Abraham, NIDDK
Beena Akolkar, NIDDK
Michael Appel, NIDDK
Sara Arnold, IFFGD
Guillermo Arreaza-Rubin, NIDDK
Michele Barnard, NIDDK
Terry Bishop, NIDDK
Olivier Blondel, NIDDK
Diane Breckenridge, NIDDK
Josephine Briggs, NIDDK
Francisco Calvo, NIDDK
Shelley Carow, NIDDK
Arthur Castle, NIDDK
Joan Chamberlain, NIDDK
Dolph Chianchiano, Nat'l Kidney Foundation
Michelle Cissell, Juvenile Diabetes Research Found.
John Connaughton, NIDDK
Catherine Cowie, NIDDK
Maria Davila-Bloom, NIDDK
Edward Doo, NIDDK
Gayla Elder-Leak, NIDDK
Thomas Eggerman, NIDDK
Paul Eggers, NIDDK
Jody Evans, NIDDK
James Everhart, NIDDK
Richard Farishian, NIDDK
Ned Feder, NIDDK
Carol Feld, NIDDK
Frances Ferguson, NIDDK
Olaf Fonville, NIDDK
Judith Fradkin, NIDDK
Lisa Gansheroff, NIDDK
Mark Geanacopoulos, NIDDK
Shefa Gordon, NIDDK
Carol Goter-Robinson, NIDDK
Janet Gregory, NIDDK
Xiaodu Guo, NIDDK
Carol Haft, NIDDK
Mary Hanlon, NIDDK
Mary Harris, NIDDK
Barbara Harrison, NIDDK
Trude Hilliard, NIDDK
Eleanor Hoff, NIDDK
Jay Hoofnagle, NIDDK
Thomas Hostetter, NIDDK
Joyce Hunter, NIDDK
James Hyde, NIDDK
Mary Lou Ingeholm, Georgetown University
Donna James, NIDDK
Stephen James, NIDDK
Ann Jerkins, CSR
Teresa Jones, NIDDK
Christian Ketchum, NIDDK
Mustaq Khan, CSR
Krish Krishnan, CSR
Robert Kuczmarski, NIDDK
Tina Lancaster, OD, ICSD
Maren Laughlin, NIDDK
Amy Lavarola, Constella Group
Ellen Leschek, NIDDK
Maxine Lesniak, NIDDK
Monica Liebert, Amer. Urological Assoc.
Barbara Linder, NIDDK
Saul Malozowski, NIDDK
Denise Manouelian, NIDDK
Ronald Margolis, NIDDK
Dan Matsumoto, NIDDK
Michael K. May, NIDDK
Julie McDermott, NIDDK
Catherine McKeon, NIDDK
Rebecca Menso, NIDDK
Barbara Merchant, NIDDK
Carolyn Miles, NIDDK
David Miller, NIDDK
Megan Miller, NIDDK
David Mineo, NIDDK
Marva Moxey-Mims, NIDDK
Christopher Mullins, NIDDK
Neal Musto, NIDDK
D.G. Patel, NIDDK
Aretina Perry-Jones, NIDDK
Judith Podskalny, NIDDK
Sharon Pope, NIDDK
Elliot Postow, CSR
Rebekah Rasooly, NIDDK
Patricia Robuck, NIDDK
Mary K. Rosenberg, NIDDK
Atul Sahai, NIDDK
Karen Salomon, NIDDK
Lakshmanan Sankaran, NIDDK
Leonard Seeff, NIDDK
Jose Serrano, NIDDK
Elizabeth Singer, NIDDK
Paul Smedberg, American Society of Nephrology
Philip Smith, NIDDK
Lisa Spain, NIDDK
Myrlene Staten, NIDDK
Karen Teff, NIDDK
Dietmar Tietz, NIDDK
Rebecca Torrance, NIDDK
Marcia Vital, NIDDK
Karen Walker, NIDDK
Robert Wellner, NIDDK
Barbara Woynarowska, NIDDK
Dorothy West, NIDDK
Gina Wrench, NIDDK
Susan Yanovski, NIDDK
Charles Zellers, NIDDK

II. CONSIDERATION OF SUMMARY MINUTES OF THE 167th COUNCIL MEETING

A motion was made, and unanimously passed by voice vote, to approve the summary minutes of the 167th NDDK Advisory Council (February 2005) as submitted.

III. FUTURE COUNCIL DATES

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

September 14 and 15, 2005
February 15 and 16, 2006
May 31 and June 1, 2006
September 20 and 21, 2006

February 21 and 22, 2007
May 30 and 31, 2007
September 19 and 20, 2007

IV. ANNOUNCEMENTS

A. APPOINTMENTS, AWARDS, AND ACKNOWLEDGEMENTS
Dr. Allen Spiegel, Director

With Regard to NDDK Advisory Council Members:

- *Dr. Jerry Palmer:* Dr. Palmer will join the Diabetes, Endocrinology, and Metabolic Diseases Subcommittee of Council as a new *ex officio* member representing the Department of Veterans Affairs. He is Director of the Division of Endocrinology, Metabolism, and Nutrition at the VA Puget Sound Health Care System, Director of the NIDDK Diabetes Endocrinology Research Center, and Professor of Medicine at the University of Washington in Seattle.

- *Dr. Jeffrey Flier:* The American Diabetes Association will honor Dr. Flier with the prestigious Banting Award. This award recognizes his work on the molecular biology of insulin action, pathophysiology of obesity and weight regulation, physiology of leptin, and transgenic models of diabetes and obesity. A long-time extramural NIDDK grantee, Dr. Flier began his career as a clinical associate in the NIDDK Intramural Diabetes Branch. He is currently Harvard Faculty Dean for Academic Programs and Chief Academic Officer at the Beth Israel Deaconess Medical Center.

Within the NIDDK:

Joining the Division of Diabetes, Endocrinology, and Metabolism is:

- *Dr. Guillermo Arreaza-Rubin*: An endocrinologist and immunologist, Dr. Arreaza-Rubin received clinical training in Venezuela and research training at the University of Toronto and the University of Western Ontario. While a scientific director at Diabetogen Biosciences in London, Ontario, he worked on immunomodulatory agents for therapy of type 1 diabetes. He will assist in managing the islet transplant consortium and will participate in NIDDK programs in type 1 diabetes to develop new therapeutics.

Joining the Division of Kidney, Urologic, and Hematologic Diseases as a new staff member is:

- *Dr. Debuene Chang:* As the Director of the women's urology programs, Dr. Chang will bring to NIDDK her expertise in clinical urology and translational work, particularly device development. After graduating *summa cum laude* from the University of California, Berkeley, with a major in biophysics and medical physics, she attended Harvard Medical School. She completed her general surgery residency and urology residency at Massachusetts General Hospital and has since been in private practice in California. In addition to her expertise in clinical urology, Dr. Chang has conducted

research on the use of lasers for surgical applications, in both the bladder and urinary tract.

Joining the NIDDK Review Branch as Scientific Review Administrators are:

- *Dr. Atul Sahai:* Dr. Sahai joins the NIDDK from Northwestern University, where he was an associate professor. After receiving his Ph.D. in biochemistry from Howard University, Dr. Sahai completed a postdoctoral fellowship at NIH and has since held faculty positions at various academic institutions. Dr. Sahai has experience in renal research, particularly diabetic nephropathy and renal tubular cell biology. His recent work is on obesity and diabetes in gastrointestinal diseases, including non-alcoholic steatohepatitis.

- *Dr. Robert Wellner:* With a Ph.D. in biochemistry from the State University of New York Upstate Medical Center, Dr. Wellner's research background includes intracellular trafficking of proteins, epithelial ion and water transport, and gene therapy. He has served as a research physiologist at the U.S. Army Medical Research Institute of Infectious Diseases at Fort Detrick in Frederick, Maryland, and as a biologist in the Gene Therapy and Therapeutics Branch of the National Institute of Dental and Craniofacial Research.

NIDDK staff members receiving awards and honors are:

- *Dr. Saul Malozowski and Ms. Elizabeth Singer:* Dr. Malozowski, a senior advisor in the Division of Diabetes, Endocrinology, and Metabolic Diseases, and Ms. Singer, Director of the Office of Communications and Public Liaison, received the 2004 NIH Hispanic Health Communications Award in recognition of their service and commitment to the Nation's health. Dr. Malozowski was a spokesperson for the 2004 NIH and Department of Health and Human Services (DHHS) Hispanic Health Initiative, "Celebra La Vida Con Salud." In this capacity, he participated in radio public service announcements and in interviews aired in a number of U.S. cities.

- *Dr. Nancy Nossal:* Chief of the intramural Laboratory of Molecular and Cellular Biology, Dr. Nossal was elected this year to the American Academy of Arts and Sciences. She is recognized for her important work on the mechanisms of DNA replication.

Within the NIH Community:

- *Dr. Antonio Scarpa:* Dr. Scarpa joins NIH as Director of the Center for Scientific Review. At Case Western Reserve University, he was the David and Inez Myers Professor and Chair of the Department of Physiology and Biophysics. He is internationally recognized for his biophysical research into cellular and molecular mechanisms of ion transport and the metabolic consequences induced by transport. Dr.

Scarpa's work has been supported by NIH, including NIDDK, as well as the American Heart Association.

- *Dr. Judith Vaitukaitis:* The former Director of the National Center for Research Resources (NCRR), Dr. Vaitukaitis has been named Senior Advisor on Scientific Infrastructure and Resources to Dr. Zerhouni. While the search for a new NCRR Director is under way, the Acting Director is Dr. Barbara Alving, former Deputy Director of the National Heart, Lung, and Blood Institute and continues to serve as the Director of the Women's Health Initiative.

- *Dr. Robert Star:* Dr. Star has been named Senior Advisor on Clinical and Translational Sciences to Dr. Alving, Acting Director, NCRR. Dr. Star has worked on clinical research issues for the Re-engineering the Clinical Research Enterprise component of the NIH Roadmap and he co-chairs the Roadmap Trans-NIH Clinical Research Workforce Committee. In his new position, he will lead the effort to broaden the vision for this component of the Roadmap--particularly focusing on the concept of Regional Translational Research Centers.

B. CONFIDENTIALITY AND CONFLICT OF INTEREST
Dr. Robert Hammond, Director, Division of Extramural Activities

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

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

V. REPORT FROM THE NIDDK DIRECTOR
Dr. Allen Spiegel, Director

NIDDK Division of Extramural Activities Director To Retire

With sadness, Dr. Spiegel announced that Dr. Robert Hammond, Director of the NIDDK's Division of Extramural Activities and NDDK Advisory Council Executive Secretary, will retire

at the end of June 2005. His contributions to both NIDDK and NIH have been invaluable. His objectivity and excellent judgment were critical in the Institute's dealing with challenges ranging from issues of scientific integrity to prioritization, strategic planning, and fairness in review. He also made vital contributions at the trans-NIH level with regard to locus of review and the loan repayment program. While Dr. Hammond will be greatly missed, the Institute is nevertheless moving vigorously to recruit a new Division Director. Interviews are under way, and some excellent candidates have been identified.

NIH Reauthorization

Efforts are currently underway to formally reauthorize NIH programs. Leading this process is Representative Joe Barton (R-TX), Chairman of the House Committee on Energy and Commerce, which has jurisdiction over the NIH statutory authorities. To this end, a series of congressional hearings has been conducted and NIH Director, Dr. Elias Zerhouni has provided testimony. One specific hearing dealt with recommendations of an Institute of Medicine report regarding the NIH organizational structure, which was discussed in this Council after its publication. During the most recent of these hearings, held in March 2005, Representative Barton delineated three key areas that would likely be addressed by the reauthorization process:

1. Expand the authority of the NIH Director, including his budgetary authority.

2. Better align budget lines to ensure that funding allocations and mechanisms meet scientific demands.

3. Create a new, more transparent and more streamlined reporting system regarding NIH research activities.

One concept outlined by Dr. Zerhouni in his testimony is the creation of a new office to promote research coordination among NIH components. Specifically, he recommended an Office of Portfolio Analysis and Strategic Initiatives (OPASI). This Office would facilitate collaboration and pooling of resources among the ICs, expedite research, and facilitate adaptation to changes in science.

Dr. Spiegel noted that, at the March 2005 Planning Retreat, NIH Institute and Center Directors addressed the following themes with the NIH Director.

- Balancing trans-NIH priorities with Institute-specific priorities;
- Establishing infrastructure priorities and funding decisions;
- Developing long-term strategies to enhance trans-NIH cost efficiencies;
- Clarifying the role of the NIH Intramural Research Program in light of a challenging budgetary climate; and
- Evaluating current funding policies to maximize funding of the highest priority programs in challenging times.

Part 1 of the Council Forum will focus on the intramural theme, while Part 2 of the Forum will highlight some of the other Retreat topics, around which the NIH Director has established internal working groups for the purpose of conducting more detailed analyses.

VI. REPORT FROM THE NIDDK DEPUTY DIRECTOR
Dr. Griffin Rodgers, Deputy Director

NIDDK Appropriations for FY06: The FY06 budget is still pending. The President's request proposes an increase of 0.5 percent in funding for NIDDK, which is in line with the overall request for the NIH. Dr. Zerhouni has testified at hearings on the budget before both the House and Senate Labor/HHS Appropriations Committees.

Update on NIH Conflict-of-Interest Policies: In February 2005, "Interim Final Regulations" were issued in response to concerns about the need to strengthen NIH's conflict-of-interest policies. Developed by the Department, the new supplemental regulations would place substantial limitations on NIH employees in three areas: outside activities, types of financial holdings, and receipt of awards. Debate has ensued regarding whether the regulations would adversely affect the ability of the NIH to recruit and/or retain senior scientists. Thus far, the regulations on stock divestiture have not been implemented.

VII. ADVISORY COUNCIL FORUM--PART 1
Report on the NIDDK Intramural Research Program (IRP)
Dr. Ed Holmes, Member, 2005 Blue Ribbon Panel (BRP) Review
Dr. Marvin Gershengorn, Director, NIDDK Division of Intramural Research

Following up on the intramural theme of the March Planning Retreat, Dr. Spiegel presented a budget overview. Since 1986, the NIH IRP budget has increased in absolute dollars, but has decreased proportionately as a percent of the NIH total by about two percent and its real purchasing power (in 1986 dollars) has remained relatively stable since 2002. The NIDDK's IRP budget has followed a similar trend. As a percentage of the NIDDK total appropriation, the Institute's IRP budget has decreased approximately two percent since 1994--from approximately 11.7 percent of the budget to 9.7 percent. The sharp decline that occurred from 1998 to 2001 reflected a deliberate NIDDK effort to enhance the extramural program as the NIH entered its five-year period of budget doubling starting in FY 1999. The NIDDK intramural budget has since stabilized at around 9.7 percent of the Institute's total appropriation, below the NIH average and thirteenth among the Institutes.

Blue Ribbon Panel Review and Draft NIDDK Implementation Plan

In 2005, a Blue Ribbon Panel (BRP) convened to review the NIDDK IRP. Chair of the panel was Dr. Lee Limbird, a vice-Dean at Vanderbilt University. Panelists included current and former Council members, as well as representatives with expertise in basic, clinical, and translational research: Barrie Carter, VP, Targeted Genetics Corp., Richard Goodman, Director Vollum Institute for Advanced Biomedical Research, Edward Holmes, Dean, UCSD Medcial School, Brian Matthews, Professor, Institute of Molecular Biology, Uinversity of Oregon, and Michael Thorner, Chair, Dept. of Medicine, University of Virginia. The panel met three times to review materials provided by NIDDK, to interview approximately 50 IRP staff, and to review comments received from approximately 30 individuals. This process resulted in a report that presents recommendations in the following four major areas, which were summarized by Dr. Ed

Holmes. Dr. Marvin Gershengorn, Director of the NIDDK Division of Intramural Research, then described the IRP's draft implementation plan for responding to the recommendations.

1. Continue To Conduct Strong and Productive Research: The BRP commended the innovative and high-impact research conducted within the NIDDK's IRP. In addition, the presence of 13 members of the National Academy of Science within this program, from a total of 52 members within the NIH, attests to the high quality of its investigators. The IRP's outstanding intellectual environment enables it to take on high-risk projects, and it has had great success in these efforts. Recognizing the accomplishments of the IRP in basic science, the BRP encouraged the program to also channel its resources toward the success of clinical research endeavors.

2. Balance Laboratory and Clinical Research: To better emphasize, foster, and sustain clinical research within NIDDK's IRP, the BRP had nine recommendations as follows:

- Recruit a nationally recognized clinical investigator to head the clinical research area;
- Identify unique clinical opportunities in which the program might invest;
- Strengthen collaboration with the Phoenix Epidemiology and Clinical Research Branch;
- Create competitive packages for patient-oriented research investigators;
- Ensure a career path in clinical research that can lead to NIH tenure;
- Develop an infrastructure that supports clinical research;
- Foster communication and collaboration between basic and clinical researchers;
- Develop funding mechanisms that promote interactions between basic and clinical researchers and across branches of NIDDK and other Institutes; and
- Develop programs that enhance research training for clinical researchers.

To develop an infrastructure that supports clinical research, the IRP plans to create a central office to supplement individual branches' resources for supporting clinical research. New office staff would include a manager, two biostaticians, a protocol specialist, a patient coordinator, and a specialist in patient recruitment to assist with the IRP's clinical research protocols. The IRP is also augmenting interactions with clinical investigators at its Phoenix branch. These efforts include instituting a new laboratory facility within the Translational Genomics Research Institute; integrating the Phoenix and Bethesda databases; enhancing collaborations between obesity researchers at the two locations via, for example, monthly videoconferences; and intensifying efforts to recruit a genetic epidemiologist.

A significant opportunity for conducting patient-oriented research in the IRP is the obesity clinical research initiative. This initiative involves organizing a group of current clinical investigators interested in obesity research, as well as recruiting a new clinical investigator. Within the Obesity Clinical Research Center, there is a metabolic research patient care unit to house patients and a facility for phenotyping obese patients. In addition, as part of a collaboration with nuclear medicine and PET colleagues, the IRP has purchased an MRI instrument to further studies of obese patients. The intent is for this facility to be the center for comprehensive obesity research and the site of extensive intramural-extramural collaboration. These and other activities planned by the IRP will help grow clinical research activities within the Institute.

3. Enhance the Quality of Postdoctoral Training and Career Development: To attract strong postdoctoral fellows to the NIDDK IRP, the BRP recommended that the IRP: (1) coordinate

retreats at which postdoctoral fellows are featured speakers, (2) offer scientifically intense coursework for fellows, and (3) develop a funding initiative to support the transition of fellows to independent research. The IRP's plans to implement these recommendations include participating in the development of a certificate-granting, trans-NIH program in translational research; strengthening the Annual Fellows Retreat; initiating a competitive fellow award based on a written grant proposal; expanding the Senior Clinical Research Fellowship (SCRF) program; and interdigitating the NIDDK SCRF with the proposed NIH-wide Assistant Clinical Investigator Program.

4. Enhance Effectiveness of BSC Review Process: To enhance the effectiveness of the BSC review process, the BRP recommended that: (1) investigators be informed of the members serving on the BSC and be able to recommend reviewers for the panel, (2) BSC members be identified during the review process, (3) feedback to IRP scientists be provided in a timely manner, and (4) mentoring teams be formed that include intra- and extramural researchers. In response to these recommendations, the IRP plans to implement the following changes to the BSC review process:

- Reference letters would be requested and *ad hoc* reviewers chosen from a list submitted by the investigator;
- Each investigator would have an individual, five-minute meeting with reviewers without the Scientific Director present;
- The Laboratory/Branch Chief would be present for the summary discussion;
- The BSC report, written by the Chair, and the individual reviewers' evaluations would be sent to the investigator and Laboratory/Branch Chief; and
- The Scientific Director and Deputy Scientific Director would meet with the investigators and Laboratory/Branch Chief to discuss the review and to plan actions soon after the BSC meeting.

A final recommendation from the BRP is to augment efforts to develop a shared vision in strategic planning and build consensus regarding the mission of the IRP.

Overall, the challenges identified by the BRP are similar to those facing intramural research programs within other Institutes and institutions. Challenges aside, the BRP considered the NIDDK IRP a robust program and outstanding intellectual environment with the unique ability to pursue high-risk projects. All BRP recommendations are being reviewed by Drs. Zerhouni and Spiegel, who will take them under advisement.

Council Questions and Comments

Defining the Success of the IRP: Has the dollar efficiency of the IRP been measured against that of extramural programs? Council discussion clarified that the "metric of success" for the IRP will have quantitative as well as qualitative elements, such as the citation impact of publications from the IRP.

Training of Clinical Investigators in Epidemiology: Did the BRP address epidemiology research within the IRP? Dr. Holmes said that the BRP favorably reviewed the opportunity that NIH investigators have to participate in the Duke Clinical Research Program, which enables them to receive training in epidemiology. Dr. Spiegel added that, in terms of ongoing epidemiology

research, there are significant population-based studies taking place at the Phoenix site, as well as several epidemiologists on the Bethesda campus who provide program oversight.

Evaluating Clinical Investigators: Did the BRP consider how NIH would assess intramural investigators in the clinical arena compared to basic investigators, which is also a concern in the extramural community? Dr. Holmes suggested that there should be consideration of the many elements that differentiate clinical from basic research. For instance, it can be difficult for clinical researchers to distinguish themselves in the field because most clinical studies are team-based and it often takes many years to complete a study and publish results. The NIH is actively working to address concerns regarding how to recognize, invest in, and promote clinical investigators. The Clinical Research Task Force of the American Association of Medical Colleges was convened to address the apparent decline in the number of investigators doing clinical research.

Increasing the Number and Quality of Postdoctoral Fellows: Has NIH identified specific factors that may have contributed to a decline in the recruitment of postdoctoral fellows to the IRP in recent years? Dr. Holmes reported that, among the factors affecting recruitment are financial issues--such as cost-of-living and salary structure, as well as a lack of infrastructure to support fellows. In addition, Dr. Spiegel pointed to bureaucratic limitations that do not permit NIH fellows to apply for NIH grants.

Defining the Mission of the IRP: *How are the goals of the intramural research programs of the various Institutes distinguished from the goals of the extramural programs?* Dr. Spiegel outlined two components central to the mission of NIH's intramural programs that make them unique: (1) conducting research that is not only high-risk, but also high-impact, and (2) linking basic and clinical research.

Preliminary Report from the Council Working Group on Extramural-Intramural Collaboration in the CRC Obesity Research Center

In March 2005, Dr. Spiegel convened a Council Working Group charged with developing plans to foster extramural-intramural collaborations that will utilize the new facilities being built in the NIH Clinical Research Center for the trans-NIH Obesity Clinical Research Center. Specifically, the group will advise the Institute regarding establishment of a policy for collaboration between the intramural and extramural community, identification of a funding mechanism to support collaborative activities, and development of a process for reviewing and prioritizing collaborations. Council members toured the obesity center and spoke with intramural investigators in obesity who are currently involved on an *ad hoc* basis with extramural investigators. These discussions underscored the significant potential for future collaborative activities using the obesity center. However, extramural obesity and nutrition center directors have expressed a need for more information about the center. Their suggestions include mini-sabbaticals, fellowships, and a K23 award. Taking these suggestions under advisement, the Working Group will conduct additional meetings and will present a full report with written recommendations at the next Council meeting in September 2005.

VIII. SUBCOMMITTEE MEETINGS

From approximately 11:00 a.m. to 1:45 p.m., separate meetings were convened by the Subcommittees for Diabetes, Endocrinology, and Metabolic Diseases; Digestive Diseases and Nutrition; and Kidney, Urologic, and Hematologic Diseases.

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

X. SCIENTIFIC PRESENTATION
Role Reversal--RNA Control of Gene Expression

Dr. Richard Goodman
Director and Senior Scientist
Vollum Institute for Advanced Biomedical Sciences
Oregon Health Sciences University

Dr. Goodman presented major accomplishments and innovations in the field of gene regulation over the last 40 years. These include the discovery and accumulation of knowledge about binding and activation domains, the role of co-activators in genetic transcription, and recent exciting discoveries concerning the role of "micro-RNAs" in gene regulation.

XI. ADVISORY COUNCIL FORUM: Part 2
Setting Priorities and Managing Resources in Challenging Times

Having discussed the intramural theme from the March 2005 NIH Planning Retreat, the Council turned to the other four themes:

- Balancing trans-NIH priorities with Institute-specific priorities;
- Establishing infrastructure priorities and funding decisions;
- Developing long-term strategies to enhance trans-NIH cost efficiencies; and
- Evaluating current funding policies to maximize funding of the highest priority programs in challenging times.

In pursuing these themes, the NIH has proposed activities in three major areas: (1) strategic planning (both trans-NIH and IC-specific), (2) grant funding policies, and (3) research training and support for new investigators. Each of these areas is addressed in greater detail below.

Strategic Planning: Trans-NIH and IC-Specific
Dr. Allen Spiegel

Dr. Spiegel referenced Dr. Zerhouni's testimony before a March 2005 hearing of the House Energy and Commerce Subcommittee on Health. Dr. Zerhouni explained that, to face the challenges of the 21st century, the NIH needs to work in a manner that will complement its processes for determining strategic research initiatives and maximize opportunities for trans-NIH collaboration. He discussed functional approaches for strengthening coordination in order to realize these objectives, rather than major structural reorganization. Along these lines, he gave the examples of the NIH Roadmap initiative, the NIH Obesity Research Task Force, and the NIH

Neuroscience Blueprint. Each of these represents coordinated efforts of existing Institutes and Centers. Along similar lines, Dr. Zerhouni now proposes creation of a new component within the Office of the NIH Director: an Office of Portfolio Analysis and Strategic Initiatives (OPASI). This new office, which would report to the NIH Director, would have three arms, as described below:

- *Strategic Analysis:* This arm would be responsible for developing and using analytic tools, including a coding system (knowledge management) that would provide a systematic understanding of the current NIH research portfolio. This arm would also provide tools to quantitate epidemiologic data in order to help gauge public health need and disease burden and, thereby, contribute to the setting of priorities across ICs.
- *Evaluation:* This arm would be responsible for evaluating the results of NIH's investments. Its success would depend on good metrics.
- *Strategic Coordination.* This arm would develop common processes and formats for NIH-wide planning and work with ICs in their planning efforts. The details of how such strategic coordination activities would be conducted are critical to the success of NIH strategic planning efforts.

All three arms of OPASI would report to an advisory committee and involve input from stakeholders to ensure accountability.

Council Questions and Comments

Approaches to Coding: The NIH has great strength in bibliographic information tools to apply to the issue of coding its research portfolio. However, in the strategic analysis arm of the newly proposed office, it appears that the NIH would be both developing the coding algorithms and applying them; would this present a conflict? Dr. Spiegel cited examples (including, for instance, the Human Nutrition Research Information Management system, or HNRIM) in which NIH, in coordination with other Federal agencies, successfully developed coding systems to capture information in a consistent manner on nutrition research and other critical topics. This is accomplished with input from scientific program managers who are experts in their respective fields.

Valuing Basic Research: While NIH is proposing to set priorities by determining disease burden, research that is in its early stages often cannot be evaluated in this manner. Dr. Spiegel reassured Council that Congress and NIH recognize the importance of investing in basic research. For example, the fourth largest institute within NIH, the National Institute of General Medical Sciences, supports basic biomedical research almost exclusively. Dr. Spiegel stressed the importance of strengthening epidemiologic data to better gauge disease burden, having the necessary knowledge base and research tools in place, and using additional measures, such as scientific opportunity, to help determine research priorities.

Implementing Strategic Plans: Without long-term commitment and follow-through, strategic planning exercises are not meaningful. Dr. Spiegel agreed on the need for an ongoing commitment to examining the research portfolio to identify areas of deficiency in the knowledge base and to capitalize on the emergence of research opportunities. He is hopeful that the long-range planning effort of a soon-to-be-formed National Digestive Diseases Commission will be dynamic in nature.

Balancing Activities: Would NIH-wide strategic coordination result in a top-down prioritization process that would detract from the individual ICs' congressional mandates and from investigator-initiated research? Dr. Spiegel emphasized the importance of: (1) striking an appropriate balance between NIH-wide and IC-specific activities, and (2) striking a balance between achieving economies of scale via NIH-wide activities, on the one hand, and supporting investigator-initiated research, on the other. The NIH recognizes that its commitment to strategic planning must be ongoing and that its approach must be dynamic in order to respond to advances in research and other emerging issues. There is an unequivocal need for increased coordination and the breaking down of organizational silos on the one hand, with a corresponding need to respect the mission-specific research authorities established by the Congress--largely in response to public health issues and needs. Untargeted investigator-initiated research remains an NIH priority. Moreover, larger, NIH-spearheaded initiatives that are targeted to research areas often include opportunities for investigators to submit regular research grant applications (R01s).

Clinical Research: This type of research needs long-term funding in order to translate scientific discoveries in ways that will directly benefit patients. Dr. Spiegel noted that this comment is relevant to the time horizon for the funding of Regional Translational Research Centers under the NIH Roadmap. The NIH is now grappling with the issue of how and when to "graduate" these types of Roadmap initiatives into the existing programs of appropriate lead Institutes and Centers and what the budget implications of that process may be.

Grant Funding Policies
Dr. Robert Hammond

In an effort to maximize funding of the highest priority programs in a challenging budget climate, NIH is evaluating whether any of its corporate grant funding policies need to be changed to include consideration of numbers of grants per investigator, percentage of grants attributed to new investigators, or other factors. Data collected in support of this effort were shared at the March 2005 NIH Director's Planning Retreat and are presented below.

- Across the NIH, between 1998 and 2004, there was a 41-percent increase in the average dollar amount awarded per Research Project Grant (RPG)—to the average amount of about $550,000 per grant in 2004. However, adjusted for inflation, this average amount did not increase significantly between 1998 and 2004.

- While there has been discussion about maximizing funding by limiting the number of grants permitted per investigator, NIH data from 1998 and 2004 show that ~75 percent of all principal investigators hold only one research project grant, ~20% hold two grants; only ~6% hold three or more.

- NIH-wide data indicating the number of investigators with RPGs from multiple ICs have also been collected and analyzed. In the case of NIDDK, for example, of the 2,640 investigators awarded RPGs in 2004, 699 investigators also held awards from another IC.

Council Questions and Comments

Investigator Participation in NIH Portfolio: Is it really advisable to limit the number of grants per investigator? Should investigators with multiple grants undergo greater scrutiny in review? Dr. Spiegel reiterated that the marginal gain from such an approach would be very limited. He further commented that there has been no discussion at NIH about possibly limiting the number of grants awarded to Howard Hughes-supported investigators, whose funding is substantial.

Training and Supporting New Investigators
Dr. Robert Hammond

Data indicate that the average age of an NIH awardee at the time of award was 47.2 years in 1994—rising to 50.2 years in 2003. For first-time awardees, the corresponding data are 39.9 years—rising to 42.6 years in the most recent year for which complete data are available. Investigators are therefore spending longer periods of time before they can set their own research directions and establish their independence. As a result, there is increasing concern that prospective investigators will choose other career paths. This would have troubling implications for the future of biomedical research in the United States. The research training and support of new biomedical investigators has therefore been identified as an NIH-wide goal. To this end, the NIH commissioned the May 2005 National Academies report entitled, "Bridges to Independence." This report identifies opportunities for and challenges to fostering the independence of new investigators in biomedical research. The report presents recommendations in four major areas:

1. Optimizing Postdoctoral Training: Recommendations under this topic included shortening postdoctoral appointments, reallocating NIH resources for postdoctoral support, providing independent funding, clarifying mentorship responsibilities, broadening educational opportunities, and conducting program evaluation.

2. Transitioning to the First Independent Position: Recommendations included creating career transition research grants to: (1) initiate an independent research program, and (2) to permit increased risk-taking during the final phase of mentored postdoctoral training and during the initial phase of the independent research effort.

3. Establishing Stable Research Programs: Recommendations included establishing a new investigator R01 grant, providing support for non-tenure track scientists, and providing for enhanced job security.

4. Enhancing Data Collection and Program Evaluation: Recommendations included developing enhanced data collection systems on all NIH-supported research, irrespective of specific funding mechanism, so that NIH can track the effectiveness of its programs and make more informed programmatic decisions.

The "Bridges to Independence" report may be viewed on the National Academies Press Web site at: http://books.nap.edu/catalog/11249.html.

Council Questions and Comments

Evaluation the Research Career (K) Mechanism: It may be too early to draw conclusions about the K23 mechanism. Dr. Spiegel noted that the K23 award program for patient-oriented career investigators began in 1999 and is a five-year program. The NIH is very much interested in tracking the success of this program. There is a determined effort, beginning now, to capture data on the cohort that is emerging from the K23 pipeline and to assess their R01 and other research activity. The NIH also continues to study the impact of the other, more well-established career award mechanisms.

Team Science Versus Independent Research Careers: *While the Roadmap emphasizes a team approach, the National Academies report focuses on fostering independent research careers. Is this a mixed message?* Dr. Spiegel responded that the intention of "Bridges to Independence," was to address the steady state of postdoctoral fellows. Statistics show that, despite an increase in the number of postdoctoral fellows in the biomedical sciences, there is no comparable increase in tenure track positions. Furthermore, the emphasis on team science and the need to foster independence are not necessarily antithetical to each other. For instance, the National Academies report, in keeping with a team science approach, recommends developing a new support mechanism for non-tenure track scientists. However, the NIH can only go so far in defining the landscape; academic health centers also have a vital role. There is also ongoing discussion within NIH and within universities about how to acknowledge co-investigators in the biological sciences, as is currently done in physics. Council members commented further that, with respect to investigative teams, universities need to be able to identify the individuals who are a driving, independent force for the research, and to promote them accordingly.

Foreign Postdoctoral Fellows: Does NIH track the career paths of foreign postdoctoral fellows to determine whether they pursue biomedical research? Dr. Spiegel said that, at present, there is no way to track foreign postdoctoral fellows in the extramural research community; however, the ratio of foreign-to-nonforeign postdoctoral fellows in NIH's intramural program is approximately 50:50. He added that, while NIH has no position on hiring nonforeign as opposed to foreign postdoctoral fellows, the agency is involved in transitioning high-quality foreign trainees to permanent residency and does support proposals and programs that involve foreign fellows in intramural research for a finite number of years.

Cost-Sharing Post-R01: The four-year cycle of funding offered via many NIH grant mechanisms may not be appropriate because science cannot be made to fit such a well-defined schedule. Dr. Spiegel responded that, for this reason, a cost-sharing approach should be further explored. In such an approach NIH and the supporting institution would share the cost of supporting the investigator during the transitional time following his or her first R01 award. Council members were interested to learn more about this approach. Some Council members expressed concern that such an approach may not be feasible on practical grounds.

Resource Allocation for Infrastructure: Infrastructure support has suffered in the current budget climate. Dr. Spiegel noted that infrastructural support will be the topic of further discussion at an upcoming IC directors' retreat.

XII. CONSIDERATION OF REVIEW OF GRANT APPLICATIONS

A total of 1,380 grant applications, requesting support of $332,968,884 were reviewed for consideration at the May 19, 2005 meeting. Funding for these 1,380 applications was recommended at the Scientific Review Group recommended level. Prior to the Advisory Council meeting, an additional 472 applications requesting $124,554,285 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 May 19 meeting.

XIII. ADJOURNMENT

Dr. Spiegel thanked the Council members for their attendance and efforts. There being no other business, the 168th meeting of the NDDK Advisory Council was adjourned at 4:45 p.m., May 19, 2005.

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

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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