APPENDIX E

SUPPLEMENTAL MATERIAL ON SCIENTIFIC CONFERENCES, WORKSHOPS, AND MEETINGS RELEVANT TO TYPE 1 DIABETES AND ITS COMPLICATIONS

In addition to input that NIH and CDC receive at meetings specifically focused on research supported by the *Special Statutory Funding Program for Type 1 Diabetes Research* (*Special Diabetes Program* or *Program*) the agencies also obtain input at scientific conferences, workshops, and meetings that are relevant to type 1 diabetes and its complications. This input informs the planning process for use the *Special Diabetes Program*.

Research Conferences And Workshops

This listing provides information on scientific conferences and workshops with relevance to type 1 diabetes and its complications that have occurred since the development of the 2007 "*Evaluation Report*" on the *Special Statutory Funding Program for Type 1 Diabetes Research* (www.T1Diabetes.nih.gov/evaluation) through March 1, 2010. Please see Appendix 4 of the 2007 report for a list of previously held conferences and workshops.

Advances Toward Measuring Diabetic Retinopathy and Neuropathy: From the Bench to the Clinic and Back Again

April 4-5, 2007, sponsored by NIDDK

This conference focused on promoting advances in phenotyping diabetic retinopathy and neuropathy in animal models. Sessions included presentations describing clinical and animal studies in diabetic retinopathy and neuropathy; current methods for identifying, quantifying, and measuring these complications; and new advances in other scientific areas that may lead to improvements in phenotyping these conditions. A series of plenary talks and discussion sessions involving international leaders in their respective fields provided a forum for evaluating the current state of the art, and for identifying needs and research opportunities, which helped to inform a pilot and feasibility program sponsored by the Mouse Metabolic Phenotyping Centers.

Clinical Proteomics in Diabetes and its Complications

July 20, 2007, sponsored by NIDDK

The main focus of this workshop was the application of proteomic technologies to clinical research relevant to diabetes and its complications. Particular emphasis was placed on research aimed at the identification of novel protein markers of diabetes and pre-diabetes, but more generally the application of proteomics to clinical studies. This workshop also provided a venue to bring together researchers with expertise in proteomics with clinical researchers interested in applying this technology to problems related to diabetes and its complications, in order to foster new collaborations.

miRNA and Epigenetic Regulations of the Immune Response

December 11-12, 2008, sponsored by NIDDK, NIAID, NIAMS, JDRF

Epigenetics is the study of stable genetic modifications that result in changes in gene expression and function without a corresponding alteration in DNA sequence. microRNAs (miRNAs) are naturally occurring molecules that can specifically silence the expression of a gene or a family of genes by blocking translation of the proteins they encode; they are involved in the regulation of a wide variety of cellular functions. Research has shown that epigenetic mechanisms and miRNAs are critically involved in immune responses. The purpose of the workshop was to bring together researchers interested in studying epigenetic and miRNA-mediated regulation of T cell development and function and their role in the immune and autoimmune responses in diseases such as type 1 diabetes.

Non-adherence in Adolescents with Chronic Illness

September 22-23, 2008, sponsored by NIDDK

Adherence to a prescribed treatment regimen can be a matter of life and death for people with chronic diseases, including people with type 1 diabetes who must check blood glucose levels several times each day and administer insulin. When seemingly rigid requirements are ignored by the adolescent going through the sometimes difficult transition to adulthood, the results can be tragic. The purpose of this workshop was to explore the risk factors for non-adherence in adolescents with kidney disease, diabetes, or gastrointestinal disease and determine ways to promote better adherence.

Towards an Artificial Pancreas: An FDA-NIH-JDRF Workshop

July 21-22, 2008, sponsored by FDA, NIH, JDRF

This workshop provided a public forum for discussing the progress and remaining challenges in the development of closed-loop systems designed to regulate blood glucose control in people with diabetes. The workshop also provided stakeholders with information to accelerate the development of an artificial pancreas. Session topics included: state-of-the-art design of closed-loop glycemic control systems; results of recently conducted clinical trials; design of clinical trials, including how to define success and failures of a closed-loop system; algorithms and *in silico* models; engineering challenges; patient considerations; metabolic monitoring; and paths for developing a marketable closed-loop system. In December 2008, with support of the *Special Diabetes Program*, NIDDK issued solicitations to support research conducted by small businesses toward the development of new technologies for an artificial pancreas.

Imaging the Pancreatic Beta Cell, 4th Workshop

April 6-7, 2009, sponsored by NIDDK

The purpose of the workshop was to explore the considerable progress and foster collaborative research in the field of imaging the pancreatic islet cell mass, function, or inflammation in health and disease. The overall intended goal of the field is to develop clinically useful imaging approaches for monitoring the mass, function, and inflammation of endogenous and transplanted islets and beta cells in people with type 1 or type 2 diabetes and those at risk for these diseases, in order to understand the natural history of disease and to monitor therapy.

Inflammation, Immunity, and Metabolism at the Interface of Type 1 and Type 2 Diabetes

May 5-6, 2009, sponsored by NIDDK

Diabetes is a heterogeneous disease that is affected by a wide spectrum of inflammatory reactions. Whereas chronic and destructive inflammation of the pancreatic islets (insulitis) is a defining causal feature of type 1 diabetes, low-grade systemic inflammation and activation of innate immunity contribute to the pathogenesis of type 2 diabetes. Recent research suggests, however, that systemic inflammation and insulin resistance also may contribute to type 1 diabetes, and the reduced beta cell mass observed in people with type 2 diabetes may in part be due to insulitis and enhanced programmed cell death. The composition and texture of these innate and adaptive immune responses and the interface with metabolic disturbances determine the inflammatory phenotype observed in the diabetes syndromes. The purpose of the workshop was to discuss: (1) the reciprocal regulation of innate and adaptive immunity, highlighting a possibly significant role in the pathogenesis of diabetes; (2) insulin resistance and chronic activation of the innate

immune system in both major forms of diabetes, and the contribution to the metabolic derangement that is common to both diseases; (3) convergence of the inflammatory and autoimmune processes on the function and survival of the beta cell, and the differences and commonalities between type 1 and type 2 diabetes; and (4) lessons learned from the investigation of other chronic autoimmune/inflammatory disorders, with an emphasis on how this information might help investigators understand diabetes pathogenesis and potential treatments.

Typology of Diabetes in Children and Young Adults

September 16-17, 2009, sponsored by NIDDK, CDC

The purpose of the meeting was to review knowledge related to the typology of diabetes in childhood, with a particular focus on the potential overlap between type 1 and type 2 diabetes. The aims of the workshop were to: review the basis of current classification methods; identify areas of uncertainty in diabetes classification; explore new data related to the typology of diabetes in childhood; and identify new areas for research, with the goal of establishing improved paradigms for the classification of pediatric diabetes.

Next Generation Beta Cell Transplantation

November 9, 2009, sponsored by NIDDK, FDA, JDRF

The success of clinical islet transplantation as a curative therapy for type 1 diabetes has been hampered by concerns regarding durability of the transplanted islets, shortages of cadaver donor pancreata, the toxic effects of chronic immunosuppression, and recurrent autoimmunity. To hasten progress and circumvent these limitations, adult human beta cell replacement alternatives are being developed for clinical investigation using both porcine islets and differentiated human stem cells. In addition, encapsulation materials designed to shield transplanted cells from destructive immunity are being evaluated. At this workshop, regulatory authorities, academia, industry, and funding bodies convened to discuss the translational landscape and technology platforms required for the next generation of beta cell transplantation. It provided an interactive venue for identifying the hurdles that need to be overcome to achieve clinical success.

Diabetes Mellitus Interagency Coordinating Committee (DMICC) Meetings Relevant to Research on Type 1 Diabetes and Its Complications

This listing provides highlights of recent DMICC meetings relevant to type 1 diabetes that have occurred since the development of the 2007 "*Evaluation Report*" on the *Special Statutory Funding Program for Type 1 Diabetes Research* (www.T1Diabetes.nih.gov/evaluation) through March 1, 2010. For descriptions of previous DMICC meetings focused on the *Special Diabetes Program* or with relevance to type 1 diabetes, please see Appendices 3 and 4 of the 2007 report.

Opportunities for Diabetes Clinical Research

January 18-19, 2007

The purpose of this meeting was to solicit input from DMICC members and external experts on opportunities for clinical research on type 1 and type 2 diabetes. Many past and present NIH-supported diabetes clinical trials have been collaborative efforts involving more than one component of NIH, CDC, and FDA, for example. Thus, the DMICC provided an ideal venue to conduct a trans-NIH and trans-HHS discussion about opportunities for agencies to work together to conduct future clinical trials. The meeting also provided an opportunity for the Committee to obtain input from external experts in diabetes and diabetes clinical trials about key areas in which a well-designed trial could make a difference in the lives of people with diabetes.

The meeting began with a series of presentations to the Committee made by external experts on the current state-of-the science, as well as on unanswered questions related to the treatment and prevention of type 2 diabetes, the treatment of type 1 diabetes, and the treatment of older people with diabetes. After the presentations, the participants formed two break-out groups focused on the areas of diabetes management and diabetes prevention to discuss a list of possible trials in each area that had been distributed prior to the meeting. The list was developed based on external input obtained before the meeting. Related to treatment of type 1 diabetes, the participants discussed opportunities to develop a closed-loop insulin pump.

The second day of the meeting included presentations by a representative from each break-out group who summarized the group discussions for all meeting participants. Participants further discussed the trials and provided additional input on all of the possible trials. External input, such as input obtained at this meeting, is critically important to inform decisions made by NIDDK and other DMICC member organizations about future diabetes clinical trials supported by regular appropriations and the *Special Diabetes Program*.

DMICC Member Overview of Diabetes-Related Activities

September 20, 2007

This meeting provided an opportunity for DMICC member agencies, with emphasis on NIH Institutes and Centers, to share their plans for new and ongoing initiatives in diabetes research. In particular, members were encouraged to present research or programs that related to the Diabetes National Plan for Action (DNPA), developed under the auspices of the U.S. Department of Health and Human Services. DNPA, which was published in December 2004, focused on both type 1 diabetes and type 2 diabetes. It can be found at: http://aspe.hhs.gov/health/NDAP/NDAP04.pdf. The goals of DNPA are to increase national awareness

of diabetes and its impact and what can be done to prevent and manage the disease; reduce the prevalence of diabetes and its risk factors; promote improved detection, monitoring, and treatment; and coordinate public and private efforts and leverage existing resources. Topics in the DNPA include strategies for addressing type 1 and type 2 diabetes for individuals and families, schools, health care providers, employers, communities, health insurance providers, media, researchers and educators, and governments. The DMICC is integral to the federal response to the DNPA.

In addition to presentations on type 2 diabetes research from NIDDK, cardiovascular clinical trials from NHLBI, and diabetes surveillance and prevention and control programs from CDC, the Centers for Medicare & Medicaid Services presented information on physician-focused care improvement initiatives to improve quality and efficiency within the Medicare system. The Agency for Healthcare Research and Quality, Health Resources and Services Administration, and Indian Health Service (IHS) also provided updates of diabetes-related initiatives. With regard to type 1 diabetes, NICHD discussed TRIGR and DirecNet. The NIDDK also provided an update on the *Special Diabetes Program* and reminded DMICC members that both "*Advances and Emerging Opportunities in Type 1 Diabetes Research: A Strategic Plan*" and the "*Evaluation Report*" on the *Special Statutory Funding Program for Type 1 Diabetes Research* can be found on NIDDK's Web site. Additionally, future plans for an external evaluation meeting to evaluate major clinical projects were discussed.

Expanding Collaborations To Translate Research into Practice

April 1, 2008

The DMICC provides a venue for discussion of current and future projects conducted by member agencies. Presentation of projects helps members to identify opportunities for collaboration and allows them to make use of each other's expertise and resources. This meeting focused on fostering new collaborations among DMICC member agencies; speakers highlighted potential opportunities at their agency or institute which could involve the participation of other DMICC member agencies. For example, it was suggested that research agencies, such as NIH and CDC, could collaborate with service provider agencies, like IHS, on the design of research studies. Early input from service provider agencies could assist in the translation of research results and dissemination of information into practice.

The NIDDK provided an update on the *Special Statutory Funding Program for Type 1 Diabetes Research* including announcement of the extension of the *Program* and the *Special Diabetes Program for Indians* through FY 2009. In response to challenges to most effectively using funds in a single year with the typical NIH funding mechanisms, NIDDK, which oversees the *Special Diabetes Program*, received NIH approval for a new multiyear funding mechanism called the DP3. In FY 2009, this funding mechanism was used to solicit applications for research on the newly discovered type 1 diabetes genes and the mechanisms by which they cause susceptibility to disease. Finally, NIDDK has organized an evaluation meeting for April 2008 for an external panel of scientific experts to

review the clinical research efforts supported by the *Special Diabetes Program* and to guide future efforts of these ongoing programs.

Strategic Planning To Enhance Federal Diabetes Programs

August 11, 2008

This meeting included several different topics, including an update on the *Special Statutory Funding Program for Type 1 Diabetes Research* from NIDDK and an update on the *Special Diabetes Program for Indians* by IHS. Regarding the type 1 diabetes *Program*, NIDDK asked for input on plans for supporting type 1 diabetes research with the funds, which had recently been extended through FY 2011. To inform decisions, NIDDK will continue to be guided by the 2006 strategic plan for Type 1 Diabetes Research, by a new diabetes strategic planning effort (described below), and by input obtained from an external evaluation panel convened in April 2008 to assess the large clinical projects that were previously funded through the *Program*. A similar meeting is planned for 2009 to discuss pre-clinical projects; the input obtained at that meeting will also guide the use of the funds. The NIDDK also reported on recent initiatives made possible by the *Special Diabetes Program*, such as the Type 1 Diabetes Pathfinder Award to attract new talent to type 1 diabetes research.

The parallel *Special Diabetes Program for Indians* had also been recently extended through FY 2011. The IHS provided an update on plans, which included a tribal consultation concerning how best to utilize the funding to the benefit of American Indians with or at risk for diabetes. In general, communities are free to determine how to direct the funds to accomplish program goals and to expand the diabetes-fighting infrastructure they already have. Already, dramatic success has been achieved in reducing the diabetes burden in the American Indian community, as evidenced by the lowering of average hemoglobin A1c (HbA1c) levels. In the future, IHS will be working to identify the approaches that are most effective in realizing these health improvements so that successes can be replicated at other sites.

Another topic of discussion was an NIDDK proposal to begin a new diabetes strategic planning process under the auspices of the DMICC to help guide the federal investment in diabetes research. In 1999, the Congressionally-mandated Diabetes Research Working Group developed and published "*Conquering Diabetes: A Strategic Plan for the 21st Century*," a comprehensive diabetes research plan that has served as a blueprint for discovery. Since that time, major changes have taken place in the understanding of diabetes. At the same time, significant data have emerged on the national burden of pre-diabetes and on the alarming increase of diabetes in children. Thus, the Committee decided that the time was right to identify high-priority opportunities for diabetes research that can be accomplished in the next 5 to 10 years. The NIDDK, as chair of the DMICC, would spearhead the new strategic planning effort with broad external input. The plan is envisioned to guide NIH, other federal agencies, and the investigative and lay communities in their pursuit of the goal of conquering diabetes. Additionally, the new plan would help to guide type 1 diabetes research supported by the *Special Statutory Funding Program for Type 1 Diabetes Research*.

Federally Supported Diabetes-related National Education Programs

May 6, 2009

Presentations at this meeting were centered on diabetes-related national education programs. The NEI's National Eye Health Education Program ensures that vision is a public health priority through the translation of eye and vision research into public and professional education programs and includes diabetic eye disease as one of its main program areas. The NIDDK and CDC's National Diabetes Education Program disseminates research results through its two campaigns, "*Control Your Diabetes. For Life*," based on the findings of the Diabetes Control and Complications Trial, and "*Small Steps. Big Rewards. Prevent type 2 Diabetes*," which translates the results of the Diabetes Prevention Program clinical trial into materials for health care providers and patients. The NIDDK's National Kidney Disease Education Program aims to reduce the morbidity and mortality caused by kidney disease and its complications through its campaigns. The NLM's Medline Plus is a resource for health information, including diabetes-related information, for patients, family, friends, and professionals. The meetings also included discussions of education activities from providers such as Veterans Health Administration and IHS.