

APPENDIX 3: SUPPLEMENTAL MATERIAL ON THE PLANNING AND IMPLEMENTATION OF THE SPECIAL FUNDING PROGRAM

This Appendix provides information on the diabetes research plans and reports, planning and evaluation meetings, and interagency coordinating committee meetings that have informed program planning and implementation of the *Special Funding Program*. As described in this Appendix, the NIH and CDC have solicited broad and extensive input from the external scientific community, patients, members of professional and lay advocacy organizations, and other Federal agencies, to inform program planning and resource allocation.

DIABETES RESEARCH PLANS AND REPORTS

1998 Administrative Plan for the Special Type 1 Diabetes Research Funding Program

In January 1998, the Director, NIH, submitted to HHS an administrative plan for the use of funds provided by the Balanced Budget Act of 1997 (P.L. 105-33) for type 1 diabetes research. The overall objective of the plan, formulated through meetings with both NIH and HHS components and the external diabetes research community, was to promote innovative, clinically relevant, and multidisciplinary research on type 1 diabetes. Particularly crucial to this initial plan were recommendations emanating from a 1997 trans-NIH symposium, “Diabetes Mellitus: Challenges and Opportunities,” which was sponsored by the Director, NIH, along with nine institute directors. In addition, the chairmen of four working groups from this conference (i.e., Type 1 Diabetes—Etiology and Pathogenesis, Therapy, Microvascular Complications, and Macrovascular Complications) were involved in formulating this initial research plan for the *Special Funding Program*.

The *Special Funding Program* was expected to bring the best research talent, the most promising research ideas, and the most technologically advanced research tools to bear on combating type 1 diabetes, with particular attention to clinical and therapeutic issues. In addition, a budget strategy was developed to stratify the deployment of funds, so that a commitment base would not be established in FY 1998 that would preclude funding of emerging scientific opportunities in the later years of the program. Within the overarching scientific and budgetary goals of the program, a plan was developed to support the immediate pursuit of highly promising, innovative science through trans-NIH research solicitations; the establishment of a CDC National Diabetes Laboratory; the development of approaches to exploit other areas of high scientific priority through small, 1-3 year funding strategies; the encouragement of technology development and application to exploit scientific opportunities through 1-year funding

commitments; and the further pursuit of initiatives supported in the early years that proved most successful.

1999 Diabetes Research Working Group Strategic Plan

The Congress established the Diabetes Research Working Group (DRWG) as an independent panel of scientific experts from academia, industry, voluntary organizations, and the NIH, through Senate and House report language accompanying the Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriations Bill, 1998. The DRWG was charged with the development of a comprehensive plan for NIH-funded diabetes research efforts. This plan covered all aspects of diabetes research, including both type 1 and type 2 diabetes.

The DRWG identified five “Extraordinary Research Opportunities”—Genetics, Autoimmunity and the Beta Cell; Cell Signaling and Cell Regulation; Obesity; and Clinical Research and Clinical Trials of Critical Importance. In addition, “Special Needs for Special Problems,” which included diabetic complications, optimizing glucose control, and others, and “Resource and Infrastructural Needs” were addressed. The full DRWG report, “Conquering Diabetes: a Strategic Plan for the 21st Century,” can be accessed on the NIDDK’s website (www.niddk.nih.gov/federal/dwg/fr.pdf). Since its completion in 1999, the plan has greatly enhanced the framing of diabetes initiatives at the NIH, including the *Special Statutory Funding Program for Type 1 Diabetes Research*. An update on new opportunities, scientific advances, and research progress made since issuance of the DRWG report was prepared in 2002 (www.niddk.nih.gov/federal/dwg/2002/dwg02.htm).

2000 Interim Evaluation Report on the Special Type 1 Diabetes Research Funds

In response to the Balanced Budget Act of 1997 that originally established the *Special Statutory Funding Program for Type 1 Diabetes Research*, an interim evaluation report was submitted to the Congress in 2000. Although it was premature at that time to assess scientific accomplishments of the *Special Funding Program*, the report evaluated the planning and implementation process that guided the use of the *Special Funds*. The full report is posted on the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) website (www.niddk.nih.gov/federal/initiative.htm).

2000 Ad Hoc External Advisory Panel Summary Report

A panel of scientific advisors met with representatives of the NIH, the CDC, the ADA, and the JDRF to consider 22 proposals, totaling \$57.65 million, submitted by the Institutes and Centers of the NIH and CDC for funding, with \$19.5 million to become available in FY 2001 under the provisions of the Balanced Budget Act of 1997.

Dr. Allen Spiegel, Director of NIDDK, asked the scientific advisors to determine which of these 22 proposals offer the best opportunity to develop knowledge that will lead to improved methods to prevent, treat, or cure type 1 diabetes. They were also encouraged to suggest other initiatives that could make important contributions toward advancing research on type 1 diabetes and its complications. Dr. Spiegel noted that Institutes and Centers had been encouraged to propose trans-NIH initiatives involving multiple components of the NIH and initiatives to which they were also willing to commit Institute funds.

Eleven of the 22 proposals were recommended with the highest enthusiasm; a twelfth highly recommended project emerged from the discussion. To achieve a total recommended budget of \$20 million in FY 2001, many proposals were

reduced in scope and allocated less than the funds requested. The proposals selected and the amount of Balanced Budget Act funding in FY 2001 for each follow.

Comprehensive Atlas of Beta Cell Biology (\$3.0M)

As initially proposed, this project included seven components. The committee recommended supporting five components as part of this project: online database to disseminate information arising from this project to the scientific community; development of a human beta cell line which maintains physiologic responsiveness to glucose and other factors involved in regulation of insulin secretion and cell growth and development; functional genomics and proteomics of the beta cell; development of monoclonal antibodies to cell surface components of the beta cell for use in stem cell identification; and functional imaging of the beta cell to detect changes in cell number, cell mass, function, and metabolism. The two additional components initially proposed as part of this initiative were recommended for inclusion as components of other proposals: diagnostic tools for beta cell transplantation was included in the human islet resource centers, and identification of single nucleotide polymorphisms (SNPs) for type 1 diabetes candidate genes was included in the Immune Response Diversity Project. It was recognized that the \$3.0 million allocated from Balanced Budget Act Funds would not be sufficient to pursue all the components of this initiative found to have outstanding merit, and the NIDDK promised to provide substantial additional Institute funds for this project.

Human Islet Transplantation (\$2.5M)

As initially proposed, this project would fund regional resource centers to supply human islet cells to researchers for use in trials of human islet transplantation. The committee recommended incorporating into these resource centers the development of methods to assess the quality, purity, and viability of harvested islets *in vivo* and the determination of optimal methods of islet preparation, using tools developed

from the functional genomics component of the Comprehensive Atlas of Beta Cell Biology Project. The committee also recommended that these resource centers screen donors for evidence of autoimmunity and provide organs not suitable for use in islet transplantation to researchers for studies of pathogenesis of type 1 diabetes. Two million dollars in Balanced Budget Act funds were recommended for these components, with additional funding for the islet resource centers in FY 2001 to be provided from the NCCR. An additional \$0.5 million was recommended to support an islet/beta cell transplant registry to collect and analyze data, both pre- and post-transplantation, from all institutions performing islet and beta cell transplants in North America.

Consortium for Development of Improved Animal Models (\$4.0M)

This project focused on development of animal models of diabetes-associated micro- and macrovascular complications. The emphasis was on the mouse, but larger animals, such as swine and other species, were proposed as well. The committee strongly supported the research proposed and recommended that, in addition to micro- and macrovascular complications, models useful for study of wound healing in diabetes be developed.

Immune Response Diversity Project (\$1.0M)

This project integrates the genomics of host immunity with advanced bioinformatics to aid discoveries in immune mediated diseases. While this proposal was felt to be highly meritorious, concern was raised about the support of aspects of the proposal that appeared to lack a focus on type 1 diabetes with funds targeted for type 1 diabetes. Reduced funding was recommended to support components of the proposal specifically focused on type 1 diabetes, particularly identification of SNPs in type 1 diabetes candidate genes.

Preventive Vaccines for Autoimmune Diabetes (\$3.0M)

This project was recommended without modification and with the highest priority. Additional regularly appropriated funds will be provided for this initiative.

Studies of New Therapies That Prevent or Reduce the Microvascular Complications of Diabetes (\$1.0M)

Several promising new drugs are under development to prevent retinopathy and other microvascular complications. Some surrogate outcomes have recently been developed which can be used for short-term pilot studies to prevent retinopathy. This initiative would support small pilot studies of promising agents to aid in the transition from the bench to clinical investigation. Additional support for these pilot trials would come from NIH and industry funds.

Gene Therapy Approaches for Type 1 Diabetes and Its Complications (\$1.0M)

The committee recommended that this project focus particularly on methods of targeting gene transfer to the beta cell *in vivo*, and on developing gene therapy approaches to prevention and treatment of complications, such as delivery of growth factors. Additional regularly appropriated funds will be required for this initiative.

Functional Genomics Approaches to Diabetes Complications (\$1.0M)

As proposed, this initiative included two components focused on hypoglycemia and microvascular complications. The committee strongly endorsed application of gene profiling techniques to studies of glucose sensing and noted that common mechanisms are involved in beta cell and brain glucose sensing. However, it was felt that this component of the initiative should be deferred until FY 2002 so that it can be developed in the context of recommendations from a planned workshop on hypoglycemia and the brain. One million dollars

was recommended in FY 2001 to fund application of gene profiling technologies to peripheral vascular tissue to aid in understanding of microvascular complications.

Population-Based Registry for Diabetes in Children (\$1.0M) and Pilot Programs for Population-Based Screening of Risk Factors for Type 1 Diabetes in Children Using State and Territorial Public Health Laboratories (\$0.5M)

It was noted that there are a number of practical problems in developing population-based registries for diabetes in children in the U.S. Despite the uncertainty of success, the committee recommended that \$1.0 million be allocated to support one or two pilot projects. Such registries are of critical importance in documenting the true incidence of type 1 and type 2 diabetes in children and in assessing changes over time in incidence and age of development of diabetes. It was felt that pilot programs for screening for risk of type 1 diabetes in the general population are feasible because assays are now available for use on dried blood spots, and the initiation of pilot studies was highly recommended.

Studies To Identify Genetic Associations in Patients with Microvascular Complications of Diabetes (\$0.5M)

The committee noted that the NIDDK and the JDRF have recently initiated efforts to identify genes for diabetic nephropathy and recommended support for the initiation of studies to identify genes predisposing and contributing to the development of retinopathy. Additional regularly appropriated funds will be provided for this initiative.

Assessment of Oral Microflora and Immune Responses in Type 1 Diabetic Patients (\$0.5M)

The committee recommended support of this initiative, which was developed based on recommendations from a recent

workshop on oral complications of diabetes. Additional regularly appropriated funds will be provided for this initiative.

Evaluation of Use of Minimally-Invasive Glucose Sensors in Children (\$1.0M)

Committee members proposed this initiative after considering a proposal to study the metabolic and developmental consequences of intensive insulin therapy in children. The committee felt that proposal was not feasible due to the very long follow-up which would be required and the likely changes in methods of glycemic control which would occur in the interim. Instead the committee recommended that new technologies should be evaluated in children. It was recommended that the use of recently developed minimally-invasive glucose sensors should be studied in children to assess their efficacy in achieving improved metabolic control and reducing the risk of hypoglycemia.

2001 Administrative Plan for the Special Type 1 Diabetes Research Funding Program

In February 2001, the Acting Director, NIH, submitted to HHS an administrative research plan for the expanded *Special Funding Program* provided by the FY 2001 Consolidated Appropriations Act (P.L. 106-554). This plan, developed through consultation with NIH and other HHS components and the diabetes research community, clearly articulated the six broad research goals that frame the *Special Program*.

Through this careful priority-setting process, the NIH developed a scientifically-meritorious research plan that was within the budgetary targets and that complemented research initiatives launched with the P.L. 105-33 funds. Importantly, budget flexibility was maintained to support modifications during the later years of the program as science developed, and to address unanticipated needs or sudden shifts in focus that would optimize the use of the *Special Funds* for the benefit of type 1 diabetes research. Advice garnered from the April 2000 *ad hoc*

Advisory Meeting was invaluable in prioritizing the allocation of the increased funds provided for FY 2001-2003.

2002 Executive Summary of the *Ad Hoc* Advisory Meeting Report

An external advisory panel of scientific and lay experts with respect to type 1 diabetes research convened at the NIH on May 16, 2002, to discuss the *Special Statutory Funding Program for Type 1 Diabetes Research*. The advisors were charged with evaluating the research efforts supported by the *Special Funds*, identifying scientific gaps and opportunities for future research, and advising the NIH and the CDC on the use of remaining funds for FY 2002 and FY 2003. This meeting constitutes a major source of input for a mandated report to the Congress evaluating the *Special Funding Program*.

The panel expressed great enthusiasm for research coordination mechanisms—consortia, clinical trial networks, repositories, databases, and registries—that have been established, in whole or in part, with the *Special Funds* and urged the development of additional programs of this nature. The importance of continuity of support for these valuable research resources and infrastructure was strongly emphasized. Several strategies for facilitating the maximal use of these resources were proposed. Significant ideas included the addition of ancillary studies to large clinical trials, an increase in coordination among the various research groups, and expansion of the core missions of some research consortia to encompass emerging issues of high scientific priority. In addition, the advisors were pleased with the support of innovative, high-impact research through funding of pilot and feasibility grants to individual investigators. They appreciated the success of solicitations issued with these funds in attracting new investigators and established investigators who were new to diabetes research. The initiatives undertaken were felt to maintain an appropriate balance between large-scale research programs and

investigator-initiated research. Moreover, these Requests for Applications (RFAs) have been issued periodically throughout the duration of the *Special Funding Program* to ensure that they attracted the best, most cutting-edge science. The advisory panel emphasized that it was not yet possible to fully assess the outcome of the *Special Funding Program* in that many projects were recently or newly initiated, not all of the FY 2002 funds had been deployed, and funding plans for FY 2003 have not yet been finalized.

Research Coordination and Connections

The advisory panel made several recommendations for extending and capitalizing on existing research coordination efforts, maximizing connections among research groups with related interests, and developing new resources to enhance cross-disciplinary research in complex scientific fields.

The panel identified the following elements as important to coordination:

- ▶ Bioinformatics initiatives to integrate data from multiple consortia and trial networks;
- ▶ A multi-Institutional Review Board (IRB) to review multi-site clinical research;
- ▶ Common informed consent documents;
- ▶ Improved assay standardization;
- ▶ Ancillary studies and other mechanisms to ensure that maximal value is obtained from research data and samples from clinical research study participants;
- ▶ Partnerships between industry and academia to spur drug development and testing, including fast track mechanisms to facilitate clinical trials;
- ▶ Mechanisms to bring discoveries with therapeutic applications that originate in academic laboratories through pre-clinical development—the NCI's Rapid Access to Intervention Development (RAID) program was discussed as a possible model.

The panel identified additional opportunities for coordination of efforts in several research areas:

- ▶ Enhancement of research on diabetic complications by:
 - Creating a central knowledge base to coordinate information on NIH-wide initiatives related to diabetic complications;
 - Improving dissemination of information about existing animal models;
 - Facilitating animal model research projects that address multiple complications and evaluate multiple tissues in the same animal(s); and
 - Stimulating the development of new animal models for complications research.
- ▶ Systematic evaluation of approaches to islet transplantation including:
 - Pancreas harvesting;
 - Islet isolation, evaluation, and preservation;
 - Site and method of islet transplantation; and
 - Immunosuppression, tolerance, and other aspects of immunomodulation.
- ▶ Expansion of the islet cell resource centers' mission to include the procurement of pancreata for basic research on insulinitis;
- ▶ Application of insights from angiogenesis research to the study of islet graft vascularization;
- ▶ Investigating hypoglycemia unawareness in new islet transplant recipients;
- ▶ Recruitment of neuroscientists and brain-imaging specialists to study similarities in the glucose-sensing mechanisms of the pancreatic beta cells, the brain, and other glucose-sensitive tissues;
- ▶ Establishment of type 1 diabetes as a reportable illness throughout the U.S.; and
- ▶ The use of type 1 diabetes as a model for understanding immunology and autoimmunity.

Major Research Opportunities

Based on recent research progress in type 1 diabetes as well as in broader areas relevant to diabetes research, the advisors recognized several critical areas of opportunity. Pursuing initiatives in these areas would expand on recent scientific advances to enhance progress on the understanding, treatment, or prevention of type 1 diabetes:

- ▶ Understanding the autoimmune basis of type 1 diabetes:
 - The role of HLA molecules in the development of autoimmunity;
 - Central tolerance and reprogramming of T cells;
 - The effect of parental type 1 diabetes on possible immune tolerization of offspring during pregnancy;
 - Beta cell antigen identity;
 - Developing assays for pathogenic T cells;
 - Applying new methodologies, such as proteomics approaches, to studying insulinitis and identifying circulating beta cell markers;
 - Designing beta cell imaging technology for use in assessing progression of autoimmune destruction of beta cells; and
 - Identifying genes conferring susceptibility to or protection from development of type 1 diabetes.
- ▶ Pursuing stem cells or stimulators of stem cells as a source of beta cells that could overcome the short supply of islets available for transplantation by current protocols;
- ▶ Improving islet transplantation procedures and documenting their risks and benefits, including issues of cost-effectiveness, quality of life, and the development of complications;
- ▶ Understanding the mechanisms of hypoglycemia unawareness and nocturnal hypoglycemia; and
- ▶ Uncovering the role of inflammation in vascular complications of diabetes, particularly functional interactions between monocytes and endothelial cells.

Conclusions

Recent progress in type 1 diabetes research has allowed great strides in our understanding of this disease, but much work remains to be done. Studies to identify how genetic propensities and environmental triggers initiate the disease process in humans are now critical. Continued research on animal and cell models will be needed to understand mechanisms and develop novel preventive agents for type 1 diabetes and its devastating complications. Ongoing investment in clinical trials and research will help scientists translate research advances into real improvements in patients' health. The research initiatives and resource development undertaken with the *Special Funding Program* to date have sparked exciting new opportunities for future, cutting-edge research on understanding, preventing, and treating type 1 diabetes.

The full report can be accessed at: www.niddk.nih.gov/federal/planning/type1summary.pdf

2003 Report on Progress and Opportunities

The *Special Funding Program* has mandated reporting requirements to the Congress. The first mandated interim report was transmitted to the Congress in 2000 (described above). The NIDDK prepared a second report to meet a January 2003 statutory reporting requirement to the Congress. That reporting requirement was changed to January 2007, as a result of the President's signature into law of P.L. 107-360. Therefore, in April 2003, the NIDDK published the second report it prepared to meet the statutory requirement as an interim report on progress and opportunities. The interim report provided an important assessment of the *Special Program* by external scientific experts, grant recipients, and NIDDK staff who analyzed the associated scientific literature and other relevant data on the *Program*. Moreover, the report contains a highly useful summary of research opportunities identified by external experts in the field. These opportunities served as a scientific guidepost in developing this program in later years. The full

report can be accessed at: www.niddk.nih.gov/federal/planning/type1_specialfund/

2005 Executive Summary of the *Ad Hoc Planning and Evaluation Meeting Report*

An external panel of 16 scientific and lay experts with expertise relevant to type 1 diabetes and its complications convened in Bethesda, MD, January 18-19, 2005, to discuss the *Special Statutory Funding Program for Type 1 Diabetes Research*. The goals of the 2-day meeting were to perform a mid-course assessment of current efforts supported by the *Program*, to identify new and emerging opportunities, and to solicit recommendations for future type 1 diabetes research. The meeting focused largely on the program's research consortia and networks. The meeting constitutes a major source of input for a congressionally-mandated program evaluation report, which is due to the Congress by January, 2007.

Type 1 Diabetes Research Goals

The meeting was framed around six major research goals that offer exceptional promise for the treatment and prevention of type 1 diabetes:

- ▶ Goal I: Identify the Genetic and Environmental Causes of Type 1 Diabetes
- ▶ Goal II: Prevent or Reverse Type 1 Diabetes
- ▶ Goal III: Develop Cell Replacement Therapy
- ▶ Goal IV: Prevent or Reduce Hypoglycemia in Type 1 Diabetes
- ▶ Goal V: Prevent or Reduce the Complications of Type 1 Diabetes
- ▶ Goal VI: Attract New Talent and Apply New Technologies to Research on Type 1 Diabetes

Cross-Cutting Recommendations

The panel was charged with reviewing specific ongoing projects supported by the program and making recommendations for future research opportunities. Throughout the meeting,

many common themes emerged, which cut across research efforts supported by the program.

The panel identified several cross-cutting opportunities to enhance and synergize type 1 diabetes research efforts:

Extend and capitalize on existing research efforts by maximizing connections among research groups with both related and distinct interests: The panel recommended that strong existing coordination across consortia be further enhanced in order to synergize research efforts. These interactions should not be limited to consortia with overlapping interests. Collaboration between researchers with distinct interests can facilitate the pursuit of novel research directions. Increased coordination can prevent duplicative work by promoting the sharing of resources and methodology, as well as by facilitating cross-disciplinary research approaches.

Develop new modes of interaction to foster diabetes research: The panel encouraged interactions between biologists and chemists to identify small molecules that could be used as therapeutics for disease. The panel strongly endorsed the use of novel mechanisms such as innovative partnership awards to foster collaboration and interaction between diabetes researchers and researchers outside of the diabetes field, such as neuroscientists and bioengineers. These types of partnerships can accelerate research progress by fostering the application of novel technologies and expertise to the type 1 diabetes research field.

Enhance opportunities for data sharing and integrated analysis: The panel recommended that bioinformatics approaches to data creation and maintenance be coordinated and integrated across the multiple research consortia in order to enhance communication and data sharing/analysis.

Foster translational research to enhance the timely transfer of important advances in the laboratory to a clinical research setting: The panel endorsed ongoing efforts and encouraged continued support of the *Special Funding Program* regarding translational research such as the T1D-RAID program. The panel stressed the importance of promoting interaction between basic and clinical scientists in order to facilitate translational research. Additionally, the NIH commitment to research clinicians, particularly at the junior faculty level, was seen as critical for attracting and retaining research talent.

Capitalize on research investments with patient follow-up: The panel recognized the opportunity to maximize data collection in longitudinal trials, particularly those involving children and newly diagnosed cases of type 1 diabetes, by maintaining contact with the patients and their families to track their medical progression.

Promote partnerships with industry to advance research: The panel encouraged interactions between type 1 diabetes clinical trials consortia and industry to promote testing of potential therapeutic agents. The panel favored utilizing the SBIR program to produce reagents that would facilitate basic science and the translation of laboratory discoveries to the clinic.

Maintain strong oversight mechanisms for ongoing efforts: The panel strongly endorsed the contributions of External Advisory Boards (EABs) that have been created to guide and monitor the progress of consortia and resources supported with the *Special Funding Program*. The panel encouraged the NIDDK to ensure that all consortia receive regular oversight from such panels.

Develop strategic plan for future type 1 diabetes research: To build upon the new and emerging opportunities identified at the meeting, the panel strongly endorsed a broad state-of-the-science review and development of a long-range plan for type 1 diabetes research.

Major Research Opportunities

The expert panel recognized several critical areas of research opportunity that will accelerate research progress in type 1 diabetes. Pursuing initiatives in these areas would expand on recent scientific advances to enhance progress in the understanding, treatment, and prevention of type 1 diabetes:

- ▶ Identifying novel biomarkers and surrogate endpoints that would enhance therapeutic development and the conduct of type 1 diabetes clinical trials;
- ▶ Understanding the autoimmune basis of type 1 diabetes by enhancing research in the field of human type 1 diabetes and regulatory T cells;
- ▶ Exploring the role of the gastrointestinal mucosal barrier in the pathogenesis and prevention of type 1 diabetes;
- ▶ Creating a renewable source of human beta cells by developing approaches to expanding functional islets and to creating conditions to differentiate embryonic and adult stem cells to islet/beta cells;
- ▶ Defining normal glucose profiles in children;
- ▶ Improving animal models to study type 1 diabetes and its complications;
- ▶ Alleviating type 1 diabetes and its complications by understanding regenerative pathways;
- ▶ Promoting collaborative research by supporting multidisciplinary “self-assembled” research consortia to tackle current barriers that limit progress in type 1 diabetes research;
- ▶ Providing support to investigators to pursue high-risk, high-payoff projects without requiring extensive preliminary data; and

- ▶ Supporting focused “innovative partnership” programs that facilitate collaborative interactions and attract new research talent.

Conclusions

The *Special Funding Program* has supported research that has greatly increased our understanding of type 1 diabetes. Because many of the programs are newly established, the future potential for directly impacting patients’ health is extremely high. However, there is still much work to be done. It is critical to coordinate efforts of these consortia and networks in order to provide an integrated understanding of the disease. Continued support of basic research will help to provide insights on the molecular underpinnings of disease development, as well as to identify novel therapeutic targets and agents. Ongoing investment in basic and clinical research will help investigators translate positive results from the laboratory to the clinic to improvements in patients’ health. The projects supported by the program and the future research opportunities endorsed by the panel are critical to the understanding, prevention, and treatment of type 1 diabetes.

The full report can be accessed on the NIDDK’s website (www.niddk.nih.gov/federal/planning/Jan-18-19-T1D-Final.pdf).

2006 Advances and Emerging Opportunities in Type 1 Diabetes Research: A Strategic Plan

At a January 2005, *ad hoc* planning and evaluation meeting of external scientific and lay experts with expertise relevant to type 1 diabetes and its complications (described above), one of the recommendations emanating from the meeting was to initiate a much broader review of the entire state-of-the-science with respect to type 1 diabetes, including recent research advances and emerging opportunities. In response

to this recommendation, the NIDDK Director announced in March 2005, that the statutory Diabetes Mellitus Interagency Coordinating Committee (DMICC), chaired by the NIDDK, would spearhead a new type 1 diabetes research strategic planning effort. The membership of the DMICC includes all NIH components involved in diabetes research, as well as other relevant federal agencies. Based on the same general content, two versions of the Strategic Plan were developed with broad external input from scientists, patients, and representatives of patient advocacy organizations. One version of the Plan was developed for patients and the public, and the other version of

the Plan was developed for the scientific research community. The purpose of the Strategic Plan is to serve as a scientific guidepost to the NIH and to the investigative and lay communities by identifying compelling research opportunities that will inform the priority-setting process for the type 1 diabetes research field and propel research progress on the understanding, prevention, treatment, and cure of type 1 diabetes and its complications. The “Summary and Recommendations” section of the Strategic Plan is found in Appendix 6; both versions of the Plan can be accessed on the NIDDK’s website (www.T1Diabetes.nih.gov/plan).

DIABETES MELLITUS INTERAGENCY COORDINATING COMMITTEE (DMICC) MEETINGS FOCUSED ON THE *SPECIAL STATUTORY FUNDING PROGRAM FOR TYPE 1 DIABETES RESEARCH*

This listing provides highlights of DMICC meetings specifically focused on the *Special Funding Program*. For a listing of other recent DMICC meetings on topics relevant to type 1 diabetes and its complications, please see Appendix 4.

Diabetes Mellitus Interagency Coordinating Committee Overview

The DMICC, chaired by the NIDDK, was authorized by Public Law 93-354 and was established in the fall of 1974. It includes representatives from Federal departments and agencies whose programs are relevant to diabetes mellitus and its complications. The DMICC facilitates cooperation, communication, and collaboration among agencies that conduct or support diabetes-related activities. DMICC meetings and projects currently tend to focus on bringing together in depth information from the varied programs represented by the member organizations; being the catalyst for the initiation of projects; and guiding the progress of projects involving several agencies. The following recent DMICC meetings were used as a venue to discuss research relevant to type 1 diabetes and its complications, and in some cases, to solicit input from members on program planning and evaluation of the *Special Statutory Funding Program for Type 1 Diabetes Research*.

Type 1 Diabetes Initiatives (January 15, 1999)

This DMICC meeting focused on the process of setting priorities for the use of *Special Statutory Funds*. DMICC members provided updates of type 1 diabetes activities in their Institute, Center, or agency. The NIDDK also provided an update to DMICC on the use of the *Special Funds*, as well as the awards funded under recent initiatives. The summary minutes can be accessed at: www.niddk.nih.gov/federal/dmicc/minutes_19990115.htm.

Use of *Special Funds* for Type 1 Diabetes Research (April 14, 2003)

This meeting began with a brief legislative history of the *Special Funding Program*, which has grown from the original \$30 million per year in 1998 to \$150 million per year for FY 2004–2008, for a total of \$1.14 billion for FY 1998–2008. The discussion then centered around six major goals for type 1 diabetes research: a description of each goal was provided, followed by discussion regarding recommendations and potential research opportunities. A proposal was discussed outlining a mechanism to seed collaborative research supplements for shared resources. Finally, reports were provided on the consortia and resources, new and re-issued research solicitations, and potential SBIR and STTR program announcement topics. The summary minutes can be accessed at: www.niddk.nih.gov/federal/dmicc/Final-Edited-DMICC-4-13-03.pdf.

Meeting on the *Special Statutory Funding Program for Type 1 Diabetes Research* (July 28, 2004)

This meeting opened with an update about the *Special Statutory Funding Program for Type 1 Diabetes Research* and a discussion to help plan for an evaluation of the program. Much of the funding had been devoted to: establishing large-scale collaborative, infrastructure-intensive fundamental initiatives that could not be pursued with R01 funds; creating major clinical trials networks; promoting innovative, high-risk, high-impact research that is different from typical R01 research; and promoting translational research to develop new therapies. An update was provided on *Special Program* initiatives started between April 2003 and July 2004. The DMICC used the meeting to plan for the January 2005 *ad hoc* planning and evaluation meeting (described above), discussing the goals and topics of the meeting, as well as the advice to be obtained

by the expert panel. Finally, an introduction was provided to the mandated program evaluation due to Congress by January 1, 2007. The summary minutes can be accessed at: www.niddk.nih.gov/federal/dmicc/Final-July-28-Summary.pdf.

Update on Current and Planned Initiatives (March 21, 2005)

A review was provided of the implementation status of recommendations from the January 2005 *ad hoc* planning and evaluation meeting on the *Special Statutory Funding Program for Type 1 Diabetes Research*. One recommendation of the expert

panel was to initiate a broader review of the entire state-of-the-science regarding type 1 diabetes with an emphasis on new and emerging opportunities that could be pursued with the *Special Funds*. To implement this recommendation, the NIDDK launched a new strategic planning effort in type 1 diabetes research (described above) to be spearheaded by the DMICC. The DMICC was apprised of current plans and asked for input into the strategic planning process. It also received updates on diabetes-related activities by its members. The summary minutes can be accessed at: www.niddk.nih.gov/federal/dmicc/2005/03-21-05-Summary-Final.pdf.

SOLICITATION OF INNOVATIVE IDEAS FROM THE BROAD EXTERNAL SCIENTIFIC COMMUNITY

Since the inception of the *Special Funding Program*, the NIH has solicited input and recommendations from scientists external to the NIH through forums such as scientific and planning/evaluation panel meetings, as described in this Appendix. To solicit broader input for future research opportunities from the scientific community as a whole, the NIDDK issued a Request for Information (RFI) calling for innovative ideas to advance prevention, treatment, and cure of type 1 diabetes (see “Text of RFI,” below). The RFI—initially suggested at a DMICC meeting on July 28, 2004—was announced to the scientific community in the NIH Guide for Grants and Contracts and in the journal *Science*. The NIDDK’s announcement made clear that ideas submitted would not be treated as confidential or proprietary and that there was no research funding associated with this process. The NIDDK collected ideas for 7 weeks.

The NIDDK received over 80 submissions, which were presented to the expert panel at the January 2005 *ad hoc* planning and evaluation meeting focused on the *Special Funding Program* (described above). The panel members were given the submitted innovative ideas in advance of the meeting and were asked to consider them. During the meeting, time was set aside to discuss and consider the ideas. A synopsis of the discussions is found under each “Goal” chapter in the summary of the January 2005 meeting (accessed at: www.niddk.nih.gov/federal/planning/Jan-18-19-T1D-Final.pdf).

Text of RFI

Release Date: August 31, 2004

Notice Number: NOT-DK-04-013

Issued by: NIDDK (www.niddk.nih.gov/)

Purpose: To invite ideas for opportunities that can accelerate research progress and overcome current research barriers to

the prevention, treatment and cure of type 1 diabetes and its complications.

Background: The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH), leads a Special Statutory Funding Program (\$150 million/year) for Type 1 Diabetes Research, on behalf of the Secretary of the Department of Health and Human Services. The *Special Program* supports research to pursue compelling opportunities in type 1 diabetes research (more information on the program can be found at: www.T1Diabetes.nih.gov). The program is framed around six broad, scientific goals: Goal I: Identify the Genetic and Environmental Causes of Type 1 Diabetes, Goal II: Prevent or Reverse Type 1 Diabetes, Goal III: Develop Cell Replacement Therapy, Goal IV: Prevent or Reduce Hypoglycemia, Goal V: Prevent or Reduce the Complications of Type 1 Diabetes, Goal VI: Attract New Talent and Apply New Technologies to Research on Type 1 Diabetes.

Information Requested: The NIDDK invites submission of innovative ideas and approaches toward accelerating progress and overcoming research barriers to the prevention, treatment and cure of type 1 diabetes and its complications. There is significant flexibility in the use of the special funds; opportunities could be pursued through solicitations for traditional research grants or through mechanisms to support larger collaborative efforts. Suggestions should focus on identifying the opportunity and approaches, technology and expertise useful for its development rather than on a funding instrument or solicitation design. Suggestions that will involve creative scientists and scientific communities not currently working on type 1 diabetes, and with the potential to contribute to prevention, treatment and cure of type 1 diabetes, are particularly encouraged.

Response and Process: Submissions in response to this RFI will be considered by NIH and CDC scientists and by an *ad hoc* evaluation panel to be convened by the NIDDK as part of the process guiding use of the *Special Statutory Funding Program for Type 1 Diabetes Research*.

This Request for Information is for information and planning purposes only and shall not be construed as a solicitation or as an obligation on the part of the NIDDK. The NIDDK does not intend to award a grant or contract on the basis of responses nor otherwise pay for the preparation of any information submitted or the Government's use of such information. Acknowledgment of receipt of responses will not be made, nor

will respondents be notified of the Institute's evaluation of the information received. Responses will not be held in a confidential manner. Responses may be anonymous.

Please describe your suggested opportunity or approach including: (1) how it could potentially have a major, positive impact on one or more of the six goals above, and/or (2) the current research barriers it could help overcome. You may submit more than one idea, but please limit the description of each to one page in length.

For full consideration, submissions are due by Friday, October 22, 2004.
