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

The *Special Statutory Funding Program for Type 1 Diabetes Research* has enabled the establishment of a unique, extraordinarily collaborative, scientifically comprehensive, and managerially sound research program. This program stands as an effective model for deploying funds that support cross-organizational initiatives of impressive scientific power and synergism. The *Special Funds* have both propelled and enabled researchers to capitalize on remarkable opportunities in diabetes research in ways not typically possible through traditional funding approaches and program-development mechanisms.

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 Program* toward this goal, but also to describe and analyze the innovative process by which the Department of Health and Human Services (HHS) approached this challenge. The multipronged scientific structure of the *Special 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 chapter describes the multiple evaluation approaches used to assess the scientific and clinical outcomes of the research; it also explains the decision processes used in developing the scientific emphases and allocating the resources of the *Special Program*.

This evaluation has been guided by the following questions:

- What impact has the *Special Program* made on the field of type 1 diabetes? How has the field progressed in the past 9 years since its inception?
- What objective measures can be used to benchmark the progress of the *Special 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 Program* and to what extent has the program been able to adapt to emerging research opportunities and recommendations from external advisors?
- To what extent has the planning process for the *Special Program* relied on perspectives of various scientific and lay stakeholders?
- How effectively has the *Special Program* been administered by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), which was delegated this responsibility by the Secretary, HHS? To what extent do the scientific initiatives and the distribution of resources reflect a coordinated strategic plan?
- In which ways could the research supported by the *Special Program* be enhanced?
- How are the collaborative research consortia and clinical trial networks perceived by scientists not affiliated with these projects?
- Which funding mechanisms have been most effective in stimulating progress?
- To what extent has the *Special Program* stimulated high-risk, high-impact research, or diabetes research in new fields that have not previously addressed diabetes?
- How successful has the *Special Program* been in cultivating cross-disciplinary interactions and coordination?
- How successful has the *Special 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 Funding 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 Program*, the clinical 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 Funding Program*, new insights into the biology of this disease and its therapy are continuing to develop. For example, the *Special Program* has initiated long-term prospective clinical studies, including one enrolling 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 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.
- *Professional Assessment*: Scientific judgment of external experts in the type 1 diabetes field garnered from specific assessments of the program at meetings convened in May 2002 and January 2005. Each individual project has ongoing assessment, but these two meetings assessed research supported by the *Special Funding Program* as a whole.
- *Stakeholder Input*: Assessment by program grantees of the impact of the *Special Program* on their research and careers, as obtained through their responses to surveys administered by the NIH.
- *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, stimulation of clinical research, and success in catalyzing continued research in the field.
- *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 grantee surveys, annual progress reports of funded investigators, or meetings of External Advisory Committees (EACs).

Cut-off Dates for Data Collection

In order to prepare this evaluation report to meet the statutory deadline, data collection on research progress was terminated on March 1, 2006. 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 this chapter and in Appendix 1 are reported through the end of Fiscal Year (FY) 2005. However, the collection of references for scientific journal publications was limited to articles published prior to January 1, 2006.

EMPLOYMENT OF AN INNOVATIVE PARADIGM FOR TRANS-HHS, CROSS-DISCIPLINARY, AND TRANSPARENT RESEARCH PLANNING AND MANAGEMENT

As designated by the Secretary, HHS, the NIDDK has coordinated the development of a sound planning, implementation, and evaluation process for the *Special Funding Program*. The allocation of funds has been performed in a scientifically competitive manner in cooperation with multiple Institutes and Centers of the NIH, the Centers for Disease Control and Prevention (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 the *Special Funds*. These plans, released in 1998 and 2001, established the framework for initiatives and research priorities to be pursued. Notably, the *Special Funding 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 an excellent model for a scientifically targeted and managerially integrated program because it is a systemic disease that is addressed by multiple NIH and HHS components. Type 1 diabetes involves the body's endocrine and metabolic functions (NIDDK) and immune system (NIAID); multi-organ complications affecting the heart and arteries (NHLBI), eyes (NEI), kidneys and urologic tract (NIDDK), nervous system (NINDS, NIMH), and oral cavity (NIDCR); the special problems of a disease diagnosed primarily in children and adolescents (NICHD); critically important and complex genetic (NHGRI) and environmental (NIEHS) factors; and the need for novel imaging technologies (NIBIB) and specialized research resources, such as islet isolation centers (NCRR). Diabetes complications have intersected with drug development pathways in cancer research (NCI). Type 1 diabetes is also of importance to other NIH components such as NIA, NINR, NLM, and ODS, and other HHS agencies, such as the CDC, FDA, HRSA, CMS, and AHRQ. Thus, the *Special Funding 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 Program. *(The annual funding levels for this* Program *since its inception are shown in Table 1.)*

Goal I: Identify the Genetic and Environmental Causes of Type 1 Diabetes

- Type 1 diabetes results from complex interactions of inherited genes and unknown environmental triggers. Long-term epidemiological research is required to pinpoint environmental factors for this complex disease. Large-scale collection and analysis of genetic samples are needed to identify the multiple genes involved.

Goal II: Prevent or Reverse Type 1 Diabetes

- Type 1 diabetes is caused by autoimmune destruction of the pancreatic beta cells. Focused research on the immune system and well-designed clinical studies are critically important to advance understanding of the mechanism of diabetic autoimmunity and to find new means of blocking or reversing this process.

Goal III: Develop Cell Replacement Therapy

- Replacement or regeneration of the pancreatic beta cells that are lost in type 1 diabetes would relieve patients of the need for insulin therapy, restore proper glucose control, and drastically reduce the risk of long-term complications. Further research on beta cell biology, immune modulation, and islet transplantation protocols could transform these highly experimental, but promising, treatments into a viable cure for type 1 diabetes patients.

Goal IV: Prevent or Reduce Hypoglycemia in Type 1 Diabetes

- Extremely low blood glucose—hypoglycemia—is a serious, acute complication of type 1 diabetes that can be life-threatening in extreme cases. It is the major factor that limits achievement of metabolic control shown to prevent complications. Research on the brain functions needed to recognize and avert hypoglycemia, and on the development of sensors to optimize the daily management of blood glucose levels, could not only significantly improve patients' quality of life, but could also improve control and avert complications.

Goal V: Prevent or Reduce the Complications of Type 1 Diabetes

- Over time, the high blood glucose levels of diabetes cause extensive damage to many of the body's organ systems. The development of new therapies or behavioral interventions to treat or prevent such complications could substantially reduce the health and financial costs of type 1 diabetes. Importantly, individuals with type 2 diabetes also benefit from research on diabetic complications.

Goal VI: Attract New Talent and Apply New Technologies to Research on Type 1 Diabetes

- Type 1 diabetes is an extremely complex disease in terms of its origin, daily management, and clinical progression. The pace and scope of type 1 diabetes research would be greatly enhanced by recruiting researchers from a variety of scientific fields who have not yet applied their expertise to the study of diabetes, and by expanding the pool of talented researchers whose main focus is on type 1 diabetes.

Table 1. Budget of the *Special Funding Program* by Goal (FY 1998-2005)±

	1998	1999	2000	2001	2002	2003	2004	2005
Goal I	493,436	2,070,192	4,463,743	22,535,131	16,378,537	19,717,454	34,808,000	45,084,403
Goal II	9,247,235	6,211,806	5,615,924	25,888,609	21,934,292	21,631,424	19,367,709	15,176,867
Goal III	6,379,977	6,293,237	5,881,222	25,204,681	19,346,899	19,701,970	47,148,270	41,716,120
Goal IV	3,470,740	3,672,012	2,579,693	2,674,074	8,993,845	7,643,699	8,389,536	7,680,901
Goal V	10,339,294	11,725,416	11,344,751	19,435,977	21,402,845	15,017,921	16,359,078	17,748,844
Goal VI	0*	0*	0*	4,049,000	11,793,551	16,130,672	23,789,681	22,056,018
Administrative (e.g., conferences, personnel)	69,318	27,337	114,667	212,528	150,031	156,860	137,726	536,847
TOTAL	**30,000,000**	**30,000,000**	**30,000,000**	**100,000,000**	**100,000,000**	**100,000,000**	**150,000,000**	**150,000,000**

± Please see Appendix 1 for a detailed budget analysis.

* Prior to FY 2001, 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. 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 launched relative to Goal VI.

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 Funds* (see Appendix 3). One challenge in managing large-scale science is the time required to accelerate or decelerate research programs in response to availability of funds. The dynamic interdependence of the efforts of NIH program managers and the external scientific and diabetes voluntary communities has helped the scientific priorities develop to reflect the changing needs of research.

Based on this scientific framework, a comprehensive management strategy has been used to promote maximum flexibility, to respond to new scientific opportunities, and to plan and initiate broad, multidisciplinary projects that would not have been undertaken without the *Special Funds*. The *Special Program* has included both short-term and long-term initiatives. Short-term grant supplements and pilot and feasibility grants have enabled the *Special 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 large-scale research projects of critical importance.

The *Special 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 the 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. Moreover, several initiatives launched with the *Special Funds* have attracted investment from private foundations, industry, or other non-federal government sources with an interest in type 1 diabetes research. The total budget distribution of the *Special Program* by Goal from FY 1998 through FY 2005 is displayed in Figure 3.

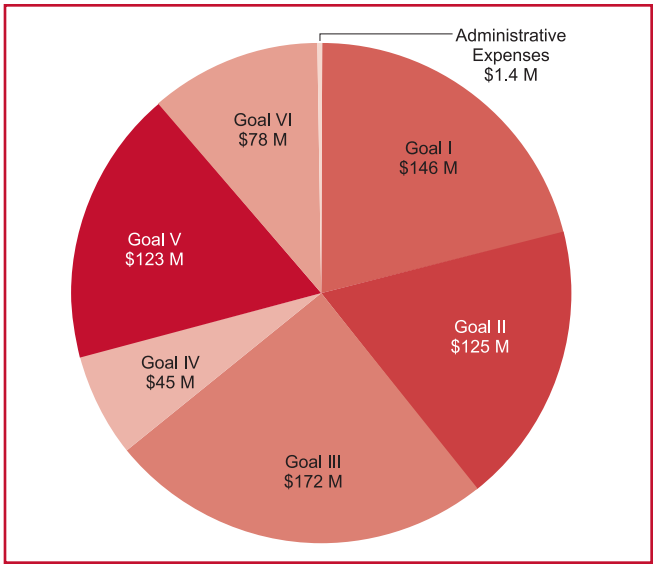

Figure 3: Total budget distribution by Goal, FY 1998-2005.

ESTABLISHMENT OF LARGE-SCALE, COLLABORATIVE, AND INFRASTRUCTURAL INITIATIVES

In the first years (FY 1998-2000), the *Special 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 Program* enabled the initiation of these high-impact research efforts at a scientifically optimal scale. The majority of the *Funds* since 2001 has 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 distribution of funds among these different types of research mechanisms is shown in Figure 4.

The collaborative initiatives, which have become a hallmark of the *Special Program*, include genetics consortia, long-term epidemiological efforts, a beta cell biology consortium, animal models consortia, the 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 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 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.

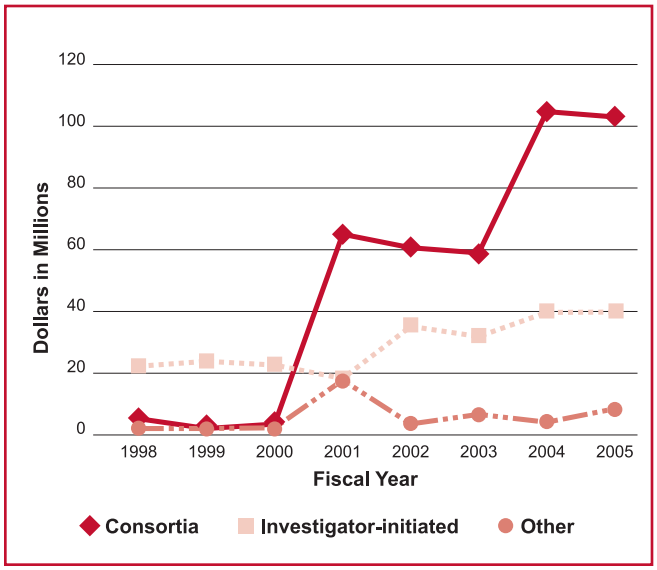

Figure 4: Distribution of funds over the course of the *Special Funding Program*. Data show the funding levels for research consortia (◆; e.g., U mechanism grants), investigator-initiated research efforts (■; e.g., R01 and R21 grants), and other efforts (●; e.g., training grants, contracts) over the course of the *Special Funding Program* from FY 1998 through FY 2005.

IMPROVING PATIENTS' HEALTH BY PROPELLING RESEARCH PROGRESS ON THE UNDERSTANDING, PREVENTION, TREATMENT, AND CURE OF TYPE 1 DIABETES AND ITS COMPLICATIONS

In the 85 years since the discovery of insulin, diabetes research and the medical treatment of diabetes patients 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 9 years since its inception, the Special Funding 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 quality of life of people with type 1 diabetes. Examples of scientific advances follow.*

Greatly Improved Prognosis for Americans with Type 1 Diabetes: New research has provided some very good news for Americans with type 1 diabetes: incidence of certain major complications of the disease is down, and overall life expectancy is up. Scientists examined the rate of premature death and of various complications 20-30 years after diagnosis in people diagnosed in the 1950s through the 1970s. Although the scientists found that the rates of some complications, such as heart disease, have not improved significantly among people with type 1 diabetes, they found that people diagnosed more recently were nevertheless much more likely to live longer, healthier lives than those diagnosed earlier. In particular, kidney failure, diabetic nerve damage, and death are now all less likely to occur during the 20- to 30-year period following a diagnosis of type 1 diabetes than they used to be.

Hemoglobin A1c (HbA1c) Standardization Improves Care for People with Diabetes: The *Special Funding Program* and the CDC launched the HbA1c Standardization Program in 1998 as a key tool to enable translation of tight blood glucose control proven to reduce complications into common practice. Now, clinical test values obtained in commercial laboratories nationwide are comparable to those in the landmark clinical trial that established the value of the HbA1c measurement. The standardization effort has been a great success, and has facilitated vital, life-saving and life-improving efforts for people with diabetes.

New Glucose Monitoring Tools for Controlling Blood Glucose Levels: The *Special Funding Program* and the NIH supported the development of recently 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 tight control necessary to prevent disease complications.

Long-Term Benefit of Near-Term Blood Glucose Control: The *Special Funding Program* enhanced the long-term continuation of the follow-on to the landmark Diabetes Control and Complications Trial (DCCT), called the Epidemiology of Diabetes Interventions and Complications (EDIC) Study. Surprisingly, the former intensively-treated group continued to have long-term benefits compared to those in the control group, despite similar HbA1c levels during EDIC—an effect termed "metabolic memory." Thus, physicians and patients now know that it is particularly valuable to intensively control blood glucose levels early in the course of disease. Importantly, EDIC has also now shown that close control lowers the risk of heart disease and stroke by about 50 percent in people with type 1 diabetes.

Novel Drugs for Treating Complications: Elucidation of molecular pathways by which increased blood glucose damages tissues has resulted in the development of novel drugs

to treat diabetes complications. For example, NIH-supported scientists developed a therapeutic agent that inhibits a protein called protein kinase C beta (PKC beta), which is being tested as a treatment for diabetic eye disease. Other examples of promising therapeutic agents for diabetic eye disease being developed with support from the *Special Funding Program* are drugs that inhibit excessive angiogenesis (new blood vessel growth) in the eye.

Advances in Islet Transplantation as a Therapeutic Approach for Type 1 Diabetes Patients: The *Special Program* supported the first islet transplantation trial in the United States using a procedure referred to as the "Edmonton protocol." Through the Immune Tolerance Network (ITN), the *Special Program* also supported the first international, multicenter trial of islet transplantation using the protocol. These studies have confirmed and extended the demonstration that islet transplantation may become an alternative to whole pancreas transplantation for treatment of type 1 diabetes. The *Special Funding 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 lifelong immunosuppressive medication.

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

To stimulate continued progress in type 1 diabetes research over the next several years, the *Special Program* has invested in a range of activities from basic research into the cellular and molecular mechanisms causing type 1 diabetes and its complications, to genetic and epidemiological studies that may inform preventing or reversing the disease, to translational and clinical research that is leading to new therapies. The *Special Program* investments in type 1 diabetes research resources will pay dividends in future years as ongoing efforts come to fruition and by facilitating new avenues of research; likewise, the training of clinical investigators will ensure a competent pool of talent to conduct that research.

Bibliometric Analysis

Compendium of *Special Funding 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 therefore searched for scientific publications associated with grants funded through the *Special Program*, identifying 4,755 articles published from January 1, 1998, and prior to January 1, 2006. However, the final collection of papers analyzed in this evaluation report is almost certainly an under-representation 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.

For purposes of the bibliometric analysis, these papers were divided into two pools.

- *Pool A-1,552 Publications*: Generally speaking, the publications in Pool A are from grants awarded through initiatives, clinical trials, or research consortia made possible through the *Special Funding Program*. With few exceptions, these grants are new since the inception of the Program.
- *Pool B-3,203 Publications*: The publications in Pool B typically cite pre-existing grants that were augmented through the *Special Funding Program*. Many of the Pool B grants augmented 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 the papers in Pool B were made possible by the additional funding, and which were more related to the prior award, more detailed analyses were restricted to the publications in Pool A.

The publications, and a complete definition of Pools A and B, can be found at: www.niddk.nih.gov/fund/diabetesspecialfunds/investigator/data.htm

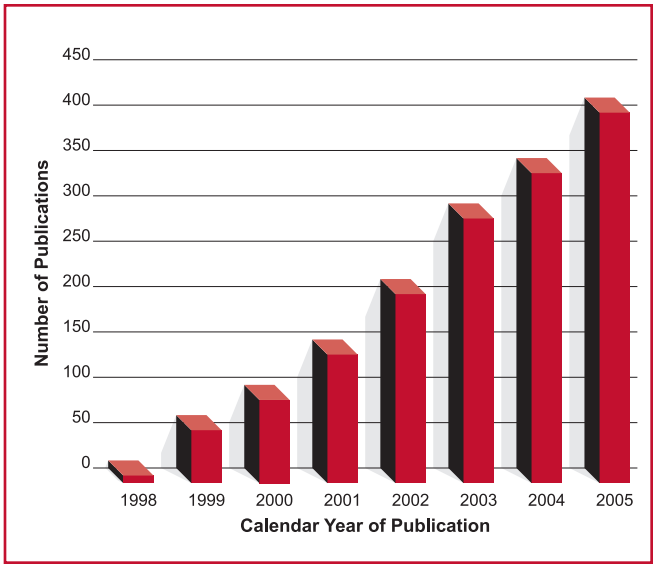

Figure 5: Scientific publications in Pool A supported by the *Special Funds*. This graph represents the number of papers in Pool A published each calendar year. Data only include the identified 1,552 papers published before January 1, 2006, produced from *Special Program* funding.

Table 2. Citation Analysis for Pool A Scientific Papers

Year	Total Papers	Papers with Available Citation Data	Maximum Citations	Mean Citations	Median Citations	Total Citations
1998	10	10	227	73	52	730
1999	65	64	157	31	20	1,986
2000	91	84	247	33	20	2,780
2001	144	138	177	24	17	3,329
2002	215	209	355	21	12	4,367
2003	283	270	137	13	9	3,524
2004	334	321	109	6	4	2,082
2005	410	382	22	1	0	422
1998-2005 Total	**1,552**	**1,478**	**355**	**13**	**5**	**19,220**

Citation Analysis for Pool A Scientific Papers

The 1,552 papers in Pool A were analyzed to evaluate their impact on the scientific community (Table 2, Figure 5, Figure 6, and Figure 7). 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. Citation data were collected with Internet-based databases; for methodology, please see Appendix 5. The data for each paper are reported in the compendium of publications at the website listed previously. 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 are available for 1,478 of the Pool A research publications (Table 2, column 3). In general, citation data are missing for the remaining 74 papers because the publications' journals are not listed in the commercial citation database. These 74 references include 22 papers published in the journal *Diabetes Technology and Therapeutics*. It is important to note that a large proportion of articles published on glucose monitors, technology pertaining to the development of an artificial pancreas, and related topics, were published in this journal, including the results of some important clinical trials. Thus, it is not possible to apply the citation analysis method of impact assessment to this area of *Special Funds*-supported research.

Among the 1,478 papers for which citation data are available, the number of citations prior to January 1, 2006, ranged from 0 to 355, with an average (mean) of 13 and a median of 5. As expected, the average number of citations per paper is dramatically higher for the papers published early in the *Program* than for those published later (Figure 6). Also, as expected, the publication output of papers per year has increased annually, as the *Program* has matured (Table 2, Figure 5).

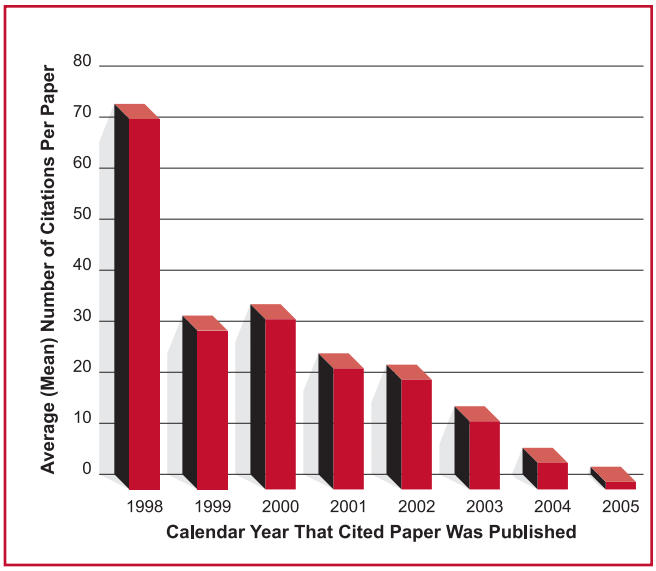

Figure 6: Average number of times Pool A *Special Funds*-supported papers were cited in other scientific publications. Mean citations are grouped by the calendar year during which the cited papers were published. The cited papers are the subset of 1,478 papers in Pool A for which citation data are available. Citations appearing in papers published on January 1, 2006, 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 most citation data of it appear in a scientific journal, the average number of citations is lower in more recently published papers.

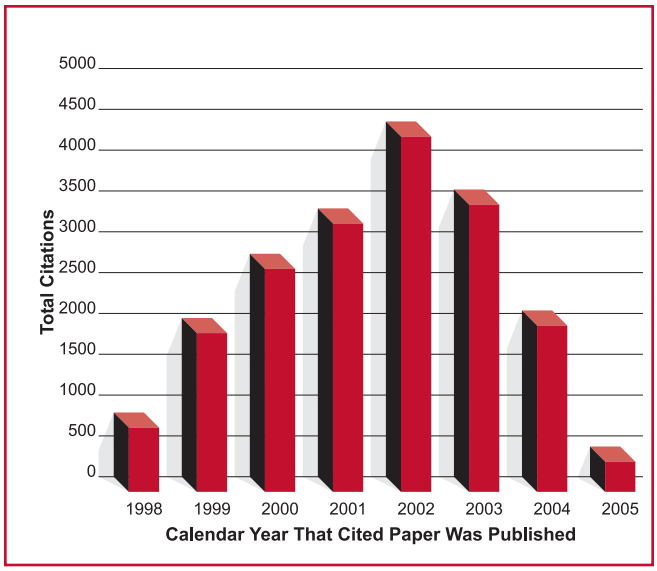

Figure 7: Total citations of Pool A *Special Funds*-supported research publications. Citations are grouped by the calendar year during which the cited papers were published. The cited papers are the subset of 1,478 Pool A papers for which citation data are available. Citations appearing in papers published on January 1, 2006, or later were not included in this analysis.

Survey of Independent Investigators

To augment the bibliometric analysis and to provide a more complete understanding of the progress from investigator-initiated research projects, the NIDDK conducted an Office of Management and Budget-approved survey. The survey was distributed to researchers who received NIH grants supported by the *Special Funds*, but which were not associated with one of the research consortia or clinical trial networks. Of 334 surveys distributed to grantees, the NIDDK received 274 complete responses (82 percent response rate) from 239 unique investigators (some investigators had more than one grant). Investigators were asked to assess the impact of *Special Program* on their research and careers and also to provide evidence of patent applications, scientific publications, research resources produced and distributed, funding history, and follow-up funding applications. These data were incorporated into the following sections of this chapter and in the sections on "Evaluation of Investigator-Initiated Research" in the chapters for each scientific goal. For the survey instrument, methodology, and further details on the survey, please refer to Appendix 5.

Patents and Technology Transfer Agreements

Patents and patent applications represent an objective metric of productivity. Investigators responding to the survey were asked to report patents filed with the U.S. Patent and Trademark Office (USPTO). The issued patents were verified from the searchable database on the USPTO website. Investigators reported 25 U.S. patents that derived from research supported

by the *Special Program*. Issued patents are listed in Appendix 5. Additionally, grantees reported 39 patents that had been filed with the USPTO, but had not yet been issued. A provisional patent is a 1-year intellectual property protection, often used as a preliminary step before filing a non-provisional patent. Survey respondents reported eight provisional patents that had been allowed by the USPTO. In some cases, the technology was patented by the academic institution and licensed to the private sector for further development. In other cases, grantees described technology transfer agreements in which the private sector filed the patents. The breakdown for the total of 72 filed patents is summarized in Table 3.

Table 3. U.S. Patents*

Patents issued	25
Patents filed but not yet issued	39
Provisional Patents	8
Total Patents Filed	**72**

*Patents reported by investigators in grantee survey. Table does not include patents derived from research supported in consortia, networks, centers, training programs, grants to small businesses, and supplements to ongoing research grants.

Research Resources

Research resources are research tools, technologies, biological samples, or other scientific materials that are produced or collected to enable scientific experimentation. A focus of the *Special 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 type 1 diabetes research enterprise. Fifteen percent of the grants to individual investigators covered in the investigator survey used resources provided by the consortia and networks (41/274 unique grants to 239 investigators). The NIDDK maintains a website (www.T1Diabetes.nih.gov) that lists resources that can be shared or purchased at low cost. Additionally, the website provides data and protocols from several of the consortia and networks. A large majority (81 percent; 77/95) of investigators who were aware of the type 1 diabetes website reported that they found it useful.

Examples of research resources developed by the consortia supported by the *Special Program* include:

- Animal models
- Antibodies
- Assays
- Data sets
- DNA sequencing support
- Human pancreatic islets
- Microarrays
- Pre-clinical development of therapeutic agents
- Samples from clinical research networks (e.g., blood cells, serum, plasma, genetic samples)

Examples of research resources developed by individual investigators, as reported in the survey of *Special Program* grant recipients include:

- Animal models and new strains of mice
- Antibodies
- Assays and reagents for diagnostic tests
- Bioinformatics databases and resources on the Internet
- Cell lines
- Computer-based algorithms to: model blood glucose values; predict genetic risks for developing type 1 diabetes or its complications; and enhance imaging technologies
- Imaging technology resources
- Immune monitoring core to analyze cell signaling pathways
- Glucose sensors
- Microarrays
- Tools for genetic engineering and gene therapy (e.g., DNA constructs and vectors)

PROMOTION OF DIVERSE, INNOVATIVE, AND PATIENT-ORIENTED RESEARCH ON TYPE 1 DIABETES

Diverse Research Portfolio

Research proposals for support by the *Special 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 2005, a total of 58 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 investigator-initiated research, or in some cases to attract applications for participation in a consortium. Solicitations for investigator-initiated research projects 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 Program* provided full or partial support for projects associated with 2 Requests for Proposals (RFPs), 1 Notice, and 20 other initiatives and consortia (see Appendix 1 for a complete list of funding announcements and initiatives). A breakdown of activity in terms of the *Special Program*'s funding mechanisms is provided in Table 4.

The *Special Program* funded 534 grants and supplements and 24 contracts through the NIH. Individual investigators predominantly received short-term or long-term research project grants. In some cases, the *Special 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 Funds* 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 Funding Program* also supported nine 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

Table 4. *Special Program* Funding Mechanisms (FY 1998-2005)

Activity for NIH-supported projects	New Awards	Supplements	Grants + Supplements
Research Project Grants (R01, R21, R24, R29, R33, R37)	354	19	373
Small Business Grants (STTR: R41; SBIR: R43, R44)	9	0	9
Research Programs and Centers (P01, P30, P40, P50, P51, P60, M01)	3	45	48
Cooperative Agreements (U01, U10, U19, U24, U42)	84	6	90
Training Awards (Career: K12, Institutional: T32)	14	0	14
Contracts	23	1	24
Total NIH projects	**487**	**71**	**558**

as coordinating trial networks, maintaining genetic and tissue sample repositories, supporting bioinformatics integration, coordinating patient recruitment for clinical trials, and DNA sequencing. Other programs, such as a major epidemiological study, and efforts to standardize techniques to measure diagnostic biomarkers, are supported by the CDC using the *Special Funds*.

Innovative and Exploratory Research

The *Special Funding Program* has promoted innovative, cutting-edge research that has the potential to quickly advance the field. The pilot and feasibility grant mechanism, known as an R21 grant, is one means of achieving this goal. In addition to supporting innovative, high-risk/high-impact investigations, R21 grants, which are typically 2-3 years in duration, have helped to ensure budget flexibility in the later years of the *Special Funding Program*. This short-term funding mechanism has helped to free up funds for reallocation as scientific opportunities have emerged. This flexibility allows the program to quickly respond to changes in science, while providing sufficient seed money for investigators to gather data for a full grant application if their hypotheses prove worthy of further pursuit. On the continuum of funding mechanisms, R01 research grants are often based on stronger preliminary evidence and, thus, are considered to be of lower risk and may have a longer funding period, typically 4-5 years. These mechanisms are complementary, and pilot and feasibility grants can often gain the necessary preliminary data to facilitate a successful R01 grant application to the NIH, or funding by a non-profit group or other research organization.

As shown in data on new research grants displayed in Table 5, from FY 1998 through FY 2005, slightly more new R21 grants than R01 grants were awarded through the RFAs issued under the *Special Funding Program*. This level of R21 grant support differs markedly from the NIH-wide pattern; the *Special Funding Program* awarded a much higher percentage of R21 grants in relationship to R01 grants than did NIH as a whole during the same time period. In addition, nearly 92 percent of the responses to the investigator survey (252/274 unique grants to 239 investigators) indicated that these grants supported innovative or high-risk research that the investigators would not otherwise have been able to pursue.

Table 5. New Research Grants (FY 1998-2005): R01 and R21*

	R21	R01	Total R21+R01	Percent R21
Special Funding Program	182	162	344	53 %
NIH-Wide Grant Funding	7,187	32,865	40,052	18 %

*Totals do not include grant supplements. Source: NIH Office of Extramural Research: http://grants1.nih.gov/grants/award/success/Success_ByActivity.cfm

NIH Involvement in Research Programs Supported by the *Special Funds*

As noted previously, cooperative agreements (or U mechanism awards) are those in which the NIH is significantly involved with the external scientists in the framing and achievements of the research program. As shown in Table 6, *Special Funding Program* support for cooperative agreements differs markedly from the NIH-wide pattern; the *Special Funding 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. This data demonstrates that the *Special Funds* 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.

Table 6. New Research Grants (FY 1998-2005): U and R Mechanisms*

	U Mechanism	R Mechanism	Total U+R	Percent U Mechanism
Special Funding Program	84	363	447	18.8 %
NIH-wide Grant Funding	1,650	47,412	49,062	3.4 %

*Totals do not include supplements. Source: NIH Office of Extramural Research: http://grants1.nih.gov/grants/award/success/Success_ByActivity.cfm

Clinical and Translational Research

In addition to encouraging innovative research studies, the *Special Funding 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 with the statutory language establishing the *Special Program*. The clinical research portfolio (FY 1998-2005) was evaluated by searching the NIH database of funded grants and grant applications for research projects that were coded for human subject research (excluding research coded for human subject research, but that only involved human tissue samples). Of the 439 grants included in the analysis (R and U mechanisms), 162 were categorized as clinical research (37 percent). (For methodology, see Appendix 5). By comparison, 33.7 percent of grants supported by the NIH matched this definition of clinical research (29,688 of 88,097 competing grants using R or U funding mechanisms). Furthermore, 14 of the grants supported by the *Special Funds* involved Phase III clinical trials, the final stage required before a therapy can be approved by the FDA. In each year, between 25 and 55 percent of the new projects had clinical components (Figure 8). The clinical research portfolio was greatly augmented when Congress expanded the *Special Funds* in 2001, enabling the initiation of the clinical trials networks and consortia.

Of the 27 consortia described in this evaluation report, 16 have a clinical focus (59 percent) and an additional 7 support projects to translate basic research into clinical research. Although research project grants tend to have a more basic science focus than the research consortia and clinical trial networks, nearly 42 percent of responses to the grantee survey (116/274 unique grants to 239 investigators) reported that the research required approval from an Institutional Review Board (IRB) that is necessary for research on human subjects, and 78 percent (214/274 grants) described the research as clinically relevant. In addition, 9.5 percent of grants (26/274) used large animals (e.g., pigs, non-human primates), which is often indicative of pre-clinical research.

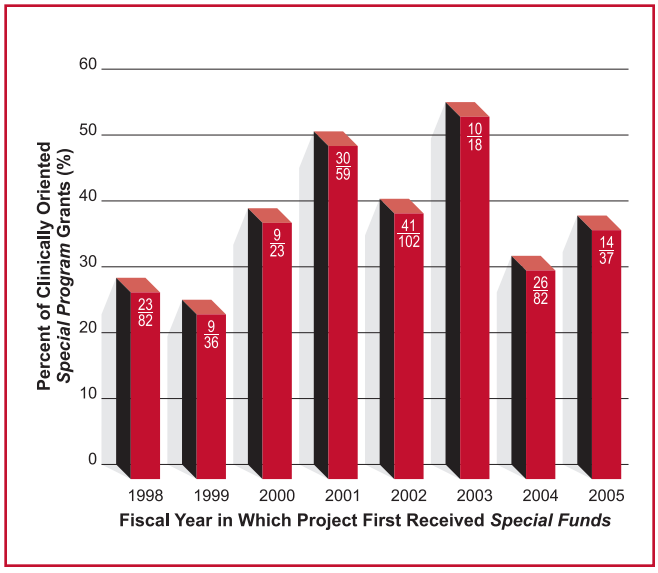

Figure 8: Percent of clinically-oriented grants (R and U mechanisms) supported by the *Special Funding Program* each Fiscal Year. Each bar shows the number of new clinically-oriented grants over the total number of new grants.

The *Special Funding Program* has also engendered significant research that translates basic discoveries to the clinical setting. An innovative series of initiatives initially launched in 2002 promoted "bench to bedside" research in which cutting-edge scientific proposals were given 2 years of exploratory funding for pre-clinical research that could be converted to a longer-term clinical grant if the research proved to be promising and certain benchmarks were achieved. Of the eight projects eligible to convert before March 1, 2006, five were translated into clinical research grants (63 percent). In addition, 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. To facilitate the pipeline of drug development, the *Special Funding Program* also worked with the NCI to provide a resource for translational research: Type 1 Diabetes—Rapid Access to Intervention Development (T1D–RAID). The T1D–RAID program provides resources for the manufacture and pre-clinical development of drugs, natural products, and biologics that will be tested in type 1 diabetes clinical trials. The *Special Funding 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.

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 of operation.
- R21 and R01 projects supported by the *Special Funds* responded to targeted solicitations to tackle difficult problems and overcome obstacles to research progress.
- Greater percentage of exploratory research (R21) grants and cooperative agreement (U mechanism) grants were supported by *Special Funds* compared to NIH as a whole.
- Innovative funding mechanisms fostered interdisciplinary collaborations and scientific partnerships.
- *Special Funding Program* initiatives attracted investigators who had not previously received NIH funding, as well as scientists who were new to diabetes research.
- Focused on the creation of resources for use by the scientific research community.

RECRUITMENT AND SUPPORT OF DIABETES RESEARCHERS

A high priority of the **Special 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.*

New Investigators

The *Special Funding 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. As noted previously, 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. 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 Funding Program* attracted investigators who had not previously received NIH funding, as well as scientists who were new to diabetes research.

From FY 1999 through FY 2005, the *Special Program* awarded 258 new research project grants (R01 and R21; this total does not include supplements to ongoing R01 grants). NIH application database records indicated that 61 (24 percent) of these were grants to new NIH investigators. These data are comparable with NIH-wide data for grant applications from new investigators (25 percent) using data from the same NIH database (for methodology, please see Appendix 5). The distribution of grants to new investigators by the *Special Funding Program* each year is summarized in Figure 9. Because of the limitations in available grant application-based data in archival databases, the number of new investigators reported here is likely an under-representation. In fact, a parallel analysis of the NIH-wide portfolio using investigator-based data indicates that an average of 36 percent* of NIH grants went to new investigators during a comparable time period. These data are consistent with the responses to the survey in which 83 of the 239 unique investigators (35 percent) indicated that the *Special Funding Program* provided the first independent NIH-supported research grant for which they were the Principal Investigator (PI). Thus, the *Special Funding Program* is extending NIH's efforts to invest in human research capital by attracting and supporting new investigators.

* Of 34,663 competing R01 and R21 grants awarded between FY 1998 and 2004, 12,442 were awarded to new investigators (source data: NIH Office of Extramural Research, http://grants.nih.gov/grants/new_investigators/New_Invest_by_Activity.xls and http://grants1.nih.gov/grants/award/success/Success_ByActivity.cfm).

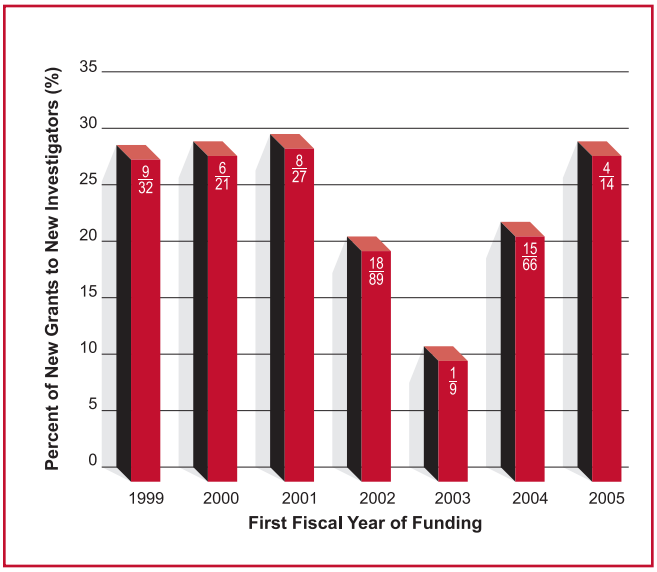

Figure 9: Recruitment of new investigators. Data on *Special Program*-funded investigators collected from NIH grant application database (IMPAC II). NIH grant applications collecting data on new investigators were phased in starting in 1999, so data are not available for 1998 and may be disproportionally lower for 1999.

In addition to attracting new investigators to diabetes research, the *Special Funding Program* sought to attract established investigators who had not previously worked on diabetes. Survey data revealed that the *Special Funding Program* provided their first grant, from any funding source, related to type 1 diabetes research for 100 of 239 unique investigators (42 percent). Of these 100 "new-to-diabetes" respondents, 78 investigators also indicated that they have continued to pursue diabetes research. Thus, the *Special Program* has been highly successful at bringing new scientific talent to bear on research issues in type 1 diabetes. Without this *Program*, it is highly unlikely that these investigators would have ventured into the type 1 diabetes research field or explored new research concepts for the future benefit of patients. Support for the recruitment of new talent to type 1 diabetes research under the *Special Funding Program* is summarized in Table 7.

Table 7. Recruitment of New Talent to Type 1 Diabetes Research

***Special Program* Stimulated:**	**Source**	**Fraction**	**Percent**
Investigators receiving first NIH grant	NIH database FY 1999-2005	61/258*	24 %
Investigators receiving first NIH grant	Grantee survey	83/239†	35 %
Investigators receiving first diabetes-related grant	Grantee survey	100/239†	42 %
Subset of investigators who received first diabetes-related grant and then continued in the field	Grantee survey	78/100	78 %
Newly recruited diabetes researchers (fraction of *Program* grantees who had not previously received any diabetes grant prior to the *Program* but subsequently continued in diabetes field)	Grantee survey	78/239†	33 %

*258 investigators were analyzed using the NIH database, which may underestimate new investigator status (see text).

†239 unique investigators responded to the survey representing 274 grants.

Continuation of NIH Research Funding

One goal of the *Special Funding Program* is to stimulate new lines of successful scientific research in the field of type 1 diabetes. Successful research efforts are often competitively renewed, and R01 research grants continuing along the same line of inquiry will retain the same grant number once they are competitively renewed. From 100 R01 grants initially awarded with *Special Funds* with a project end date before September 30, 2005, there were 54 applications to the NIH for continuation of support with regular NIH funds via recompetition through the peer-review system (Table 8) as of July 2006. Of these, 26 renewal applications had been awarded and funding decisions had not been made for four additional applications (see methodology, Appendix 5). The success rate for continuation of support (48 percent) is slightly higher than the average NIH continuation rate for the funding of competing renewal applications, which was 45.7 percent for FY 2000-2005.* Moreover, those applications included renewals of long-term projects that had successfully competed in previous renewal applications. Four of the *Special Funding Program* grants have been successfully renewed twice. Data on continuation of grant activity under the *Special Funding Program* are summarized in Table 8.

Table 8. Resubmission Rate of R01 Grants Funded by the *Special Funding Program* Compared to NIH-wide Data (FY 2000-2005)

R01 *Special Funds* Grants Eligible for Resubmission	100
Applications Reviewed	54
Applications Pending Funding Decisions	4
Competing Continuations Awarded	26 (48 %)
R01 Special Grants Renewed Twice	4
Survey Responses Indicating Continued Funding in Same Line of Research†	59 %
NIH Competing Renewals Awarded	45.7 %

†Only grants that had ended by the time of the survey were included in this analysis.

Importantly, 59 percent of survey responses (93/158 unique grants that had ended by the time of the survey) reported continued funding for the same line of research. Several additional researchers whose grants were ongoing at the time of the survey had already secured continued support for their research efforts. Some investigators cited NIH support by means other than recompetition of the original grant (e.g., through participation in TrialNet or other research consortia). In addition, several researchers obtained continued funding from non-NIH sources, including: the ADA, American Heart Association, Canadian Diabetes Association, Canadian Institutes of Health Research, Department of Defense, Department of Veterans Affairs, Dutch Diabetes Research Foundation, Endocrine Society, CDC, European Union, Heart and Stroke Foundation (Canada), JDRF, March of Dimes, Michigan Life Science Corridor Funding, National Health and Medical Research Council (Australia), National Institute of Standards and Technology, and the New York State Department of Health. At the time of the survey, additional respondents reported being in the midst of preparing or having recently submitted grants for continued research funding. Together, these data indicate that the *Special Funding Program* has enabled the establishment of a viable research enterprise that continues to make progress toward realizing the scientific goals of the program. Moreover, the research funded by this *Program* has garnered support from a broad array of research funding agencies.

*The NIH received 32,879 competing R01 applications for continued grant support for FY 2000-2005. Applications that have one or more amendments in the same fiscal year are only counted once (source data: NIH Office of Extramural Research, http://grants1.nih.gov/grants/award/success/Success_ByActivity.cfm).

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 Funding Program *has been critical to its success. Leading scientific and lay experts with expertise relevant to type 1 diabetes and its complications have participated in the priority-setting process for framing special type 1 diabetes research initiatives, helped to evaluate the accomplishments of the program, and identified new opportunities for future research that have emerged from the* Special Funding Program.**

Advisory Meetings

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 Funding Program* was launched the next year. Moreover, the chairs of four relevant subpanels from the symposium reconvened in 1998 to advise the NIH on the initial deployment of the funds under this *Program*.

Three additional *ad hoc* panels of external scientific experts (described below) have provided input on the implementation of the *Special Funding Program*. Executive summaries from these meetings have been reproduced in Appendix 3.

Planning New Initiatives, 2000

In April 2000, scientific advisors helped to prioritize proposed research initiatives for the deployment of a portion of the *Special Funds* that became available after completion of short-term projects launched in FY 1998 and 1999. The deliberations of this group were especially valuable for rapidly identifying high-priority initiatives when the *Special Funding Program* was expanded in duration and funding level in FY 2001.

Implementation and Prioritization, 2002

A similar panel of advisors met in May 2002 to review the use of the *Special Funds* 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 Funding Program*. The recommendations of this panel constitute a significant guide to the NIH's ongoing 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 Funding Program*. The panel's specific recommendations for each Consortium are included in the relevant sections within the chapters of this report that address each scientific Goal.

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 Funding 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.

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

Responding to a recommendation from the January 2005 *ad hoc* mid-course assessment of the *Special Funding 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 "Summary and Recommendations" section of the Strategic Plan is reproduced in Appendix 6. The Strategic Plan can also be accessed at: www.T1Diabetes.nih.gov/plan.

Peer Review

Grants, cooperative agreements, and contracts supported by the *Special Funding Program* have been subject to peer-review mechanisms of the 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 Funding Program*. A limited number of supplemental research awards were also made to existing peer-reviewed projects.

External Advisory Committees

For most large consortia supported by the *Special Funding Program*, the 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 advice on allocation of resources and future directions for the consortia.

Solicitation of Innovative Ideas for Research

To solicit broader input for future research opportunities from the external scientific community as a whole, the NIDDK issued a Request for Information (RFI) in 2004 calling for innovative ideas to advance prevention, treatment, and cure of type 1 diabetes. Over 80 submissions were reviewed by the expert panel during the January 2005 *ad hoc* mid-course assessment meeting. The RFI is further described in Appendix 3.

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

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

COORDINATING TYPE 1 DIABETES RESEARCH EFFORTS

The research efforts supported by the *Special Funding Program* span a wide range of scientific areas. However, many of the large-scale research efforts have elements in common. For example, several research consortia are studying the genetics of type 1 diabetes or of specific complications; there are multiple consortia enrolling newborns in studies and following them to examine different environmental triggers. In order to maximize research progress, the NIH has facilitated coordination among research consortia with both overlapping and distinct interests. The NIH has organized meetings to facilitate broad coordination efforts as well as focused meetings of consortia that share common interests. Coordination helps to prevent duplicative work by promoting the sharing of resources and methodology as well as by facilitating cross-disciplinary research approaches. Furthermore, collaboration between researchers with distinct interests facilitates the pursuit of novel research directions.

In response to recommendations from *ad hoc* panels of external scientific and lay experts to enhance ongoing collaboration and coordination among the research consortia and networks supported by the *Special Funding Program*, the NIDDK established the Type 1 Diabetes Consortia Coordinating Committee. The Committee spearheaded the development of websites for type 1 diabetes patients (www.T1Diabetes.nih.gov/patient) and researchers (www.T1Diabetes.nih.gov/investigator). The website for patients describes clinical research studies recruiting patients and has contact information for the studies if patients are interested in enrolling. The website for investigators includes information on research consortia and clinical trial networks; research resources available to the broad scientific community; and information on research funding opportunities. These websites not only enhance patient recruitment efforts, but provide researchers with access to information, data, and protocols generated by the type 1 diabetes research consortia, thereby facilitating resource sharing and coordination. Additional information on coordination efforts is found in Appendix 2.

NIH Websites Dedicated to Research Supported by the *Special Funding Program*

For Patients: www.T1Diabetes.nih.gov/patient

For Scientists: www.T1Diabetes.nih.gov/investigator

Organization of the Evaluation Report

The following chapters of this Evaluation Report are framed around the six overarching Goals of type 1 diabetes research. Goal chapters include the following components:

Introduction and Background: Scientific background for each Goal, explaining the research challenges in the context of the Goal's medical importance for the lives of patients.

Evaluation of Major Research Consortia, Networks, and Resources: An evaluation of major research efforts that are supported under the Goal. These sections were developed so that all the information on a single Consortium is found under that Consortium, rather than cross-referencing other sections of the document. Therefore, information that is relevant to two different consortia will be repeated under each Consortium. This approach, although repetitive, was intentionally used so that complete information could be found in each Consortium's evaluation in a self-contained way.

Consortium evaluations include the following sections:

- *Program Description*: The value added by the Consortium in the context of the overall research portfolio.
- *Highlights of Progress*: Examples of the progress achieved to date.
- *Anticipated Outcomes*: Description of anticipated future progress and the impact that the research effort could have on the health of type 1 diabetes patients.
- *External Evaluation by Expert Panel*: Highlights of input received from an *ad hoc* meeting of external experts who performed a mid-course assessment of the *Special Funding Program* in January 2005.
- *Actions Taken in Response to Expert Panel Recommendations*: Responses to recommendations from the January 2005 *ad hoc* panel.
- *Ongoing Evaluation*: Descriptions of regular oversight mechanisms, such as reviews by external advisory panels.
- *Coordination with Other Research Efforts*: Examples of how the research Consortium or network collaborates and coordinates its efforts with other research efforts to maximize and synergize progress.
- *Administrative History*: Programmatic details, including years of duration and agencies that support the Consortium.

Evaluation of Investigator-Initiated Research: An evaluation of research conducted through investigator-initiated research projects supported by the *Special Funding Program*. This section includes:

- *Impact of Special Funding Program on Extramural Grantees*: Self-reported descriptions of the impact that the *Program* had on the careers and research programs of scientists who received a grant under the Goal.

Emerging Research Opportunities Resulting from the *Special Statutory Funding Program for Type 1 Diabetes Research*: Highlights of future research opportunities that have been fueled by the *Special Funding Program*. The emerging opportunities were identified by scientific and lay experts external to the NIH and the CDC during a recent type 1 diabetes research strategic planning process.