DRAFT

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

June 11-12, 2003

I. CALL TO ORDER

The NIDDK Director, Dr. Allen M. Spiegel, called to order the 162nd National Diabetes and Digestive and Kidney Diseases Advisory Council meeting on June 11, 2003, at 8:31 a.m. in Conference Room E1/E2, Building 45, on the NIH campus in Bethesda, MD. Dr. Spiegel opened the meeting with the following general announcements.

< With respect to new Council members, Dr. Robert J. Alpern from the University of Texas Southwestern Medical Center in Dallas and Dr. Edwin Darracott Vaughan, Jr. from the Weill Medical College of Cornell University will be joining the Kidney, Urologic, and Hematologic Diseases Subcommittee. Dr. Raymond N. DuBois, Jr., from Vanderbilt University Medical Center and Dr. Robert H. Eckel from the University of Colorado Health Sciences Center will be joining the Digestive Diseases and Nutrition Subcommittee. Finally, Dr. Linda A. Sherman from the Scripps Research Institute will be joining the Diabetes, Endocrinology, and Metabolic Diseases Subcommittee. Curricula vitae of all council members were made available on the CD provided to all council members.

< Several NIDDK-supported investigators are among the newly elected National Academy of Sciences members: Dr. John Baxter, an endocrinologist at the University of California, San Francisco; Dr. Dennis Carson, Professor of Medicine at the University of California, San Diego; Dr. Barry Coller, a hematologist at Rockefeller University; Dr. Diane Matthis, an immunologist at the Joslin Diabetes Center; Dr. Catherine Ross, a nutrition professor at Pennsylvania State University; and Dr. Avram Hershko, a former Lasker Awardee and a newly elected Foreign Associate.

< Dr. Joseph Shiloach, an intramural researcher, is a recipient of the Department of Health and Human Services Secretary's Award for Distinguished Service for participating in a team that produced a *Staphylococcus aureus* vaccine.

< Two new staff appointments have been made: Ms. Elisa Gladstone, Associate Director of the National Kidney Disease Education Program; and Dr. Ellen Leschek, Type 1 Diabetes TrialNet Program Director, Division of Diabetes, Endocrinology and Metabolic Diseases.

A. ATTENDANCE – COUNCIL MEMBERS PRESENT

Dr. Robert J. Alpern
Dr. Edward Benz
Ms. Mary E. Clark
Dr. Raymond N. DuBois
Dr. Robert H. Eckel
Dr. Richard H. Goodman
Hon. Levan Gordon
Dr. Earl Harrison (*Ex officio*)
Dr. Edward W. Holmes
Dr. James W. Kikendall (*Ex officio*)
Dr. Sum P. Lee
Ms. Nancy J. Norton
Dr. Daniel Porte
Dr. Sandra Puczynski
Dr. Vicki Ratner
Dr. Linda A. Sherman
Dr. E. Darracott Vaughan
Dr. W. Allan Walker

Absent Council Members:
Mr. David Baldridge
Dr. Jose Caro
Dr. Carolyn Kelly

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. Some NIDDK staff listed below attended via videocast from 2 Democracy Plaza, Room 701. Guests were present during the open sessions of the meeting. Attendees included the following:

Kristen Abraham, NIDDK
Lawrence Agodoa, NIDDK
Beena Alkolkar, NIDDK
Sara Arnold, IFFGD
David Badman, NIDDK
Michele Barnard, NIDDK
Najma Begum, CSR
Carolyn Benson, NIDDK
Tawana Berry, NIDDK
Terry Bishop, NIDDK
Sharon Bourque, NIDDK
Josephine Briggs, NIDDK
Danita Byrd-Holt, SSS
Francisco Calvo, NIDDK
Joan Chamberlain, NIDDK
Dolph Chianchiano, Nat. Kid. Fd.
Jordana Choucair, IFFGD
John Connaughton, NIDDK
Randy Copeland, NIDDK
Leslie Curtis, NIDDK
Florence Danshes, NIDDK
Linda Edgeman, NIDDK
Michael Edwards, NIDDK
Thomas Eggerman, NIDDK
Paul Eggers, NIDDK
Gayla Elder-Leak, NIDDK
Donald Ellis, NIDDK
Jody Evans, NIDDK
James Everhart, NIDDK
Richard Farishian, NIDDK
Ned Feder, NIDDK
Carol Feld, NIDDK
Teresa Fitzpatrick, NIDDK
Olaf L. Fonville, NIDDK
Judith Fradkin, NIDDK
Lisa Gansheroff, NIDDK
Sanford Garfield, NIDDK
Derek Gault, NIDDK
Elisa Gladstone, NIDDK
Robert Goldstein, JDRF
Maria Gonzalez, Constella Grp
Janet Gregory, NIDDK
Carol Haft, NIDDK
Frank Hamilton, NIDDK
Mary Hanlon, NIDDK
Dana Harris, NIDDK
Mary Harris, NIDDK
Barbara Harrison, NIDDK
Trude Hilliard, NIDDK
Gladys H. Hirschman, NIDDK
Eleanor Hoff, NIDDK
Jay Hoofnagle, NIDDK
Ann Karen Howard, NIDDK
Van Hubbard, NIDDK

Donna Huggins, NIDDK
Joyce Hunter, NIDDK
James Hyde, NIDDK
Donna James, NIDDK
Stephen James, NIDDK
Scott Jenkins, The Blue Sheet
Valerie Johnson, NIDDK
Robert Karp, NIDDK
Melissa Keefe, Am. Urol. Assoc.
Charlette Kenley, NIDDK
Christian Ketchum, NIDDK
M.A. Khan, CSR
Kathy Kranzfelder, NIDDK
Krish Krishnan, CSR
Robert Kuczmarski, NIDDK
John Kusek, NIDDK
Maren Laughlin, NIDDK
Kim Law, NIDDK
Todd Le, NIDDK
Melissa Lee, NIDDK
Ellen Leschek, NIDDK
Maxine Lesniak, CSR
Monica Liebert, Am. Urol. Assoc.
Helen Ling, NIDDK
Billie Mackey, NIDDK
Denise Manouelian, NIDDK
Ronald Margolis, NIDDK
Teresa Marquette, NIDDK
Winnie Martinez, NIDDK
Dan Matsumoto, NIDDK
Michael K. May, NIDDK
Julie McDermott, NIDDK
Barbara Merchant, NIDDK
Catherine Meyers, NIDDK
Carolyn Miles, CSR
David Miller, NIDDK
David Mineo, NIDDK
Marva Moxey-Mims, NIDDK
Christopher Mullins, NIDDK
Neal Musto, NIDDK
Leroy Nyberg, NIDDK
Diana O'Donovan, NIDDK
Denise Payne, NIDDK
Peter Perrin, CSR
Aretina Perry-Jones, NIDDK
Roberta Peterson, McKessa
Judith Podskalny, NIDDK
Sharon Pope, NIDDK
Elliot Postow, CDR
Rebekah Rasooly, NIDDK
Patricia Robuck, NIDDK
Ruth Robinson, NIDDK
Paul Rushing, NIDDK
Lakshmanan Sankaran, NIDDK
Sheryl M. Sato, NIDDK
Leonard Seef, NIDDK
Jose Serrano, NIDDK
David Serreze, Jackson Lab
Kathleen Shino, NIDDK
Michelle Shorter, NIDDK
Elizabeth Singer, NIDDK
Philip Smith, NIDDK
Rosa Sorrell, NIDDK
Robert Star, NIDDK
Lisa Thompson, NIDDK
Mehrdad Tondravi, NIDDK
George Tucker, NIDDK
Whitney Tull, NephCure Foun.
Renetta Washington, NIDDK
Dorothy West, NIDDK
Elizabeth Wilder, NIDDK
Gina Wrench, NIDDK
Susan Yanovski, NIDDK
Charles Zellers, NIDDK

II. CONSIDERATION OF SUMMARY MINUTES OF THE 161ST COUNCIL MEETING

A motion was made, and unanimously passed by voice vote, to accept the summary minutes of the 161st Council as submitted.

III. FUTURE COUNCIL DATES

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

September 24-25, 2003
February 4-5, 2004
May 26-27, 2004
September 22-23, 2004
February 23-24, 2005
May 19-20, 2005
September 14-15, 2005

IV. ANNOUNCEMENTS: CONFIDENTIALITY AND CONFLICT OF INTEREST
Dr. Robert Hammond

Dr. Hammond called to the Council's attention the procedures to guarantee 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. Council members were reminded that materials furnished to them are considered privileged information and are to be used for the purpose of review and discussion only during the closed portions of the meeting. The outcome of closed session discussions may be disclosed only by staff and under appropriate circumstances. All communications from applicants and grantees 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. They do not need to do so for *en bloc* actions.

Regarding multi-campus institutions of higher education, an employee may participate in any particular matter affecting one campus of a state multi-campus institution of higher education if the employee's disqualifying financial interest is employment at a separate campus of the same multi-campus institution and a position with no multi-campus responsibilities. Finally, Dr. Hammond underscored that the Council members are special government employees and are governed by the Department of Health and Human Services (DHHS) standards of conduct during the days they are paid for duty. During those periods, members cannot transact personal business, enter into discussions with members of the legislative or executive branches of the government, or discuss matters pertaining to their institution's funded activities with NIH staff. Furthermore, Council members must not discuss with members of the Congress proposed or pending legislation or appropriations that concern the Public Health Service or the Department during this period.

V. REPORT FROM THE NIDDK DIRECTOR
Dr. Allen Spiegel

Dr. Spiegel called Council members' attention to a document entitled: "Highlights of the NIDDK Program Planning Process." Many items noted in this document reflect the diversity of science funded and/or conducted by the NIDDK, the evolving program planning process, the collaborations with many patient-oriented and professional organizations, and the input obtained from the scientific community and the public. Dr. Spiegel asked Council members to review the document and to share their thoughts and ideas with NIDDK staff and Subcommittee participants.

Focus of Future Advisory Council Discussions: Shortly before the February 2003 Council meeting, Dr. Hammond asked the Council members to identify issues that they considered to be the most productive for Council consideration. The view of the majority was that the Council should focus on the "big picture" rather than more detailed or specific issues that could be deferred in many instances to Institute staff. During the February 2003 Advisory Council teleconference, participants discussed a number of such broad topics.

Research Centers Mechanism: One of the "big picture" central themes that will be discussed with Council members is the Research Centers mechanism. Although Centers represent only about 5 percent of the NIDDK budget, the investment is significant. Given the magnitude of the

investment and the uniqueness of the mechanism, important questions need to be asked across all Centers to ensure that taxpayers' dollars are being used in the most cost-effective, productive, and meaningful way. In order to determine if this is the case, Dr. Spiegel asked Council members to propose an appropriate framework and relevant questions. Because NIDDK Centers encompass all program areas, there may be questions that are specific to a given discipline, which should be discussed at the Subcommittee level. However, broad, generic issues also exist. For instance, the Centers mechanism has the potential to be an outstanding vehicle for addressing not only translational and clinical research, but multidisciplinary and interdisciplinary research as well. This enhancement effort is viewed by the Institute to be the best way to promote efficiency and cost-effectiveness in order to have a real impact on public health. As the enhancement effort progresses, details of the process will be posted on the NIDDK Website at http://www.niddk.nih.gov.

New Liver Disease Branch: A new organizational unit, a Liver Disease Branch, has been established within the Digestive Diseases and Nutrition (DDN) Division. Consistent with the recommendations of a search committee--which was chaired by Dr. Rodgers and composed of both lay members and gastrointestinal and liver experts--Dr. Spiegel has appointed Dr. Jay Hoofnagle as the new Branch Chief. Dr. Hoofnagle is an internationally recognized expert in liver disease research, who has pioneered studies of interferon therapy in various forms of hepatitis. Dr. Hoofnagle sees this new appointment as an opportunity to focus on areas of great need and opportunity. He will continue to play an important role in the NIDDK Intramural Program and to help catalyze liver disease research across the NIH. In the interim, Dr. Stephen James has been appointed as the Acting Director of the DDN Division, the position Dr. Hoofnagle previously held. Another national search will be launched shortly to identify a new permanent Division Director and Dr. Rodgers will chair that search committee.

NIDDK Office of Obesity Research: Last February, Council members were informed of the establishment of a new Office of Obesity Research within NIDDK. During that Advisory Council teleconference, Drs. Philip Smith (Division of Diabetes, Endocrinology and Metabolic Diseases) and Dr. Sue Yanovski (Division of Digestive Diseases and Nutrition) outlined some of their ideas, with input from an NIDDK Obesity Research Working Group, with regard to initiatives and steps that the Institute would be taking to address this public health crisis.

NIH Obesity Research Task Force: In April 2003, the NIH Director, Dr. Elias Zerhouni, established an NIH Obesity Research Task Force, co-chaired by Dr. Spiegel and Dr. Claude Lenfant, Director of the National Heart, Lung, and Blood Institute (NHLBI). The charge to the task force includes: (1) Develop an NIH strategic plan for obesity research based on the identification of areas of greatest scientific opportunity and need; (2) Monitor the implementation of the plan and report to the NIH Director and IC Directors; and (3) Serve as a point of contact between the NIH and external organizations. The current membership of the Task Force includes representatives from most ICs with programmatic interests in obesity research. Given the important behavioral component of obesity, the NIH Office of Behavioral and Social Science Research, the National Institute of Mental Health, and the National Institute on Drug Abuse also are involved.

Input to Inform the NIH Obesity Research Plan: Input from intramural scientists, lay leaders, and the public is necessary to inform the development of the NIH Obesity Research Plan. Reversing

the tide of the obesity epidemic will require national changes, cooperation at all levels of government, and public-private partnership. The NIH has a vital role to play and that role should be informed by external input. The source of this input will include general scientific meetings (e.g., the January 2003 Keystone Symposium on Obesity); meetings convened by NIH ICs for research planning advice (e.g., NHLBI Think Tank on Enhancing Obesity Research); panels of experts associated with NIH ICs (e.g., the NIDDK Advisory Council and NIDDK Clinical Obesity Research Panel); and specific requests to external experts.

Categorizing Obesity Research Activities: The Task Force is currently developing a framework for organizing and coordinating obesity research activities. The consensus of the group to date reflects six broad areas: (1) Identification of the genetic, behavioral, and environmental factors causing obesity; (2) Understanding the pathogenesis of obesity and its co-morbidities; (3) Prevention and treatment of obesity; (4) Policy, health services, economics, translation to practice; (5) Enabling technologies; and (6) Development of multidisciplinary research teams.

Refining NIH Obesity Research Goals: The NIH Obesity Research Task Force is generating a cohesive set of goals. A broad spectrum of obesity research areas will be organized into a "matrix" according to risk (difficulty in attainment) juxtaposed to expected timeframe. This matrix will be an important planning tool. The NIH strategic plan for obesity research will seek to maximize collaboration among the NIH ICs and to capitalize on their expertise and interests in initiative development. The cohesive, coordinated, and synergistic efforts of the Task Force will aid the realization of the stated goals. The NIH obesity research plan will have an intramural component, which will be framed by Dr. Michael Gottesman, NIH Deputy Director for Intramural Research, and a steering committee of scientific directors chaired by Dr. Marvin Gershengorn, Director of the Division of Intramural Research, NIDDK. The intramural research focus will be on animal models, translation, and clinical research.

Dr. Spiegel expressed optimism that the work of the new NIH Obesity Research Task Force will enable the NIH to make important inroads in combating the obesity epidemic. At the same time, due to the daunting nature of the task, intense focus, efforts and coordination are required at all levels of government, as well as the private and nonprofit sectors, in order to combat this national problem. The Secretary of the Department of Health and Human Services has noted that this is a major priority of his administration.

General Discussion:

A Council member commented that the food industry is now looking at producing products that provide healthier alternatives to the public. Another Council member inquired about how to address the environmental issues that relate to the daunting problem of obesity. Dr. Spiegel noted that there needs to be not only objective evidence supporting the effectiveness of an intervention, but also a demonstration that the intervention works in the general population. For instance, the Diabetes Prevention Program, a type 2 diabetes prevention study supported by the NIDDK, was a study that showed that, in a highly controlled setting of a clinical trial, a lifestyle intervention had a major impact in reducing the development of type 2 diabetes in high-risk individuals. However, the question of how to translate this information to the general population remains. For obesity, a plan is needed that will: (1) identify areas where there is no solid, objective evidence base, and (2) provide the required evidence base across disciplines. To succeed in conquering obesity, we need a multi-faceted effort.

A Council member suggested that the NIH Obesity Research Task Force historically review the National Cancer Institute's (NCI) experience with the Comprehensive Cancer Center core grants. For example, incentives were incorporated into these grants to encourage investigators to engage in discovery-oriented research, as well as interact with the community and other agencies. Dr. Spiegel acknowledged that there are many lessons to be learned from the experiences of Obesity and Nutrition Research Centers, Clinical and Nutrition Research Units, and other centers.

REPORT FROM THE NIDDK DEPUTY DIRECTOR

Dr. Griffin Rodgers

Dr. Rodgers discussed broad funding mechanisms for Fiscal Year 2002 (FY02) and FY03. While activity in almost all of these categories has increased, it is important to note that FY03 is the fifth and final year of the NIH budget doubling period. The expectation in growth rates in FY04 and in future years will be much more modest.

Dr. Rodgers reviewed how the NIDDK's percentage distribution of funds among mechanisms has changed over the 5-year budget doubling period (from 1999 to 2003). In the following examples, all figures are expressed as percentages of the total appropriation, unless stated otherwise:

- Cooperative agreements increased from 6.5 percent of the budget in 1999 to roughly 9.6 percent in 2003.
- Research centers have fallen from 6.4 percent of the budget in 1999 to about 5 percent in 2003. However, the total spending at each Center has increased as a result of a raising of level of the funding caps.
- Research careers, the K award series, have increased from 2.8 percent to 3.3 percent.
- The "Other Research" category has increased from about 0.5 percent to about 1.8 percent. This category includes the biotechnology centers and the mouse metabolic phenotyping centers. Because both of these activities are intentionally time-limited, these funds will be redeployed to other parts of the budget in the future, as funding needs are identified.
- The National Research Service Award (NRSA) category has decreased from 3.6 percent to 3.1 percent. The NIH has continued to grant annual stipend increases while holding the NRSA numbers to a modest increase. Both of these practices are congruent with the recommendations of the National Academy of Sciences to address the national demand for entry-level investigators.
- Research contracts have increased from 2.9 percent to 5.1 percent. A part of this increase reflects funding of the loan repayment program. The increase also reflects reprogramming and departmental transfers.
- The Intramural Program has decreased from 10.7 percent to 9.7 percent of the total NIDDK budget.
- The NIDDK continues to have one of the lowest administrative cost rates at the NIH, at slightly over 3 percent of the total budget.

< After remaining fairly flat between 1993 and 1998, funding for research project grants increased significantly during the budget-doubling period and continues to be the primary NIDDK research funding mechanism.

The NIDDK funds a range of clinical trials. In addition, the NIDDK has encouraged the development of ancillary studies to ongoing clinical trials, as well as efforts to promote the gathering of specimens and data into central repositories to enable the greatest use of these research resources by investigators. The NIDDK has also used cooperative agreements to establish longitudinal and cohort studies to address important questions not appropriate for clinical trial settings. In this new science era, biomedical research depends increasingly on multidisciplinary teams, on shared specialized services, and on major, shared databases.

NIH Extramural Loan Repayment Programs
Dr. Robert Hammond

The purpose of the NIH Extramural Loan Repayment programs is to recruit and retain highly qualified health professionals as clinical investigators and pediatric researchers. Individuals may apply through this contract mechanism for repayment of educational loans of up to $35,000 per year for up to 2 years at a single time, plus a federal tax liability offset. The NIH has increased funding for this program across the board. In 2003, NIDDK has targeted approximately $4 million total for the two repayment programs, twice the amount targeted in 2002. This year, under a new feature, the clinical and pediatric research activity may be supported through an NIH grant, any nonprofit source, or a combination of the two. For those individuals who receive support through the NIH, any research grant mechanism is acceptable. For example, individuals who are supported at least 50-percent time for their research efforts through an R01 award or a nonprofit source would qualify for a loan repayment this year if they meet other eligibility criteria, such as amount of debt load. They would not have qualified under last year's criteria.

Clinical research and pediatric research are two different tracks, and applicants for repayment of loans must specify one. Last year, NIDDK received and reviewed 34 applications for the clinical research track and 29 for the pediatric track, a total of 63 applications. This year, NIDDK received 93 applications for clinical research and 78 for pediatric research, a total of 171 applications. The numbers for FY03, however, are preliminary. If NIDDK is unable to fund all the applications that have merit, other Institutes may be able to support selected applications.

Regarding the FY03 timeline, applications will be reviewed in July 2003 by the NIDDK Review Branch. Shortly thereafter, NIDDK will develop a funding plan, and awards will be made in August. A full, informational report will be given at the September Council meeting; however, because loan repayments are made through the contract mechanism, they do not require Council review. In response to questions, Drs. Hammond and Spiegel made the following comments about the loan repayment programs.

Success Rate: As stated in September, for 2002, NIDDK had an 87 percent success rate, funding about 57 of 63 applications. Dr. Spiegel observed that the different Institutes had substantially different numbers of applications; several were "oversubscribed," and some were "under-subscribed." The NIDDK's 87 percent success rate occurred after it transferred some of the

unsuccessful, but otherwise well-qualified, applicants to other NIH ICs.

Degrees of Successful Applicants: Irrespective of degree held, applicants have to have outstanding debt that is at least 20 percent of their salary in order to qualify for the loan repayment programs. In the pediatric research track, applicants must be doing pediatric-relevant research of any kind. Although a Ph.D. can qualify, as a matter of practice, the Ph.D. with a graduate assistantship does not have much qualifying debt. Similarly, an M.D./Ph.D. in the Medical Scientist Training Program (MSTP) does not have much, if any, qualifying debt. Thus, the debt pool consists largely of M.D. applicants. In the clinical research program, the only type of Ph.D. who qualifies does population-based research; for example, a biostatistician or an epidemiologist.

Review Process: The NIDDK will use an Internet-assisted review process in which electronic applications will be sent to the review group. Heavy consideration will be placed on the applicant's research plan for the next 2 years.

For years, people have advocated this kind of program, noting that debt forgiveness is an important way to counter the dearth of investigators in critical areas. Medical school debt now averages over $100,000 per graduating student. It will be important for this program to provide evidence that those individuals who receive debt forgiveness will ultimately be productive in a research career. Consequently, the program needs to be evaluated over time.

Evaluation of NIDDK-Supported Centers – Introduction
Dr. Hammond

The NIDDK proposes to assess the extent to which its Research Centers enhance research, including the overall contribution of Centers to biomedical research progress, the advantages and disadvantages of specific Center types (e.g., core centers *versus* specialized research), and possible untapped roles of Centers. The overarching goal is to ensure that NIDDK is maximizing the benefit of this mechanism. The areas of intended study are: (1) growth of the research base and program base at institutions with Centers as opposed to institutions without Centers; (2) use of cores; (3) exploitation of new advances; (4) role of Centers in the research career development of new investigators (e.g., success of pilot and feasibility studies in leading to first R01s); (5) contribution of Centers to collaborative and multidisciplinary efforts; and (6) role of Centers in fostering translational and clinical research.

The NIDDK has notified the principal investigators of currently funded Centers about this study. The process will include the gathering of information from multiple sources, and, therefore, grantees may be contacted over the next few months. The purpose of seeking input from grantees is not to modify the funding ceilings on Centers, but to determine how effectively NIDDK is using the mechanism. As NIDDK develops the enhancement study, it will post updates on its internet website (http://www.niddk.nih.gov). The advice of Council members will be central to the development of a valid, useful approach to enhancing NIDDK Centers. A preliminary report is expected in September 2003.

VI. SCIENTIFIC PRESENTATION

"Hype and Promise of Stem Cells"
Dr. Catherine Verfaillie
Professor of Medicine and Director of the Stem Cell Institute
University of Minnesota

Dr. Verfaillie discussed her laboratory's stem cell research within the context of a broader perspective on both embryonic stem (ES) cells and adult stem cell plasticity. Stem cells undergo self-renewing cell divisions; a single stem cell can differentiate into multiple different functional cell types; and when administered to a human or animal, stem cells can functionally reconstitute an organ that had been destroyed. There has been recent excitement about ES cells because they can differentiate into all of the body's cell types and maintain differentiation capacity when grown in the laboratory for long periods of time; thus, these cells might constitute an unlimited source of cells for therapies. However, several difficulties are associated with potential clinical use of human ES cells. These cells would be obtained from a donor and might thus be rejected by the patient; they could form tumors (teratomas); and the generation of these cells from blastocysts (early embryos) is a controversial procedure. Adult stem cell research is viewed with excitement, but many questions remain. On the positive side, adult stem cells are already being used for such therapies as bone marrow transplantation. These cells could be obtained directly from the patient. Moreover, because adults, not embryos, are the source of the cells, the research is not controversial. Finally, adult stem cells appear to be more potent, or have greater "plasticity," than previously thought. That is, there are numerous reports that an adult stem cell from one tissue can differentiate into specific cell types normally found in other tissues. (As one example, Dr. Verfaillie's laboratory discovered cells from bone marrow, which they call multipotent adult progenitor cells or MAPCs, that can be induced to differentiate into nerve cells, muscle cells, liver cells, and other cell types.) At the same time, however, emerging evidence calls into question some of the earlier reports of adult stem cell plasticity; for example, certain observations of apparent plasticity have been found to result from the fusion of an adult stem cell fusing with another cell type rather than its differentiation into another cell type. It is possible that, clinically, adult stem cells might prove to be a better cell source for repair of some tissues, while ES cells may be more suitable for others. As investigators gain increased understanding of self-renewal and differentiation, research on these cells may facilitate the discovery of drugs to repair damage to tissues; these cells may also be useful for drug toxicity screening; and they may be useful for cell-based therapies, as has been suggested by research in animal models of disease. Additionally, experiments are under way to bioengineer tissues, such as arteries, from MAPCs. Dr. Verfaillie believes that clinical trials are likely 5 to 10 years away, with much additional research still needed in preparation.

VII. ADJOURN FOR LUNCH

Dr. Spiegel thanked all the presenters and then adjourned the open session of the full Council.

VIII. SUBCOMMITTEE MEETINGS

At approximately 1:00 p.m., separate meetings were convened of the Subcommittees for Diabetes,

Endocrinology and Metabolic Diseases; Digestive Diseases and Nutrition; and Kidney, Urologic and Hematologic Diseases.

IX. REPORT FROM THE NIH DIRECTOR
Dr. Elias Zerhouni

Dr. Zerhouni expressed his pleasure at being able to address the NDDK Advisory Council and then highlighted several challenges and opportunities the agency is facing.

Budget Doubling: A key issue is the completion in FY03 of the 5-year period of budget doubling for the NIH. The transition between FY03 and FY04 may be difficult to manage because of the general economy, an increasing budget deficit, homeland security needs, and other competing national priorities. The NIH IC Directors, the Office of the NIH Director, the DHHS, and the Office of Management and Budget (OMB) have worked towards completing the five-year period of budget doubling in FY03, and toward minimizing the impact on investigators of deceleration in the growth of the budget in FY04 and subsequent years, while maintaining the "momentum of science." One action that this has required is the reinvesting of one-time expenditures, such as those for biodefense, back into the grant pool. The total change from the FY03 NIH funding level to the FY04 President's Budget request is an increase of approximately 2.6 percent or a $550 million net increase.

Expectations are high in many quarters about the ways that the NIH will effectively transform the doubled budget into real scientific and medical gains. In response to questions from public policy makers and constituency groups, the NIH must be accountable for the stewardship and productive investment of its increased budgetary base. Accountability includes documenting, with compelling arguments and a compelling vision, the results that we have achieved, and proposing promising research strategies for the future. We are already doing this in congressional testimony and in other venues.

Roadmap: A second critical issue is the "Roadmap for NIH Research and Strategy," which is a vision of opportunities to be exploited, as well as roadblocks to overcome, within the context of the heightened expectations mentioned previously. Topic-oriented groups composed of representatives from the extramural and intramural scientific communities, along with relevant IC Directors, met on several occasions between September and October 2002 to develop the "Roadmap" topics. They focused very specifically on changes in science that need to be considered as NIH charts its future course, as well as on areas that a single Institute or Center simply cannot tackle all by itself and for which a multi-institute effort, as part of a NIH vision, is really required. After extensive discussion about points of scientific convergence and commonality across disciplines in areas such as cell signaling, and the enormous opportunities and impacts of new technologies such as high-throughput methods, three broad themes emerged from these meetings: (1) *Paths to Discovery:* The role of the NIH will be to enhance this process across all ICs, because the pathways will likely not be specific to diseases or disciplines; (2) *Research Teams of the Future:* It is imperative to make new and enhanced technologies available to investigators; to encourage the formation of multidisciplinary research teams, including computer scientists and statisticians; and to increase the number of young investigators; and (3) *Re-engineering the Clinical Research Enterprise*: Culturally, over the past 20 to 25 years, clinical

research has not been recognized as well as it should have been within its own environment; academic health centers have a challenged economic base. The ability to do clinical research has also been made more difficult because of regulatory pressures, and the significant research costs in both dollar and human terms. There is also a sense that clinical research is more complex than it used to be. It is a discipline in its own right that requires infrastructure so that young physicians are supported when they explore translation. One roadblock is the difficulty in moving from a target that is identified in early research to proof-of-principle. The bold and difficult goal to be achieved is to take a different approach: the NIH leadership and external advisors are being tasked to look at this enterprise as a whole.

Many clinical studies are conducted overseas where health care and information systems are not as fragmented as in the U.S. Foreign health information systems are more harmonized and have an intrinsic ease that facilitates long-term studies in which patient identification is standardized. This is not necessarily possible now in this country given the system that is in place, and it might become even more difficult in the future. Therefore, one of the issues that the NIH leadership would like to address is the informatics infrastructure for clinical research and the integration of clinical research teams within the translational context. A balance is needed in terms of approaching both the science itself, and the translation of science, in a way that does not perturb balances within the overall system.

The NIH IC directors have not had any difficulty in identifying common themes to direct concerted efforts. National Advisory Councils and other external scientific and lay experts can help the NIH leadership further enhance and energize these common areas, and support the IC directors in identifying what can reasonably be done. Synergy is needed and can be accomplished across Institutes, even in a time when constraints are increasing, and the critical mass required to make a difference in science is higher.

National Advisory Councils have an important role in framing the NIH strategy in the post-budget-doubling era, in defining a compelling vision that invigorates the leadership of the agency in terms of both science and the translation of science, and in identifying programs and priorities within ICs that converge with other NIH components and for which co-investments are very important, whether in the area of human capital, infrastructure, or technology. Without the 21,000 reviewers and advisors who serve NIH selflessly, including the many National Advisory Council members, the NIH would not be the crown jewel that it is.

General Discussion:

Dr. Zerhouni affirmed the need to pursue a cross-departmental and cross-sector collaboration to accelerate the movement of research from discovery to translation, and then on toward application. Leaders of federal science agencies and industry are challenged by finding ways to bring a medical research discovery to bear on disease prevention and treatment. Organizations are seeking ways to synergize their resources with others. For instance, the FDA Commissioner is interested in integrating the discovery and the approval process to accelerate drug development. Furthermore, the CDC and the NIH have collectively focused on biodefense, which has paid off by way of the spectacular, fundamental advances made in historically record time in response to Severe Acute Respiratory Syndrome (SARS). In industry, an important issue relates to molecular libraries. Industry does not believe that it has the capability to truly exploit chemical space, whether it be

proteins, antibodies, or small molecules. If an intellectual property medium can be provided whereby industry's ability to contribute to the research community is not diminished, as it is today, some success may be achieved. Encouragingly, academic health centers are increasingly working together, as demonstrated by the impressive, multi-institutional biodefense proposals that are being submitted to the NIH.

A Council member asked Dr. Zerhouni what NIH can do to remedy the "post-NIH or pre-license gap," a gap that impedes the commercial development of important ideas that could potentially improve human health. This gap occurs when investigators come to a certain point in their research at which entering the private sector to develop a product or a device is a logical progression, but for which there is no support to make this happen. Dr. Zerhouni affirmed that these types of limitations exist, as a "translational block," especially with the multiplication of targets of opportunity that scientists are identifying. However, the activation energy required to reach the next step is high. Issues of prototyping exist, and developing the first molecular entities or any of the original early steps is challenging. For instance, a subspecialty critical to the life sciences, organic chemistry, is currently experiencing a great shortage in research manpower worldwide. Informatics is in similar dire straights. An understanding of targets has developed, but the necessary effectors are not readily available to scientists in academia or in industry. A way to accelerate translational progress is to transform universities into discovery and development engines, which they used to be in the past. Although there is no clear solution to this issue, it is included in the Roadmap.

In response to a Council member's question about his timetable related to the obesity initiative, Dr. Zerhouni emphasized that the NIH is moving rapidly, consistent with the heightened level of concern across the country, about the obesity epidemic. An integrated view on this problem is non-existent, not just in terms of research, but in terms of what to do as a nation. The NIH needs to: (1) have a responsive and proactive program in obesity research, both intramurally and extramurally, with a critical mass of investigators, and (2) frame the debate as to what the issues are. Obesity is one of those "environmental/genetic" disconnects that accompany social evolution. In less than 100 years, humans have moved from millions of years of evolution in which starvation and conservation of energy were the rule to an environment of largesse in the Western world. Although we are designed to endure starvation and conserve energy, the environment has changed so abruptly that there is no way that the resulting evolutionary stress can be tackled by standard processes. The knowledge gathered on obesity will be the needed weapon to address this evolutionary dilemma. Obesity cannot be addressed by a "band-aid" approach. The NIH is thinking of obesity in both a reactive and proactive way, and positioning itself as a leading research engine for problem-resolution.

When questioned about his expectations in obesity research, Dr. Zerhouni responded that some important goals are to find a way to stop the growth of the obesity epidemic, given that obesity is likely driving the rising rates of diabetes, and also, to prevent "syndrome X." Programmatically, a compelling vision should be developed by the NIH Obesity Research Task Force in a matter of months, to be followed by a more detailed approach on how to combat obesity through research. Importantly, this effort is not limited to the NIH. The CDC is very involved and willing to collaborate, as are other agencies in the Department under the leadership of Secretary Thompson, as well as other sectors. However, the NIH must first define more precisely the complex problem of obesity. Obesity is not an issue that can be dealt with just by the NIDDK, the NCI, or any other

single organizational entity. Obesity is also a behavioral and social sciences problem, and a problem of neurological controls and environmental cues.

Dr. Spiegel elaborated further regarding Dr. Zerhouni's establishment of the NIH Obesity Research Task Force. Input from leaders in the community and health advocates is being sought. The NIH has been conducting intensive investigations in this field, but obesity has become such a critical problem that opportunities for coordinated, synergistic approaches must be seized. The NIH will likely have a role in terms of identifying targets, some of which will be developed into effective drugs. However, the behavioral and preventive components require a multi-pronged approach that will need partnership with organizations beyond the NIH.

In response to a question regarding the lack of young investigators, Dr. Zerhouni noted that Dr. Kirschstein, Senior Advisor to the NIH Director, has been asked to coordinate between the Advisory Committee to the NIH Director and the various IC Directors, as well as the Institute of Medicine (IOM) of the National Academy of Sciences, to generate a white paper that will include potential approaches to this issue. In addition, this issue will be addressed through the Roadmap. Essential to these efforts will be the collaboration and integration of NIH activities with academic health centers and other entities.

X. SUBCOMMITTEE MEETINGS: CONTINUED

Subcommittee meetings were convened at approximately 4:15 p.m. and continued until approximately 5:30 p.m. Subcommittee members met once again on June 12, 2003 from 8:00 a.m. to 9:30 a.m.

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

At approximately 9:59 a.m. on Thursday, June 12, 2003, Dr. Spiegel reconvened the open session of the full Council.

XII. REPORT FROM THE NIDDK INTRAMURAL RESEARCH PROGRAM

Dr. Marvin Gershengorn

Dr. Spiegel provided background information on the NIDDK Division of Intramural Research. The program represents approximately 10 percent of the overall NIDDK budget, on the order of $150 million. The Deputy Director for Intramural Research, Michael Gottesman, is currently arranging for a review of the program by a blue ribbon panel, consistent with a recommendation from an external committee convened by former NIH Director, Dr. Harold Varmus, that such reviews be conducted for every Institute on a periodic basis. The panel will include a member of the NIH Director's Advisory Committee, a member of the NIDDK Advisory Council, a recent chair of the Board of Scientific Counselors (BSC), and three *ad hoc* members representing a spectrum of disciplines, from basic science to clinical research, that is reflective of the science in the NIDDK Division of Intramural Research. Every tenured and tenure-track scientist is already

reviewed on a periodic basis, every four years at a minimum, by a distinguished BSC. In contrast, the blue ribbon panel will look at the totality of the program and the direction it takes, and will offer recommendations for future and possibly new directions.

Dr. Gershengorn noted that the Intramural Program at NIDDK ranges from the most basic research to clinical research. He reviewed the current staffing profile, noting that tenured scientists are reviewed every 4 years by the BSC and tenure-track scientists are given resources for an average of 6 years, during which time their research accomplishments and productivity are evaluated after 3 years and a decision for-or-against tenure is made after 6 years. A new subcategory of staff scientists direct the Intramural Program's core facilities. Changes in the Intramural Division in the last 12 to 18 months are intended to move the program further ahead in specific areas, and to establish core resources that will help intramural scientists achieve this. For example, six search committees are currently seeking to recruit talented investigators to expand or complement research in the following areas: (1) Biological Modeling; (2) Insulin/IGF-1 Action in Obesity; (3) Endocrine Pancreas Development; (4) Clinical Endocrinology–Nuclear Receptor Biology; (5) Endocrine/Metabolism–Patient-Oriented Research; and (6) Digestive Diseases–Patient-Oriented Research. Another change is the establishment of a series of facilities that can be shared by intramural investigators to enable the Intramural Program to move further ahead synergistically. Two such laboratories have been in place for a number of years: one to generate "knock-out" mice and another to generate transgenic animals. The Intramural Program is in the process of setting up the following core facilities: (1) a Mouse Metabolism Laboratory, (2) a Microarray Facility, (3) a Chemical Biology Laboratory, (4) a Fellowship Recruitment and Career Development Office, (5) an Office of Technology Transfer, and (6) a Mass Spectroscopy/Proteomics Laboratory. The first NIDDK Intramural-wide retreat was held in May 2003. Approximately 160 scientists attended the event. Fruitful collaborations were initiated by interactions at this retreat, which will become an annual event.

General Discussion:

A Council member asked whether there is a need for a large-scale core that would allow people to do random mutagenesis studies for which there is significant interest, how this would be approached, and whether there is a need for Good Manufacturing Practice (GMP) facilities. Dr. Gershengorn responded that, for the moment, establishing such a facility is an enormous endeavor and is not within NIDDK's Intramural Program's plan. Regarding GMP, the scope for the Intramural Program's chemical biology initiative will be limited to the probe stage. Going beyond probes to potential drugs would require partnering with pharmaceutical companies, probably through Cooperative Research and Development Agreements (CRADAs). However, establishing GMP facilities is a goal in the NIH Molecular Libraries Roadmap, which has a large extramural component and is led by the National Human Genome Research Institute (NHGRI).

Dr. Spiegel offered a broader perspective regarding NIH shared or core facilities to illustrate that there is both a critical mass of scientists at the NIH and significant interaction. Importantly, there is a Shared Resources Committee of the Scientific Directors. Current entities include:

< An Intramural High-Throughput Sequencing Center, which is run by the NHGRI, but which all the ICs will utilize.

< An *in vivo* Nuclear Magnetic Resonance (NMR) Center, which is also a consortium of all the ICs.

< The Center for Inherited Disease Research (CIDR), also run by the NHGRI for high-throughput genotyping. Although it is located on the Bayview Campus at Johns Hopkins University, it is accessible to both extramural and intramural researchers.

< A new Vaccine Center that has a small GMP facility created for biologics and vaccines.

At Dr. Spiegel's request, Dr. Gershengorn commented on ways that the Intramural Program can contribute to the efforts of the NIH Obesity Research Task Force. Dr. Gershengorn noted that any single Institute would find it very difficult to have all of the facilities, expertise, and other resources that are needed to understand obesity. Much of the required expertise and facilities is available in certain extramural research sites and in one or two places within the NIH intramural campus, but not in a cohesive way and not under one umbrella. The intramural initiative envisioned by the NIH Obesity Task Force is based on establishing collaborations across ICs and extramurally. For example, a facility for phenotyping the obese individual could be established at the NIH and made available to patients of leaders of extramural obesity centers funded by NIDDK and to other obesity researchers. The NIDDK has a great deal to contribute to this effort because, although most of its intramural research occurs in the Bethesda campus (including obesity research), a very important branch located in Phoenix, Arizona, has conducted studies focusing on type 2 diabetes and obesity in the Pima Indians for more than 30 years.

One of the Council members commented positively on the concept. He noted that, in his institution alone, there are a limited number of resources that can be devoted to expensive technologies such as NMR spectroscopy and Positron Emission Tomography (PET) scanning capabilities. Even when instruments are available, their use is often limited to clinical care. Although there are instrumentation grant applications that can be submitted to the National Center for Research Resources (NCRR) to fund equipment, the idea of high-end spectroscopy capabilities at the NIH through which investigators could have patients travel to obtain those kinds of measurements would certainly complement what is going on in extramural research institutions.

A Council member asked about the process through which the Intramural Program develops its plans. Dr. Gershengorn explained that a group of senior NIDDK scientific managers meets and discusses these important issues on a monthly basis. Moreover, he has recently established a new committee of senior investigators within the Intramural Program called the Executive Advisory Committee, which meets monthly to discuss a strategic research development plan for the program. The intent of these processes is to build on the program's already existing strengths.

In response to a question regarding the relationship between the Intramural Program's Chemical Biology Laboratory and the larger Roadmap Molecular Library initiative, Dr. Gershengorn clarified that he was referring to a brand new NIH initiative in which 500,000 chemically diverse, small molecules will be accumulated within a central repository under the NHGRI. This effort will then serve as a basis for high-throughput screening. One Center will be established within the Intramural Program on the Bethesda campus, and two others extramurally. Once hits are identified, medicinal and organic chemists will translate those hits into probes. Within its own chemical biology initiative, the NIDDK Intramural Program will complement what is being done across the NIH. The intent of the NIDDK's Chemical Biology Laboratory will not be high-

throughput screening, but the development and application of more rational approaches, using chemistry and molecular modeling approaches to translate hits into probes. In response to another question, Dr. Gershengorn assured the Council that extramural researchers would be granted access to these high-throughput sites and compounds, but that the process to do so is not yet in place.

XIII. ADVISORY COUNCIL FORUM: ENHANCEMENT OF NIDDK-SUPPORTED RESEARCH CENTERS

Dr. Robert Hammond

In follow-up to his presentation to Council the preceding day, Dr. Hammond led a discussion on the upcoming evaluation of NIDDK-supported Research Centers, seeking an overview from each of the Subcommittees.

Digestive Diseases and Nutrition (DDN) Subcommittee: Centers should be evaluated both at the outset of funding and at different points during their evolution. Pilot and Feasibility (P&F) Projects have been very successful; however, their true impact should be assessed more closely, particularly with regard to potential candidates and awardees. It is critical that NIDDK develop strategies to attract new investigators and groom them. Core facilities should be dynamic and evolve as the needs of the research base develop within a Center. Thus, Centers should not only seek ways to provide a service, but also identify the appropriate technologies for answering research questions. Given the importance of attracting new investigators and to evaluating P&F project impact, DDN Subcommittee members suggested that these two goals be accomplished in one step by coupling P&F project funding with other approaches. For example, a K awardee could combine a P&F project with a General Clinical Research Center (GCRC) grant to do clinical studies. This would enhance P&F funding and simultaneously promote clinical investigation. Other suggestions included using the R24 mechanism to bring in communities that are not as broad-based as those which initially received Center grants, and to couple them, through the R18 mechanism, to fund a specific area that uses Centers as a way to promote clinical investigation. The need to examine how some Centers successfully bring their disciplines to the forefront was also discussed. In particular, the questions to be asked are: (1) how are these Centers used within the institution to leverage other components of research; (2) how do these Centers work with other Centers to bring in new capabilities, such as the biotechnology cores that provide new technology for a broader based group; and (3) to what extent might these Centers train individuals in the discipline?

Kidney, Urologic, and Hematologic (KUH) Subcommittee: Distinguishing features should be clarified among P50, P01, and P30 Centers. In addition, specific circumstances should be delineated that would justify an emphasis on core resources. Because areas of intended Center enhancement effort are not really germane to the P50 mechanism, which represents the bulk of the KUH Division Center portfolio, the Division may be better served by using a P30 mechanism. Centers should focus on providing core mechanisms that can support the strengths that are already present in the best research centers, and perhaps support research broadly across the country. Also, Center investigators should be encouraged to support research beyond their institution, to focus on attracting new investigators, and to foster translational and clinical research. The O'Brien Center program has made a significant difference in crystallizing the efforts of investigators at different institutions who are working on urology and sometimes urology/nephrology problems.

There has also been a "halo effect" of the Centers in urology. As the group in the O'Brien Center became organized, other people began to interact with these investigators and a number of clinically oriented people were attracted to doing research. The training these Centers provide has been oriented toward clinical translation of research. However, it is difficult for a single institution to have all the tools to put together an excellent application, and the multi-institutional characteristic of the early O'Brien Centers should be revisited. Although the O'Brien Centers have been extremely successful, there is a need for continuous assessment and strengthening.

Diabetes, Endocrinology, and Metabolic Diseases (DEM) Subcommittee: Although Subcommittee members recognize the added value of a Center, such as its ability to supply the necessary infrastructure, several challenges remain. Centers need to be state-of-the-art, keeping pace with the rapid advance of technology development. With respect to projects, consideration needs to be given to whether "transition-to-independent-support" is the best indicator of success. Perhaps recognition should be given to Centers that place more importance on higher-risk projects. Although the term "Center" implies a specific location, emphasis should be placed on the formation of multi-institutional and multi-site Centers. Rather than dwelling on assessing Centers as they exist today, NIDDK should focus on what Centers should be in the future.

General Discussion:

In opening the floor for general discussion, Dr. Spiegel noted that the NIDDK would be best served by formulating a strategic vision of what Centers should be, and by encouraging translational and clinical research. However, he also stressed the need to assess current Centers to ensure that goals and targets are being met and that Center strengths and weaknesses are being identified. The logical end product of the Center enhancement effort would be to take the form of modifications in Requests for Applications (RFAs) in which new targets and expectations would be clearly set. With respect to P&F projects, there is an inherent "Catch-22" problem. If projects are really high risk, failure will sometimes be the outcome. Therefore, it may be necessary to use a different metric than a formulaic approach to determine the high-impact results that could derive from a project, and what would be lost if it is not funded. The following points remain to be considered by the Council: (1) research training as a key aspect of Centers, and (2) whether the Center mechanism is a good way of attracting investigators from other fields who have expertise relevant to the aims of the Center.

With respect to core facilities, Dr. Spiegel indicated that, while cores derive a certain amount of support from Centers, they draw on a variety of other resources as well (e.g., the dean, the institution, etc.). The germ-free animal facilities are an example of a vital core resource for research, difficult to create, but potentially capable of empowering research at a number of other institutions. However, administrative barriers might militate against the notion that cores (such as those at the Digestive Diseases Centers) can be used on a more expanded basis and whether this could be resolved by instituting a fee-for-service.

The NIDDK staff inquired as to how Centers might tap into the extensive investment in GCRCs while avoiding redundancies. A Council member noted that there are tremendous opportunities in marrying the GCRCs with a DDN, KUH or DEM Center. These arrangements provide a great opportunity to foster translational research because virtually all of the resources needed for clinical research are made available by the GCRC. The GCRC directors are interested in good, hard

science that is done well in human patients, that is appropriately peer reviewed, and that has accounted for all the Institutional Review Board (IRB) considerations. Council members discussed a number of barriers to the conduct of clinical research, several of which impact upon the use of GCRCs.

Speaking about the Biomedical Informatics Research Network (BIRN), another Council member explained that the group has attempted to network through the GCRCs to pull together about 10 Centers, because no one institution has the critical mass of patients. BIRN is standardizing human data related largely to imaging. It would be useful for the NIDDK Advisory Council to have a presentation about BIRN. Dr. Spiegel hoped that NIDDK might work with NCRR on these issues to search for ways to better utilize the GCRCs and foster more interaction.

The Roadmap for NIH Research and Strategy
Dr. Allen Spiegel

Responding to a question from a new Council member, Dr. Spiegel elaborated further on the Roadmap. He explained that, at the February Council meeting, a single page document was circulated, listing three broad headings: New Pathways to Discovery; Research Teams of the Future; and Re-engineering the Clinical Research Enterprise. Listed under those headings are about 15 subheadings. Dr. Zerhouni believes that the doubling of the NIH budget opened up tremendous opportunities for research progress; however, there are compelling goals--such as re-engineering the entire clinical research enterprise--that cannot be accomplished by any single Institute and must therefore be spearheaded by the NIH proper. The Roadmap is intended to address this issue. To this end, Dr. Zerhouni convened focus groups last August, including distinguished panels of investigators from around the country and from multiple disciplines. These meetings were followed by a 2-day summit on clinical research. Based on each of the Roadmap headings, an internal working group of NIH staff was formed. Each group was co-chaired by two IC Directors. The working groups, populated by program staff from all the Institutes, created the "Zerhouni matrix." This is a three-by-three matrix that contains a series of initiatives organized by degree of difficulty in attainment, and by an expected timeline with an accompanying vision statement. These working groups did not function in a vacuum; rather, they interacted via teleconference with a variety of distinguished extramural investigators in areas such as systems biology and proteomics. Although this effort will coalesce at a budget retreat on June 20th, 2003, an iterative process will continue. Dr. Zerhouni intends to seek input from National Advisory Councils, health advocacy groups and professional organizations, and the public.

NIDDK Priorities
Dr. Spiegel

Dr. Spiegel reported that one of his management priorities during the period of budget doubling was to maintain robust pay lines, supplemented by special emphasis funding for areas identified by the Council. At the same time, the budget doubling also enabled the NIDDK to mount an impressive list of new clinical trials and multi-institutional consortia and arrangements not previously possible. Now that the doubling of the NIH budget has been completed, the NIDDK will strive to maintain pay lines, and will also emphasize the funding of new investigators to sustain research on the many chronic diseases within the Institute's mission.

Facilitation of Patient-Oriented Research:
Dr. Spiegel

A Council member asked what the NIH is doing with respect to the trend toward increased IRB requirements and the resulting concerns among clinical investigators regarding the huge amount of associated paperwork. Acknowledging the severity of the problem, Dr. Spiegel indicated that the NIH is exerting leadership through a trans-NIH committee that is carefully examining these issues. Moreover, the NIH participates, through a standing representative, in an IOM Clinical Research Roundtable. This group is looking at all aspects of clinical research in a multi-dimensional way. Dr. Spiegel also noted that, in an FY02 competitive process, the NIH awarded $25.1 million to a number of institutions around the country for a human subjects research enhancement program. This competition, to be repeated in FY03, is designed to enable institutions to acquire the necessary infrastructure (i.e., websites, tracking of patients, training of individuals) to facilitate the work of IRBs. On another front, the NCI has been piloting a central IRB process that may facilitate reduction of the burden on investigators and still preserve accountability in ensuring the safety of research patients. The paramount principles of protecting patient safety and avoiding inappropriate conflicts of interest will remain critically important as the research community seeks to streamline clinical research processes. Dr. Briggs, Director of the Division of KUH, added that the Roadmap effort has placed a priority on "harmonization." The term refers to trying to ensure, at an agency level, that regulatory issues are handled in a harmonious way by the different DHHS agencies. Dr. Rodgers also pointed out that the IC Directors are concerned about the implications and the interpretations of the new Health Insurance Portability and Accountability Act (HIPAA) and the effects that the regulations may have on the continuation of clinical trials.

XIV. CONSIDERATION OF REVIEW OF GRANT APPLICATIONS

A total of 1,384 grant applications, requesting support of $290,634,844 were reviewed for consideration at the June 11-12, 2003 meeting. Funding for those 1,384 applications was recommended at a level of $290,284,844.

XV. ADJOURNMENT

Dr. Spiegel thanked Council members for their attendance and advice. There being no other business, Dr. Spiegel adjourned the 162nd meeting of the NIDDK National Advisory Council on June 12, 2003, at 11:42 a.m.

I hereby certify that, to the best of my knowledge, the foregoing summary minutes 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