APPENDIX 2: TYPE 1 DIABETES CONSORTIA COORDINATION

This Appendix describes the numerous collaborative efforts among the type 1 diabetes consortia and networks that have occurred or are ongoing. It also describes the steps that the NIH and CDC have taken to enhance coordination and collaboration among research programs with related and distinct interests.

TYPE 1 DIABETES CONSORTIA COORDINATING COMMITTEE

At an* ad hoc *planning and evaluation meeting convened in January 2005, on the* Special Statutory Funding Program for Type 1 Diabetes Research *(see Appendix 3), an expert panel strongly recommended that the NIH and CDC extend and capitalize on existing research efforts by maximizing connections among research groups with both related and distinct interests. The panel recommended that strong existing coordination across consortia be further enhanced to synergize research efforts. These interactions should not be limited to consortia with overlapping interests. Collaboration between researchers with distinct interests could facilitate the pursuit of novel research directions. In addition, increased coordination can prevent duplicative work by promoting the sharing of resources and methodology, as well as by facilitating cross-disciplinary research approaches.

In 2003, the NIDDK established a Type 1 Diabetes Consortia Coordinating Committee, which consists of representatives from multiple research consortia, and networks to enhance ongoing collaboration and coordination among the research consortia and networks supported by the *Special Funding Program*. The charge of this Committee has been to coordinate issues of recruitment and enrollment; standardize assays, phenotyping, and consents; promote the use of clinical populations for development and validation of assays for immune and metabolic monitoring; and coordinate bioinformatics issues and ancillary studies.

This Committee met multiple times via teleconference and once in person to discuss issues of coordination and collaboration. The Committee also spearheaded the development of a website to aid type 1 diabetes patient recruitment efforts (www.T1Diabetes.nih.gov/patient), as well as a website to facilitate resource sharing across consortia (www.T1Diabetes.nih.gov/investigator).

EXAMPLES OF MEETINGS TO FACILITATE COLLABORATION AND COORDINATION AMONG TYPE 1 DIABETES CONSORTIA

Type 1 Diabetes Consortia Coordinating Committee Meeting

May 15, 2005, Boston, MA

The expert panel at the January 2005, meeting on the *Special Funding Program* recommended a face-to-face meeting of the Type 1 Diabetes Consortia Coordinating Committee to explore novel avenues for collaboration. In response to this recommendation, the NIDDK convened a meeting of the Committee in association with the annual meeting of the Federation of Clinical Immunology Societies (FOCIS) in Boston. Over 20 representatives from consortia and networks supported by the *Special Funding Program* attended the meeting and discussed ongoing research efforts and areas for enhanced collaboration.

One of the recommendations emanating from this meeting was for the NIDDK to expand its website on the *Special Funding Program* so that it could be used as a resource for sharing across consortia. The Committee recommended that the following types of information and resources be posted on the website for public dissemination: organization charts showing committees and committee charges; consortia policies (e.g., publications and presentations, ancillary studies, quality control, intellectual property); opportunities available through consortia for new investigators; case report forms; standardized vocabularies; research resources (e.g., antibodies, animal models, cell lines, microarrays). In addition, because many of the consortia have data, biosamples, and protocols that are available to share with the broader research community, the Committee strongly recommended that this material also be posted on the NIDDK's website.

In response to this recommendation, the NIDDK launched an expanded public website dedicated to research supported by the *Special Funding Program* in February 2006 (www.T1Diabetes.nih.gov). The website includes information for both researchers and patients/family members. Patients can search for clinical research studies that are enrolling participants; read brief descriptions of the studies to help them determine if they are eligible; and find out who to call if they are interested in enrolling (www.T1Diabetes.nih.gov/patient). Investigators can access current funding opportunities; descriptions of ongoing research consortia and networks; information on research resources (such as those described above); and descriptions of upcoming and past meetings relevant to type 1 diabetes research (www.T1Diabetes.nih.gov/investigator). The public website permits investigators in the broad scientific community to access resources, data, and materials generated by the research consortia, thereby maximizing the investment in these research efforts.

Coordination of Type 1 Diabetes Studies Involving Newborns

May 15, 2005, Boston, MA

Prior to the larger type 1 diabetes Committee meeting (described above), representatives from consortia studying newborns (TEDDY, TRIGR, and TrialNet) met to discuss opportunities for enhancing coordination and collaboration. The participants discussed how to obtain the most useful information when looking at these studies as a group. Common data variables across the studies and future analytic strategies were also discussed.

Genetics of Diabetes and Its Complications: Consortia Meeting

July 20, 2005, Bethesda, MD
Meeting Summary: www.niddk.nih.gov/fund/other/genetics-diabetes/Workshopexecsummary.pdf

The expert panel at the January 2005 meeting on the *Special Funding Program* strongly encouraged enhanced coordination among the four major genetics consortia supported by

the *Special Program*: Family Investigation of Nephropathy and Diabetes (FIND), Genetics of Kidneys in Diabetes Study (GoKinD), Epidemiology of Diabetes Interventions and Complications Study (EDIC), and Type 1 Diabetes Genetics Consortium (T1DGC). In response to this recommendation, the NIDDK convened a meeting with representatives from all four genetics consortia. At the meeting, recommendations were developed for facilitating interactions among the studies and for future analytic strategies. The importance of interactions between consortia was emphasized to enhance the value of the individual studies that aim to develop new strategies for prevention and treatment to alleviate the suffering from type 1 diabetes.

Table A3: "At a Glance" Matrix of Type 1 Diabetes Consortia Coordination Activities

Red-shaded squares indicate collaboration between the consortia	AMDCC	Prevention Centers	BCBC	CIT	CITR	EDIC	FIND	GoKinD	ITN	Immunobiology of Xenotransplantation	ICRs	Mouse Repositories	NHPCSG	SEARCH	Standardization Programs	TEDDY	TRIGR	T1DGC	T1D-RAID	TrialNet
Animal Models of Diabetic Complications Consortium (AMDCC)	■					■	■	■												
Cooperative Study Group for Autoimmune Disease Prevention		■									■									
Beta Cell Biology Consortium (BCBC)			■								■	■								
Clinical Islet Transplantation Consortium (CIT)				■	■				■		■		■			■		■	■	■
Collaborative Islet Transplant Registry (CITR)				■	■				■		■									
Epidemiology of Diabetes Interventions and Complications (EDIC)	■					■	■	■							■			■		
Family Investigation of Nephropathy and Diabetes (FIND)	■					■	■	■										■		
Genetics of Kidneys and Diabetes Study (GoKinD)	■					■	■	■										■		
Immune Tolerance Network (ITN)				■	■				■				■			■	■		■	■
Immunobiology of Xenotransplantation Cooperative Research Program										■			■							
Islet Cell Resource Centers (ICRs)		■	■	■	■			■	■		■			■			■		■	
Mouse Repositories			■									■								
NHP Transplantation Tolerance Cooperative Study Group (NHPCSG)				■					■	■			■				■		■	
SEARCH for Diabetes in Youth											■			■	■	■		■		■
Standardization Programs (C-peptide, HbA1c, DASP)						■								■	■	■		■		■
The Environmental Determinants of Diabetes in the Young (TEDDY)				■					■					■	■	■	■	■		■
Trial to Reduce IDDM in the Genetically At Risk (TRIGR)									■					■		■	■			■
Type 1 Diabetes Genetics Consortium (T1DGC)				■		■	■	■						■	■	■		■		■
Type 1 Diabetes-Rapid Access to Intervention Development (T1D-RAID)				■					■		■		■						■	■
Type 1 Diabetes TrialNet (TrialNet)				■					■					■	■	■	■	■	■	■

HIGHLIGHTS OF TYPE 1 DIABETES CONSORTIA COLLABORATION AND COORDINATION

The following section highlights the ongoing collaborations and coordination efforts among type 1 diabetes research consortia and networks supported by the *Special Funding Program* (please see Appendix 7 for a list of program abbreviations and websites). Because this section is organized by consortium, collaborative efforts appear more than once. For example, collaborations between TEDDY and TRIGR are listed under each consortium. A matrix (Table A3) provides a concise analysis of these collaborations.

Animal Models of Diabetic Complications Consortium (AMDCC)

FIND, GoKinD, and EDIC: The AMDCC semi-annual meeting on March 22-24, 2005, included presentations by representatives from FIND, GoKinD, and EDIC to initiate collaborations such that data originating from the genetics consortia will direct the creation of new animal models by the AMDCC, which will, in turn, validate the findings of the genetics consortia.

Mouse Metabolic Phenotyping Centers (MMPCs): The AMDCC and the MMPCs have formed a new partnership. The mission of the MMPCs is to conduct detailed metabolic phenotyping of genetically-altered mice. Thus, it is a logical extension of both consortia to have all mice generated by the AMDCC shipped to MMPC facilities. This close partnership will not only allow a number of organizational efficiencies, but more importantly, will make certain that all animals generated by the AMDCC are fully phenotyped across each relevant metabolic and diabetic complication.

Cooperative Study Group for Autoimmune Disease Prevention (Prevention Centers)

ICRs: Investigators participating in the Prevention Centers receive islets for basic research through the ICR basic science human islet distribution program.

Beta Cell Biology Consortium (BCBC)

ICRs:

- BCBC website announces availability of human islets for basic research through the ICRs (www.betacell.org/news/index.php?view=41).
- BCBC investigators use human islets obtained through the ICR basic science human islet distribution program.
- Data collected from BCBC investigators using ICR samples are reposited with the informatics coordination center of the ICRs.
- PancChips made available for potential ICR quality assessments.
- Provision of islets for BCBC investigators pursuing studies under RFA-DK03-021 (Pilot and Feasibility Program in Human Islet Biology).

Mouse Repositories:

- Mouse strains developed by BCBC investigators are available through NCRR-funded repositories (T1DR and the Mutant Mouse Regional Resource Centers [MMRRC]), which provides greater access to these resources by the scientific community.
- BCBC mouse database design based on International Mouse Strain Resource (IMSR) model used by The Jackson Laboratory's repositories, including T1DR and MMRRC.
- BCBC mouse database designed to directly interface with IMSR, T1DR, and MMRRC.

Clinical Islet Transplantation Consortium (CIT)

CITR: CITR is planning to list all active islet transplantation protocols on their website. CIT plans to use this information as part of their informed consent process for enrollees.

CITR and ICRs:

- On-site data review of transplantation centers is performed by the CITR and is provided to the ICRs. These data include determination of islet quality and collection of transplant outcome information.
- CIT investigators who use ICR resources must agree to place their clinical study data in the CITR.
- Data sharing agreements have been developed between CIT, CITR, and the ICRs. These agreements include use of shared data dictionaries and source verification of data by CIT clinical site monitors with corrections transmitted to all participants. Monthly teleconferences ensure communication about maintaining up-to-date information. This effort will minimize redundancy in data collection and will enhance its dissemination.

ICRs: Clinical grade islets are provided for islet transplantation trials. CIT investigators receive islets for basic research through the ICR basic science human islet distribution program.

ITN: CIT and ITN are sharing expertise and coordinating efforts in the planning of immunologic assays in CIT trials. ITN core labs will be used for selected assays in CIT trials.

NHPCSG: Cross-representation of investigators between NHPCSG and CIT led to collaborative design of pre-clinical studies and pre-clinical testing of therapeutics in non-human primates.

NHPCSG and ITN: CIT, ITN, and NHPCSG are interested in utilizing similar reagents for use as immune modulators for the treatment of type 1 diabetes or for islet transplantation.

TEDDY, T1DGC, and TrialNet: Collaborative media effort between TEDDY, T1DGC, TrialNet, and CIT. Media needs of all of these groups are being jointly handled by a single media contract to optimize coordination of type 1 diabetes clinical trials.

T1D-RAID: Provision of novel reagents for testing to reduce islet autoimmune destruction after transplantation.

Collaborative Islet Transplant Registry (CITR)

ICRs:

- Monthly conference calls are held between CITR and the ICRs to discuss status of initiatives and any logistical concern between the two projects.
- Investigators who use ICRs must agree to place their clinical study data in CITR.

ICRs and CIT:

- On-site data review of transplantation centers is performed by CITR and is provided to the ICRs. These data include determination of islet quality and collection of transplant outcome information.
- Data sharing agreements have been developed between CIT, CITR, and the ICRs. These agreements include use of shared data dictionaries and source verification of data by CIT clinical site monitors with corrections transmitted to all participants. Monthly teleconferences ensure communication about maintaining up-to-date information. This effort will minimize redundancy in data collection and will enhance its dissemination.

ITN: Results of pertinent trials are archived.

Epidemiology of Diabetes Interventions and Complications (EDIC)

AMDCC: The AMDCC semi-annual meeting on March 22-24, 2005, included presentations by representatives from FIND, GoKinD, and EDIC to initiate collaborations such that data originating from the genetics consortia will direct the creation of new animal models by the AMDCC, which will, in turn, validate the findings of the genetics consortia.

FIND and GoKinD:

- A series of ongoing database coordination meetings between EDIC, FIND, and GoKinD is seeking to standardize patient consent forms and permit investigators to search data across databases.
- The NIDDK is coordinating an integrated database of the parameters in the genetics studies of kidney disease in diabetes, which will include EDIC, GoKinD, and FIND.

FIND, GoKinD, and T1DGC: In July 2005, consortia supported by the *Special Funding Program* that study genetics (GoKinD, FIND, EDIC) participated in a meeting with T1DGC. In response to recommendations from this meeting, new initiatives are being developed to coordinate future efforts among the studies. A summary of the meeting can be accessed on the NIDDK's website (www.niddk.nih.gov/fund/other/genetics-diabetes/Workshopexecsummary.pdf).

Standardization Programs: The National Glycohemoglobin Standardization Program certifies clinical laboratories to use the standard set by DCCT/EDIC for measurements of HbA1c.

Family Investigation of Nephropathy and Diabetes (FIND)

AMDCC: The AMDCC semi-annual meeting on March 22-24, 2005, included presentations by representatives from FIND, GoKinD, and EDIC to initiate collaborations such that data originating from the genetics consortia will direct the creation of new animal models by the AMDCC, which will, in turn, validate the findings of the genetics consortia.

GoKinD, EDIC, and T1DGC:

- In July 2005, consortia supported by the *Special Funding Program* that study genetics (GoKinD, FIND, EDIC) participated in a meeting with T1DGC. In response to recommendations from this meeting, new initiatives are being developed to coordinate future efforts among the studies. A summary of the meeting can be accessed on the NIDDK's website (www.niddk.nih.gov/fund/other/genetics-diabetes/Workshopexecsummary.pdf).
- FIND Steering Committee meetings from the past 4 years have frequently included presentations by GoKinD and EDIC study representatives.
- The NIDDK is coordinating an integrated database of the parameters in the genetic studies of kidney disease in diabetes, which will include EDIC, GoKinD, and FIND.
- A series of ongoing database coordination meetings between EDIC, FIND, and GoKinD is seeking to standardize patient consent forms and permit investigators to search data across databases.

GoKinD: Key personnel from FIND serve in official advisory capacities for GoKinD.

Genetics of Kidneys in Diabetes Study (GoKinD)

AMDCC: The AMDCC semi-annual meeting on March 22-24, 2005, included presentations by representatives from FIND, GoKinD, and EDIC to initiate collaborations such that data originating from the genetics consortia will direct the creation of new animal models by the AMDCC, which will, in turn, validate the findings of the genetics consortia.

FIND: There has been a coordination conference call with FIND representatives.

FIND and EDIC: A series of ongoing database coordination meetings between EDIC, FIND, and GoKinD is seeking to standardize patient consent forms and permit investigators to search data across databases.

FIND, EDIC, and T1DGC:

- In July 2005, consortia supported by the *Special Funding Program* that study genetics (GoKinD, FIND, EDIC) participated in a meeting with T1DGC. In response to recommendations from this meeting, new initiatives are being developed to coordinate future efforts among the studies. A summary of the meeting can be accessed on the NIDDK's website (www.niddk.nih.gov/fund/other/genetics-diabetes/Workshopexecsummary.pdf.
- The NIDDK is coordinating an integrated database of the parameters in the genetic studies of kidney disease in diabetes, which will include EDIC, GoKinD, and FIND.

ICRs: GoKinD investigators receive islets for basic research through the ICR basic science human islet distribution program.

Immune Tolerance Network (ITN)

CIT: CIT and ITN are sharing expertise and coordinating efforts in the planning of immunologic assays in CIT trials. ITN core labs will be used for selected assays in CIT trials.

CITR: Results of trials archived with CITR.

ICRs: Islet sources for multicentered clinical study sites utilizing the Edmonton Protocol. ITN investigators receive islets for basic research through the ICR basic science human islet distribution program.

NHPCSG:

- Cross-representation of investigators between the NHPCSG and ITN.
- ITN priorities for pre-clinical testing of new therapeutics considered in evaluating Opportunities Pool applications. Several of the high priority strategies are currently funded as pilot projects.
- NIAID program staff attend ITN transplantation mechanistic assay meetings to represent NHPCSG interests.

NHPCSG and CIT: CIT, ITN, and NHPCSG are interested in utilizing similar reagents for use as immune modulators for the treatment of type 1 diabetes or for islet transplantation.

TEDDY: TEDDY had several discussions with ITN and has adopted the ITN standard for messenger RNA (mRNA) extraction.

T1D-RAID: Provision and pre-clinical testing of novel reagents.

TrialNet:

- ITN collaborates with TrialNet on the development and implementation of protocols in type 1 diabetes, where both parties agree it is beneficial. The studies in which TrialNet and ITN collaborate include: (1) Natural History Study; (2) Mycophenolate Mofetil – Daclizumab (MMF/DZB); (3) T Cell Validation Study; and (4) The Effects of Rituximab on the Progression of Type 1 Diabetes in New Onset Patients.
- The ITN supplies collection kits and training to laboratories for isolating peripheral blood mononuclear cells (PBMCs).
- ITN provides RNA isolation on batched specimens.
- ITN coordinates the transfer of frozen PBMCs, RNA, and plasma specimens to the NIDDK Repository from laboratories for studies, as applicable.

- ITN coordinates the collection of blood and the transfer of samples from the clinical sites to the Flow Core Laboratory for analysis.
- Research staff from ITN and TrialNet collaborate on joint studies, communicating daily and convening 1 hour weekly to discuss critical site/study/technical issues. They also use this time to update each other regarding each Center's status in ongoing studies.
- ITN and the TrialNet Coordinating Center participate in monthly meetings where key study members discuss the status and any pending problems or issues with ongoing studies.
- ITN and TrialNet use a common Data and Safety Monitoring Board.
- Protocols potentially of interest to both TrialNet and ITN are considered by both Networks with the goal of joint sponsorship.
- TrialNet and ITN did a joint mailing (with the help of JDRF, New England chapter) to introduce/advertise the TrialNet Natural History Study and the ITN Insulin Study.

TRIGR: There is coordination of T cell assays being done by TRIGR and ITN.

Immunobiology of Xenotransplantation Cooperative Research Program

NHPCSG:

- Cross representation between programs, both at the Principal Investigator (PI) and Program Director levels.
- Plans are in place for sharing of reagents, techniques, and protocols that may be relevant to the two programs.

Islet Cell Resource Centers (ICRs)

Multiple Consortia: Investigators from the following consortia supported by the *Special Funding Program* receive islets for basic research through the ICR basic science human islet distribution program: Cooperative Study Group for Autoimmune Disease Prevention, BCBC, CIT, GoKinD, ITN, and SEARCH.

BCBC:

- BCBC website announces availability of human islets for research from ICRs (www.betacell.org/news/index.php?view=41).
- Data collected from BCBC investigators using ICR samples are reposited with the informatics coordination center of the ICRs.
- PancChips made available for potential ICR quality assessments.
- Provision of islets for BCBC investigators pursuing studies under RFA-DK03-021 (Pilot and Feasibility Program in Human Islet Biology).

CIT: Clinical grade islets are provided for CIT transplantation trials.

CITR: Investigators who use ICR resources must agree to place their clinical study data in the CITR.

CIT and CITR:

- On-site data review of transplantation centers is performed by the CITR and is provided to the ICRs. These data include determination of islet quality and collection of transplant outcome information.
- Data sharing agreements have been developed between CIT, CITR, and the ICRs. These agreements include use of shared data dictionaries and source verification of data by CIT clinical site monitors with corrections transmitted to all participants. Monthly teleconferences ensure

communication about maintaining up-to-date information. This effort will minimize redundancy in data collection and will enhance its dissemination.

ITN: Islet source for multicenter clinical studies utilizing the Edmonton Protocol.

T1D-RAID: Provision of novel reagents as media additives to improve function and survival of islets in culture.

Mouse Repositories: Type 1 Diabetes Mouse Repository (T1DR) and Mutant Mouse Regional Resource Centers (MMRRC)

BCBC:

- Mouse strains developed by BCBC investigators are available through NCRR-funded repositories (T1DR and MMRRC), which provides greater access to these resources by the scientific community.
- BCBC mouse database design based on IMSR model used by the Jackson Laboratory's repositories, including T1DR and MMRRC.
- BCBC mouse database designed to directly interface with IMSR, T1DR, and MMRRC.

Non Human Primate Transplantation Tolerance Cooperative Study Group (NHPCSG)

CIT: Cross-representation of investigators between NHPCSG and CIT led to collaborative design of pre-clinical studies and pre-clinical testing of therapeutics in non-human primates.

Immunobiology of Xenotransplantation Cooperative Research Program:

- Cross representation between programs, both at the PI and Program Director levels.
- Plans are in place for sharing of reagents, techniques, and protocols that may be relevant to the two programs.

ITN:

- Cross-representation of investigators between the ITN and NHPCSG.
- ITN priorities for pre-clinical testing of new therapeutics considered in evaluating Opportunities Pool applications. Several of the ITN high priority strategies are currently funded as pilot projects.
- NIAID program staff attend ITN transplantation mechanistic assay meetings to represent NHPCSG interests.

ITN and CIT: CIT, ITN and NHPCSG are interested in utilizing similar reagents for use as immune modulators for the treatment of type 1 diabetes or for islet transplantation.

T1D-RAID: Provision of novel reagents and potential for pre-clinical testing.

Search for Diabetes in Youth (SEARCH)

ICRs: SEARCH investigators receive islets for basic research studies through the ICR basic science human islet distribution program.

T1DGC: Four SEARCH sites (Cincinnati, Southern California, Seattle, and South Carolina) are participating as recruitment centers for the T1DGC North American Network. Investigators and staff from the SEARCH sites have attended T1DGC training sessions (December 2003) and the annual T1DGC North American Network meeting (January 2005).

TEDDY:

- Investigators at the Denver SEARCH site are directly collaborating with TEDDY, or are PIs of TEDDY.
- The PIs of the South Carolina SEARCH site is an EAB member of the TEDDY study.

TrialNet:

- A TrialNet researcher has provided a coordinating function by leading development of the TrialNet protocol to compare C-peptide stimulation tests and assess variability of test results, participating on the C-peptide measurement standardization working group, and working with SEARCH investigators to analyze SEARCH C-peptide data.
- In Colorado and in South Carolina, SEARCH is collaborating with TrialNet by helping them recruit eligible cases. They are informing SEARCH participants about TrialNet and referring them to the TrialNet coordinator.
- A SEARCH investigator is establishing an affiliate site with the TrialNet University of Florida Center. SEARCH will serve as one of the recruitment sources for this affiliate site.

TrialNet and T1DGC: The PI for the T1DGC North American Network provided coordination between TrialNet, SEARCH, and T1DGC through her involvement in all three studies. Procedures across the three studies were standardized to the extent possible.

TRIGR:

- The Kaiser Permanente Southern California SEARCH site is participating in the TRIGR study. Institutional Review Board (IRB)-approved passive recruitment site: identify physicians and other health care providers (e.g., pediatric endocrinologists, endocrinologists, perinatalogists, obstetricians) who would work with families eligible for the study, provide education/information about the study to these providers, put study recruitment brochures and flyers in their waiting rooms, answer questions from potential participants who then self-refer to TRIGR's UCLA study site.
- The Denver SEARCH site is distributing brochures about TRIGR.

Standardization Programs

Diabetes Autoantibody Standardization Program (DASP)

SEARCH: The SEARCH central laboratory at the University of Washington, Seattle, is participating in DASP.

TEDDY, T1DGC, and TrialNet: DASP interacts with the TEDDY, T1DGC, and TrialNet autoantibody labs, by providing laboratory materials and proficiency testing to facilitate their autoantibody measurements.

Type 1 Diabetes Proteomics Investigators: DASP is working with NIDDK-supported investigators studying proteomics and type 1 diabetes, and collaborating with Pacific Northwest Laboratories, to find new biomarkers to improve diagnosis of and prediction of risk for this disease. This collaborative project will use blood samples collected by DASP from newly-diagnosed type 1 diabetes patients and healthy people. The samples will be analyzed with proteomic and metabolomic technologies; that is, large-scale profiling and characterization of the component proteins and small molecules, respectively. Differences identified between samples from patients and healthy individuals can be further investigated for potential predictive or diagnostic value.

C-peptide Standardization

C-peptide Standardization Committee: Performed studies at the Diabetes Diagnostic Laboratory, University of Missouri, for the C-peptide Standardization Committee to evaluate C-peptide stability.

TrialNet:

- The Diabetes Diagnostic Laboratory, University of Missouri, conducted an international round-robin comparison of C-peptide assays, which included two labs from TrialNet. The results from the comparison study illustrated the need to identify and minimize the major sources of variation in C-peptide measurements in multicenter, multi-laboratory clinical studies.
- A TrialNet investigator participates on the C-peptide measurement standardization working group.

HbA1c Standardization

EDIC and TrialNet: EDIC, TrialNet, and other clinical studies supported by the *Special Funding Program* use laboratories certified through the program.

The Environmental Determinants of Diabetes in the Young (TEDDY)

ITN: TEDDY had several discussions with ITN and has adopted the ITN standard for mRNA extraction.

NIDDK Central Repositories: TEDDY is repositing biological samples and data into the Repository and will make the material available to the broad scientific community. The NIDDK has developed an initiative to support investigator-initiated ancillary studies to ongoing studies, including TEDDY (PAR-06-216, Ancillary Studies to Major Ongoing NIDDK and NHLBI Clinical Research Studies).

SEARCH:

- Investigators at the Denver SEARCH site are directly collaborating with TEDDY or are PIs of TEDDY.
- The PI of the South Carolina SEARCH site is an External Advisory Board member of the TEDDY study.

Standardization Programs: DASP interacts with the TEDDY autoantibody lab by providing laboratory materials and proficiency testing to facilitate laboratory measurements.

TrialNet:

- The central human leukocyte antigen (HLA) laboratory for TEDDY is the same laboratory that provides the HLA strips to the central HLA laboratory for TrialNet. Both laboratories perform HLA typing using the same methodology. This coordination will permit direct comparison between results obtained in both studies.
- TEDDY has shared HLA screening procedures, data forms, and parts of the Manual of Operation concerning follow-up of high-risk children with TrialNet investigators during the development of the Nutritional Intervention To Prevent (NIP) Type 1 Diabetes Study. Investigators in the two studies have avoided direct competition for eligible participants through concerted action to define exclusive study geographic areas.

TrialNet and T1DGC:

- TEDDY, TrialNet, and T1DGC share the same laboratories for measurement of autoantibodies (IA-2 and GAD65). This fact permitted coordination of efforts to bring the laboratories together in a common protocol and quality control effort. This coordination will permit direct comparison between TEDDY, T1DGC, and TrialNet data.
- The central HLA laboratory for TEDDY and the North American network HLA laboratory for T1DGC are the same. The rest of the networks in T1DGC are performing HLA in an identical manner. TrialNet gets the HLA strips from the same laboratory as TEDDY and T1DGC. This will permit direct comparison between results obtained in TEDDY, T1DGC, and TrialNet.

TrialNet, T1DGC, and CIT: Collaborative media effort between TEDDY, T1DGC, TrialNet, and CIT. Media needs of all of these groups are being jointly handled by a single media contract to optimize coordination of type 1 diabetes clinical trials.

TRIGR:

- TEDDY and TRIGR share the same Data Coordinating Center, which has resulted in implementation of similar standards in data collection, entry, and management quality control and analyses for both studies.
- TEDDY and TRIGR have implemented similar standards in data collection and entry, thus permitting direct comparison between results obtained in each study.
- The same investigator is the Director of the HLA screening laboratory for the Germany and Finland sites in TEDDY and for all European sites in TRIGR. This will permit the direct comparison between HLA results in the studies.

TRIGR and TrialNet: TEDDY participated in a coordination meeting in May 2005, with investigators from TRIGR and TrialNet's NIP Diabetes Study to discuss how to obtain the most useful information when looking at these studies as a group. Common data variables across the studies and future analytic strategies were discussed.

Trial To Reduce IDDM in the Genetically at Risk (TRIGR)

ITN: There is coordination of T cell assays being done by TRIGR and ITN.

SEARCH:

- The Kaiser Permanente Southern California SEARCH site is participating in the TRIGR study. IRB-approved passive recruitment site: identify physicians and other health care providers (e.g., pediatric endocrinologists, endocrinologists, perinatalogists, obstetricians) that would work with families eligible for the study, provide education/information about the study to these providers, put study recruitment brochures and flyers in their waiting rooms, answer questions from potential participants who then self-refer to TRIGR's UCLA study site.
- The Denver SEARCH site is distributing brochures about TRIGR.

TEDDY:

- TEDDY and TRIGR share the same Data Coordinating Center, which has resulted in implementation of similar standards in data collection, entry, and management quality control and analyses for both studies.
- TEDDY and TRIGR have implemented similar standards in data collection and entry, thus permitting direct comparison between results obtained in each study.
- The same investigator is the Director of the HLA screening laboratory for the Germany and Finland sites in TEDDY and for all European sites in TRIGR. This will permit the direct comparison between results for HLA.

TEDDY and TrialNet: TRIGR participated in a coordination meeting in May 2005, with investigators from TEDDY and TrialNet to discuss how to obtain the most useful information when looking at these studies as a group. Common data variables across the studies and future analytic strategies were discussed.

Type 1 Diabetes Genetics Consortium (T1DGC)

GoKinD, EDIC, and FIND: In July 2005, consortia supported by the *Special Funding Program* that study genetics (GoKinD, FIND, EDIC) participated in a meeting with T1DGC. In response to recommendations from this meeting, new initiatives are being developed to coordinate future efforts among the studies. A summary of the meeting can be accessed on the

NIDDK's website (www.niddk.nih.gov/fund/other/genetics-diabetes/Workshopexecsummary.pdf).

NIDDK Central Repositories: T1DGC is repositing samples and data in all three Repositories (Biosamples, Genetics, and Data).

SEARCH: Four SEARCH sites are participating as recruitment centers for the T1DGC North American Network. Investigators and staff from the SEARCH sites have attended T1DGC training sessions (December 2003) and the annual T1DGC North American Network meeting (January 2005).

Standardization Programs: DASP interacts with the T1DGC autoantibody lab by providing laboratory materials and proficiency testing to facilitate laboratory measurements.

TrialNet:

- All 14 TrialNet centers participate as recruitment centers for the T1DGC North American Network. Investigators and staff from the TrialNet sites have attended T1DGC training sessions (December 2003) and the annual T1DGC North American Network meeting (January 2005).
- The Deputy Director and Project Manager at the T1DGC Coordinating Center participated in conference calls to assist the TrialNet Coordinating Center staff in establishing their international sites. A comprehensive list of issues and topics related to implementing international data collection formed the basis of these calls. As requested by the TrialNet Coordinating Center, the T1DGC Coordinating Center provided a study form related to destruction of samples and provided the ethnicity categories adopted for use in the T1DGC.

TrialNet and SEARCH: The PI for the T1DGC North American Network provided coordination between TrialNet, SEARCH, and T1DGC through her involvement in all three studies. Procedures across the three studies were standardized to the extent possible.

TrialNet and TEDDY: T1DGC, TrialNet, and TEDDY share the same laboratories for measurement of autoantibodies (IA-2 and GAD65). This fact permitted coordination of efforts to bring the laboratories together in a common protocol and quality control effort. This coordination will permit direct comparison between results obtained in each study.

TrialNet, TEDDY, and CIT: Collaborative media effort between TEDDY, T1DGC, TrialNet, and CIT. Media needs of all of these groups are being jointly handled by a single media contract to optimize coordination of type 1 diabetes clinical trials.

Type 1 Diabetes—Rapid Access to Intervention Development (T1D-RAID)

CIT: T1D-RAID is supporting the manufacture of lisofylline, which will be tested in the CIT to determine if it can reduce islet autoimmune destruction after transplantation.

ICRs: Provision of novel reagents as media additives to improve function and prolong survival of islets in culture.

ITN and TrialNet: T1D-RAID is assisting in the manufacture of hOKT3-Gamma-1 (Ala-Ala) monoclonal antibody, which will be tested in a clinical trial conducted by ITN to determine if it can halt further destruction of beta cells in new-onset type 1 diabetes patients. The agent is also to be used in a possible TrialNet study.

NHPCSG: Provision of novel reagents and potential for preclinical testing.

Type 1 Diabetes TrialNet (TrialNet)

ICRs: TrialNet investigators receive islets for basic research through the ICR basic science human islet distribution program.

ITN:

- ITN collaborates with TrialNet on the development and implementation of protocols in type 1 diabetes when both parties agree it is beneficial. The studies in which TrialNet and ITN collaborate include: (1) Natural History Study; (2) Mycophenolate Mofetil – Daclizumab (MMF/DZB); (3) T Cell Validation Study; and (4) The Effects of Rituximab on the Progression of Type 1 Diabetes in New Onset Patients.
- The ITN supplies collection kits and training to laboratories for isolating PBMCs.
- ITN provides RNA isolation on batched specimens.
- Coordinates the transfer of frozen PBMCs, RNA, and plasma specimens to the NIDDK Repository from laboratories for studies, as applicable.
- Coordinates the collection of blood and the transfer of samples from the clinical sites to the Flow Core Laboratory for analysis.
- Research staff from ITN and TrialNet collaborate on joint studies, communicating daily and convening 1 hour weekly to discuss critical site/study/technical issues. They also use this time to update each other regarding each Center's status in ongoing studies.
- ITN and the TrialNet Coordinating Center participate in monthly meetings where key study members discuss the status and any pending problems or issues with ongoing studies.
- ITN and TrialNet use a common Data and Safety Monitoring Board.
- Protocols potentially of interest to both TrialNet and ITN are considered by both Networks with the goal of joint sponsorship.
- TrialNet and ITN did a joint mailing (with the help of JDRF, New England chapter) to introduce/advertise the TrialNet Natural History Study and the ITN Insulin Study.

SEARCH:

- A TrialNet investigator has provided a coordinating function by leading development of the TrialNet protocol to compare C-peptide stimulation tests and assess variability of test results, participating on the C-peptide measurement standardization working group, and working with SEARCH investigators to analyze SEARCH C-peptide data.
- In Denver, SEARCH is collaborating with TrialNet by helping them recruit eligible cases. They are informing SEARCH participants about TrialNet and referring them to the TrialNet coordinator.
- A SEARCH investigator is establishing an affiliate site with the TrialNet University of Florida Center. SEARCH will serve as a recruitment source for this affiliate site.

Standardization Programs:

- A TrialNet investigator participates on the C-peptide measurement standardization working group.
- The Diabetes Diagnostic Laboratory, University of Missouri, conducted an international round-robin comparison of C-peptide assays which included two TrialNet laboratories. The results from the comparison study illustrated the need to identify and minimize the major sources of variation in C-peptide measurements in multi-center, multi-laboratory clinical studies.
- TrialNet uses laboratories certified through the HbA1c standardization program.

T1DGC:

- TrialNet collects/provides samples for T1DGC.
- All 14 TrialNet centers are participating as recruitment

centers for the T1DGC North American Network. Investigators and staff from the TrialNet sites have attended T1DGC training sessions (December 2003) and the annual T1DGC North American Network meeting (January 2005).

- The PI for the T1DGC North American Network provided coordination between TrialNet and TIDGC through her involvement in both studies. Procedures across both studies were standardized to the extent possible.
- The Deputy Director and Project Manager at the T1DGC Coordinating Center participated in conference calls to assist the TrialNet Coordinating Center staff in establishing their international sites. A comprehensive list of issues and topics related to implementing international data collection formed the basis of these calls. As requested by the TrialNet Coordinating Center, the T1DGC Coordinating Center provided a study form related to destruction of samples and provided the ethnicity categories adopted for use in the T1DGC.
- The North American Network HLA laboratory for T1DGC provides the HLA strips to the central HLA laboratory for TrialNet. Both laboratories perform HLA using the same methodology. This will permit direct comparison between results obtained in both studies.
- T1DGC and TrialNet share the same North American laboratory for measurement of autoantibodies. This coordination will permit direct comparison between results obtained in each study.

TEDDY:

- TEDDY and TrialNet share the same laboratories for measurement of autoantibodies (IA-2 and GAD65). This will permit direct comparison between results obtained in each study.
- The central HLA laboratory for TEDDY is the same laboratory that provides the HLA strips to the central HLA laboratory for TrialNet. Both laboratories perform HLA typing using the same methodology. This will permit direct comparison between results obtained in both studies.
- TEDDY has shared HLA-screening procedures, data forms, and parts of the Manual of Operation concerning follow-up of high-risk children, with TrialNet investigators during the development of the NIP Diabetes Study. Investigators in the two studies have avoided direct competition for eligible participants through concerted action to define exclusive study geographic areas.

TEDDY and TRIGR:

- TrialNet participated in a coordination meeting in May 2005, with investigators from TEDDY and TRIGR to discuss how to obtain the most useful information when looking at these studies as a group. Common data variables across the studies and future analytic strategies were discussed.
- The mechanistic samples obtained from each of the consortia can be used to make up a larger common database.
- The sites are not competing for patient recruitment (coordination of recruiting effort).

TEDDY, T1DGC, and CIT: Collaborative media effort between TEDDY, T1DGC, TrialNet, and CIT. Media needs of all of these groups are being jointly handled by a single media contract to optimize coordination of type 1 diabetes clinical trials.