DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Fiscal Year 2006 Budget Request

Witness appearing before the
House Subcommittee on Labor-HHS-Education Appropriations

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National Institute of Diabetes and Digestive and Kidney Diseases

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William Beldon, Deputy Assistant Secretary, Budget

Mr. Chairman and Members of the Committee:

I am pleased to present the Fiscal Year (FY) 2006 President's budget request for the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) a sum of $1,872,146,000, which includes $150,000,000 for the Special Appropriation for Research on Type 1 Diabetes through Sec. 330B of the Public Health Service Act. The NIDDK transfers some of these funds to other institutes of the NIH and to the Centers for Disease Control and Prevention (CDC). Adjusted for mandatory funds, this is an increase of $8,562,000 over the FY 2005 enacted level of $1,863,584,000 comparable for transfers proposed in the President's request.

I appreciate the opportunity to testify on behalf of the NIDDK. Our Institute supports research to combat a wide range of debilitating chronic health problems, including diabetes and other endocrine and metabolic diseases; digestive diseases; kidney and urologic diseases; blood diseases; and obesity. Through vigorous support of investigator-initiated research and Institute-initiated efforts, the NIDDK will continue to elucidate the fundamental biology underlying health and disease and to explore new strategies for disease diagnosis, treatment, and ultimately, prevention.

FROM THE LABORATORY BENCH TO THE PATIENT'S BEDSIDE

In recent years, ever-advancing technologies have led to an explosion of biomedical knowledge. It is imperative that scientists harness new discoveries to improve medical care. Thus, in addition to supporting critical basic and clinical research, the NIDDK is also bolstering "translational" research, to accelerate the progression of scientific

discovery from basic to clinical studies to directly benefit patients. In one stage of translational research, insights gained at the laboratory "bench" spur the design of new strategies for prevention or intervention, which investigators then test in clinical studies—at the patient "bedside." In a second stage of translational research, investigators explore ways to bring successful interventions and lifesaving knowledge from the clinical research setting into the realm of healthcare practice.

With the goal of directing NIDDK translational research investments to enhance efforts on multiple diseases, I established a Trans-NIDDK Translational Research Working Group to identify research obstacles and opportunities. The Working Group charted the progression from basic to clinical research to medical practice for a number of health conditions to identify common themes for future research. These analyses were considered by NIDDK's National Advisory Council; external advice was also received at other scientific meetings.

By way of example, translational research relating to the assessment of blood sugar (glucose) levels has greatly benefited diabetes care. Scientists discovered that levels of a variant of the red blood cell protein hemoglobin, called hemoglobin A_{1c} (HbA_{1c}), correlate with blood sugar levels. In the 1990s, a landmark NIDDK-supported clinical trial demonstrated that people with type 1 diabetes can reduce the risk of eye, kidney, and nerve complications by lowering their HbA_{1c} levels through intensive treatment of blood sugar. As a result of this research, target levels for HbA_{1c} were set, thus improving patient care by encouraging medical practitioners to use a combination of methods to better control blood sugar. This research further led to the FDA's acceptance of the HbA_{1c} level as an end-point sufficiently robust to define clinical

benefit in clinical trials. "Biomarkers," such as the level of HbA_{1c}, can facilitate clinical trials and thus stimulate the development of new therapeutic agents. Many new drugs for diabetes have now been FDA-approved based on HbA_{1c} as an outcome.

In another example of successful bench-to-bedside research, NIDDK-supported investigators elucidated the biological defect responsible for the devastating inherited metabolic disease, MPS I; discovered a naturally-occurring dog model for the disease; and tested a potential therapy in dogs. Following clinical testing, this therapeutic agent is now produced by industry and available on the market to treat this disease. These two examples illustrate the critical role of NIH investment in research from bench-to-bedside. Both also spanned several decades from the initial basic research discoveries to clinical application. Thus, a critical goal of NIDDK's new translational research efforts is to accelerate this process.

In one planned translational research effort, the NIDDK will pursue the development of new biomarkers. Examples of diseases or conditions for which such biomarkers would be valuable include acute kidney failure, liver and kidney fibrosis, type 1 diabetes, and insulin resistance—which is associated with type 2 diabetes. The NIDDK will also foster research on biomarkers for interstitial cystitis, including the evaluation of a potential diagnostic marker that emerged from prior NIDDK-funded research.

Among other translational research efforts, the NIDDK will strengthen research to bring new non-invasive imaging techniques from the laboratory to the clinical setting to enhance clinical research on liver, pancreatic, kidney, and urologic diseases. The Institute will also encourage the development of new animal models suitable for preclinical testing of diagnostic, preventive, or therapeutic interventions for diseases

within NIDDK's mission. Although a wealth of information about human biology has been and continues to be gleaned from studies of mice and other animals, in many cases existing animal models are insufficient for preclinical testing. Other translational research efforts are capitalizing on fundamental knowledge about how proteins assume their proper structures. This approach, informed by a recent NIDDK-sponsored conference, will help propel the search for therapies for cystic fibrosis and certain liver and kidney diseases, which are caused by defects in protein "folding" or "processing." Translational research promoted by the NIH Roadmap will synergize with these NIDDK efforts to accelerate progress.

Insights gained from clinical observations can open new avenues for basic research studies, which, in turn, will spur new clinical research endeavors. Several NIDDK initiatives are fostering increased collaboration between basic and clinical researchers, including support for ancillary studies to major ongoing NIDDK clinical trials. Such studies will also maximize the Institute's investment in these trials. As part of our new efforts to enhance our research centers programs, the NIDDK will encourage basic and clinical research partnerships to take advantage of the opportunities of research centers.

In addition to the bench-to-bedside research just described, the NIDDK is pursuing strategies to best translate successful clinical research results from patient study volunteers to the public. These efforts include, for example, translating the results of the Diabetes Prevention Program (DPP) clinical trial, which demonstrated that people at high risk for type 2 diabetes can dramatically reduce risk of disease onset through modest weight loss and exercise. To promote these positive findings, the NIDDK launched its campaign, *"Small Steps. Big Rewards. Prevent Type 2 Diabetes,"* with

tailored messages and materials developed for ethnic groups at high risk for type 2 diabetes, older adults, and a general audience. In parallel, the Institute is supporting research demonstration and dissemination projects to explore new strategies for effectively translating the DPP results, from clinical trial to community. This research includes testing programs that target different age groups and minority populations.

New translation efforts to combat kidney disease are building upon the recent finding that even modestly-impaired kidney function increases risk of cardiovascular disease and premature death. Avoiding these devastating outcomes requires early awareness of kidney disease and appropriate treatment. Critically important is detection of deterioration in the kidneys' filtering capacity, the glomerular filtration rate (GFR). While GFR is difficult to measure directly, it can be estimated from routinely measured serum creatinine. The NIDDK's National Kidney Disease Education Program (NKDEP) is thus encouraging laboratories that measure serum creatinine to provide clinicians with GFR values. The NKDEP recently launched an education campaign emphasizing the importance of early detection and treatment, and targeting this message to primary care providers and those at high risk for kidney disease.

EXAMPLES OF BASIC AND CLINICAL RESEARCH ENHANCEMENTS

Underscoring a growing health crisis among our Nation's children, this past year an NIDDK-supported pilot study of middle school students uncovered high levels of the "metabolic syndrome," which is a cluster of health problems associated with obesity and increased risk for diabetes and cardiovascular disease. To address the health

threats posed by obesity, we developed and published a *Strategic Plan for NIH Obesity Research*. Informed by extensive input from scientific and lay experts, the Strategic Plan was developed by the NIH Obesity Research Task Force. Since its inception by the NIH Director, I have had the privilege of co-chairing the Task Force with the NHLBI Director, with the aims of synergizing and accelerating obesity research across the NIH. Consistent with the goals of the *Strategic Plan*, the NIDDK is pursuing a multifaceted obesity research agenda, from basic molecular investigations to novel intervention studies to translational research. For example, the NIDDK is spearheading a new trans-NIH initiative to study how factors such as maternal weight during pregnancy can lead to obesity in offspring. This research has important implications for public health.

In the area of digestive diseases, the *Action Plan for Liver Disease Research* has now been published. It was developed through NIDDK-led efforts with broad external input from the research, professional, and patient-advocacy communities. Examples of the many areas addressed by the *Action Plan* include developing or improving therapies for hepatitis C; developing tools for early liver cancer detection; and research on living donor liver transplantation. The *Action Plan* will direct new liver disease research; the NIDDK will also continue major ongoing clinical studies on hepatitis C; biliary atresia, a disease that strikes children; and non-alcoholic steatohepatitis, a fatty liver disease.

The *Action Plan for Liver Disease Research* is part of a larger planning process for research on digestive diseases, which have an enormous burden on the U.S. population. For inflammatory bowel disease, external advice received in previous planning efforts will continue to inform the NIDDK research agenda. New planning efforts will aim to

strengthen research on irritable bowel syndrome and other functional gastrointestinal disorders, which are debilitating and highly prevalent but not well understood. Following focused planning efforts relevant to gastroparesis, the NIDDK will establish a new clinical research consortium to study this debilitating syndrome of nausea, vomiting, bloating, and other symptoms which complicates diabetes and other diseases.

In the areas of kidney and urologic diseases, in addition to the efforts described earlier, the NIDDK will encourage partnerships to pursue promising new therapies for polycystic kidney disease, and will launch a new clinical intervention study of children with vesicoureteral reflux, a bladder condition which can impair kidney function.

I have highlighted today examples of NIDDK's many and diverse research plans and efforts. These reflect our strong commitment to improving human health.

Thank you, Mr. Chairman. I would be pleased to answer any questions that the Committee may have.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
National Institute of Diabetes and Digestive and Kidney Diseases
Biographical Sketch

NAME: Allen M. Spiegel, M.D.

POSITION: Director, National Institute of Diabetes and Digestive and Kidney Diseases

BIRTHPLACE : Germany

DATE: May 18, 1946

EDUCATION: B.A., Columbia College, 1967
M.D., Harvard Medical School, 1971

EXPERIENCE:

1999-present	Director, National Institute of Diabetes and Digestive and Kidney Diseases, NIH
1990-1999	Director, Division of Intramural Research, National Institute of Diabetes and Digestive and Kidney Diseases, NIH
1993-present	Chief, Metabolic Diseases Branch, National Institute of Diabetes and Digestive and Kidney Diseases, NIH
1988-1993	Chief, Molecular Pathophysiology Branch, Metabolic Diseases Branch, National Institute of Diabetes and Digestive and Kidney Diseases, NIH
1985-1988	Chief, Section on Molecular Pathophysiology, Metabolic Diseases Branch, National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, NIH
1977-1984	Senior Investigator, Metabolic Diseases Branch, National Institute of Arthritis, Metabolism, and Digestive Diseases, NIH
1973-1976	Fellow, NIH Endocrinology Training Program, Clinical Associate, Metabolic Diseases Branch (Dr. G. D. Aurbach, Chief), National Institute of Arthritis, Metabolism, and Digestive Diseases, NIH
1971-1973	Intern and Assistant Resident in Medicine, Massachusetts General Hospital, (Dr. Alexander Leaf, Chief)

HONORS AND AWARDS:

1966 - Elected to Phi Beta Kappa
1967 - B.A. Summa Cum Laude
1971 - Elected to Alpha Omega Alpha
1971 - M.D. Cum Laude
1988 - Outstanding Service Medal - U.S. Public Health Service
1990 - Meritorious Service Medal - U.S. Public Health Service
1990 - Jacobaeus Prize - Nordisk Insulin Foundation
1993 - Plenary Lecturer - Japan Endocrine Society

1993 - Aurbach Memorial Lecturer - American Society for Bone and Mineral Research
1994 - Harrison Memorial Lecturer - Endocrine Society of Australia
1996 - Komrower Memorial Lecturer - Society for the Study of Inborn Errors of Metabolism
1998 - Edwin B. Astwood Lecture Award - Endocrine Society (U.S.A.)

PROFESSIONAL ORGANIZATIONS:
American Federation for Clinical Research
The Endocrine Society
American Society for Bone and Mineral Research
American Society for Clinical Investigation
American Society for Biochemistry and Molecular Biology
Association of American Physicians
Institute of Medicine of the National Academy of Sciences

LICENSURE AND CERTIFICATION:
Diplomate American Board of Internal Medicine, 1974
Board Certified in Endocrinology, 1975
Licensed in Medicine, Maryland

Department of Health and Human Services
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William R. Beldon

Mr. Beldon is currently serving as Deputy Assistant Secretary, Budget in the Department of Health and Human Services. He has been a Division Director in the Budget Office for sixteen years, most recently as Director of the Division of Discretionary Programs. Mr. Beldon started in federal service as an auditor in the Health, Education and Welfare Financial Management Intern program. Over the course of more than 30 years in the Budget Office, Mr. Beldon has held Program Analyst, Branch Chief and Division Director positions. Mr. Beldon received a Bachelor's Degree in History and Political Science from Marshall University and attended the University of Pittsburgh where he studied Public Administration. He resides in Fort Washington, Maryland.