APPENDIX B

ASSESSMENT OF THE *SPECIAL STATUTORY FUNDING PROGRAM FOR TYPE 1 DIABETES RESEARCH*

Evaluation Objectives

In designating special set-aside funds to "provide for research into the prevention and cure of type 1 diabetes," the Congress recognized the opportunity to finally overcome this devastating, long-standing disease and its complications. The intent of this congressionally mandated evaluation report is not only to highlight and assess the significant progress made by the *Special Statutory Funding Program for Type 1 Diabetes Research* (*Special Diabetes Program* or *Program*) toward this goal, but also to describe and analyze the innovative process by which the U.S. Department of Health and Human Services (HHS) approached this challenge. The multipronged scientific structure of the *Program*; the establishment of large collaborative research consortia and clinical trials networks; the incentives to promote high-risk, pioneering research; and the major investments in translational research, clinical investigator training, scientific infrastructure, and technology and resource development represent a significant departure from traditional mechanisms of funding smaller-scale research in type 1 diabetes. This appendix describes the multiple evaluation approaches used to assess the scientific and clinical outcomes of the research; it also explains the decision process used in developing the scientific emphases and allocating the resources of the *Special Diabetes Program*.

This evaluation has been guided by the following questions:

- What impact has the *Special Diabetes Program* made on the field of type 1 diabetes? How has the field progressed since the *Program*'s inception?
- What objective measures can be used to benchmark the progress of the *Special Diabetes Program*, both scientifically and programmatically?
- To what extent has the scientific progress already benefited patients, and what additional anticipated outcomes could affect the lives of patients living with the disease or at risk of developing it?
- How appropriate is the scientific focus of the *Special Diabetes Program* and to what extent has the program been able to adapt to emerging research opportunities and input from external experts?
- To what extent has the planning process for the *Special Diabetes Program* relied on perspectives of various scientific and lay stakeholders?
- How effectively has the *Special Diabetes Program* been administered by NIDDK, which was delegated this responsibility by the Secretary, HHS? To what extent do the scientific initiatives and distribution of resources reflect a coordinated strategic plan?
- In which ways could the research supported by the *Special Diabetes Program* be enhanced?
- How are the collaborative research consortia and clinical trial networks perceived by scientists not affiliated with these projects?

- Has the creation of large, collaborative consortia enabled unique research opportunities and enhanced research in type 1 diabetes?
- Has there been added value in supporting collaborative consortia tackling specific major barriers to progress in type 1 diabetes research, rather than supporting individual researchers tackling those particular areas?
- To what extent has the *Special Diabetes Program* stimulated high-risk, high-impact research, or diabetes research in new fields that have not previously addressed diabetes?
- How successful has the *Special Diabetes Program* been in cultivating cross-disciplinary interactions and coordination?
- How successful has the *Special Diabetes Program* been in recruiting new investigators to apply their talents to type 1 diabetes research? What impact has it had on their careers?
- How effectively have strategies promoted clinical and translational research?

Evaluation Approaches

Multiple approaches were taken to evaluate the planning and implementation processes involved in administration of the *Special Diabetes Program*, and the scientific accomplishments of initiatives supported by this *Program*. It must be emphasized that achievement in biomedical research is a process that reflects the progressive accumulation of knowledge; the incremental building of scientific knowledge can therefore be a long-term process. Although many promising scientific findings have begun to emerge from research initiated by the *Special Diabetes Program*, the public health impact of this program is not yet fully manifest and thus cannot yet be fully assessed.

Type 1 diabetes is a chronic disease often diagnosed in childhood, adolescence, or young adulthood, with complications sometimes appearing decades later. From the *Special Diabetes Program*, new insights into the biology of this disease and its therapy are continuing to develop. For example, the *Special Diabetes Program* has initiated long-term prospective clinical studies, including one that has enrolled newborns who will be followed until they reach age 15; it has also supported infrastructure development to facilitate future research, such as the creation of animal models and the invaluable collections of genetic and tissue samples that are being stored in a repository for later analysis. Thus, many results from the evaluation approaches described in this report represent only a preliminary assessment of the advances that can be expected to flow from the *Special Diabetes Program*.

The major parameters that guided the evaluation process include:

- *Research Accomplishments:* Review of scientific advances and technological developments that have had positive impacts on patients or enabled future basic and clinical research. These data are primarily obtained from research publications, as well as from research advances included in "*Advances and Emerging Opportunities in Diabetes Research: A Strategic Planning Report of the DMICC*."

- *Professional Assessment:* Scientific judgment of external experts in the type 1 diabetes field garnered from specific assessments of clinical and pre-clinical consortia supported by the *Program* at meetings convened in April 2008 and June 2009 respectively. Additionally, each individual consortium or project has ongoing assessment.
- *Bibliometric Analysis:* Compendium of *Program*-associated publications in peer-reviewed scientific journals and the impact of these publications as determined by a citation analysis.
- *Grant Portfolio Analysis:* Use of NIH archival databases to determine program effectiveness in terms of dimensions such as recruitment of new investigators and stimulation of clinical research.
- *Interviews with Consortia Investigators:* Sample consortia investigators provided input on the importance and value of consortia supported by the *Special Diabetes Program*.
- *Other Metrics of Progress:* Outcome measures including patents, research resources (*e.g.*, microarray chips, antibodies, genetic and tissue samples, Internet-accessible data sets, animal models), and progress toward patient recruitment goals. These data are primarily obtained from annual progress reports or meetings of external review committees.

Cut-off Dates

In order to prepare this evaluation to meet the statutory deadline, data collection on research progress was terminated in spring 2010. Although there have been notable scientific advances between the cut-off date and the publication of this report, the cut-off date has been maintained, and these examples have not been included to ensure that data reporting is consistent from project to project. Budget data in Appendix A are reported through the end of Fiscal Year (FY) 2009. However, the collection of references for scientific journal publications was limited to articles published prior to January 1, 2010.

Data Sources

Several sources were used to collect data needed to evaluate the *Special Diabetes Program*:

- **electronic Scientific Portfolio Assistant (e-SPA)**: The NIDDK utilized NIAID's electronic Scientific Portfolio Assistant (e-SPA) to collect data on a portfolio of grants (see below) supported by the *Special Diabetes Program*. The data collected through e-SPA included: *Program*-associated publications in peer-review journals and the number of times those publications were cited in other papers; patent activity resulting from the *Special Diabetes Program*; the number of new investigators recruited to research; and the number of grants coded as clinical research supported by the *Program*. e-SPA was also utilized to capture NIH-wide comparison data. e-SPA is an application that combines modern search and business intelligence reporting tools to provide indicators on quality, relevance, and impact using data from IMPAC II (Information for Management, Planning, Analysis, and Coordination), iEdison, NIH Intramural Database, NLM MEDLINE, Thomson Reuters Web of Science and Journal Citation Reports, and U.S. Patent and Trademark Office (USPTO) Patent Applications and Grants. The initial production system was launched in 2008.
- ***Special Diabetes Program* Grant Portfolio**: The total portfolio of grants and contracts supported by the *Special Diabetes Program* for FY 1998-2009 is found in Appendix A. A subset of these projects was included in the e-SPA analyses. The

following award types were excluded: (1) contracts, because the e-SPA tool does not capture complete data on contracts; (2) supplements to existing grants or centers, because it would not be possible to determine if the data collected related to the supplement portion of the grant or only to the primary grant.

- **Other NIH Archival Databases**: In addition to e-SPA, NIDDK used other NIH archival databases to collect data for this evaluation, including IMPAC II, Research Portfolio Online Reporting Tools Expenditures and Results (NIH RePORTER), and PubMed.
- **Reports on Progress**: The NIDDK used progress reports prepared for planning and evaluation meetings on the *Special Diabetes Program* and Web sites of the research consortia to obtain data on outcome measures such as development of research resources, progress toward patient recruitment goals, and scientific accomplishments.
- **2007 "*Evaluation Report*" on the *Special Statutory Funding Program for Type 1 Diabetes Research:*** A previous evaluation was published in 2007 to meet a congressional reporting requirement (www.T1Diabetes.nih.gov/evaluation). The NIDDK used data collected for the 2007 evaluation to supplement or verify data collected for this Report.

Changes in Data Sources Since the 2007 Evaluation of the *Special Diabetes Program*: For the 2007 Report, the data collection was performed manually, with database searches to obtain data on metrics such as publications resulting from the *Special Diabetes Program*. Data to supplement the manual searches, such as information on patent activity, was obtained through a survey of grantees supported by the *Program*.

Since that time, NIAID developed e-SPA, which automates data collection on a variety of metrics, as described above. The new availability of e-SPA enabled NIDDK to collect data that was only available via grantee survey for the 2007 evaluation. Because of the availability of e-SPA, NIDDK did not administer another grantee survey.

Employment of an Innovative Paradigm for Trans-HHS, Cross-Disciplinary, and Transparent Research Planning and Management

As designated by the Secretary of HHS, NIDDK has coordinated the development of a sound planning, implementation, and evaluation process for the *Special Diabetes Program*. The allocation of funds has been performed in a scientifically competitive manner in cooperation with multiple Institutes and Centers of NIH, CDC, and other components of HHS with expertise in type 1 diabetes. A series of planning meetings—involving these agencies, Institutes and Centers, and members of the diabetes patient-advocacy community—resulted in administrative plans for allocation of funds of the *Special Diabetes Program*. These plans, released in 1998 and 2001, established the framework for initiatives and research priorities to be pursued.

Since that time, critical sources of input that have informed program planning have included a variety of scientific workshops and conferences; meetings of the statutory Diabetes Mellitus Interagency Coordinating Committee (DMICC); a series of planning and evaluation meetings in which NIDDK convened panels of external scientific and lay experts to provide input on the *Special Diabetes Program* and future directions; and strategic planning processes, with broad external

input, that have culminated in the publication of two reports: "*Advances and Emerging Opportunities in Type 1 Diabetes Research: A Strategic Plan*" and "*Advances and Emerging Opportunities in Diabetes Research: A Strategic Planning Report of the DMICC*." Notably, the *Special Diabetes Program* ties a set of HHS-wide research planning and evaluation efforts to the deployment of a specified amount of budgetary resources in a highly effective and efficient research management process.

Type 1 diabetes is a systemic disease that requires a multidisciplinary research approach and therefore is addressed by multiple components of NIH and HHS. The disease involves the body's endocrine and metabolic functions (NIDDK) and immune system (NIAID); complications affecting the heart and arteries (NHLBI), eyes (NEI), kidneys and digestive and urologic tracts (NIDDK), nervous system (NINDS, NIMH), and oral cavity (NIDCR); the special problems of a disease diagnosed primarily in children and adolescents (NICHD); complex genetic (NHGRI) and environmental (NIEHS) factors; the need for novel imaging technologies (NIBIB); data on disease incidence and prevalence in the United States (CDC); development of research resources (NCRR); and services for pre-clinical testing of therapeutics (NCI).

The *Special Diabetes Program* supports a spectrum of research within these NIH and HHS components, making it a model trans-NIH and trans-HHS program. In addition to the components listed above, the NIH Office of Research on Women's Health, NIH Office of Dietary Supplements, National Institute on Aging, National Center on Minority Health and Health Disparities, National Center for Complementary and Alternative Medicine, and National Institute of Nursing Research have also participated in the *Special Diabetes Program*. Thus, the *Special Diabetes Program* has catalyzed and synergized the efforts of a wide range of HHS components to combat type 1 diabetes and its complications.

Pursuit of a Scientifically Focused, but Flexible, Budgeting Process

Six major, scientific research Goals that offer exceptional promise for the treatment and prevention of type 1 diabetes form the basis of the planning and allocation processes of the *Special Diabetes Program*:

- 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

More information on each Goal, and the research supported under those Goals, is found in the main body of the report. The annual funding levels by Goal for FY 1998-2009 are shown in Table B1. The total budget distribution of the *Program* by Goal from FY 1998-2009 is displayed in Figure B1. A detailed budget analysis is found in Appendix A.

The professional judgment of scientific and lay expert panels has repeatedly endorsed the structure of these Goals as an appropriate and effective framework to manage the *Special Diabetes Program* (see section later in this Appendix on the "Broadly Consultative Planning

Process for Priority Setting and Resource Distribution"). One challenge in managing large-scale science is the time required to accelerate or decelerate research programs in response to the availability of funds. The dynamic interdependence of the efforts of government program managers and the external scientific and diabetes voluntary communities has helped the scientific priorities develop to reflect the changing needs of research.

Table B1: Budget of the *Special Diabetes Program* by Goal (FY 1998-2009)[a]

	Goal I	Goal II	Goal III	Goal IV	Goal V	Goal VI	Administrative (*e.g.*, personnel, conferences)	TOTAL
1998	493,436	9,247,235	6,379,977	3,470,740	10,339,294	0[b]	69,318	30,000,000
1999	2,070,192	6,211,806	6,293,237	3,672,012	11,725,416	0[b]	27,337	30,000,000
2000	4,463,743	5,615,924	5,881,222	2,579,693	11,344,751	0[b]	114,667	30,000,000
2001	22,535,131	25,888,609	25,204,681	2,674,074	19,435,977	4,049,000	212,528	100,000,000
2002	16,378,537	21,934,292	19,346,899	8,993,845	21,402,845	11,793,551	150,031	100,000,000
2003	19,717,454	21,631,424	19,701,970	7,643,699	15,017,921	16,130,672	156,860	100,000,000
2004	34,808,000	19,367,709	47,148,270	8,389,536	16,359,078	23,789,681	137,726	150,000,000
2005	45,084,403	15,176,867	41,716,120	7,680,901	17,748,844	22,056,018	536,847	150,000,000
2006	37,706,975	15,090,798	53,200,058	4,425,237	26,948,806	11,825,222	802,904	150,000,000
2007	63,186,097	26,064,134	29,809,919	4,301,484	15,322,431	10,611,551	704,384	150,000,000
2008	21,179,111	60,227,685	21,567,125	3,845,729	11,514,911	31,077,754	587,685	150,000,000
2009	59,761,987	37,755,958	33,859,097	7,461,138	6,130,362	4,167,000	864,458	150,000,000
Total	**327,385,066**	**264,212,441**	**310,108,575**	**65,138,088**	**183,290,636**	**135,500,449**	**4,364,745**	**1,290,000,000**

[a] Please see Appendix A for detailed budget analysis.

[b] In addition to solicitations focused exclusively on attracting new talent to type 1 diabetes research, Goal VI was addressed by solicitations for research projects that encouraged the participation of new investigators and the submission of applications for pilot and feasibility awards, as well as the development of new technology in the context of Goals I-V. These early efforts relative to Goal VI are thus embedded in other Goals during the FY 1998-2000 period of the *Program*. Starting in FY 2001, specific initiatives were also launched relative to Goal VI.

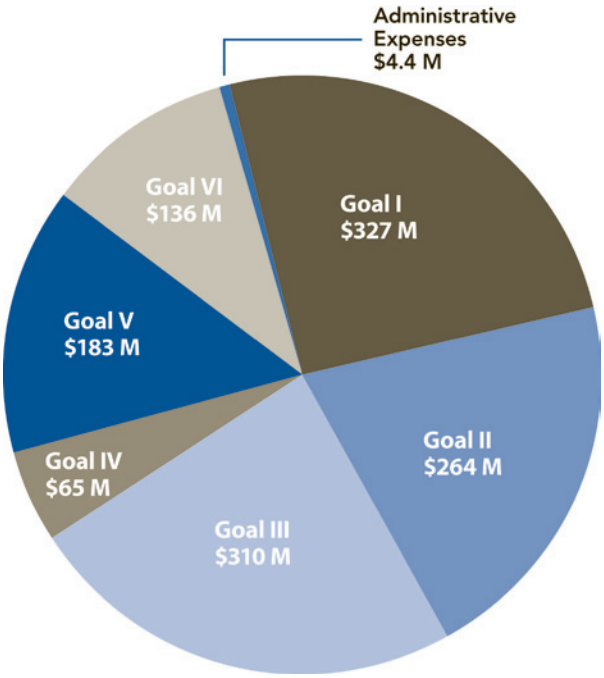

Figure B1: Total budget distribution by Goal, FY 1998-2009

Based on this scientific framework, a comprehensive management strategy has been used to: promote maximum flexibility; respond to new scientific opportunities; and plan and initiate broad, multidisciplinary projects that would not have been undertaken without the *Special Diabetes Program*. The *Special Diabetes Program* has included both short-term and long-term initiatives. Short-term grant supplements and pilot and feasibility grants have enabled the *Program* to capitalize quickly on emerging research opportunities of high priority. Longer-term research grants and consortia and research infrastructure initiatives have been pursued to initiate unique, ambitious, large-scale research projects of critical importance. Because of the uncertainty of future funding of a time-limited *Program*, the NIH has employed novel funding mechanisms to support new research projects in later years of the *Program* in order to capitalize on new and emerging research opportunities.

The *Special Diabetes Program* has also established targeted type 1 diabetes-relevant components within initiatives that are supported in part by regularly appropriated funds. This strategy has maximized NIH and CDC's investment in type 1 diabetes research by building upon and realizing the greatest potential benefits from existing research infrastructure and ongoing clinical trials. Conversely, now that numerous clinical research studies and clinical trials networks have been established through support from the *Special Diabetes Program*, scientists are taking advantage of the existing infrastructure to conduct ancillary studies to maximize the research investment. Ancillary studies have been supported by the *Special Diabetes Program* or other sources (*e.g.*, regular NIH appropriations, the American Recovery and Reinvestment Act, diabetes voluntary organizations), which saves resources by building upon established studies and using data that have already been collected. Samples from ongoing studies are also being stored in the NIDDK Central Repositories, so that they can serve as a resource to the scientific community for additional research on type 1 diabetes and its complications, which maximizes the investment into these unique research studies. Moreover, several initiatives launched by the *Special Diabetes Program* have attracted investment from private foundations, industry, or other non-federal government sources with an interest in type 1 diabetes research.

Establishment of Large-Scale, Collaborative, and Infrastructural Initiatives

In the first years (FY 1998-2000), the *Special Diabetes Program* primarily supported initiatives soliciting research from independent investigators on topics of urgent and unmet need. When the *Program* was augmented in FY 2001, the additional funds enabled the creation of unique, innovative, and collaborative research consortia and clinical trials networks. The *Special Diabetes Program* enabled the initiation of these high-impact research efforts at a scientifically optimal scale. The majority of the funds since 2001 have supported these collaborative research efforts, with a goal of promoting progress in type 1 diabetes research that could not be achieved by a single laboratory. The collaborative initiatives, which have become a hallmark of the *Special Diabetes Program*, include genetics consortia, long-term epidemiological efforts, a beta cell biology consortium, animal models consortia, a clinical islet transplantation consortium, and clinical trials networks. Such projects are significantly different in size, scope, duration, and nature from investigator-initiated type 1 diabetes research efforts supported through the *Special Diabetes Program* or regular NIH appropriations. Most NIH research takes the form of 3- to 5-year hypothesis-driven research grants, either initiated by investigators in the field or submitted in response to NIH research solicitations. Such grants and funding initiatives often involve only a single NIH funding component and are carried out in a single, academic research laboratory. In contrast, the infrastructural and other large-scale research initiatives of the *Special Diabetes Program* represent a new paradigm in that overt trans-NIH and NIH-CDC collaborations are integral and essential to their successful operation, and the involvement of multiple research groups is required. For examples of the infrastructure that has been established to support research consortia, please see the main body of the report: "Critical Investment in Infrastructure for Type 1 Diabetes Research" feature (Goal I) and "The Beta Cell Biology Consortium: An Experiment in Team Science" feature (Goal III).

This approach has yielded remarkable progress. For example, collecting DNA from thousands of volunteers through the Type 1 Diabetes Genetics Consortium has resulted in the identification of over 40 new genes and gene regions associated with type 1 diabetes. Researchers working together in the Beta Cell Biology Consortium have made tremendous progress that can inform the development of cell replacement therapy for type 1 diabetes. Researchers collaborating in Type 1 Diabetes TrialNet have identified a new cellular target for possibly preventing or treating type 1 diabetes. Even more progress is expected in the future as research continues to build on this progress.

This Report describes several metrics for evaluating the scientific progress of the collaborative research consortia. One key metric was the evaluation of consortia by ad hoc groups of external scientific and lay experts in April 2008 and June 2009 (see descriptions of meetings later in this Appendix). These meetings provided critical sources of input for enhancing research being conducted by the consortia and future research directions. A second evaluation metric was obtaining input from scientists participating in research consortia to determine if there has been benefit in conducting the research as a collaborative endeavor. That input is found in "Investigator Profiles" in the main body of the report. Third, evaluation of major research consortia, networks, and resources is found in Appendix C. Finally, scientific

output from the consortia is included in the bibliometric analysis found later in this Appendix.

Improving Patients' Health

In the 89 years since the discovery of insulin, diabetes research and the medical treatment of people with diabetes have witnessed many "modern miracles." Yet, scientific research is both serendipitous and incremental, a process in which advances typically accrue and build upon each other over a relatively extensive time period. In the 12 years since its inception, the *Special Diabetes Program* has accelerated this process, uniting government and privately funded medical research with medical providers and biotechnology and pharmaceutical companies to bring about many improvements in the health and quality of life of people with type 1 diabetes. Examples of scientific advances follow.

Greatly Improved Prognosis for Americans with Type 1 Diabetes: Because of research progress over the last 2 decades, including research supported by the *Special Diabetes Program*, people with the disease are living longer and healthier lives than ever before and experiencing lower rates of disease complications. A recent study of the clinical course of type 1 diabetes concluded that starting intensive control of blood glucose as soon as possible after diagnosis greatly improves the long-term prognosis for patients. The study also found that the outlook for people with longstanding type 1 diabetes has greatly improved over the past 20 years due to a better understanding of the importance of intensive glucose control, as well as advances in insulin formulations and delivery, glucose monitoring, and the treatment of cardiovascular disease risk factors. These findings come from analyses of the long-term health outcomes for people who participated in NIDDK's landmark Diabetes Control and Complications Trial (DCCT) and its ongoing, *Special Diabetes Program*-supported, follow-up study, the Epidemiology of Diabetes Interventions and Complications, which began in 1993. This study reinforced and extended the DCCT's initial findings that intensive blood glucose control dramatically reduces the risk of eye, kidney, and nerve damage due to diabetes. In particular, researchers found that, among DCCT participants who had received intensive glucose control during the trial, rates of vision loss and kidney failure had fallen to much lower levels than seen historically. Achieving and maintaining intensive glucose control is not easy for people with type 1 diabetes; the 21st century picture of clinical outcomes provided by this study can aid health care providers in discussing the tremendous health benefits of intensive control with their patients and reinforces the need for research to develop less burdensome approaches to help patients achieve these goals.

Newly Discovered Type 1 Diabetes Genes: Using new and emerging genetics technologies, scientists in the NIDDK-led and *Special Diabetes Program*-supported Type 1 Diabetes Genetics Consortium and their collaborators identified over 40 different genes or genetic regions that influence a person's risk of developing type 1 diabetes, bringing the total number of known regions to near 50—up from only three known genes a few years ago. Now, the challenge is to understand how those genes may influence disease development. Further research is ongoing to pinpoint the exact genes and understand their function in type 1 diabetes. Understanding the genetic underpinnings of type 1 diabetes can aid the ability to predict risk, as well as inform the development of new prevention and treatment strategies.

Adult Pancreas Cells Reprogrammed to Insulin-producing Beta Cells: Scientists in the NIDDK-led and *Special Diabetes Program*-supported Beta Cell Biology Consortium (BCBC) have made tremendous progress in understanding beta cell biology toward the goal of developing cell-based therapies for diabetes. For example, in order to promote the formation of new beta cells, BCBC scientists are determining when and how certain pancreatic progenitor cells become "committed" to developing into specific pancreatic cell types and discovering flexibility in these cells. In one study, scientists made an exciting discovery that a type of adult cell in the mouse pancreas, called exocrine cells, can be reprogrammed to become insulin-producing beta cells. Using a genetically engineered virus and a combination of just three transcription factors, the researchers were able to reprogram some of the exocrine cells into beta cells. The newly formed beta cells produced enough insulin to decrease high blood glucose levels in diabetic mice. If the same type of approach can be developed to work safely and effectively in humans, this discovery could have a dramatic impact on the ability to increase beta cell mass in people with diabetes.

In another study, scientists uncovered plasticity in another pancreatic cell type—the alpha cell. Using genetic techniques in mice, the researchers increased the levels of a protein called Pax4, which is known to be involved in promoting cells to develop into the pancreatic beta cell type. They found that mice with high levels of Pax4 had oversized clusters of beta cells, which resulted from alpha-beta precursor cells and established alpha cells being induced to form beta cells. In addition, in a mouse model of diabetes, high levels of Pax4 promoted generation of new beta cells and overcame the diabetic state. In another study, BCBC scientists observed spontaneous conversion in beta cell-depleted mice of alpha cells to insulin-producing cells. These discoveries--that adult pancreatic cells have the potential to convert to beta cells--generate a fuller picture of pancreatic development and may pave the way toward new cell-based therapies for diabetes.

Hemoglobin A1c (HbA1c) Standardization Improves Care for People with Diabetes: HbA1c is a component of blood that is a good surrogate measure of long-term blood glucose control and, as such, reflects risk of diabetic complications. Clinical guidelines for controlling blood glucose to reduce diabetes complications set targets for control of blood glucose as assessed by this key test based on results from two landmark clinical trials: the DCCT for type 1 diabetes and the United Kingdom Prospective Diabetes Study for type 2 diabetes. To enable translation of these targets for control of blood glucose into common medical practice, the CDC and NIDDK, with support from the *Special Diabetes Program*, launched the HbA1c Standardization Program in 1998. This program improved the standardization and reliability in measures of HbA1c so that clinical laboratory results can be used by health care providers and patients to accurately and meaningfully assess blood glucose control and risks for complications. The standardization effort has been a great success and has facilitated national campaigns to improve control of blood glucose. As a result, the percentage of Americans with diabetes who had excellent glucose control increased from 37 percent in 1999-2000 to 56 percent in 2003-2004.[30] The American Diabetes Association (ADA) built on

[30] Hoerger TJ, Segel JE, Gregg EW, et al: Is glycemic control improving in U.S. adults? Diabetes Care 31: 81-86, 2008.

the tremendous success of the HbA1c Standardization Program to set treatment goals for glucose control in all forms of diabetes based on the test and has recommended HbA1c as a more convenient approach to diagnose type 2 diabetes.

New Glucose Monitoring Tools for Controlling Blood Glucose Levels: Research supported by the *Special Diabetes Program* contributed to the development of U.S. Food and Drug Administration (FDA)-approved continuous glucose monitors, which reveal the dynamic changes in blood glucose levels. Alarms warn the patient if blood glucose becomes too high or too low, thereby reducing the need for invasive finger sticks to monitor blood glucose levels. This revolutionary technology can make it easier for patients to keep blood glucose at healthy levels and can enhance their ability to achieve the intensive control necessary to prevent or delay disease complications. In addition, this technology, when linked to insulin delivery (known as an "artificial pancreas"), has the potential to have a further positive impact on patients' health and quality of life, and alleviate an enormous amount of patient burden.

Novel Drugs for Treating Complications: The *Special Diabetes Program* has supported the development and clinical testing of new therapeutic agents for diabetic eye disease. For example, a recent comparative effectiveness research study, conducted by the National Eye Institute (NEI)-led Diabetic Retinopathy Clinical Research Network, found that a therapeutic called ranibizumab, in combination with laser therapy, was substantially better than laser therapy alone or laser therapy with a different drug, at treating diabetic macular edema, a swelling in the eye that often accompanies and aggravates diabetic retinopathy. Ranibizumab with laser therapy substantially improved vision among study patients, and could become the new standard of care for diabetic macular edema.

Advances in Islet Transplantation as a Therapeutic Approach for People with Type 1 Diabetes: The *Special Diabetes Program* supported the first islet transplantation trial in the United States using a procedure referred to as the "Edmonton protocol" that dramatically improved islet survival and rendered many patients insulin-free. Through the Immune Tolerance Network (ITN), which is led by the National Institute of Allergy and Infectious Diseases (NIAID), the *Special Diabetes Program* also supported the first international, multicenter trial of islet transplantation using the protocol. Additionally, research supported by the *Program* laid the foundation for an unprecedented islet transplant to an American airman, sparing him from a life-long insulin requirement after pancreatic damage from wounds suffered while serving in Afghanistan. Improved approaches to islet transplantation are important not only as an alternative to whole pancreas transplantation for treatment of type 1 diabetes but also to avoid diabetes through auto-transplantation after removal of the pancreas due to pancreatitis or injury. The *Special Diabetes Program* is supporting multifaceted research efforts to overcome barriers to making islet transplantation a viable therapy, such as the shortage of available islets and the toxicity associated with the life-long immunosuppressive medication.

Promise of Therapies that Target Specific Lymphocytes in Preventing and Reversing Type 1 Diabetes: Previous clinical trials have suggested that preserving patients' remaining beta cell function can have dramatic, long-term health benefits. Researchers in NIDDK's Type 1 Diabetes TrialNet, which is supported by the *Special Diabetes Program*, reported that an immunosuppressive drug

(rituximab), which destroys immune system cells called B lymphocytes, preserved the function of insulin-producing beta cells in people newly diagnosed with type 1 diabetes. Improved insulin production was maintained 1 year after the drug was administered, but the effect dissipated at 2 years. As drugs such as rituximab broadly deplete B lymphocytes, they can increase the risk of infection and therefore can have significant side effects. Nonetheless, the finding is very important because it will propel research to find drugs targeting the specific B lymphocytes involved in type 1 diabetes without the associated side effects of drugs like rituximab.

In another study, researchers in NIAID's ITN, also supported by the *Special Diabetes Program*, are building on an earlier study showing benefits of teplizumab, a humanized anti-CD3 monoclonal antibody that targets white blood cells known as "T cells" that are involved in the autoimmune attack on the beta cells. A pilot study of teplizumab showed that a single course of the antibody could delay progression of the disease over a 2-year period. The new trial is a larger follow-up study, in which two courses of the antibody are administered, one year apart, in an effort to extend its effects on beta cell preservation.

Testing Novel Type 1 Diabetes Prevention Strategies: Research supported by the *Special Diabetes Program* has enabled testing of new type 1 diabetes prevention strategies and demonstrated that it is possible to predict with great accuracy a person's risk of developing type 1 diabetes. Moreover, while an oral insulin type 1 diabetes prevention trial (now part of TrialNet) did not demonstrate protection in the entire study population, it suggested a possible effect in the subgroup with highest insulin antibody titers. This knowledge has set the stage for screening and enrolling patients into new type 1 diabetes prevention trials, including a new trial through TrialNet that is testing oral insulin in a subgroup of people with high levels of insulin autoantibodies.

Building on findings from successful trials in newly diagnosed patients, TrialNet has developed a new paradigm: therapeutics demonstrated to be effective in new-onset patients are then tested for their prevention potential. One such prevention trial was recently launched with teplizumab, a monoclonal antibody engineered to alter the balance between destructive and protective T cells. Based on promising results in preserving beta cell function in patients newly diagnosed with type 1 diabetes, teplizumab is now being studied in family members of type 1 diabetes who are at 80 percent risk of developing type 1 diabetes over the next 5 years. This effort builds not only on the earlier success with teplizumab but also on the proven accuracy of tests to predict type 1 diabetes risk.

Scientific Productivity

Bibliometric Analysis

Compendium of *Special Diabetes Program*-supported Scientific Publications: Perhaps the most accepted metric for assessing scientific productivity is to look at peer-reviewed publications in scientific and medical journals. Peer-reviewed publication is the forum in which scientists report their discoveries and propound new ideas, and it is one means by which productivity is measured for NIH grant applications, faculty appointments, and tenure decisions. The NIDDK used e-SPA to search for scientific publications associated with grants funded through the *Special Diabetes Program*, and identified 2,793 unique articles published from January 1, 1998, and prior to January 1, 2010.

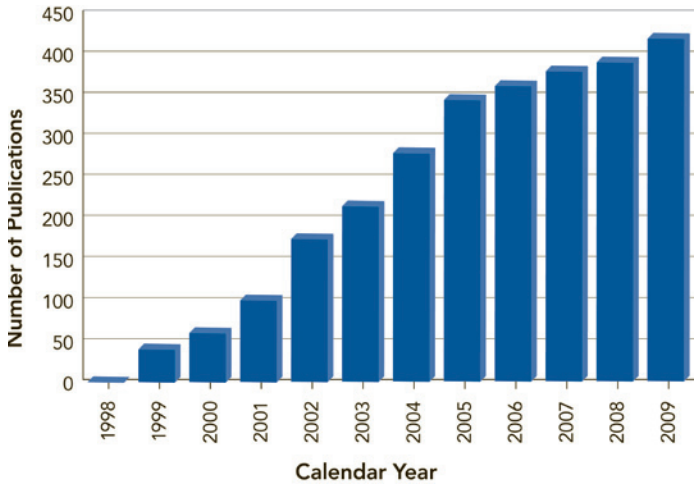

Figure B2: Number of Scientific Publications Supported by the *Special Diabetes Program*
The graph represents the number of papers published each calendar year. Data include the 2,793 papers published before January 1, 2010, produced from initiatives, clinical trials, or research consortia made possible by the *Special Diabetes Program*.

The identified set includes only publications from grants awarded through initiatives, clinical trials, or research consortia made possible through the *Special Diabetes Program*. Pre-existing grants that were augmented through the *Program* were not included in the bibliometric analysis. The final collection of papers analyzed in this evaluation report is almost certainly an underrepresentation of the actual publication output, because it is impossible to capture all published papers that do not give attribution to the grants that supported the research.

Figure B2 displays the number of articles published in each calendar year of the *Special Diabetes Program*. As would be expected, fewer articles were published in the early years of the *Program*; a scientific project can take many years from design of the project to publication of the results. The data show an increasing trend and in the later years of the *Special Diabetes Program*, there is a robust output of scientific articles.

Citation Analysis for Scientific Papers: The 2,793 papers were analyzed to evaluate their impact on the scientific community (Table B2, Figure B2, Figure B3, and Figure B4). One of the most objective methods for assessing the scientific impact of a publication is to analyze how frequently the work has been cited in other scientific publications. A higher number of citations may indicate that the paper has had a particularly large influence on subsequent work in the field, introducing a new experimental technique, for example. However, it takes time to design and carry out new experiments, so there is typically a lag time of 3 to 5 years after a paper is published before most citations of it appear in the scientific literature. Therefore, papers published in more recent years will likely generate many more citations in the future than are reported here.

Citation data obtained from e-SPA was derived from the Thomson Web of Science database and includes citation activity that occurred through December 31, 2009. A few publications were not included in the Web of Science database and therefore citation data was not reported for a limited number of publications. These publications were not included in statistical analysis of citation data. Citation data are available for 2,574 publications and, therefore, missing for 219 papers. The citation data, therefore, are likely underreported and thus limit any conclusion of impact assessment from citation analysis.

Among the 2,574 papers for which citation data are available, there are 52,739 total citations prior to January 1, 2010 (Table B2). The number of citations ranged from

Table B2: Citation Analysis of Scientific Papers

Year	Total Papers	Papers with Available Citation Data	Maximum Citations	Mean Citations	Median Citations	Total Citations
1998	2	2	261	158	158	316
1999	38	38	111	43	38	1,638
2000	62	60	226	42	31	2,522
2001	102	93	222	39	26	3,610
2002	175	163	743	47	29	7,687
2003	216	196	489	39	23	7,576
2004	291	274	528	28	18	7,751
2005	346	318	166	23	15	7,409
2006	358	345	406	19	12	6,678
2007	390	370	248	14	8	5,089
2008	397	374	121	6	3	2,103
2009	416	341	27	1	0	360
1998-2009 Total	**2,793**	**2,574**	**743**	**38**	**21**	**52,739**

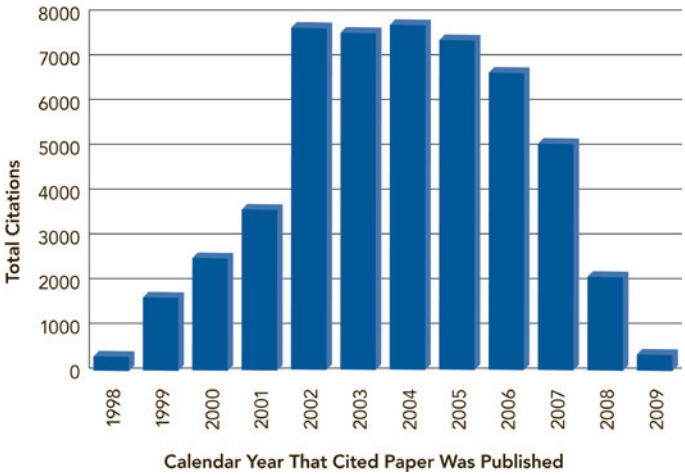

Figure B3: Total Citations of *Special Diabetes Program*-supported Research Publications
The cited papers are the subset of papers for which citation data are available. Citations appearing in papers published on January 1, 2010, or later were not included in this analysis.

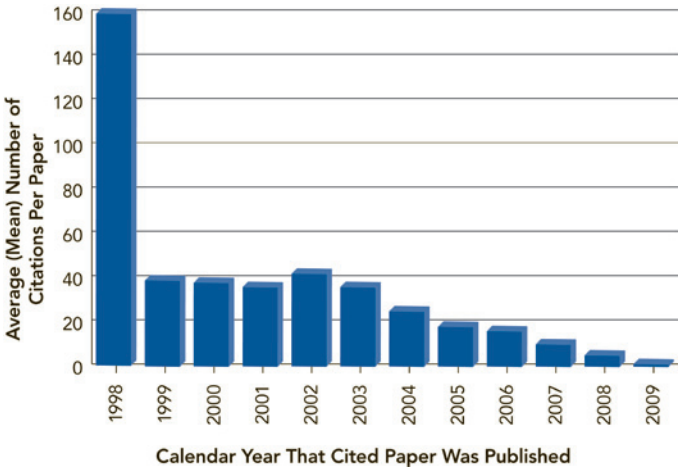

Figure B4: Average Citations of *Special Diabetes Program*-supported Research Publications
Mean citations are grouped by the calendar year during which the cited papers were published. The cited papers are a subset of papers for which citation data are available. Citations appearing in papers published on January 1, 2010, or later were not included in this analysis. Because there is typically a lag time of 3-5 years after a paper is published before the majority of citations occur, the average number of citations is lower for more recently published papers.

0 to 743, with an average (mean) of 38 and a median of 21. The total number of citations per year is dramatically higher for the papers published a few years after the inception of the *Program* (Figure B3). This likely reflects the years necessary for the projects funded early in the *Program* to publish results, but also that a sufficient number of years have passed to achieve a high number of citations. As expected, the average number of citations per paper is higher for papers published early in the *Program* than for those published later (Figure B4).

Comparison to Data from 2007 Report: It is important to note that data reported here differ from the data previously reported in the 2007 "*Evaluation Report*." The bibliometric analysis previously conducted identified 4,755 articles published from January 1, 1998, and prior to January 1, 2006. This number included publications that cited pre-existing grants that were augmented through the *Special Diabetes Program*. Many of these grants supplemented existing research project grants or Diabetes Research Centers grants at academic institutions, allowing innovative pilot projects or development of resources relevant to type 1 diabetes. Because it was not possible to determine which of these publications were made possible by the additional funding, and which were more related to the prior award, they were eliminated from the bibliometric analysis for the 2007 report. Also for this reason, they were not included in the bibliometric analysis reported here. In 2007, a total of 1,552 publications from grants awarded through initiatives, clinical trials, or research consortia made possible through the *Special Diabetes Program* were collected and used for the citation analysis in the 2007 "*Evaluation Report*."

Two additional methods used to supplement the previous publications list were not used for the data collection in this report. This includes the investigator survey, which was used to collect additional publications. Additionally, for the 2007 report, the publications list was supplemented by scientific program directors at NIH responsible for management of *Special Diabetes Program* consortia and trial networks. In order to keep the eSPA the sole variable for data collection and to keep the data as consistent as possible, these methods were not employed for the bibliometric analysis reported here.

Patents

Patents represent an objective metric of productivity. The e-SPA tool was used to collect data on patent activity on the portfolio of research grants supported by the *Special Diabetes Program* from FY 1998-2009. e-SPA interfaced with the U.S. Patent and Trademark Office (USPTO) database to search issued patents for the inclusion of specified grant numbers. If the issued patent acknowledged support from a grant, it was identified by e-SPA as associated with that grant.

The e-SPA analysis yielded a total of 23 unique, issued patents that were tied to *Program* grants (see Table B3). A previous evaluation of the *Special Diabetes Program* published in 2007 identified 15 additional issued patents that were associated with the *Special Diabetes Program* but not identified by e-SPA. Those patents were captured through self-report data from a grantee survey. Further analysis revealed that the relevant grant numbers were not included in those 15 patents filed with the USPTO, which is why they were not identified by

e-SPA. Combining datasets shows that there are at least 38 issued patents associated with the *Special Diabetes Program* (Table B3). Information on issued patents is shown in Table B4.

The estimate of 38 issued patents is likely an underestimation due to the limitations of using e-SPA. Because e-SPA is an automated system, if the patent did not cite a grant number, cited an incorrect grant number, or cited only the funding agency, it was not identified by e-SPA. However, because of the availability of the new automated e-SPA tool for identifying patent data, which was not available during the 2007 *Program* evaluation, NIDDK chose not to conduct a grantee survey. Thus, the two datasets were combined to obtain a conservative estimate of patent activity resulting from the *Special Diabetes Program*.

Research Resources

Research resources are research tools, technologies, biological samples, data, or other scientific materials that are produced or collected to enable scientific experimentation. A focus of the *Special Diabetes Program* has been to promote development of resources that can be used by the broad scientific community. Therefore, the resources are not only benefiting researchers funded by the *Program*, but the entire diabetes research enterprise. In addition, researchers outside of diabetes also use the resources. For example, scientists studying pancreatic cancer use resources developed by the Beta Cell Biology Consortium. Examples of available research resources are shown in Table B5 (more information on resources generated by research consortia is found in Appendix C). Several consortia—such as SEARCH, TEDDY, and others—also make protocols, study forms, and publications available to the scientific community through a public Web site. Furthermore, some consortia were established specifically to serve as a resource to the scientific community, such as the T1D-RAID program that provides resources for pre-clinical drug development.

Table B3: U.S. Patents

Patents Issued – e-SPA dataset	23
Patents Issued – identified in grantee survey from 2007 "*Evaluation Report*"(non-overlapping with e-SPA dataset)	15
TOTAL PATENTS ISSUED	**38**

In addition to the numerous resources that have already been developed with support from the *Program*, other resources are expected to become available in the future. For example, several clinical consortia, such as TEDDY and TRIGR, are currently collecting biological samples that will be made available and serve as invaluable resources to scientists in their quest to understand the underlying mechanisms of type 1 diabetes and to identify environmental triggers of disease.

Promotion of Diverse, Innovative, and Patient-Oriented Research on Type 1 Diabetes

Diverse Research Portfolio

Research proposals for support by the *Special Diabetes Program* are received through a variety of mechanisms, including Requests for Applications (RFAs) for grant and cooperative agreement awards, and requests for administrative supplements for pilot or ancillary studies related to ongoing projects. From FY 1998 through FY 2009, a total of 74 RFAs were issued for the support of focused research of critical importance to the prevention and cure of type 1 diabetes and its complications. RFAs solicit research on a specific scientific topic of high relevance to program goals; they are used to solicit individual research projects, or in some cases to

Table B4: Issued Patents*

U.S. Patent Number	Year Issued	Inventor(s)	Title
5,723,333	1998	Levine F, Wang S, Beattie G, Hayek A	Human Pancreatic Cell Lines: Developments and Uses
6,110,743	2000	Levine F, Wang S, Beattie G, Hayek A	Development and Use of Human Pancreatic Cell Lines
6,122,536	2000	Sun X, Joseph J, Crothall K	Implantable Sensor and System for Measurement and Control of Blood Constituent Levels
6,197,534	2001	Lakowicz J, Tolosa L, Eichhorn L, Rao G	Engineered Proteins for Analyte Sensing
6,348,429	2002	Lim D, Gough D, Rourke A	Polymers From Vinylic Monomers Peroxides and Amines
6,448,045	2002	Levine F, Dufayet D	Inducing Insulin Gene Expression in Pancreas Cells Expressing Recombinant PDX-1
6,497,729	2002	Moussy F, Kreutzer D, Burgess D, Koberstein J, Papadimitrakopoulos F, Huang S	Implant Coating for Control of Tissue/Implant Interactions
6,544,800	2003	Asher S	Polymerized Crystalline Colloidal Arrays
6,589,452	2003	Asher S, Kamenjicki M, Lednev I, Meier V	Photochemically Controlled Photonic Crystal Diffraction
6,592,746	2003	Schmid-Schoenbein G, Baker D, Gough D	Sensor Probe for Determining Hydrogen Peroxide Concentration and Method of Use Thereof
6,673,596	2004	Sayler GS, Simpson ML, Applegate BM, Ripp SA	*In vivo* Biosensor Apparatus and Method of Use
6,673,625	2004	Satcher, Jr. J, Lane S, Darrow C, Cary D, Tran J	Saccharide Sensing Molecules Having Enhanced Fluorescent Properties
6,682,938	2004	Satcher, Jr. J, Lane S, Darrow C, Cary D	Glucose Sensing Molecules Having Selected Fluorescent Properties
6,721,587	2004	Gough DA	Membrane and Electrode Structure for Implantable Sensor
6,753,191	2004	Asher SA, Reese CE	Polymerized Crystalline Colloidal Array Chemical Sensing Materials for Use in High Ionic Strength Solutions
6,766,183	2004	Walsh J, Heiss A, Noronha G, Vachon D, Lane S, Satcher, Jr. J, Peyser T, Van Antwerp W, Mastrototaro J	Long Wave Fluorophore Sensor Compounds and Other Fluorescent Sensor Compounds in Polymers
6,777,546	2004	Langridge W, Arakawa T	Methods and Substances for Preventing and Treating Autoimmune Disease
6,811,785	2004	Brumeanu T, Casares S, Bona C	Multivalent MHC Class II - Peptide Chimeras
6,835,545	2004	Halperin J	Methods, Products and Treatments for Diabetes
6,884,785	2005	von Herrath MG	Compositions and Methods for the Treatment or Prevention of Autoimmune Diabetes
6,884,585	2005	Levine F, Dufayet D	Induction of Beta Cell Differentiation in Human Cells by Stimulation of the GLP-1 Receptor
6,893,552	2005	Wang J, Zhang X, Lu F	Microsensors for Glucose and Insulin Monitoring
6,911,324	2005	Levine F, Gouty D, Itkin-Ansari P	Induction of Beta Cell Differentiation in Human Cells
6,916,660	2005	Wang B, Weston B, Yang W	Fluorescent Sensor Compounds for Detecting Saccharides
6,979,542	2005	Cheung VG, Spielman RS	Methods for Identifying Heterozygous Carriers of Autosomal Recessive Diseases
7,014,998	2006	Rothstein DM, Basadonna GP	Screening Immunomodulatory Agents by CTLA-4 Upregulation
7,026,294	2006	Fasano A, Watts T	Method of Use of Peptide Antagonists of Zonulin to Prevent or Delay the Onset of Diabetes
7,049,082	2006	Halperin J	Methods, Products and Treatments for Diabetes
7,059,719	2006	Asher S	Contact Lenses Colored With Crystalline Colloidal Array Technology
7,071,298	2006	Brown TR, Kappler F	Compounds and Methods for Treating Glycogen Storage Disease and other Pathological Conditions Resulting from Formation of Age-Proteins
7,094,555	2006	Kwok WW, Nepom G, Gebe J, Reijonen H, Liu A	Methods of MHC Class II Epitope Mapping, Detection of Autoimmune T Cells and Antigens, and Autoimmune Treatment
7,105,352	2006	Asher SA, Alexeev VL, Lednev IK, Sharma AC, Wilcox C	Intelligent Polymerized Crystalline Colloidal Array Carbohydrate Sensors
7,336,984	2008	Gough DA, Lucisano JY	Membrane and Electrode Structure for Implantable Sensor
7,402,153	2008	Steil GM, Rebrin K	Closed-loop Method for Controlling Insulin Infusion
7,439,330	2008	Halperin J	Anti-glycated CD59 Antibodies and Uses Thereof
7,491,389	2009	Scott EW, Grant M, May WS	Modulating Angiogenesis
7,615,528	2009	Brown TR, Keppler F	Methods for Alleviating Deleterious Effects of 3-Deoxyglucosone
7,622,117	2009	Tobia A, Kappler F	3-Deoxyglucosone and Skin

* Data obtained from the USPTO database (http://www.uspto.gov/patents/process/search/). Patents in light blue boxes were identified from 2007 self-reported survey data provided by grantees supported by the *Special Diabetes Program*; see Appendix 5 of the 2007 "*Evaluation Report*" (www.T1Diabetes.nih.gov/evaluation) for more information on the survey. Other patents were identified using e-SPA.

attract applications for participation in a consortium. Solicitations asked for creative approaches to solve particularly difficult problems. These solicitations encouraged high-risk, discovery research to overcome obstacles to research progress. Additionally, the *Special Diabetes Program* provided full or partial support for projects associated with Requests for Proposals (RFPs) and Program Announcements (PAs); notices were used to announce availability of funding or research resources (see Appendix A for a complete list of funding announcements and initiatives). A breakdown of activity in terms of the *Special Diabetes Program*'s funding mechanisms is provided in Table B6.

The *Special Diabetes Program* supported 648 grants and supplements and 29 contracts. Individual investigators predominantly received short-term or long-term research project grants. In some cases, the

Table B5: Examples of Available Research Resources*

CONSORTIUM	RESOURCE
Animal Models of Diabetic Complications Consortium	➢ Over 40 animal models of type 1 diabetes that closely mimic various aspects of the human complications of diabetes ➢ Standardized assays for phenotyping diabetic complications in animal models ➢ Validation criteria for animal models of diabetic complications ➢ Phenotype database ➢ Comprehensive Web site (www.amdcc.org) with public access to AMDCC resources and data
Type 1 Diabetes Mouse Resource	➢ Maintain over 199 stocks of mice important to diabetes research that are available to the scientific community ➢ Generated 19 new mouse strains that are sensitized to the development of diabetes complications for use by the research community.
Beta Cell Biology Consortium	➢ Public Web site (www.betacell.org) with over 300 unique and useful resources, of which 70 percent are publically available (those that are not remain in development and are released after validation and/or publication) ➢ 110 antibodies against markers expressed at different stages of stem cell to beta cell maturation ➢ Four PancChips (microarrays) for studying genes expressed in the pancreas/islets of both humans and mice, as well as over 36,000 gene promoter regions in mice ➢ 50 new lines of genetically engineered mice or mouse embryonic stem cells ➢ Genomics.betacell.org, which is a searchable database that provides search tools for genes, their transcripts, and their profiles in expression studies
Cooperative Study Group for Autoimmune Disease Prevention	➢ Class II human MHC tetramers ➢ NOD microarray database ➢ Antibody proteomic arrays
Type 1 Diabetes TrialNet	➢ DPT-1 dataset ➢ Biological samples
Collaborative Islet Transplant Registry	➢ Annual reports with international data on islet transplantation
Diabetic Retinopathy Clinical Research Network	➢ Study data
Diabetes Research in Children Network	➢ Study data
Type 1 Diabetes Genetics Consortium	➢ Study data ➢ Biological samples
Epidemiology of Diabetes Interventions and Complications	➢ Study data ➢ Biological samples
Genetics of Kidneys in Diabetes Study	➢ Study data ➢ Biological samples
Family Investigation of Nephropathy and Diabetes	➢ Study data ➢ Biological samples

* Data obtained from reports on progress of research consortia developed for planning and evaluation meetings, consortia Web sites, and/or NIDDK Central Repositories Web site.

Special Diabetes Program funded 1-year supplements to ongoing NIH grants for ancillary research. Research consortia and networks were funded either through cooperative agreement mechanisms, which allow NIH program officials to have significant involvement with the external scientists in the framing and achievement of a specified research goal, or with contracts or project grants (R01). The *Special Diabetes Program* established resource centers or provided supplements to established research centers to augment their type 1 diabetes research investments. These centers included animal model facilities, non-human primate centers, general clinical research centers, specialized centers, and centers that provided certain resources, such as islets for transplantation or basic research. The *Special Diabetes Program* also supported 28 grants to small businesses—Small Business Innovation Research grants (SBIR) and Small Business Technology Transfer Research grants (STTR)—to promote the development of innovative technologies such as sensors for continuous glucose monitors. Contracts were used for services such as coordinating trial networks, maintaining genetic and tissue sample repositories, supporting bioinformatics integration, coordinating patient recruitment for clinical trials, and DNA sequencing.

NIH Involvement in Research Programs Supported by the *Special Diabetes Program*

Cooperative agreements (or U mechanism awards) are those in which NIH is significantly involved with the external scientists in the framing and achievements of the research program. As shown in Table B7, *Special Diabetes Program* support for cooperative agreements differs markedly from the NIH-wide pattern; the *Program* funded a significantly higher percentage of U awards in relationship to R awards than did NIH as a whole during the same time period. These data demonstrate that the funds of the *Special Diabetes Program* have been deployed so that NIH and the research community work in partnership to develop the research programs and ensure that progress is being made.

Clinical and Translational Research

The *Special Diabetes Program* has a clear focus on clinically relevant research that can improve the health and well-being of individuals with type 1 diabetes or at risk for developing the disease. This focus is consistent

Table B6: *Special Diabetes Program* Funding Mechanisms (FY 1998-2009)

Activity	New Awards	Supplements	Grants+Supplements
Research Project Grants (R01, R21, R24, R29, R33, R37)	379	28	407
Small Business Grants (STTR: R41; SBIR: R43, R44)	28	0	28
Research Programs and Centers (P01, P30, P40, P50, P51, P60, M01)	2	50	52
Cooperative Agreements (U01, U10, U19, U24, U42)	126	6	132
Training Awards (Career: K12; Institutional: T32)	14	0	14
Training Projects (DP2, DP3)	15	0	15
Contracts	28	1	29
TOTAL PROJECTS	**592**	**85**	**677**

Table B7: New Research Grants (FY 1998-2009)

* Data from e-SPA.

with the statutory language establishing the *Program*. An analysis was conducted (see methodology below) to determine the number of funded grants that were coded for human subject research (excluding research coded for human subject research, but that only involved human tissue samples). Of the 539 grants included in the analysis (R and U mechanisms), 225 (42 percent) were categorized as clinical research (see Table B8). By comparison, 40 percent of grants supported by NIH over the same time period matched the same definition of clinical research (42,554 of 105,000 grants using R or U mechanisms). A higher percentage of U grants supported by the *Special Diabetes Program* were categorized as clinical (63 percent, or 80 of 126 grants) compared to U grants supported by NIH during the same time period (56 percent, or 4,451 of 7,986). The *Special Diabetes Program* has had a particular focus on supporting clinical research through U mechanism grants. This focus is thus reflected in the high percentage of U mechanism grants supported by the *Program* that are clinically relevant. Furthermore, 23 of the grants supported by the *Special Diabetes Program* involved Phase III clinical trials, the final stage required before a therapy can be approved by FDA.

To complement the above grants analysis on the absolute number of grants supported by the *Program* that are categorized as clinical research, another analysis was performed to determine the percent of the overall budget that has supported clinical research projects. As shown in Figure B5, 63 percent of the budget of the *Special Diabetes Program* from FY 1998-2009 was used to support clinical research. This budget analysis included not only R and U mechanism grants, but also contracts, training grants, and others (see methodology below). Using available data from NIH databases[31] showed that approximately one-third of the NIH budget in recent Fiscal Years (FY 2006-2009) has been categorized as clinical research. To be consistent with the statutory language establishing the *Program*, funds of the *Special Diabetes Program* have been deployed in a different way than regular NIH appropriations, which includes having a greater focus on clinical research and a correspondingly larger budget dedicated to it.

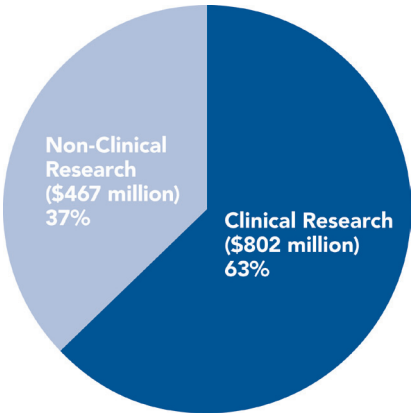

Figure B5: Budget of *Special Diabetes Program* Supporting Clinical Research, FY 1998-2009
Analysis includes R, U, T, K, DP2, and DP3 mechanism grants, as well as contracts; it excludes supplements to grants or centers because it would not be possible to determine if the categorization of the research as clinical related to the supplement portion of the grant or only to the primary grant. Thus, because the analysis excluded supplements, those budgets were also excluded from the denominator to calculate the percent clinical budget. The FY 1998-2009 budget used in the denominator of this calculation is $1.27 billion (rather than $1.29 billion, which is the total budget of the *Special Diabetes Program* over that time period).

[31] Analysis included data from: (1) NIH RePORTER (http://report.nih.gov/rcdc/categories/) for budget levels categorized as clinical research; and (2) the NIH almanac for historical total NIH budget figures (www.nih.gov/about/almanac/appropriations/index.htm).

In addition to clinical research, the *Special Diabetes Program* has also engendered significant research that translates basic research discoveries to the clinical setting. For example, animal models consortia—such as a consortium that evaluates the safety and efficacy of novel therapies to induce immune tolerance in non-human primate models of islet, kidney, heart, and lung transplantation—expedite the translation of promising therapies into clinical research. Indeed, one therapy that was tested by this consortium has been approved for testing in a human clinical trial. To further facilitate the pipeline of drug development, the Type 1 Diabetes—Rapid Access to Intervention Development (T1D–RAID) program was established to provide resources for the manufacture and pre-clinical development of drugs, natural products, and biologics that will be tested in type 1 diabetes clinical trials. Several agents have been manufactured through T1D-RAID and are being tested, or are planned for testing, in clinical trials. In addition, the Pre-clinical Testing Program associated with T1D-RAID has developed better methods for using rodent models for pre-clinical testing and has initiated testing of several new possible therapeutics. Overall, the *Special Diabetes Program* has supported a research continuum from basic to pre-clinical to clinical research, in which promising new therapeutic agents are being identified in the laboratory and subsequently tested in patients.

Methodology

- **Clinical Research Portfolio (analysis of R and U mechanism grants):** In this Report, clinical research was defined as all human subject research, excluding research labeled as human subject research but that only involved human tissue samples. To identify grants from FY 1998-2009 that fit this definition, the type 1 diabetes grant portfolio (as described under "Data Sources" earlier in this Appendix) was analyzed by e-SPA to obtain the IMPAC II human subject code for each grant application in order to classify projects as involving clinical research. Codes 10 and E4 were used to determine if a project was non-clinical; all other codes were considered clinical research. E4 projects were excluded because they involve the use of "human tissue samples," and this exclusion is consistent with the NIH decision to classify E4 projects as non-clinical research (described at http://grants.nih.gov/grants/policy/hs/faqs_specimens.htm; accessed May 19, 2010).

Table B8: Clinical Research Grants (FY 1998-2009)*

	***Special Diabetes Program* Grants**		**NIH-wide Grants**	
	Fraction of Clinical Research Grants	Percent	Fraction of Clinical Research Grants	Percent
R Mechanism	145/413	35	38,089/97,307	39
U Mechanism	80/126	63	4,451/7,968	56
TOTAL (R+U)	**225/539**	**42**	**42,554/105,400**	**40**

* Data from e-SPA. This analysis included only R and U mechanism grants.

KEY FEATURES OF RESEARCH SUPPORTED BY THE *SPECIAL STATUTORY FUNDING PROGRAM FOR TYPE 1 DIABETES RESEARCH*

- Enabled the establishment of large-scale, collaborative research consortia and networks at a scientifically optimal scale.
- R21 and R01 projects supported by the *Special Program* responded to targeted solicitations to tackle difficult problems and overcome obstacles to research progress.
- Greater percentage of cooperative agreement (U mechanism) grants supported by the *Special Diabetes Program* compared to NIH as a whole, showcasing the *Program's* focus on NIH and the research community working in partnership.
- Focused on supporting clinical research, including testing new therapies in people with or at-risk for type 1 diabetes.
- Innovative funding mechanisms fostered interdisciplinary collaborations, scientific partnerships, and the recruitment of new investigators.
- Focused on creation of resources for use by the scientific research community.
- Fostered a research pipeline of basic, pre-clinical, and clinical research.

Sometimes, research grants in the NIH database were not flagged as clinical research in the first year or more of funding, but this flag was applied to the research in later years. Any research grant that was coded as clinical research at any point in its grant history was considered "clinical research" for the purpose of this analysis.

Data from the NIH comparison set was collected through e-SPA, using the same definitions for clinical research.

- **Phase III Clinical Trials:** *Special Diabetes Program* grants coded as clinical research in the above analysis were analyzed further using IMPAC II to determine if they were also coded as a Phase III clinical trial. If the grant had a Phase III clinical trial code during any 1 or more years of the project period, it was counted as Phase III for the purpose of this analysis.
- **Analysis of *Special Diabetes Program* Budget Supporting Clinical Research:** For clinical research consortia (T1DGC, TrialNet, TEDDY, SEARCH, ITN, CIT, CITR, DRCR.net, TRIGR, DirecNet, GoKinD, EDIC, and FIND), the entire research budget was included in the analysis. For non-consortia grants, grants coded as clinical research in the above analysis were further analyzed using IMPAC II to capture budget data by year. If a project year was coded as clinical research, the budget for that year was included in the budget total for clinical research. If a project year was coded as non-clinical research (codes 10 or E4), the budget for that year was not included in the analysis. Only funds from the *Special Diabetes Program* were included in the analysis; if grants received funds from regular NIH or CDC appropriations, those budgets were not included.

The total clinical research budget was then calculated by adding the budgets of the clinical research consortia with the budgets of clinical years of the non-consortia grants. The analysis included the entire grant portfolio analyzed by e-SPA, including R, U, K, T, DP2, and DP3 mechanism grants. It also included contracts, but excluded supplements to grants or centers.

The total budget over this time period was $1.29 billion. However, to calculate the percent clinical budget, the denominator was reduced by the budgets of the supplements that were excluded from the analysis. Thus, the FY 1998-2009 budget used in the denominator of this calculation was $1.27 billion.

Recruitment and Support of Diabetes Researchers

A high priority of the *Special Diabetes Program* is the recruitment and retention of new investigators into diabetes-related research. Understanding the underlying causes of type 1 diabetes and finding new ways to prevent and cure this disease requires the concerted efforts of many investigators with diverse expertise. Relevant fields of scientific inquiry that can contribute to diabetes research include genetics, epidemiology, bioinformatics, genomics and proteomics, immunology, pathogen discovery, cell biology, bioengineering, transplantation surgery, neuroscience, cardiology, nephrology, ophthalmology, radiology, and others.

The *Special Diabetes Program* has used several mechanisms to attract new talent to type 1 diabetes research. Institutional clinical investigator training and career development programs for pediatric endocrinologists were established at seven medical institutions. Pilot and feasibility grants give new researchers the opportunity to test novel hypotheses that have conceptual promise. This type of award is also useful for established investigators who want to explore a new application or direction for their research. In addition, new research talent has been recruited through initiatives that pair established diabetes investigators with other scientists who can bring a new perspective or technology to the field. Finally, new research talent has been specifically recruited through an initiative directed to new investigators—the DP2 grant mechanism, also known as the Type 1 Diabetes Pathfinder Award. These mechanisms can be a magnet for drawing to diabetes research bright, capable investigators with creative research ideas to undertake innovative studies. Through these mechanisms, the *Special Diabetes Program* attracted investigators who had not previously received NIH funding, as well as scientists who were new to diabetes research.

In this evaluation, two approaches were considered to determine whether a grant supported by the *Special Diabetes Program* was submitted by a new investigator. First, grant applications in the NIH database IMPAC II have a "New Investigator" flag that denotes whether the grantee has had prior NIH funding. However, tracking of this parameter by the NIH began in 1999 and has been phased in over time. Therefore, it does not provide an accurate estimate of the number of new investigators for the date range of this evaluation. In a second approach, which was employed here, the investigator's earliest funded grant that disqualified him/her from being a new investigator was identified using IMPAC II. As currently defined by the NIH, an investigator can still be considered a "New Investigator" on a grant application if they previously held NIH subprojects or grants with

the following activity codes: D43, G07, G08, G11, G13, G20, L30, L32, L40, L50, L60, R00, R03, R13, R15, R21, R25, R34, R36, R41, R43, R55, R56, R90, RL5, RL9, S10, S15, S21, S22, SC2, and SC3. In addition, previous F, K, and T grant mechanisms were not considered in the selection of an investigator's earliest grant application. NIH definition of a new investigator was accessed at: http://grants.nih.gov/grants/new_investigators/#definition in February 2010. The earliest funded grant application that disqualifies an investigator from "New Investigator" status was compared to the grant application funded by the *Special Diabetes Program*. A project was considered to have a "New Investigator" if the fiscal year of the *Special Diabetes Program* grant was the same as, or earlier than, the investigator's earliest disqualifying grant application. Data for the NIH-wide comparison group was collected using the same methodology.

From the inception of the program, FY 1998, through FY 2009, the *Special Diabetes Program* awarded 384 new research project grants (R01, R21, and DP2; this total does not include supplements to ongoing R01 grants). The analysis described above indicated that 147 (38 percent) of these were grants to new NIH investigators. These data are comparable with NIH-wide data for grant applications from new investigators (39 percent). The distribution of grants to new investigators by the *Special Diabetes Program* each year is summarized in Figure B6. Thus, the *Special Diabetes Program* is extending NIH's efforts to invest in human research capital by attracting and supporting new investigators.

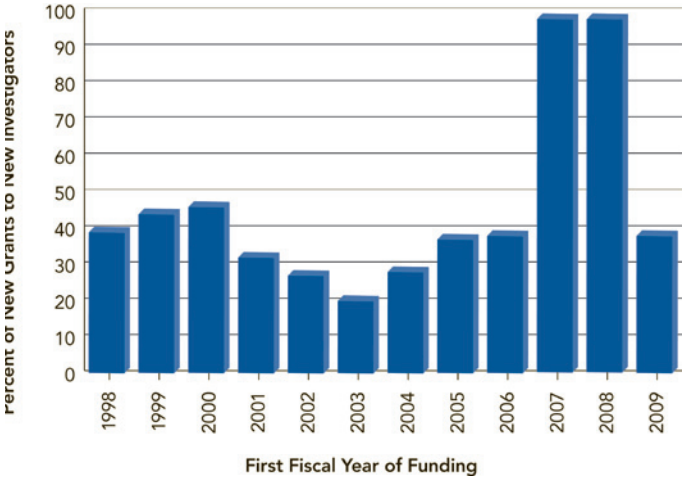

Figure B6: Recruitment of New Investigators
Data on *Special Diabetes Program*-funded investigators collected from NIH grant application database.

Broadly Consultative Planning Process for Priority Setting and Resource Distribution

The input of the diabetes research and voluntary communities in all aspects of planning, implementing, and evaluating the use of the *Special Diabetes Program* has been critical to its success. Leading scientific and lay experts with expertise relevant to type 1 diabetes and its complications have provided input on the priority-setting process for framing special type 1 diabetes initiatives, helped to evaluate the accomplishments of the *Program*, and identified new opportunities for future research that have emerged from the *Special Diabetes Program*.

External Evaluation Meetings

The NIH and CDC have convened a series of planning and evaluation meetings since the inception of the *Special Diabetes Program* to seek external scientific and lay input on ongoing and future research efforts. These meetings have constituted critical sources of input to program planning and management.

State-of-the-Science, 1997

In 1997, a trans-NIH conference entitled "Diabetes Mellitus: Challenges and Opportunities" met to discuss the state of research on diabetes and its complications. Symposium participants recommended that diabetes research be intensified in order to close research gaps, take advantage of new technologies, and capitalize on highly promising research leads and advances. The specific conclusions of this group were a critical source of input when the *Special Diabetes Program* was launched the next year. Moreover, the chairs of four relevant subpanels from the symposium reconvened in 1998 to provide input to NIH on the initial deployment of the funds under this *Program*.

Planning New Initiatives, 2000

In April 2000, scientific experts provided input on proposed research initiatives for the deployment of a portion of the funds of the *Special Diabetes Program* that became available after completion of short-term projects launched in FY 1998 and 1999. The input from this group were especially valuable for rapidly identifying high-priority initiatives when the *Special Diabetes Program* was expanded in duration and funding level in FY 2001.

Implementation, 2002

A similar panel of external experts met in May 2002 to review the use of the *Special Diabetes Program* at that time and to identify new research objectives and opportunities that arose from the expansion of research efforts on type 1 diabetes through the *Special Diabetes Program*. The input from this panel constituted a significant guide to NIH's research efforts on type 1 diabetes.

Mid-course Assessment, 2005

In January 2005, a third panel was convened for a 2-day meeting for a mid-course program assessment. The focus of the meeting was to evaluate the progress of 25 major research consortia, trial networks, and infrastructure-development initiatives. The panel also reviewed innovative research ideas proposed by the larger research community and discussed other emerging opportunities for research in type 1 diabetes that were enabled by the *Special Diabetes Program*.

Planning and Evaluation, 2008 and 2009

Conduct of *ad hoc* External Evaluation Meetings: In order to obtain external input on the progress and future directions of consortia supported by the *Special Diabetes Program*, NIDDK convened two recent ad hoc external evaluation meetings. These meetings were conducted similarly, as described below.

Panel members were identified by NIH and CDC for participation based on their scientific expertise. Panelists were asked to identify any potential conflicts of interest prior to the meeting and were dismissed for discussions that would qualify as a conflict of interest. Prior to the meeting panelists received a briefing binder prepared by NIH and CDC staff. This briefing binder contained introductory material about the *Special Diabetes Program*, instructions to the panel, and information on the consortia to be discussed. For each consortium to be discussed, the briefing binder contained:

- Administrative summary
- Description
- Goals
- Top five accomplishments

- Details of program management
- Details of resources provided to the scientific community
- Problems encountered
- Future directions if the *Special Diabetes Program* is extended
- Future directions if the *Special Diabetes Program* is not extended
- Most recent External Evaluation Committee report and/or report of the Data and Safety Monitoring Board
- List of publications generated

Panelists were informed prior to the meetings that the discussion was to serve as a means to obtain input on both current efforts and future directions on each consortium or network. The panel was asked to address the following questions:

- Does the consortium address a compelling scientific opportunity?
- How might scientific progress of each consortium be improved?
- Are processes in place to modify consortium plans in response to new scientific discoveries?
- Are there opportunities to better use resources generated by the consortium to advance type 1 diabetes research?
- Are there additional opportunities for coordination of consortia with each other and with other efforts?

The meetings were organized by consortium. Each session, which focused on a particular consortium, began with a presentation from a scientist participating in that consortium. The presentation provided an overview of the consortium, scientific accomplishments to date, current efforts, and future directions. The scientist then answered questions from the panel before leaving the room for the panel discussion. Non-federal attendees, other than the panelists, were asked to leave the room for the panel discussion. Individual panel members were designated as primary or secondary chairs for each discussion prior to the meeting based on their scientific field. The primary and secondary chairs for each session made introductory remarks and led the group discussion on each consortium or network. Following the introductory remarks, the chairs opened the floor to comments from the other panelists. Panelists provided individual input and opinions on the consortium and the discussion questions. At the end of the meeting, each panel member had an opportunity to provide input on future directions for research outside of the context of the ongoing programs.

Meeting on Clinical Research Supported by the *Special Statutory Funding Program for Type 1 Diabetes Research*, 2008: An external panel of 13 scientific experts with expertise in clinical trials, autoimmune diseases, immunology, transplantation, epidemiology, and biostatistics convened in Rockville, Maryland on April 29-30, 2008 (see Acknowledgments for a list of panelists). The goal of the 2-day planning and evaluation meeting was to perform a mid-course assessment of ongoing clinical research efforts supported by the *Special Statutory Funding Program for Type 1 Diabetes Research*.

The meeting was devoted to sessions to evaluate the following nine clinical research consortia supported by the *Special Diabetes Program*:

- Type 1 Diabetes TrialNet
- Immune Tolerance Network (ITN)
- Clinical Islet Transplantation (CIT) Consortium
- Collaborative Islet Transplant Registry (CITR)
- Diabetic Retinopathy Clinical Research Network (DRCR.net)
- The Environmental Determinants of Diabetes in the Young (TEDDY)
- Trial To Reduce IDDM in the Genetically at Risk (TRIGR)
- SEARCH for Diabetes in Youth (SEARCH)
- Diabetes Research in Children Network (DirecNet)

Much of the input provided by members of the expert panel cut across multiple research efforts. Cross-cutting input included:

- **Continue ongoing studies:** To capitalize on the investment made to date, it is important to continue all ongoing clinical research studies. All of the consortia have the potential to have a dramatic impact on the prevention and treatment of type 1 diabetes, and ending them prematurely would jeopardize the ability to acquire the extensive knowledge that can be gained through the studies.
- **Enhance collaboration among consortia:** The panel members acknowledged the efforts of the NIH, CDC, and the research consortia to coordinate their activities and noted that enhanced collaboration and coordination could propel research progress.
- **Develop a means to broadly advertise and distribute resources to the type 1 diabetes research community:** The consortia are collecting a significant number of biosamples and generating copious amounts of data that will be of benefit to the diabetes research community. It would be valuable for research consortia to develop a means to advertise the availability of biosamples and data and to ensure that policies and methods are in place to efficiently distribute these resources.
- **Encourage ancillary studies of ongoing clinical trials:** In order to maximize the investment in ongoing research programs, several panel members stressed the importance of engaging the scientific community in conducting ancillary studies of ongoing clinical trials.
- **Encourage mechanistic studies:** It is important that clinical trials be accompanied by mechanistic studies to understand why a particular therapy was or was not successful. These studies can also uncover new knowledge about mechanisms underlying type 1 diabetes disease onset and progression.

After reviewing the clinical consortia portfolio, the panel members commended NIH and CDC on the many accomplishments that have been achieved through the *Special Diabetes Program* in such a short period of time and noted that the research portfolio that has been established under the NIDDK's leadership has been a very wise investment of funding.

Meeting on Pre-Clinical Research Supported by the *Special Statutory Funding Program for Type 1 Diabetes Research*, 2009: An external panel of 14 scientific experts with expertise in beta cell biology,

immunology, diabetes complications, and animal models convened in Rockville, Maryland on June 17-18, 2009 (see Acknowledgments for a list of panelists). The goal of the 2-day planning and evaluation meeting was to perform a mid-course assessment of ongoing pre-clinical research efforts supported by the *Special Statutory Funding Program for Type 1 Diabetes Research*.

The meeting was devoted to sessions to evaluate the following nine pre-clinical research consortia supported by the *Special Diabetes Program*:

- Type 1 Diabetes-Rapid Access to Intervention Development (T1D-RAID)
- Testing for Preclinical Efficacy in Prevention or Reversal of Type 1 Diabetes in Rodent Models (Type 1 Diabetes Preclinical Testing Program [T1D-PTP])
- Testing for Preclinical Efficacy in Prevention or Reversal of Diabetic Complications in Rodent Models (Type 1 Diabetes Preclinical Testing Program [T1D-PTP])
- Animal Models of Diabetic Complications Consortium (AMDCC)
- Type 1 Diabetes Mouse Resource (T1DR)
- Beta Cell Biology Consortium (BCBC)
- Cooperative Study Group for Autoimmune Disease Prevention
- Immunobiology of Xenotransplantation Cooperative Research Program (IXCRP)
- Non-Human Primate Transplantation Tolerance Cooperative Study Group (NHPCSG)

Cross-cutting input provided by the panel regarding pre-clinical research included:

- **Enhance utilization of resources:** Many of the pre-clinical consortia generate resources or provide services to assist research in this field. Suggestions from individual panelists included improving advertising of these resources, offering more flexible receipt dates for applications for services, and increasing the availability of biosamples generated by pre-clinical research consortia.
- **Enhance collaboration among consortia:** The panel members acknowledged the efforts of NIH, CDC, and the research consortia to coordinate their activities and noted that enhanced collaboration and coordination could propel research progress.
- **Improve animal models of human disease:** Many panel members felt that efforts to improve animal models of human disease so that they are more representative of disease are important research opportunities.

After reviewing the pre-clinical program portfolio, the panel members were enthusiastic about the progress and accomplishments of the pre-clinical consortia supported by the *Special Diabetes Program*. The NIDDK and NIAID were commended for their leadership of these consortia.

The input obtained at these evaluation meetings has been critically important for informing the government's program planning efforts for this time-limited appropriation. For example, at both meetings, panel members encouraged the government to enhance coordination across existing research consortia, to make the best use of existing resources and maximize research progress. One example of how coordination has been enhanced is through collaboration on a new clinical trial. Two research consortia—one with expertise in glucose

monitoring technology and another with expertise in testing therapies for early treatment of type 1 diabetes—are collaborating on a clinical trial testing whether early and intensive blood glucose control at disease onset could preserve insulin production. In the trial, patients are placed on an inpatient closed-loop system and sent home with a sensor-augmented insulin pump. Thus, the combined expertise of the two consortia has been instrumental in enabling the conduct of this trial.

At the pre-clinical research meeting, the panel evaluated a consortium studying porcine to non-human primate models of xenotransplantation (solid organ, tissue, or cell transplantation between species). Panel members felt that the consortium's research was extremely valuable as an approach to relieve the shortage of solid organs for transplantation, but the research was less relevant to islet transplantation. Based on that feedback, the consortium is no longer supported by the *Special Diabetes Program*, but does continue to receive support from regularly appropriated funds for research on solid organ transplantation. Panel members at the clinical meeting felt that it was important to bolster research toward the development of an artificial pancreas. Based on this input, NIDDK developed new initiatives, with support from the *Special Diabetes Program*, to solicit research proposals from small businesses toward developing new technologies to inform development of an artificial pancreas. This example demonstrates how external evaluation led to a shift in use of the funds based on ongoing surveillance of scientific opportunities and how NIH has implemented input from the evaluation panels to enhance research supported by the *Special Diabetes Program*. The input received at these meetings continues to be invaluable as the government makes plans for future research directions.

Strategic Planning for Diabetes Research

The NIH utilizes strategic planning, with broad external input, to inform research directions, including research supported by the *Special Diabetes Program*. Strategic planning efforts that have informed program planning are described below.

1999 Diabetes Research Working Group Strategic Plan

In 1999, the independent, congressionally established Diabetes Research Working Group (DRWG) issued its strategic research plan for conquering diabetes, including both type 1 and type 2 diabetes. This panel of scientific experts engaged in a year-long, in-depth process to gather input from the diabetes research and voluntary communities. The DRWG's recommendations of relevance to type 1 diabetes have informed the planning and implementation of the *Special Diabetes Program*. These areas of DRWG emphasis include research opportunities identified in the areas of genetics; autoimmunity and the beta cell; clinical research and clinical trials; diabetic complications; special populations, including children; and resource needs. The Report can be accessed at: http://www2.niddk.nih.gov/NR/rdonlyres/95751201-0104-400D-AF6D-DC32E6BE74FE/0/DWG_1999_Report.pdf

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

Responding to input from the January 2005 *ad hoc* mid-course assessment of the *Special Diabetes Program*, the Director, NIDDK, launched the development of a strategic plan for type 1 diabetes research under the auspices of the statutory Diabetes Mellitus Interagency Coordinating Committee (DMICC). The 18-month planning process involved creating five scientifically

focused working groups to evaluate the state-of-the-science and to propose research objectives for type 1 diabetes research for the next 10 years. Each working group was composed of external scientific experts, members of the DMICC and other NIH officials, representatives from patient advocacy organizations, and lay members. The Type 1 Diabetes Research Strategic Plan can be accessed at: www.T1Diabetes.nih.gov/plan

2010 *"Advances and Emerging Opportunities in Diabetes Research: A Strategic Planning Report of the DMICC"*

In August 2008, the DMICC determined that the time was right to identify high-priority opportunities for diabetes research that can be accomplished in the next 5 to 10 years. As chair of the DMICC, NIDDK spearheaded the collaborative effort across federal agencies and with input from the external research and patient advocacy communities to develop a new Diabetes Research Strategic Plan. To formulate the Strategic Plan, working groups were convened to address each of 10 scientific areas of extraordinary opportunity in diabetes research. An additional working group composed of representatives from each of the other 10 groups addressed overarching needs for scientific expertise, tools, technologies, and shared resources. Each working group was chaired by a scientist external to NIH, and was comprised of external scientific experts—including basic scientists, clinicians, and engineers—as well as representatives of DMICC member organizations and diabetes voluntary organizations. This Plan will guide NIH, other federal agencies, and the investigative and lay communities in their pursuit of the goal of conquering diabetes. The Diabetes Research Strategic Plan can be accessed at: http://diabetesplan.niddk.nih.gov

Peer Review

Grants, cooperative agreements, and contracts supported by the *Special Diabetes Program* have been subject to peer-review mechanisms of NIH and CDC funding processes. This review system ensures that the funds are expended for scientifically- and technically-meritorious research that is responsive to the goals and priorities of the *Special Diabetes Program*. A limited number of administrative supplemental research awards were also made to existing projects.

Consortia External Evaluation Committees

For most large consortia supported by the *Special Diabetes Program*, NIH and CDC have established panels of scientists external to the consortia to provide ongoing oversight. These panels meet regularly to review progress and provide input on allocation of resources and future directions for the consortia.

Collaboration with the Diabetes Voluntary Community and Other Non-Federal Funding Sources

The major diabetes voluntary organizations—ADA and JDRF—have been committed and essential partners with HHS in providing critical input on the scientific goals and strategies of the *Special Diabetes Program*. Representatives of these groups have participated in the planning, assessment, and evaluation meetings that have aided in the formulation of a scientifically credible and productive plan for the *Special Diabetes Program*. Moreover, by co-sponsoring several of the special type 1 diabetes research initiatives, these organizations help HHS to maximize the resources available for achieving the goals of the *Special Diabetes Program*.