**Meeting Minutes**
**Department of Health and Human Services**
**National Institutes of Health**
**National Diabetes and Digestive and Kidney Diseases Advisory Council**
**February 24, 2010**

## I. CALL TO ORDER

***Dr. Griffin P. Rodgers, Director***

Dr. Griffin P. Rodgers, Director, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) called to order the 182nd meeting of the National Diabetes and Digestive and Kidney Diseases Advisory Council at 8:30 a.m., Wednesday, February 24, 2010, in Building 31, C Wing, 6th Floor, Conference Room 10.

## A. ATTENDANCE – COUNCIL MEMBERS PRESENT

Dr. David Altshuler
Dr. Nancy Andrews
Ms. LaVarne Burton
Dr. Charles Elson, III
Dr. Robert Flanigan
Dr. James Freston
Dr. Christopher Glass
Dr. Gregory Gores
Ms. Jane Holt
Ms. Judy Hunt
Dr. Francine Kaufman
Dr. David Klurfeld
Dr. Mark Magnuson
Dr. William Mitch
Dr. Jerry Palmer
Dr. Anil Rustgi
Dr. Anthony Schaeffer
Dr. John Sedor
Dr. Patrick Tso

**Also Present:**

Dr. Francis Collins, Director, NIH
Dr. Griffin P. Rodgers, Director, NIDDK, and Chairperson, NIDDK Advisory Council
Dr. Gregory Germino, Deputy Director, NIDDK
Dr. Brent Stanfield, Executive Secretary, NIDDK Advisory Council

## B. NIDDK STAFF AND GUESTS

Abankwah, Dora – NIDDK
Abraham, Kristin – NIDDK
Akolkar, Beena – NIDDK
Ameen, Vanessa – NIDDK
Arreaza-Rubin, Guillerno – NIDDK
Barnard, Michele – NIDDK
Begg, Lisa – NIDDK
Bethea, Gina – NIDDK
Blondel, Olivier – NIDDK
Bloom-Davila, Maria – NIDDK
Calvo, Francisco – NIDDK
Carrington, Jill – NIDDK
Castle, Arthur – NIDDK
Chamberlain, Joan – NIDDK
Chanetsa, Fungai – CSR
Cheng, Richard – NIDDK
Chianchiano, Dolph – National Kidney Foundation
Chon Lee, Angie – NIDDK
Connaughton, John – NIDDK

Cowie, Catherine – NIDDK
Curtis, Leslie – NIDDK
Densmore, Christine – NIDDK
Doherty, Dee – NIDDK
Donohue, Patrick – NIDDK
Doo, Edward – NIDDK
Durrant, Valerie – CSR
Edwards, Michael – NIDDK
Eggerman, Thomas – NIDDK
Evans, Mary – NIDDK
Everhart, James – NIDDK
Farishian, Richard – NIDDK
Feldman, Blay – Association of Independent Research Institutes
Fonville, Olaf – NIDDK
Fradkin, Judith – NIDDK
Friedman, Heidi – CSR
Gallivan, Joanne – NIDDK
Gansheroff, Lisa – NIDDK
Garfield, Sanford – NIDDK
Garofaco, Robert – CSR
Garte, Sy – CSR
Goter-Robinson, Carol – NIDDK
Greene, Lucy – NIDDK
Grey, Michael-NIDDK
Gross, Barbara – NIDDK
Groves, Reed – CSR
Guo, Xiaodu – NIDDK
Haft, Carol – NIDDK
Hamilton, Frank – NIDDK
Hann, Della – OER
Hanlon, Mary – NIDDK
Harris, Kimberly – NIDDK
Harris, Mary – NIDDK
Hilliard, Trude – NIDDK
Hoff, Eleanor – NIDDK
Hoofnagle, Jay – NIDDK
Horlick, Mary – NIDDK
Hoshizaki, Deborah – NIDDK
Hubbard, Van – NIDDK
Hunter, Christine – NIDDK
Hyde, James – NIDDK
James, Stephen – NIDDK
Jerkins, Ann – CSR
Jones, Teresa – NIDDK
Karp, Robert – NIDDK
Ketchum, Christian – NIDDK
Kim, Sooja – CSR
Klausing, Thomas – NIDDK
Kranzfelder, Kathy – NIDDK
Kuczmarski, Robert – NIDDK
Kusek, John – NIDDK
Leschek, Ellen – NIDDK
Linder, Barbara – NIDDK
Loveless, Natasha – NIDDK
Magra, Amy – NIDDK
Malik, Karl – NIDDK
Malozowski, Saul – NIDDK
Manouelian, Denise – NIDDK
Margolis, Ronald – NIDDK
Martinez, Winnie – NIDDK
Matsumoto, Dan – NIDDK
May, Ken – NIDDK
McKeon, Catherine – NIDDK
Miles, Carolyn – NIDDK
Miller, David – NIDDK
Miller, Megan – NIDDK
Moxey-Mims, Marva – NIDDK
Mullins, Christopher – NIDDK
Narva, Andrews – NIDDK
Newman, Eileen – NIDDK
Nguyen, Van – NIDDK
Nicholson, Katherine – NIDDK
Paterson, Beth – NIDDK
Perry-Jones, Aretina – NIDDK
Pike, Robert – NIDDK
Podskalny, Judith – NIDDK
Rankin, Tracy – NIDDK
Rasooly, Rebekah – NIDDK
Roberts, Tibor – NIDDK
Robuck, Patricia – NIDDK
Rosenberg, Mary Kay – NIDDK
Rushing, Paul – NIDDK
Sagan, Rebekah – NIDDK
Sahai, Atul – NIDDK
Salomon, Karen – NIDDK
Sankaran, Lakshmanan – NIDDK
Sato, Sheryl – NIDDK
Savage, Peter – NIDDK
Scanlon, Elizabeth – NIDDK
Scheiderer, Cary – OER
Sechi, Salvatore – NIDDK

Seeff, Leonard – NIDDK
Secis, Bronka – Social and Scientific Systems, Inc.
Serrano, Jose – NIDDK
Sheard, Nancy – CSR
Shepherd, Aliecia – NIDDK
Smith, Philip – NIDDK
Spain, Lisa – NIDDK
Star, Robert – NIDDK
Tatham, Thomas – NIDDK
Tinkler, Emily – NIDDK
Torrance, Rebecca – NIDDK
Tubb, Desiree – NIDDK
Tuncer, Diane – NIDDK
Wallace, Julie – NIDDK
Weinberg, David – CSR
Woynarowska, Barbara – NIDDK
Wright, Daniel – NIDDK
Wright, Elizabeth – NIDDK
Yanovski, Susan – NIDDK

## C. ANNOUNCEMENTS

Dr. Rodgers welcomed the new and continuing Council members, thanked them for their participation, and made the following announcements.

**New Council Members**

Joining the Subcouncil for the Division of Diabetes, Endocrinology and Metabolic Diseases are Ms. Judy Hunt and Dr. Francine Kaufman.

- *Ms. Judy Hunt* is a long-time diabetes research and education advocate and will serve as one of six public members on the Council. Ms. Hunt currently serves on the International Board of Directors of the Juvenile Diabetes Research Foundation International (JDRF) and as Chair of their Lay Review Committee. Since 1987, Ms. Hunt has served and held high-profile appointments in a number of diabetes-associated organizations in addition to the JRDF, including: the American Diabetes Association, Texas Diabetes Council, Pennsylvania Professional Diabetes Academy, American Association of Diabetes Educators, and National Certification Board for Diabetes Educators.

- *Dr. Francine Kaufman* is Chief Medical Officer and Vice President of Global Medical, Clinical and Health Affairs at Medtronic Diabetes, which she joined after a 30-year academic career. Until last year, she was Professor of Pediatrics at the University of Southern California's Keck School of Medicine and Head of the Center for Diabetes, Endocrinology and Metabolism at Childrens Hospital of Los Angeles. Dr. Kaufman is a former President of the American Diabetes Association and former Chair of the National Diabetes Education Program. Dr. Kaufman served as Chair of the Steering Committees overseeing two major NIDDK-led trials: The Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY) study and the HEALTHY study. She was also a principal investigator for the Type 1 Diabetes TrialNet. Dr. Kaufman has published over 120 peer-reviewed papers and over 30 books or book chapters. She earned her M.D. at Chicago Medical School, and did her internship, residency and fellowship work at Childrens Hospital of Los Angeles.

Joining the Subcouncil for the Division of Digestive Diseases and Nutrition are Dr. Gregory Gores, Ms. Jane Holt and Dr. Anil Rustgi.

- *Dr. Gregory Gores* is Professor of Physiology and Medicine and Chair of the Gastroenterology and Hepatology Departments at the Mayo Clinic. His laboratory-based research program is focused on liver cell death, especially the mechanisms by which cancer cells escape cell death and undergo malignant transformation and metastasis. Dr. Gores also develops and participates in clinical research protocols, with a focus on the treatment of hepatobiliary neoplasia. His research has been supported by NIDDK since 1989, and he presently has an NIDDK MERIT Award and two additional R01 projects. He has published nearly 300 articles, book chapters and reviews. Dr. Gores earned his M.D. from the University of North Dakota and did his residency and fellowship work at the Mayo Graduate School of Medicine.

- *Ms. Jane Holt* is co-president of the National Pancreas Foundation and is also Vice-Chair of the Digestive Diseases National Coalition. She joins the Council as one of six public members. Ms. Holt co-founded the National Pancreas Foundation in 1998 and has been tireless in her efforts to provide educational information and support for patients with pancreatic disease and to raise funds for medical research.

- *Dr. Anil Rustgi* is the T. Grier Miller Professor of Medicine and Genetics, and Chief of the Gastroenterology Division, at the University of Pennsylvania School of Medicine. Dr. Rustgi is also Director of the University's Digestive Diseases and Liver Clinical Center. His research focuses on the cell-type and tissue-type specific actions of certain oncogenes and tumor suppressor genes in modulating gastrointestinal cancers. In addition to holding two R01 awards from NIDDK, Dr. Rustgi is the Principal Investigator on an NIDDK Cooperative Agreement (U01) focused on intestinal stem cells. He also holds P01 and U01 awards from the National Cancer Institute, and he is a co-Principal Investigator on two Challenge Grants funded through the American Recovery and Reinvestment Act (ARRA). In 2006, Dr. Rustgi became Editor of the journal *Gastroenterology*. Over the last eight years he has published more than 70 papers and review articles. Dr. Rustgi earned his M.D. at Duke University and did his internship, residency, and fellowship work at Harvard Medical School--both at Beth Israel and Massachusetts General Hospital.

**Changes in the Professional Positions of Council Members and NIDDK Staff**

Dr. Rodgers announced that the following individuals had changed their professional positions.

- *Mr. Jim Schlicht,* who served on the Council as a public member since 2008, has taken a position as Legislative Liaison at the National Heart, Lung and Blood Institute. Because NIH employees may not serve on in this capacity on an NIH advisory council, Mr. Schlicht resigned prior to joining NHLBI. The NIDDK appreciates Mr. Schlicht's service to the Council, and to the Subcouncil for Diabetes, Endocrinology and Metabolic Diseases, and wishes him well in his new position.

- *Dr. Leonard Seeff,* Special Expert on Viral Hepatitis within the Liver Diseases Research Branch of the Division of Digestive Diseases and Nutrition, has retired after more than 40

years of government service at the VA and NIH. Dr. Seeff made many outstanding contributions to the field of viral hepatitis and drug-induced liver injury over the years. The NIDDK will miss his expertise and wishes him the best in retirement.

- *Dr. Debuene Chang,* Senior Scientific Officer for Women's Urologic Health Programs, recently left NIDDK's Division of Kidney, Urologic and Hematologic Diseases. Dr. Chang was a Program Officer for the Urinary Incontinence Treatment Network (UITN), which carried out several large-scale clinical trials. In addition, Dr. Chang oversaw the O'Brien Urology Research Centers program, the urology Specialized Centers of Research (SCOR) program, and the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs. Dr. Chang's personal research interests focused on urolithiasis. The Institute wishes her well on her future career endeavors.

- *Dr. Vanessa Ameen* is joining the Division of Digestive Diseases and Nutrition as Senior Scientific Advisor for Clinical and Translational Research in Digestive Diseases. She is a board-certified pediatric gastroenterologist with twenty-five years of experience in academic and clinical medicine and the pharmaceutical industry. Dr. Ameen attended medical school at the University of the West Indies in Jamaica, with a pediatric residency at the University of Medicine and Dentistry of New Jersey. She completed postdoctoral fellowships in pediatric gastroenterology and nutrition at the University of Medicine and Dentistry of New Jersey and the University of Texas Medical Branch at Galveston. After working in clinical and academic medicine at the University of Texas Medical Branch, Medical College of Wisconsin, Indiana University, and Temple University, Dr. Ameen redirected her career to the pharmaceutical industry, where she focused on nutritional support, functional gastrointestinal disorders and inflammatory bowel disease. In her most recent position, she served as the Senior Director for Clinical Development, Safety and Medical Affairs for gastrointestinal diagnostic and therapeutic products at Prometheus Therapeutics and Diagnostics in San Diego, California. Dr. Rodgers welcomed her to the Institute.

## Publication of Reports

Dr. Rodgers brought two publications to the Council's attention. He acknowledged the contributions of the NIDDK Office of Scientific Program and Policy Analysis and the extramural and intramural scientific divisions to both reports, which are posted on the NIDDK website.

- The annual NIDDK compendium of "Recent Advances & Emerging Opportunities" highlights examples of exciting NIDDK-supported research advances reported in fiscal year 2009, longer-term "stories of discovery," and profiles of patients who are benefiting from NIDDK-supported research. The report also summarizes scientific presentations made to the Advisory Council during 2009.

- The compendium, "NIDDK: 60 Years of Advancing Research To Improve Health," highlights examples of research discoveries made by NIDDK-supported scientists, both extramural and intramural, since the Institute was established. It celebrates the Institute's 60$^{th}$ anniversary in 2010.

## II. CONSIDERATION OF SUMMARY MINUTES OF THE 181st COUNCIL MEETING

Following a motion, the Council approved by voice vote the Summary Minutes of the 181st Council meeting.

## III. FUTURE COUNCIL DATES

Dr. Rodgers called the Council's attention to the following future meeting dates. Although most meetings will be a single day, Council members were asked to reserve both days to ensure flexibility should a situation arise where a longer meeting is required.

2010
May 12-13 (Wednesday and Thursday)
September 22-23 (Wednesday and Thursday)
*The Council was reminded that NIDDK's 60th Anniversary celebrations will culminate on Tuesday, September 21, 2010 with an Anniversary Scientific Symposium at NIH and an Anniversary Celebratory Dinner at the Bethesda North Marriott Hotel and Conference Center.*

2011
February 16-17, 2011 (Wednesday and Thursday)
May 11-12, 2011 (Wednesday and Thursday)
September 7-8, 2011 (Wednesday and Thursday)

2012
February 15-16 (Wednesday and Thursday)
May 16-17 (Wednesday and Thursday)
September 12-13 (Wednesday and Thursday)

## IV. ANNOUNCEMENTS
***Dr. Stanfield***

**Confidentiality**

Council members were reminded that material furnished for review purposes and discussion during the closed portion of the meeting is considered confidential. The content of discussions taking place during the closed session may be disclosed only by the staff and only under appropriate circumstances. Any communication from investigators to Council members regarding actions on an application must be referred to the Institute. Any attempts by Council members to handle questions from applicants could create difficult or embarrassing situations for the members, the Institute, and/or the investigators.

**Conflict of Interest**

Dr. Stanfield underscored that advisors and consultants serving as members of public advisory committees, such as the NIDDK National Advisory Council, may not participate in situations in which any violation of conflict of interest laws and regulations may occur. Responsible NIDDK staff shall assist each Council member to help ensure that the member does not participate in, and is not present during review of applications or projects in which, to the member's knowledge, any of the following has a financial interest: the member, or his or her spouse, minor child, partner (including close professional associates), or an organization with which the member is connected.

Dr. Stanfield noted that, at Council meetings at which applications are reviewed in groups without discussion, that is, "en bloc" action, all Council members may be present and may participate. The vote of an individual member in such instances does not apply to applications for which the member might be in conflict. Regarding multi-campus institutions of higher education, Dr. Stanfield pointed out that an employee may participate in any particular matter affecting one campus of a multi-campus institution of higher education, if the employee's financial interest is solely employment in a position at a separate campus of the same multi-campus institution, and the employee has no multi-campus responsibilities.

To ensure that a Council member does not participate in the discussion of, nor vote on, an application in which he/she is in conflict, a written certification is required. A statement is provided for the signature of the member, and this statement becomes a part of the meeting file. Dr. Stanfield directed each Council member to his or her folder containing a statement regarding the conflict of interest in his or her review of applications. He asked each Council member to read the statement carefully, sign it, and return it to NIDDK prior to leaving the meeting.

**Annual Approval of Council Operating Procedures**

Dr. Stanfield said that every year, during its winter meeting, the NIDDK Council approves its Council Operating Procedures. Last year, he consolidated the Council Operating Procedures and the En Bloc Early Concurrence Procedures into one document. The change was made simply to streamline documentation. This year, he is not recommending any further changes to the Council Operating Procedures, which were included for Council members' review in the pre-meeting materials in the Electronic Council Book and also made available in each member's folder should there be any questions. Dr. Stanfield asked if there were any questions or concerns regarding the Council Operating Procedures for 2010 and, hearing none, then asked for a motion to accept the Procedures for this year. A motion was made and seconded to accept the procedures, and they were adopted by voice vote.

## V. NIH DIRECTOR'S UPDATE
***Dr. Francis Collins***

*Dr. Rodgers introduced Francis S. Collins, M.D., Ph.D., who was sworn in as the 16th Director of NIH during the summer of 2009, following the Senate's unanimous confirmation of his nomination by President Barack Obama. Dr. Collins is a physician-geneticist known for his landmark discoveries of disease genes and his leadership of the Human Genome Project. He served as Director of the National Human Genome Research Institute (NHGRI) at the NIH from*

*1993-2008. Dr. Collins' own research laboratory has discovered a number of important genes, including those involved in cystic fibrosis, neurofibromatosis, Huntington's disease, a familial endocrine cancer syndrome, and most recently, genes for type 2 diabetes and for Hutchinson-Gilford progeria syndrome. Dr. Collins received a B.S. in chemistry from the University of Virginia, a Ph.D. in physical chemistry from Yale University, and an M.D. with honors from the University of North Carolina at Chapel Hill. Prior to coming to the NIH in 1993, he spent nine years on the faculty of the University of Michigan, where he was a Howard Hughes Medical Institute investigator. He is an elected member of the Institute of Medicine of the National Academy of Sciences. Dr. Collins was awarded the Presidential Medal of Freedom in November 2007. In 2009, he received the National Medal of Science, the highest honor bestowed on scientists by the U.S. government.*

Dr. Collins thanked Dr. Rodgers and commended him for being an incredibly capable leader of NIDDK, and for helping to address many of the corporate issues and policy questions facing NIH. He then focused his remarks on the future directions of the NIH, in a time of unprecedented research opportunities and resource challenges.

Prior to his confirmation, Dr. Collins contemplated ways in which the NIH could structure the exceptional opportunities it now has. He has developed five guiding themes which were outlined in *Science* in January 2010 ("Opportunities for Research and NIH," *Science* 327:36-37, 2010). The themes are: (1) to apply high-throughput technologies to understand fundamental biology, including genomics, but also many other areas such as nanotechnology, imaging and computational biology; (2) to focus on translational efforts to move basic science discoveries into clinical applications; (3) to put science to work for the benefit of health care reform; (4) to encourage a greater focus on global health, especially with respect to the therapeutics and prevention of disorders that are present in many different countries and thus, collectively, pose global heath problems; and (5) to ensure that the NIH's most important resource--the biomedical research community--is invigorated and empowered. To this end, the NIH can inspire innovation and recruit the next generation of researchers for a stable, vibrant research community.

Dr. Collins said that his remarks to the Council would focus on several points that can be used to make the case to the public and to policy makers about the achievements of NIH, especially with respect to the translation of basic science discoveries to the clinical arena, the benefits that NIH research brings to the economy, and the research opportunities that are ripe for exploitation.

**Advancing Knowledge through Basic Research**

Dr. Collins noted that the NIH track record in basic research is phenomenal. These achievements are congruent with an important part of the NIH mission statement: "science in pursuit of fundamental knowledge about the nature and behavior of living systems." One of the major contributors to fundamental knowledge was the late Nobel Laureate Marshall Nirenberg who, along with Heinrich Matthaei, deciphered the genetic code. This fundamental discovery has had direct translational implications--as evidenced in the large number of genetic variants that have now been correlated with common diseases through genome-wide association studies. An incredibly rich array of discoveries has emerged--each of which provides a potential clue to the pathogenesis of disease. While these genetic variants may not predict specific diseases, they are

pointing toward pathways that may be involved in disease processes, and thus, they could be extremely valuable in identifying potential therapeutic targets. A major challenge to the research community will be to prioritize the variety of potential targets for investigation, and to ensure that researchers in the public and private sectors are fully empowered to make the most of these exceptional opportunities. Dr. Collins commented that Marshall Nirenberg and many other Nobelists whose careers flourished at NIH had strong connections with NIDDK--connections the Institute can proudly reflect on as it celebrates its 60th anniversary year.

**Using Discoveries To Improve Health**

Dr. Collins described the challenge of translating the knowledge derived from basic discoveries into clinically relevant findings that can lead to improvements in human health. This challenge is reflected in another part of the NIH mission statement: "the application of (that) knowledge to extend healthy life and reduce the burden of illness and disability." When one looks at the course of human health in the U.S. over the past several decades, the effects of NIH research are evident with respect to changes in medical practice. For example, in the last 10 years or so, there has been a continual drop in age-adjusted death rates and an increase in longevity in the U.S. About every six years, the average lifespan increases by about one year, and it is hoped that this progress will not be curtailed because of the obesity epidemic. The NIH has also provided solutions for disability. For example, in 1982, about 26 percent of the population was disabled, but now that figure has dropped to about 20 percent and is continuing to decline. In many respects, a direct line can be drawn from NIH research to the reasons for these encouraging trends. It is essential that NIH stakeholders put forward these and other examples of the health benefits flowing from NIH investments.

**Benefiting the Economy**

Dr. Collins noted that the case for NIH should include the benefits of research to the economy--an issue of great current interest to national decision makers. As noted in the National Academy of Science's 2007 study, "Rising Above the Gathering Storm," some economists estimate that about half of U.S. economic growth since World War II has been the result of technological innovation. For example, in the current year, the NIH budget of $31 billion will be invested in all kinds of projects--each grant on average generating an estimated seven jobs. A study conducted by Families USA indicated that, in Fiscal Year 2007, every $1 million that NIH invested generated $2.21 million in new state business activity ("In Your Own Backyard: How NIH Funding Helps Your State's Economy. A Report from Families USA," June 2008). http://www.familiesusa.org/issues/global-health/publications/backyard-key-findings.html

Clearly, NIH funding provides an impressive return on investment. The economic benefits of NIH funding well justify the $10 billion dollars provided directly to the agency through the American Recovery and Reinvestment Act (ARRA) over the two-year period of FY 2009 and FY 2010, and the additional $400 million provided indirectly, via a transfer of funds targeted for comparative effectiveness research.

Dr. Collins acknowledged the tremendous efforts of NIH staff and the research community whose work made it possible for applications to be developed, submitted, reviewed and funded

under the Recovery Act in a timely manner. As of January 5, 2010, the NIH had awarded approximately $5 billion of Recovery Act funds, including $4.4 billion in grants to support over 13,000 projects, and nearly $500 million in contracts for over 350 projects. Twenty-eight of the funded institutions were first-time NIH award recipients, including some small businesses, and 1,885 of the funded individuals were new investigators. It is estimated that the Recovery Act funds provided to NIH will result in the creation or retention of 50,000 jobs over two years. On September 30, 2009, Dr. Collins had the opportunity to highlight the use of Recovery Act funds for President Obama and Secretary Sebelius during their visit to NIH.

Scientifically, the Recovery Act has helped to further many areas of research, some of which are of special importance to the NIDDK and its Council. For example, $8 million of Recovery Act funds were used to enhance the Beta Cell Biology Consortium, which now involves 50 scientists, both nationally and internationally, in the sharing of resources to understand the biology of these insulin-producing pancreatic cells, pinpoint the reasons for their impairment in diabetes, and discover how they can be used for cell-based therapeutic approaches to diabetes.

**Ensuring the Future: Opportunities for Tomorrow**

As NIH looks to the future, innovation continues to be a paramount concern. Many in the community have wondered whether innovation has suffered because an overburdened peer review system is functioning in a flat budget landscape. When budgets are limited, it is often difficult for peer reviewers to assess the relative benefits of funding solid, traditional scientific proposals on the one hand, and innovative, high-risk proposals on the other. To foster innovation, the NIH has developed new mechanisms that require applicants to develop transformative ideas. Three such mechanisms are the NIH Director's Pioneer Award program, the NIH Director's New Innovator Award program, and the Transformative Research Projects program.

All three of these awards are supported by the NIH Common Fund. The Congress has established the Common Fund in NIH statute and incorporated within it the NIH Roadmap Initiative. The Common Fund is used to support programs that no single Institute would be able to support, that are transformative, and that will likely have an impact on many diseases. The Common Fund now accounts for about a half billion dollars of the NIH budget, and these three programs use a major portion of that funding. Dr. Collins believes that these programs are making important accomplishments, which should be broadly cited in support of NIH investments. It is his hope that the NIH Institutes and Centers will develop similar efforts by using their individual resources to encourage innovative ideas and to capitalize on the momentum provided by recent discoveries.

Turning to the NIH budget landscape, Dr. Collins noted the difficulties the agency faced between FY 2003 and FY 2008--following the end of the five-year NIH budget doubling. The budget did not keep pace with inflation, and effectively lost about 15 percent in real purchasing power. While FY 2009 and FY 2010 brought considerable new resources through the American Recovery and Reinvestment Act (ARRA), these special funds were provided for only those two years, and investigators came forth with many more proposals than could be supported. Because science does not operate on two-year cycles, the NIH will probably see stress on its funding system when ARRA funding ends. In FY 2011 and FY 2012, there may be a great demand on

the NIH budget as the normal influx of new and competitive renewal applications expands to include ARRA-funded investigators who want to continue their work. One factor that may ease this stress is that investigators who received two-year ARRA grants are allowed to apply for no-cost extensions. Another positive factor is that the FY 2011 President's Budget request for the NIH proposes to add $1 billion in funding to the agency's base appropriation. However, because of the size of the NIH budget base, an additional billion dollars translates into an increase of about 3.2 percent over non-ARRA FY 2010 funding. The predicted inflation rate for biomedical research in 2011 is also about 3.2 percent.

At this point, it is not possible to know how the Congress will respond to the President's budget request and what the final NIH appropriation will be for FY 2011. What is known is that the NIH will be seriously challenged with respect to managing its resources at a time of such great scientific opportunity, and when the research community has been stimulated by Recovery Act funding that will draw to a close in FY 2010. The challenges are apparent in the comparison between historical *versus* projected success rates for grant applications (i.e., the percentage of reviewed research project grant applications receiving funding, computed on a fiscal year basis). Historic success rates back to 1979 were on the order of about 25-35 percent, and the research community generally considered them manageable. However, with the flattening of the budget that occurred following the NIH five-year budget doubling period, grant applications continued to increase in number, the average cost of grants continued to increase, and success rates began to fall. In FY 2010, it is estimated that NIH success rates will be about 20 percent and the prospects for FY 2011 may be even bleaker--perhaps even historically low success rates--depending upon the numbers of applications eligible for award vis-à-vis available funds.

## Making the Case for NIH

In concluding his remarks, Dr. Collins stated that he is privileged to be the NIH Director at such an exciting scientific time. He encouraged everyone to make the case for the importance of NIH endeavors by conveying the many health and economic benefits that are derived from its research investments. Dr. Collins is engaged in personal outreach about the value of NIH, and urged others to be proactive through educational programs, media, and other avenues for educating the nation about the importance of biomedical research, inspiring passion for science in the next generation, and eliciting feedback. He noted that a new brochure, "NIH: Turning Discovery into Health," provides a useful demonstration of NIH achievements. An NIH website gathers comments and suggestions from all interested parties: NIH-LISTENS@nih.gov.
Dr. Collins closed his visit to the Council by responding to comments and questions.

## Questions and Discussion

*What can NIH do to address the difficulty in attracting young people, especially medical students to a research career?* Dr. Collins replied that there are components to the process that need to be bolstered in order to improve the recruitment of talented individuals to careers in science, particularly medical students. Part of the problem is the financial burden that students carry following their training, coupled with the lure of a lucrative practice or other non-research career. The NIH Loan Repayment Program has helped in this regard, but may need to be enhanced. In addition, research should be featured in medical school curricula, and the NIH brainstorms with

the Association of American Medical Colleges (AAMC) about ways to improve curriculum development. It is also important to focus on early education (kindergarten through grade 12) to develop pathways that will encourage students to be excited about research. For example, President Obama is propelling educational improvements with his "Race to the Top" plan. Research needs to have greater visibility so that students can feel the excitement of discovery and see the enormous potential of research to improve lives.

*In a relatively flat economic environment, how can NIH maintain a balance between strong basic science and the translation of emerging fundamental discoveries into clinical advances?* Dr. Collins said that this is a constant challenge. Both basic science and the translation of its discoveries into clinical advances are encompassed in the NIH mission statement, but there is no prescription for how to strike an appropriate balance between them. Clearly, the mainstay of NIH progress will continue to be the individual investigator and the R01 grant; however, there are also compelling opportunities for large-scale efforts to move the research agenda rapidly. If there are remarkable clinical opportunities, such as in the area of small molecules, then NIH should probably start down the therapeutic pathway with modest investments so that time and momentum are not lost. It is also important to remember that the NIH is the National Institutes of Health not the National Institutes of Basic Science. Therefore, the public expects the NIH to move fundamental discoveries forward into clinical applications. At the same time, it is imperative to have the foundation of knowledge produced by basic science as a platform for clinical progress. Without that foundation, NIH could be a translational engine with nothing to translate. Thus, we need to identify and pursue special opportunities in both basic science and clinical/translational research.

*Could you elaborate on the theme of global health issues?* Dr. Collins said that science is offering new approaches to the diagnosis and treatment of several global health issues including AIDS, tuberculosis, and malaria. There are new scientific insights regarding neglected tropical diseases, many of which are caused by pathogens whose genomes have now been sequenced, thus opening up new opportunities for intervention. Also deserving attention are the non-communicable diseases, including diabetes, which are the fastest growing cause of morbidity and mortality in low- and middle-income countries. Global health research can attract young scientists, and lead to productive research partnerships. Dr. Collins noted that he convened a meeting in January 2010 of representatives from some of the key organizations involved in global health to foster information exchange and identify areas that are already very active *versus* those that are under-served. The NIH will look for opportunities to intensify global health research, possibly through the NIH Common Fund, and through other means, such as NIH participation in the planning process for the Administration's new global health initiative.

*Does NIH have any plans to address the issue of institutional investment in science? A recent article in the Journal of the American Medical Association indicated that the average investment of academic medical centers has fallen substantially.* Dr. Collins noted that some temporary relief has come from ARRA funds for faculty recruitment, renovation/construction, and equipment. However, those funds were only provided for FY 2009 and FY 2010. If academic institutions are concerned about their futures, they will need to find ways to bring in new, talented, early-stage investigators. The NIH has recognized this need with the establishment of its Pathway to Independence awards (K99-R00) to help start investigators on the road to a

research career. However, NIH discussions with both the Association of American Universities and the Association of American Medical Colleges have reinforced that there is no easy answer to filling gaps between NIH support and institutional support. Funds may need to come from eliminating activities that are not optimally productive in order to redirect funds to exciting new opportunities.

*From the Council discussion, there seem to be three inter-connected issues: the attractiveness of a career in science, the need for innovation, and the difficulties of peer review in evaluating and managing the huge flow of proposals. Would NIH consider dramatically altering its funding approaches to support people, not projects, and to manage outputs of productivity, creativity, and impact, rather than inputs? Is this an attractive approach? Would there be logistical challenges or political backlash to adopting it?* Dr. Collins said that discussions have already occurred at NIH about this type of approach, which in a sense has been piloted for superb investigators through the NIH Director's Pioneer Award and is used by the Howard Hughes Medical Institute. The NIH probably needs to make more funding decisions based on investigators rather than the projects. However, that approach needs to complement the NIH portfolio and NIH goals, and it could reach a point of diminishing returns. For example, when encouraging established investigators to move into a new research field, the risks may be much greater if funding is investigator-based rather than project-based. Again, the issue is one of striking an appropriate balance among funding alternatives.

*What future directions are planned for the Clinical Translational and Science Awards (CTSA) program?* Dr. Collins said that that the CTSA program is a crucial part of NIH efforts to enhance the application of clinical research. The expectation is that the number of CTSAs will increase from 46 to 60 in the next few years. Dr. Collins plans to visit some CTSAs very soon to see their catalytic and synergistic effects. He wants to look at their scientific function, not just their infrastructural impacts, and is particularly interested in identifying the kind of translational advances that can be attributed to the CTSAs. Once the scientific trajectory of the CTSA program is clear, the NIH can decide whether it needs to do more to foster a collaborative spirit in the program, or to identify gaps that still aren't quite filled by the CTSA structure.

*Regarding the budget challenges that will arise when funding under the Recovery Act ends in FY 2011, has NIH considered convening non-profit groups, pharmaceutical groups and others to emphasize the potential of NIH research and to proactively seek their financial support to continue some of the most productive work?* Dr. Collins said that NIH is definitely exploring ways to encourage such partnerships. However, many of the non-profits and pharmaceutical firms are also facing economic difficulties. The challenge is to find compelling pockets of research opportunity that can elicit support. In that regard, the Foundation for NIH is a mechanism that catalyzes partnerships. Dr. Collins noted that he has a great interest in building a better catalyzed partnership between academia and the pharmaceutical industry on drug development. The NIH has a great deal to offer in terms of information on assay design, high-throughput screening centers for such assays, a library of 300,000 compounds, and medicinal chemistry expertise. The NIH also has programs such as the CTSAs and a new program, Therapeutics for Rare and Neglected Diseases (TRND). Moreover, the NIH Clinical Center can undertake Phase 1 or 2 clinical trials. Dr. Collins emphasized that the goal is not to turn NIH into a drug development company, but rather, to be a better partner with biotechnology and

pharmaceutical industry in order to mitigate the risks associated with research projects that otherwise might not be considered economically feasible. The time seems right to put together resources from both the NIH and the pharmaceutical industry to jump start a whole new era of therapeutic development.

Dr. Rodgers thanked Dr. Collins for his presentation and for his discussion with Council.

## VI. REPORT FROM THE NIDDK DIRECTOR
***Dr. Rodgers***

### 2010 Appropriation

Dr. Rodgers briefed the Council on several budget developments. Since the last Council meeting, the House and Senate Appropriations Committees came to agreement through a Conference Committee regarding a final FY 2010 appropriation level for the agency. This level is a 2.7 percent increase for NIH, which includes a 2.7 percent increase for NIDDK. The final percentage increase is near the mid-point between each Chamber's initial funding mark.

The NIH will award all non-competing research project grants at slightly less than the currently committed levels. The average inflationary increase in the commitments is three percent; however, by NIH policy, NIDDK will make awards at an average increase of two percent. The NIDDK and other NIH components will have some flexibility as to how to reach that goal. The NIH intends to maintain the number of National Research Service Award trainees at approximately the same in 2010 as in 2009. Funds are provided for a one percent increase in stipends, but no increases are included for tuition or training-related expenses.

The NIDDK plans to continue its past practice of providing the full cost necessary for large clinical studies and consortia. The Institute also plans to maintain or possibly increase the number of competing research project awards above last year's actual total of 619.

The NIDDK will transfer some funds to other Institutes in order to effect NIH research initiatives. The largest of these is the initiative on Genes, Health and the Environment. Smaller NIH initiatives address rare and neglected diseases and undiagnosed diseases. During the appropriations process, both the House and Senate expressed concerns about special funding set-asides for NIH-wide initiatives and declined the Administration's FY 2010 proposals for a large increase in cancer research and a set-aside for autism research.

### 2011 President's Budget Request

President Obama has requested a $1 billion increase for the NIH, an increase of 3.2 percent over the funding level provided for FY 2010, exclusive of funds provided through the American Recovery and Reinvestment Act (ARRA). Dr. Rodgers noted several activities included in the proposed budget.

- Therapeutics for Rare and Neglected Diseases Program ($26 million increase)
- Clinical and Translational Science Awards ($10 million increase)
- Stipends for research trainees (six percent increase)

- Program Evaluation transfer of NIH funds to the Department (2.8 percent of the NIH budget)
- NIH portion of the Administration's National Nanotechnology Initiative (increase of $22 million)
- Basic Behavioral and Social Sciences Opportunity Network--OppNet (Use of regularly appropriated funds to continue the $20 million annual effort funded through ARRA)

Dr. Rodgers emphasized that the President's budget request is the beginning of a process, with the next step being consideration by the House and Senate. While the final results are unknown, FY 2011 will be a challenging year due to the end of the ARRA funding, coupled with an expected surge in research applications.

**Financial Controls: Anti-Deficiency and Funds Reprogramming**

Dr. Rodgers informed the Council that NIH is entering a new phase of tighter accounting controls.

The first change is intended to control spending by preventing any transaction that would exceed "allowance" of appropriated funds to certain components of the budget. Controls at this level are in accord with requirements of the Federal Anti-Deficiency Act. The NIH has taken care to remain in compliance with this Act, which has severe penalties for non-compliance. However, the NIH financial systems do not presently have the type of "hard controls" that would actually block a spending transaction and, in effect, prevent an overdraft. New hard controls will be incorporated into NIH accounting systems in 2011. This change is not expected to materially affect the spending of NIDDK funds, so long as the Institute has carefully planned the amounts needed for its allowances for specified budget components such as the intramural program, the extramural program, Research Management and Support, and the Small Business Innovation Research (SBIR) program and Small Business Technology Transfer (STTR) program. The hard controls will also apply to funds appropriated for the special statutory funding program for type 1 diabetes research.

The second change involves new controls that will tighten the reprogramming of funds from one budget mechanism to another. Previously, reprogramming was possible at the total funding level of each mechanism, e.g., for all research training funds or all Research Centers funds. However, beginning this year, spending will be controlled at the level of every line on the standard NIH mechanism table, and hard controls will be implemented in the accounting system by 2013. Fortunately, funds for competing and competitive renewal Research Project Grants (RPGs) will be considered a single pool. This change has the potential for affecting the distribution of funds among budget mechanisms because reprogramming requests are only possible at certain times.

## VII. CONCEPT CLEARANCE FOR OBESITY INITIATIVE "Healthy Pregnancy: Reducing Risk of Obesity and Diabetes in Mother and Child"

***Dr. Philip Smith, Deputy Director, Division of Diabetes, Endocrinology and Metabolic Diseases, and Co-Director, NIDDK Office of Obesity Research***
***Ms. Joanne Gallivan, Director, National Diabetes Education Program***
***Dr. Susan Yanovski, Director, Obesity and Eating Disorders Program, Division of Digestive Diseases and Nutrition, and Co-Director, NIDDK Office of Obesity Research***

*Dr. Rodgers introduced the presentation of a proposed new, trans-NIDDK initiative for concept clearance by the full Council because it involves more than one Division. He noted that one of the Council's most important roles is to provide recommendations to the Institute on future research initiatives.*

**Rationale for Proposed Initiative - Dr. Smith**

Dr. Smith stated that the goal of the proposed initiative is to further healthy pregnancy in order to reduce the risks of obesity and diabetes in both the mother and child--to develop a healthy pregnancy program. The initiative would include three components: educational, observational, and interventional.

Dr. Smith described research findings that provide a rationale for this initiative. He recounted epidemiologic studies, which have demonstrated the dramatic increase in obesity in the U.S. over the last 20 years. While the Centers for Disease Control and Prevention (CDC) has recently reported an apparent stabilization of obesity prevalence in the adult population, current levels of obesity remain of great concern. Particularly troublesome are trends in overweight among children and adolescents because obesity is a risk factor for type 2 diabetes, which is also increasing among youth.

From 1963 to 2006, a dramatic increase occurred in the number of overweight youth, both in the 6-11 and 12-19 year-old age groups. One impact of these trends is that there are now an increasing number of women of child-bearing age who are either overweight or diabetic, and their offspring may have health risks due to their exposure to an obese and/or diabetic intrauterine environment. Evidence is increasing that such exposure may confer metabolic risk for adult disease in offspring. Children born after obese women have had bariatric surgery have a lower risk of obesity than those born to the same mother pre-surgery. Also, studies in the Pima Indians of Arizona have shown that offspring from diabetic pregnancies have a much greater risk of early-onset diabetes than their siblings who were born before their mothers developed diabetes. These findings suggest the existence of *in utero* factors that contribute to risk for adult obesity and diabetes--in addition to risks conferred by the genetics of one's parents and/or the social environment in which a person lives. Several studies have suggested that the body's long-term memory of metabolic conditions in the intrauterine environment--called metabolic imprinting--may result from epigenetics, i.e., the control of changes in gene function that do not involve changes in DNA sequences. There are data that relate epigenetics to obesity and to energy balance. Also, systems that control energy balance in the brain, fat tissue and liver are all susceptible to perturbation during intrauterine development.

Very little is known about the mechanisms underlying metabolic imprinting in the obese or diabetic *in utero* environment that can contribute to later morbidity in offspring. One hypothesis suggests a role for changes in the placenta and its function. It is known that inflammation associated with obesity leads to macrophage invasion of tissue. The placental tissue of obese mothers is infiltrated with macrophages in direct relationship to the extent of obesity. Inflammatory markers have been found in the cord blood from the pregnancy of those mothers. Moreover, their offspring have been found to have insulin resistance. Research in obese non-

human primates has also found a similar inflammatory process that affects liver-function markers in neonates.

One of the known risk factors for obesity is maternal gestational diabetes, a form of diabetes that occurs only in pregnancy. The Hyperglycemia Adverse Pregnancy Outcomes Study (HAPO) demonstrated that glucose levels at any point above normal can have a negative impact on the mother and on the offspring (*New England Journal of Medicine* 358;19:1991-2001, 2008). However, because tests for gestational diabetes are administered relatively late in pregnancy, damage may often occur before diagnosis. Each year, about seven percent of pregnancies have complications due to gestational diabetes. Women with a history of gestational diabetes have a 20-50 percent chance of developing type 2 diabetes within 5-10 years following pregnancy. Offspring of mothers who had gestational diabetes are at a greater future risk for obesity and diabetes. Gestational diabetes frequently occurs along with other risk factors for obesity and diabetes among individuals with a family history of gestational diabetes and in certain racial and ethnic groups. The trend toward obesity in younger adults could be fueling diabetic pregnancies in obese women which, in turn, increases the level of obesity and diabetes in their offspring. Such a vicious cycle may well contribute to at least some of the apparent epidemic levels of obesity and diabetes seen in the last 20-30 years.

The proposed initiative would target women at risk for gestational diabetes with the goal of yielding life-long benefits for the mother in terms of diabetes risk, and also for her offspring in terms of the risk of developing obesity and/or diabetes. There are several reasons for targeting this initiative to women at risk for gestational diabetes. First, it is known that pregnant mothers are very highly motivated to modify their behaviors that may affect their fetuses. Thus, women may be particularly receptive to behavior modification strategies to counter obesity and therefore reduce their risk for gestational diabetes and its effects. Second, studies have shown that short-term lifestyle interventions can be very effective, and the period of pregnancy is short. Third, it makes sense to address the problems of obesity and diabetes early in life. Avoiding damage to a fetus *in utero* could reduce the need for difficult and costly interventions for obesity and diabetes when the offspring of diabetic pregnancies reach adolescence and adulthood.

The proposed initiative would have three components. An outreach component would educate women at risk for gestational diabetes about the potential dangers to both themselves and their children. A second component would identify markers of *in utero* exposure to metabolic risks and link them to the offspring's later childhood markers and adult risk. A final component would involve lifestyle interventions that begin early in pregnancy to target weight gain and metabolic improvements, using indicators such as glucose levels and inflammatory markers.

**Educational Component of Proposed Initiative – Ms. Gallivan**

Ms. Gallivan described the initiative's educational component, called: "Increasing Early Intervention To Prevent Diabetes Following Pregnancy Complicated by Gestational Diabetes." These efforts would be pursued through the National Diabetes Education Program (NDEP) in conjunction with the NIH Office of Research on Women's Health (ORWH). The NDEP is a partnership between the NIDDK and the CDC, with the participation of over 200 public and private partners from federal, state and local levels. The goal of the NDEP is to reduce the

burden of diabetes in the U.S. by facilitating adoption of proven approaches to prevent or delay the onset and progression of diabetes and its complications. The NDEP was established approximately 13 years ago to translate the findings from the NIDDK's landmark clinical trial, the Diabetes Control and Complications Trial (DCCT). Since its inception, the NDEP has developed science-based messages and educational campaigns for patients, the public, and health professionals based on the results of several important clinical trials.

A three-year ground-breaking clinical trial, the Diabetes Prevention Program (DPP), demonstrated that the risk of developing diabetes could be substantially reduced in at-risk individuals. The lifestyle intervention, which focused on weight loss achieved through dietary change and increased physical activity, reduced the risk of developing type 2 diabetes by 58 percent, while the drug metformin reduced the risk by 31 percent. A follow-up study, the Diabetes Prevention Program Outcomes Study, showed that the benefits of the interventions persisted over a longer period of time. The combined ten-year results of the DPP and DPPOS studies demonstrated that the risk of developing type 2 diabetes could be reduced 34 percent with the lifestyle intervention, and by 18 percent with the drug metformin. Interestingly, the risk reduction in women who have had gestational diabetes was comparable to other study participants, even though they are known to have a higher incidence of the disease. Therefore, the proposed initiative in women who have had gestational diabetes would provide an opportunity to identify an intervention strategy for a very high-risk population. As a result of the DPP, the NDEP launched a national public education campaign in 2002: "Small Steps. Big Rewards. Prevent Type 2 Diabetes." A number of other educational campaigns target high-risk groups, including certain ethnic populations and the elderly.

The proposed educational component of the new initiative would build on an existing NDEP educational campaign for women with a history of gestational diabetes and their offspring, called: "It's Never Too Early To Prevent Type 2 Diabetes." With support from the NIH Office of Research on Women's Health, the following goals would be pursued: (1) to decrease the number of women with a history of gestational diabetes who go on to develop type 2 diabetes; (2) to raise awareness of the health risks of diabetes in pregnancy among families with children whose mothers have ever been diagnosed with gestational diabetes; and (3) to improve the reach of information and the delivery of health-care professional counseling regarding future health risks and the importance of adopting and maintaining healthy behaviors among those families. The initiative would feature outreach through both traditional media and social media channels to women who have had gestational diabetes.

In developing the initiative, the NIDDK recognizes the importance of encouraging the participation of health care professionals and groups, such as family physicians, pediatricians, obstetricians, and gynecologists, who interact with women of child-bearing age. The NIDDK has already conducted a series of focus groups with obstetrician-gynecologists to learn what they know about the history of women with gestational diabetes, what they tell their patients when they screen them, and what the NDEP could provide to help their patients make lifestyle changes with regard to healthful eating and nutritional intervention. In addition to these outreach efforts, the educational component of the initiative would also include a comparative effectiveness element.

**Observational and Interventional Components of Proposed Initiative – Dr. Yanovski**

Dr. Yanovski addressed the two research components of the proposed initiative. The first would be an observational cohort component aimed at identifying markers of *in utero* exposure to obesity and hyperglycemia and their relationship to later childhood markers and adult risk of metabolic health problems. Dr. Yanovski discussed the need for studying the impact of metabolic health in pregnancy. In 2009, the Institute of Medicine issued a report on weight gain during pregnancy. The report noted that a record-high proportion of American women of childbearing age are obese, but that current evidence is insufficient to make specific recommendations for gestational weight gain in women who have a body mass index equal to or greater than 35 in pregnancy. The report pointed to the need for studies in obese women, stratified by severity of obesity, on the determinants, impact and composition of gestational weight gain. In addition, the American Congress of Obstetricians and Gynecologists recently recommended reassessing glycemic control during pregnancy and the methods by which it is evaluated.

Dr. Yanovski said that, while epidemiologic findings support a direct relationship between gestational weight gain and offspring birth weight, there is a need for observational and experimental studies for direct assessment of the impact of gestational weight gain and other maternal metabolic factors on childhood outcomes, including post-natal weight gain, adiposity, and metabolic status throughout childhood and adolescence.

Few studies have investigated the effect of lifestyle interventions in overweight and obese pregnant women. Moreover, study designs to date have varied widely in terms of nutrition education, types of dietary or physical activity programs provided, rigor of the interventions, and whether efforts were made to limit or even prevent weight gain in women who were already obese. Prior studies have had homogeneous populations with small numbers of participants, and significant loss to follow-up. Results have been highly variable in terms of controlling weight during pregnancy, with little evaluation of later metabolic parameters, particularly with respect to the offspring.

The observational component of the new initiative would build upon current knowledge that maternal obesity and hyperglycemia have an impact on offspring in terms of body composition and inflammatory markers, and also, that maternal hyperglycemia significantly increases the risk for obesity and diabetes in Pima Indian offspring. In the proposed initiative, researchers would seek to identify intermediate biomarkers of metabolic risk in offspring based on the results of well-characterized pregnancies that are followed as the offspring develop into childhood and adolescence. To this end, the NIDDK proposes leveraging the rich database of the existing Hyperglycemia Adverse Pregnancy Outcomes (HAPO) study. The HAPO was a multi-center, international study that included a multi-ethnic population of over 23,000 pregnant women who did not have gestational diabetes. The study demonstrated a continuous association between maternal glucose and the primary outcomes of birth weight, cord blood C peptide, and neonatal adiposity; however, it was not designed to follow the longer term metabolic outcomes of these pregnancies as the offspring matured into childhood and adolescence. The NIDDK now proposes performing in-depth metabolic phenotyping of the offspring of the mothers who participated in the HAPO study. Data would be collected on body composition, inflammatory markers, glucose

and lipid levels, DNA, and possibly the microbiome. These data could then be analyzed and related to maternal exposures and neonatal parameters.

Turning to the third component of the proposed initiative, Dr. Yanovski described the conceptual basis for research on a lifestyle intervention program, which would start in early pregnancy. The objectives would be: (1) to support exploratory study of lifestyle interventions, which are designed to promote appropriate gestational weight gain through improved diet and physical activity, and (2) to assess the impact of these lifestyle changes on a variety of behavioral, anthropometric, and metabolic outcomes in both the mother and her offspring. The study would be designed to answer a number of questions, such as: What are the effects of diverse lifestyle interventions on the metabolic status of obese pregnant women, for example, in terms of gestational diabetes? What types of interventions might work--for example, would changes in diet composition have an impact in a high-fat *versus* low-fat diet, even in the absence of changes in weight? What would be the impact of different types of physical activity, independent of gestational weight gain? Do short-term interventions in obese pregnant women have longer-term effects in the mother, such as reduced post-partum weight retention? Do effective lifestyle interventions during pregnancy affect risk for obesity or other metabolic diseases in offspring over time?

Dr. Yanovski outlined the general design of the proposed interventional component of the proposed initiative. Exploratory research would be conducted in overweight/obese pregnant women who are recruited as early as possible in the first trimester to test the efficacy of dietary or physical activity interventions to reduce excessive weight gain during pregnancy. The study duration and size of the study population would vary, depending on the primary outcomes and expected enrollment. Follow-up would be required to continue for at least 12 months after the birth of the offspring. Investigators would be required to provide a plan for maintaining contact with the mothers and their offspring, including the involvement of pediatricians and primary care physicians. Collaboration would be required among investigators to devise a core set of measures for capturing data in study participants and their offspring. In the mothers, primary outcomes could include measures of weight or body composition during pregnancy and the post-partum period, and measures of glycemic status, including insulin sensitivity. Additional maternal outcomes could include patterns of weight gain, complications of pregnancy and delivery, and risk factors for cardiovascular disease. In the offspring, outcomes could include size at birth, neonatal body composition, post-natal growth, and body composition. This design would also provide an opportunity to examine mechanistic outcomes including markers of placental function, epigenetic markers for regulatory genes in mother and child, and the gut microbiome of the mother *versus* the neonate. The data gathered could provide a platform for gaining insights into underlying conditions that lead to childhood obesity. Additionally, data could be collected on individual, familial, and environmental variables, such as paternal body mass index, lifestyle factors, temperament, and infant feeding practices. In a sense, this research could be considered a form of primary prevention study to interdict pediatric obesity.

Dr. Yanovski identified other factors that would have to be considered in designing the study, such as the feasibility of recruiting and retaining the patient population, and the acceptability of and adherence to a lifestyle intervention in diverse populations. Other issues to be addressed would include the ability to measure relevant biological and behavioral outcomes, and the

feasibility of tracking longer-term outcomes. Important issues are the feasibility, safety, and effects on mother and offspring of limiting gestational weight gain.

Dr. Yanovski closed by pointing out some of the long-term research implications of the proposed observational and interventional research. The research has the potential for translating effective interventions into community-based and/or clinical care settings. The results may also inform larger clinical trials, which could address gestational weight gain or other identified, potentially modifiable factors related to pregnancy complications, post-partum weight retention, and/or progression to obesity, type 2 diabetes or other morbidities in the offspring.

**Council Questions and Discussion**

*How does this proposed research relate to the Barker hypothesis that reduced fetal growth is strongly associated with a number of chronic conditions later in life?* (*Barker, DJP: Maternal Nutrition, Fetal Nutrition, and Disease in Later Life. Nutrition 13(9):807-13, 1997). It would be interesting to include individuals from the Pima Indian population in the proposed research because, in addition to having high rates of diabetes and obesity, they have a high incidence of kidney disease.* Dr. Smith replied that the NIDDK would welcome suggestions regarding outcome measures across the physiological spectrum. The research concept developed thus far has focused on issues related to obesity and diabetes risk, but is inclusive of metabolic disorders of all kinds, including kidney dysfunction and cardiovascular disease. The number of disease outcomes studied would depend on partnerships with organizations who contribute funding. It is hoped that other Institutes would be interested in funding research based on well-phenotyped pregnancies for which the risks in the offspring are not only diabetes and obesity, but also other conditions such as kidney disease and cardiovascular disease. Dr. Yanovski noted that NIDDK has a good history of opening up investigations of well-phenotyped populations for ancillary studies that will maximize the knowledge that can be derived.

*Could the proposed research involve the Clinical and Translational Science Award (CTSA) program?* Dr. Yanovski responded that the proposed initiative is the type of study for which NIDDK would like to see involvement of the CTSAs. Also, managed care organizations might be able to bring in multi-specialty groups and follow the development of children. Different NIH Institutes and other federal and non-federal organizations could likewise participate.

*Would it be possible to compare offspring who have been delivered to women before and after they have had bariatric surgery--given that data show that women have lower rates of obesity and diabetes following such surgery?* Dr. Smith responded that studying any large cohort in which the pregnancy is very well-characterized metabolically would be beneficial in terms of linking what is known about the *in utero* environment and the effects on the offspring. Dr. Yanovski noted that the NIDDK is currently supporting a longitudinal assessment of bariatric surgery, through an observational cohort study. Researchers are following pregnancies in that group; however, that study was not designed to characterize the pregnancies in such a way as to follow outcomes in the offspring.

*Is it possible that obese fathers have a detrimental effect on the metabolic outcomes of offspring even if the mothers are of normal weight or underweight during pregnancy?* Dr. Smith

responded that there are clearly genetic and/or environmental factors other than the gestational weight gain of the mother than can influence the metabolic outcomes of the offspring. However, research suggests that the excess growth experienced by offspring of diabetic mothers is not due solely to genetic factors of the mother or father. The NIDDK supports considerable research on the roles and interrelationship of genetic and environmental factors in obesity; however, the influence of the obese intrauterine environment has been underappreciated as a potential cause of early-onset obesity in offspring.

*How would the proposed initiative be structured organizationally? Would it be intramural or extramural? What would be the budget, timing, and next steps?* Dr. Smith replied that the educational component is already under way, with some co-funding from the NIH Office of Research on Women's Health. The NIDDK has funds to move it forward, but the issue is the degee to which it can be expanded. Because the educational component is focused on women identified as having had gestational diabetes, it will be important to work with the Congress on Obstetrics and Gynecology to reduce the future pregnancy risks and family risks of these women. For the observational cohort study, the NIDDK is planning to use a small amount of one-year money for a planning phase and then issue a solicitation along the lines of a cooperative agreement. However, that will have to be done in a targeted way, because the intent is to build upon the existing HAPO study population. Depending upon the budgetary landscape, the observational cohort study would probably commence in 2011. Funding will depend upon the number of contributing partners the NIDDK is able to enlist to support the study. For the interventional component, the plan is to issue a Request for Applications; however, it would be important to establish common outcome measures so that comparisons can be made if different research teams or sites are involved. The funding amount has not yet been determined, but it is hoped that this part of the study would go forward in 2011, with contributions from other NIH components and agencies.

*How can you plan a large educational program that is predicated on an intervention whose results are not yet known?* Dr. Smith replied that there are data derived from interventional research on which to base the educational component. For example, gestational diabetes occurred among patients who participated in the Diabetes Prevention Program clinical trial, and they benefited from the lifestyle intervention. Moreover, it has been shown that treating gestational diabetes has a positive effect on pregnancy. What is unknown is the effect on the offspring, which can only be inferred at this point. Dr. Yanovski added that a number of epidemiologic studies show a relationship between maternal weight gain or gestational diabetes and increased birth weight in the offspring. However, the mechanism underlying this correlation has not yet been identified. The proposed initiative would attempt to extend the epidemiologic observations so that mechanisms could be pinpointed. Additionally, Dr. Smith noted that the NIDDK is in the process of testing interventions in non-human primate models.

The discussion period ended with a Council member recommending that the proposed study draw upon knowledge from the NIDDK's TEDDY study with respect to categorizing what happens over time to the newborn. It was also noted that the proposed study would be useful in drawing attention to the general importance of birth weight and the circumstances of pregnancy. Dr. Rodgers thanked the presenters and the Council members for their contributions to this concept clearance discussion.

## VIII. ADVISORY COUNCIL FORUM: "NIDDK Research Centers Program"

***Dr. James Hyde, Senior Advisor for Career Development (K) Awards and Diabetes Centers Programs within the Division of Diabetes, Endocrinology and Metabolic Diseases***

*In introducing Dr. Hyde, Dr. Rodgers noted that the NIDDK undertakes periodic reviews of its operations to gain Council input regarding ongoing and planned activities. These discussions can help identify ways to evaluate and strengthen programs.*

Dr. Hyde provided an overview of the NIDDK Research Centers program and then posed a number of evaluation-related questions to the Council members. He acknowledged the information provided by the NIDDK Centers Program Directors, Catherine McKeon, Judy Podalsky, Carolyn Miles, Marva Moxey-Mims, Terry Bishop, and Deborah Hoshizaki, and also thanked Karen Salomon, Kate Nicholson, and David Miller for their assistance.

### Purpose and Types of Centers

The Research Centers programs are intended to provide additional resources for institutions that already have a strong research base related to stated scientific themes. Resources can include biomedical and behavioral Research Cores, Pilot and Feasibility programs, an Administrative Core, an Enrichment Program, and in some cases, the direct support of research projects.

The NIH includes 17 different types of awards under the general rubric of NIH Research Center Grant Mechanisms (G12, M01, P20, P30, P40, P41, P50, P51, P60, PL1, U30, U41, U42, U50, U51, U54, and R07). Of these, the NIDDK primarily funds three types of Centers: Core Center Grants (P30) that support shared resources and facilities for use by many researchers; Specialized Centers of Research (P50s) that focus on a specific disease entity or biomedical problem; and Comprehensive Centers (P60s) that provide a multipurpose, common focus to diverse, related efforts. Dr. Hyde noted that the NIDDK's Comprehensive Centers are funded only by the Division of Diabetes, Endocrinology and Metabolic Diseases (DEM).

All three types of NIDDK-funded Centers provide funds for shared facilities through Research Cores, and for Pilot and Feasibility studies that enable the preliminary testing of ideas. In addition to that support, the Specialized Centers provide funds for research projects; whereas the Comprehensive Centers provide funds for Prevention and Control (translational) Cores. Dr. Hyde also noted that the DEM has piloted a program using the Resource-Related Research Project grant (R24). This mechanism is not technically a Research Center, but it is center-like in that it can support Research Cores that are directly related to already-funded research projects; however, it does not support Pilot and Feasibility studies.

### Funding and Scientific Scope

In FY 2009, the NIH expended approximately 10 percent of its $30.4 billion budget on Research Centers. There is variability among NIH components regarding the percentage of their budgets used to support Centers programs. For example, in FY 2008, the National Cancer Institute used about 10 percent of its budget on Centers, whereas the National Institute of Mental Health and

National Institute of General Medical Sciences spent slightly over 8 percent, and the National Institute of Neurological Disorders and Stroke spent about 6 percent. The corresponding percentage for the NIDDK was about 5 percent or $91 million. The NIDDK expends most of its Research Centers funding on Core Centers.

Collectively, the NIDDK Research Centers encompass the fields of diabetes, digestive diseases, kidney diseases, obesity, cystic fibrosis, molecular therapy, urology, and hematology. The NIDDK Research Centers program has grown in numbers and types of centers, as well as total funding amount since its inception. In 1995, the NIDDK funded 59 Centers. By the end of the NIH five-year budget doubling in 2003, the number of NIDDK Centers began to approach 80 and has remained relatively constant since then.

## History of the NIDDK Research Centers Program

The NIDDK Research Centers program began in the 1970s, with the Diabetes Research Centers (1973), followed by Clinical Nutrition Research Units and Obesity Nutrition Research Centers (both in 1979). Four additional Research Centers programs were started in the 1980s (for cystic fibrosis, digestive diseases, kidney diseases, urologic diseases). Five more were added in the 1990s (for cystic fibrosis, pediatric nephrology, molecular therapy, molecular hematology, and polycystic kidney diseases). The most recent changes were the establishment of the Digestive Diseases Research Development Centers (2003) and the merging of two earlier Core and Specialized Centers programs for cystic fibrosis into the Cystic Fibrosis Research and Translation Core Centers (2005).

## Funding and Distribution Patterns

There were funding increases for the NIDDK Research Centers program during the five-year NIH budget doubling, followed by a stabilization period. From 1995 to 2009 the overall program budget increased 65 percent. In 1995, the distribution of Centers program funds was about 46 percent for the Division of Diabetes, Endocrinology and Metabolic Diseases (DEM), about 34 percent for the Division of Digestive Diseases and Nutrition (DDN), and about 20 percent for the Division of Kidney, Urologic and Hematologic Diseases. In 2009, those percentages were 38 percent for DEM, 36 percent for DDN, and 26 percent for KUH.

In 2009, the NIDDK funded eleven Research Centers programs that involved 78 awards to 41 grantee institutions. Thirty-one grantee institutions have 1-2 NIDDK-funded centers. Ten grantee institutions have 3 or more: Children's Hospital, Boston (3); Johns Hopkins University (3); Massachusetts General Hospital (3) ; University of Michigan (3); University of North Carolina, Chapel Hill (3); University of Pennsylvania (4); Vanderbilt University (4); Washington University, St. Louis (4); Yale University (5); and University of Alabama, Birmingham (6).

About 16 percent of funds in Center grant awards support Pilot and Feasibility Projects, and about 84 percent of funds support Research Cores and Projects. Of the 314 Research Cores supported, about 232 (74 percent) are basic Research Cores; while about 82 (26 percent) are clinical Research Cores. About 38 percent of Center awards involve subcontracts with other institutions or organizations.

Dr. Hyde pointed out correlations between the funding of NIDDK Research Centers and other NIH research activities. For example, many of the institutions with Research Center grants are also major recipients of NIDDK R01 grants. About 86 percent of NIDDK-funded Research Centers also have an NIDDK-funded institutional research training grant (T32) in a relevant scientific area. About 79 percent of NIDDK-funded T32 training grants are located at Center-affiliated institutions. Approximately 85 percent of NIDDK-funded Research Centers are also associated with an NIH Clinical and Translational Science Award (CTSA).

**Questions and Discussion**

Dr. Hyde posed several questions to the Council members and elicited their comments.

*Centers Evaluation: How can NIDDK assess the value of the Centers Program and determine the appropriate level of funding? What metrics should be used by NIDDK to evaluate the value of the Centers program (and other large programs)?*

- Identify agreed-upon set(s) of goals that different Centers programs are working to achieve prior to determining appropriate metrics (e.g., goals of acquiring technologies, creating/nurturing investigative communities, supporting young investigators). Metrics used should assess progress toward reaching established goals. Another approach is to determine the value of Research Centers--for example, as a channel for developing investigators, as a means of gaining institutional commitment and support, and/or as an impetus for synergy and collaboration.

- Gauge benefits derived by investigators, especially young, new investigators, with regard to fostering career development. Track the careers of investigators (new investigators and recompeting investigators) who are associated with a Center grant (e.g., ability to garner new and competitive renewal grants and publish articles). Compare these investigators with a similar cohort in institutions without Centers.

- Assess degree to which Centers enable acquisition, integration and use of new technologies, such as high-throughput sequencing.

- Determine whether there is diversity in use of the Cores (or whether investigators are consistently using the Center grant as merely an extension of their labs).

- Find ways to determine whether Centers are accomplishing something that otherwise would not be accomplished. Metrics need to go beyond merely counting the number of grants and publications attributable to investigators associated with Centers, number of Pilot and Feasibility programs offered by Centers, and number of Center-supported investigators who went on to achieve R01 or equivalent support.

- Assess how different Centers programs cooperate synergistically to promote the availability of information in the public domain (e.g., protocols, technologies, methodologies,

biorespositories for evaluation of tissues for somatic gene mutations; blood samples for germ line studies; and databases that range from DNA to proteins to bioinformatics).

- Evaluate the existence and value of synergistic relationships among different Center programs (e.g., Diabetes Centers and Digestive Diseases Centers) and whether structural aspects of current programs promote or impede synergistic arrangements in an increasingly complex scientific landscape. It was noted that, while Centers within a given categorical area are encouraged to interact, synergy has not really been pursued across the categorical lines of Centers programs. For example, the current research emphasis on the impact of the microbiome on metabolism might provide opportunities for synergistic interactions among the Research Centers in obesity and in digestive diseases. When staff members visit a research institution, they could try to arrange a visit with all the NIDDK-funded centers there. By looking across categorical lines, the NIDDK would be in a better position to foster synergy between and among different Centers programs, and also, to ensure that there is no duplication of effort. Without changing any program or mechanism, the promotion of synergistic interactions could have positive results.

- Determine the contributions of Centers to the infrastructure of research institutions and the degree to which investigators depend on Core facilities to accomplish their work. It was noted that there is extensive cooperation between local institutions and the NIDDK Research Centers; however, perhaps research institutions housing Centers should provide them with greater funding support, especially for Pilot and Feasibility studies, given that the Centers' budgets have ceilings.

- Evaluate Centers relative to other NIH mechanisms that have similar purposes. For example, both Research Core Centers and Clinical and Translational Awards (CTSAs) generally provide funding support to institutions--not to individuals or to specific research projects. Similarly, the Pilot and Feasibility components of Research Centers are similar to the NIH Pathway to Independence Award (K99-R00) in that both mechanisms help to support young investigators. A comparative analysis of programs with similar purposes may point to the most productive allocation of funds among these mechanisms, or indicate whether a diversity of funding approaches may be advantageous. In this regard, it should be recognized that the leaders of Research Centers have considerable decision-making authority regarding which technologies, research Cores, and Pilot and Feasibility projects to pursue, and that other NIH funding mechanisms may provide a less centralized decision-making process for achieving mutual goals, such as nurturing young or new investigators. There are important program similarities and differences that could be explored in an evaluation.

- Identify the factors that contributed to some research institutions having multiple NIDDK-funded Research Centers. Was there a deliberate, resource-gaining strategy by an institution, or was there highly directed energy by independent research groups within an institution?

*Research Cores: How could the NIDDK Centers Program foster the development of more unique Research Cores (e.g., high-end organ imaging, metabolic phenotyping) vs. traditional institutional Research Cores (e.g., transgenic mouse facilities)? How could NIDDK promote more sharing and greater access to Research Core facilities through the Centers Program?*

- Promote regional or national resources and reduce redundancy. Institutions and investigators prefer to have research resources available at their own Research Center--even on their own floor-- rather than at a regional or national facility to which they must gain access. There is both the perception and the reality of limited access to regional facilities. For example, one impediment may be the lack of facilities for investigators to house tissue samples and experimental animals at a regional facility in order to take advantage of its cell imaging capabilities.

    - Favor excellence over quantity in establishing Research Cores. Avoid the tendency to create the same types of Cores at every institution. Instead of having multiple Cores serving a region, consider having one truly outstanding Core that is accessible to a group of regional academic research institutions.

    - Consider facilitating the establishment and use of large, centralized repositories for animal-model tissues and human tissues that investigators can use to generate new hypotheses and undertake validation studies. Such repositories could transcend local and regional boundaries, and facilitate high-quality research owing to carefully designed protocols for the acquisition, storage, and retrieval of tissue. These types of facilities could be made broadly available beyond the community of Research Centers, and would be a great benefit for both junior investigators and established investigators.

    - Consider whether it may be more productive for the NIH to enhance access to existing research resources, rather than to create new ones for which access is limited because funds are not specifically provided for that purpose. While it is true that some resources may need to be available locally, many types of research might be more efficiently supported through regional or national resources.

- Consider whether it would be beneficial if a modest layer of additional funds could be requested by grant applicants and provided by NIH to increase accessibility to regional resources. Such investments could make first-class regional facilities more broadly available to research institutions (e.g., a superb imaging facility). NIH funding is generally project-based, and NIH Requests for Applications don't typically require or encourage applicants to include a request for budgetary resources to maximize accessibility to research resources.

- Include in the evaluation of Research Centers an assessment of the availability and accessibility of the resources provided, as well as the identification of ways to enhance their widespread use. Utilization of the resources would be an important metric in any evaluation, especially of regional facilities.

*Use of Center Resources: Do the NIDDK Centers programs provide an appropriate balance of funds for Pilot and Feasibility projects versus Research Cores? What steps could NIDDK take to better promote highly innovative Pilot and Feasibility projects? How should NIDDK determine*

*the appropriate balance of support for resources designed for specific institutions vs. national resources?*

- Strike a feasible balance between the Pilot and Feasibility component and the Research Cores component of Research Centers--recognizing that both are valuable. It is difficult to state what that balance should be. When balancing Pilot and Feasibility *vs.* Core support, consider the size and nature of the academic institution that houses the Research Centers and the relative quality of the activities that are competing for the allocation of Centers funds. Whatever the endeavors within a Research Center program may be, a reasonable amount of funds needs to be provided to make the undertakings feasible.

- Recognize that Pilot and Feasibility components are important because they are a means of cultivating young investigators for academic careers, and this is a key driver of grant renewal.

- Use Pilot and Feasibility funds to nurture not only young investigators, but also to provide opportunities for established investigators to move into new scientific fields.

- Promote more highly innovative Pilot and Feasibility projects by regionalization. Regionalization would provide a larger pool of applications that could compete in a properly developed peer review process and this could help elevate the quality of science by enhancing competition and reducing any institutional bias.

*Future Directions: How could the NIDDK Centers programs promote more clinical and translational research? How could the Centers programs collaborate more effectively with the Clinical and Translational Science Awards (CTSAs) to leverage additional resources for NIDDK-funded investigations?*

- Ask CTSAs how they interact with Research Centers at the same institution. This question would be posed for information-gathering purposes, rather than to suggest any need for change.

- Consider the concept of adding a disease-focused module onto a CTSA grant so that NIH investments are well aligned scientifically.

- Consider assessing the interactions that occur at an institution when the same individual is both a CTSA Director and a Research Center Director. How could these effects be modeled?

- Promote more clinical and translational research within Research Centers by the use of incentives, such as special consideration for funding. Incentives are needed to overcome an inherent bias toward basic research. The current view is that basic research will be considered more favorably in peer review and has a greater probability of being funded; hence, it is favored applications. While the prospects for clinical research have improved, more incentives are needed to bolster this type of research even further.

- Reduce impediments to institutional collaboration, including the way that overhead rates and outsourcing-insourcing issues are handled for budgetary purposes. The NIH could create regional resources that address these issues, or find some other creative ways to improve the flow of funds between and among institutions to maximize the sharing of research resources.

- Carefully consider partnering with industry. Industry might be willing to contribute to the funding of Research Cores within Centers if they could have access to them.

Dr. Rodgers concluded the discussion by thanking Dr. Hyde for his presentation and the Council members for their suggestions. He indicated that the NIDDK will distill the comments received and report back to the Council members on how it plans to follow-up on their ideas.

## IX. SCIENTIFIC PRESENTATION: "Mechanisms of Intestinal Homeostasis: The Immunoregulatory Role of IgA"

***Dr. Charles Elson, III, Professor of Medicine and Microbiology, and Vice Chair for Research, Department of Medicine, University of Alabama at Birmingham, and Holder of the Basil I. Hirschowitz Chair in Gastroenterology***

The central focus of research in Dr. Elson's laboratory is the regulation of mucosal immune responses and, more specifically, the role of such regulation in the maintenance of normal homeostasis, as well as in states of chronic intestinal inflammation.

## X. REPORTS OF SUBMCOMMITTEES: CONSIDERATION OF REVIEW OF GRANT APPLICATIONS

A total of 1,720 grant applications, requesting support of $454,266,251 were reviewed for consideration at the February 24, 2010 meeting. Funding for these applications was recommended at the Scientific Review Group recommended level. Prior to the Advisory Council meeting, an additional 1,356 applications requesting $358,779,579 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 February 24, 2010 meeting.

## XI. ADJOURNMENT

Dr. Rodgers thanked the Council members for their attendance and valuable discussion. There being no other business, the 182nd meeting of the NIDDK Advisory Council was adjourned at 4:30 p.m.

Griffin P. Rodgers, M.D., M.A.C.P.
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Chairman, National Diabetes and Digestive and Kidney Diseases Advisory Council