QUALITY CONTROL
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I. INTRODUCTION

The T1DGC Coordinating Center will perform quality control studies throughout the time period that data are collected. The Coordinating Center will be assisted in the performance of these duties by the Regional Network Centers, the clinics and the Quality Control Committee.

There are two primary purposes for quality control. The most important purpose is to provide feedback to the data collection sites in order to maintain and improve the quality of the study data over the course of data collection. A secondary purpose is to historically document the level of quality for inclusion in study publications.

Quality control involves the collection of specific types of data and the subsequent analysis of that data. It is primarily a measure of the quality of data either collected by the clinics or samples analyzed by laboratories associated with the study.

Quality control is accomplished in many different ways depending upon the type of data being collected, the type of procedure being analyzed, and the associated outcome variable in question. The quality control measures used in the T1DGC study will assess the reliability and validity of the data and proper adherence to the protocol.

The tools that will be used include:

1. Monitoring:
    a. recruitment efforts
    b. specimen tracking
    c. data completeness
    d. freezer temperatures

2. Internal surveillance:
    a. editing forms (at the clinic and Regional Network Center)
    b. laboratory internal quality control procedures

3. External surveillance:
    a. variability of laboratory measurements, using split pair samples
    b. data entry error rates
    c. data edits

This section has been developed to outline the procedures to be performed in order to assure that quality data are being collected and reported.

II. COORDINATING CENTER RESPONSIBILITIES

The T1DGC Coordinating Center has primary responsibility for monitoring and ensuring the overall quality of the study data. Specific responsibilities of the Coordinating Center in developing and carrying out quality control measures are listed below:

1. Organize and conduct Regional Network Center training sessions to teach standardized data collection protocols.

2. Organize and conduct Regional Network Laboratory (DNA Repositories, Autoantibody and Storage Laboratories, and HLA Genotyping Laboratories) training sessions to teach the T1DGC Specimen Tracking System protocol.

3. Review pilot study data and certify clinic readiness to initiate T1DGC data collection.

4. Maintain an up-to-date file of all completed Regional Network Center data entry certification and clinics certified to collect data.

5. Design protocol and procedures for periodic site visits to the Regional Network Centers and Regional Network Laboratories that check for quality of performance and adherence to T1DGC standardized procedures.

6. Develop a system for monitoring study recruitment and communicate with the

Regional Network Coordinators regarding recruitment progress and issues.

7. Develop a system for promptly processing and analyzing incoming data and generating quality control reports for distribution to the Regional Network Centers and Regional Network Laboratories.

8. Identify problems and notify Regional Network Centers of the quality of performance of network and clinic personnel throughout the entire data collection period.

9. Identify problems and notify Regional Network Laboratories of the quality of performance of their laboratories throughout the entire data collection period.

10. Develop and maintain a system for tracking all T1DGC specimens from collection at the clinics to receipt at the Regional Network Laboratories and from Regional Network Laboratories to receipt at the Regional HLA Laboratories, NIDDK Central Repositories, the Center for Inherited Disease Research, contributing investigators and other facilities or entities approved by the T1DGC Steering Committee or Access Committee.

11. Report pertinent information to the Quality Control Committee, the Steering Committee and the External Advisory Board.

12. Maintain historical data that describes the quality and performance of the entire T1DGC study.

13. Produce and maintain the study documents related to T1DGC quality control: (1) the reports presented to the Quality Control Committee and Steering Committee during data collection; and (2) documents found in reports to the T1DGC External Advisory Board.

III. REGIONAL NETWORK CENTER RESPONSIBILITIES

Given the study structure, the T1DGC has a two-tiered quality control scheme. Each Regional Network Center maintains all direct contact with the clinics collecting data within their specified region. Thus, quality control measures are implemented by the Regional Network Centers at the clinic level, with specific responsibilities outlined below:

1. Organize and conduct clinic training sessions to teach standardized data collection protocols. Training sessions can be centralized, one-on-one or a combination of these techniques within any given Regional Network.

2. Notify the Coordinating Center when clinic training has been completed and when a pilot study has been performed.

3. Maintain an up-to-date file of all completed Regional Network Center data entry certification, clinics certified to collect data, and clinic staff IDs.

4. Monitor recruitment of each clinic and develop and implement strategies to achieve recruitment goals as needed.

5. Review completeness of form sets upon receipt from clinics and notify clinics of missing forms.

6. Review forms for completeness and notify clinics of missing data and errors in form completion.

7. Develop and implement a system for tracking requests for data forms, data verification or data correction from clinics in accordance with outlined procedures.

8. Design protocol and procedures for periodic site visits that check for quality of performance and adherence to T1DGC standardized procedures in clinics where specific serious problems have been identified.

9. Review *T1DGC Daily Freezer Temperature Log* from clinics on a monthly basis and notify clinic of problems noted.

10. Monitor clinic compliance with quality control scheme for blood collection and notify clinic if inadequate collection of quality control samples noted.

IV. QUALITY CONTROL COMMITTEE

T1DGC study data is primarily of two types: (1) laboratory and (2) forms. Thus, the Quality Control Committee is comprised of four subcommittees: (1) DNA Repositories, (2) Autoantibody and Storage Laboratories, (3) HLA Genotyping Laboratories, and (4) Forms Data. The overall committee includes members from each of the Regional Network Laboratories, the Regional Network Centers and the Coordinating Center. (A list of the Quality Control Committee members and an organizational chart is located in Appendix A.)

The Quality Control Committee will meet as needed to review the status of the study quality control monitoring. Decisions regarding current and proposed techniques will be discussed, as well as current issues. The committee will be kept abreast of issues through frequent correspondence with the Chair of the Quality Control Committee and the Deputy Director of the Coordinating Center.

V. SITE VISITS

A. Regional Network Center and Laboratories

During the first 6 months of data collection, and annually thereafter as needed, site visits will be made to each of the Regional Network Centers and Regional Network Laboratories. The goals of the site visits are: (1) to observe the Regional Network Center or Regional Network Laboratory under normal operating conditions for adherence to protocol; (2) to identify and resolve any data collection issues at the individual clinics (for Regional Network Center site visits only); (3) to identify and resolve any sample shipment, handling and analysis procedures (for Regional Network Laboratory site visits only); (4) to increase/improve communication between the Coordinating Center and Regional Network

Center and Regional Network Laboratory personnel; and (5) to demonstrate the study's concern for the quality of data collection.

The site visits will be conducted in a single day, unless issues within the Regional Network Center or Regional Network Laboratory necessitate an extended visit. The site visit team for the Regional Network Centers will consist of the Deputy Director (Coordinating Center), Project Manager (Coordinating Center) and, if possible, the Project Officer from NIDDK and/or a representative from the JDRF. The site visit team for the Regional Network Center Laboratories will consist of the Chair of the Quality Control Committee, the Deputy Director (Coordinating Center), and, if possible, the Project Officer from NIDDK and/or the JDRF liaison. An agenda is prepared and distributed to the Regional Network Center or Regional Network Laboratory prior to the site visit. (Appendix B contains examples of site visit agendas for Regional Network Centers and each type of Regional Network Laboratory.)

Following the site visits, a formal report is prepared. For Regional Network Center site visits, the report is written by the Deputy Director and Project Manager at the Coordinating Center; the Chair of the Quality Control Committee prepares the site visit reports for the Regional Network Laboratories. Site visit reports are distributed to the Chair of the Steering Committee, the Chair of the Quality Control Committee, the Deputy Director of the Coordinating Center, the Project Officer at NIDDK, the JDRF liaison, and the Regional Network Center or Regional Network Laboratory visited. These individuals will discuss these reports on a conference call, if required; this group will make recommendations for the follow-up and correction of problem areas in a timely manner. The Principal Investigator at the Regional Network Center or Regional Network Laboratory will be asked to respond in writing in a timely manner regarding the resolution of any major problems.

B. Regional Network Clinics

Due to the large number of clinics within the Regional Network Centers, annual site visits to all clinics are not planned. However, Regional Network Centers may identify certain clinics where continued or serious issues regarding data collection or sample shipments require a site visit. In this event, the Regional Network Center will confer with the Coordinating Center and develop an agenda for the site visit. The site visit will include observation of collection of blood and completion of forms for a family. (Appendix C contains sample check sheets for blood collection and shipping procedures.)

Following the site visit, the Network Coordinator will prepare a formal report to be distributed to the Chair of the Steering Committee, the Chair of the Quality Control Committee, the Deputy Director of the Coordinating Center, the Project Officer at NIDDK, the JDRF liaison and the Principal Investigator and Clinic Coordinator of the clinic visited. These individuals will discuss the report on a conference call with the Network Coordinator and/or Network Principal Investigator, if required; this group will make recommendations for the follow-up and correction of problem areas in a timely manner. Each Clinic Coordinator and Principal Investigator will be asked to respond in writing in a timely manner regarding the resolution of any major problems.

VI. QUALITY CONTROL PROCEDURES

This section details the quality control procedures that are to be carried out for specified components.

A. Identifying Participants for Duplicate Blood Collection

The Clinic Coordinator is responsible for identifying the T1DGC participants for whom the quality control duplicate blood collection will be performed. The participants selected are referred to as "QC participants". A *T1DGC Participant and QC Selection Log* has been developed to assist in the selection and tracking of quality control participants. In the event that the additional sample cannot be collected on the identified participant, the nurse or technician collects the duplicate sample on the next appropriate participant.

Given the overall volume of blood being collected, the additional quality control tube is collected only in participants that are at least 16 years old (or large for their age). The additional serum and plasma volume required for quality control is split between two participants: QC-Red for autoantibodies and serum storage and (2) QC-Purple for plasma storage and DNA extraction from the cell pack. A QC-Red participant must be an affected individual (*i.e.*, must have type 1 diabetes). A QC-Purple participant can be any age (or size) eligible individual in the family.

The quality control sampling for the QC-Red participant within each clinic is outlined below:

1. There is no QC-Red collected during the clinic's pilot study.
2. An affected individual (proband or affected sibling) from the first two T1DGC families will have an additional serum tube collected. The selected affected siblings should not be in the same family.
3. After the collection of the first two QC-Red samples, every 10th affected participant will have an additional serum tube collected.
4. After the collection of an additional five QC-Red samples (for a total of seven QC-Red samples), every 20th affected individual will have an additional serum tube collected.
5. For clinics with primarily pediatric populations, a QC-Red sample should be collected from every age (or size) eligible participants to provide adequate duplicate samples.

The quality control sampling for the QC-Purple participant within each clinic is outlined below:

1. There is one QC-Purple collected during the clinic's pilot study.
2. Any age (or size) eligible individual from the first two T1DGC families will have an additional plasma tube collected. These participants should not be in the same family.
3. After the collection of the first two QC-Purple samples, every 10th participant will have an additional plasma tube collected.

4. After the collection of additional five QC-Purple samples (for a total of seven QC-Purple samples), every 20th participant will have an additional plasma tube collected.

Once a participant is identified as a QC-Red or QC Purple participant, the Clinic Coordinator should provide the appropriate label set to the nurse or technician. The nurse will place a quality control ID label on the Blood Collection Form, the duplicate sample, the duplicate aliquots (for serum and plasma) and the shipping forms. (See Appendix D for a schematic of the duplicate blood collection sampling procedures and the contents of the QC label sets.)

B. Regional Network Laboratories

The Coordinating Center will receive laboratory results for examined participants on a monthly basis from each type of laboratory as outlined below:

1. DNA Repositories: data for the DNA yield from the EDTA cell pack and/or cell line and for the cell line transformation success/failure.
2. Autoantibody and Storage Laboratories: data for autoantibody measures (GAD65 and IA-2ic) on probands and affected siblings.
3. HLA Genotyping Laboratories: data for HLA-A, B, C, DP, DQ, DRB1 and subtypes and CTLA4 and INS SNPs for all participants

The quality of performance in the DNA Repositories will be based largely on the cell line transformation rate and the DNA yield from cell packs and /or cell lines. Further, those using the DNA (*e.g.*, the HLA Genotyping Laboratories) will report any issues with the quality of the samples to the Coordinating Center. The Chair of the Quality Control Committee and the Deputy Director at the Coordinating Center will investigate any noted problems regarding DNA quality.

To assess the quality of the measures from the Autoantibody Laboratories Laboratories, a two-pronged system will be implemented. First, univariate analyses will be

conducted on the monthly data results uploaded to the Coordinating Center. Within each laboratory, comparison of data results over time will be recorded. Based on these analyses, summary statistics (*e.g.*, means, variances) and out-of-range values will be obtained and, if necessary, investigated further.

Second, duplicate measures will be performed on an approximate 5% random sample of participants for autoantibody measures. Duplicate serum samples will be sent by the clinics to the laboratory in the sample shipments. To the extent possible, the laboratory will be blinded as to which samples were paired.

In addition to graphical inspection of the data, reliability will be assessed using correlation coefficients and the technical error measurement for autoantibody measures. (The technical error is the square root of the pooled between measures variance as a percent of the sample mean: ((Sqrt(Σ d^2/2n))/sample mean)* 100.) The technical error is compared to the laboratories internal coefficient of variation. If there is evidence of high technical error then the laboratory will be contacted and queried for an explanation.

Duplicate HLA genotype measures will be performed on a random 5% of samples. Under the direction of the Coordinating Center, the DNA Repositories will provide duplicate DNA samples within each set of 92 samples sent to the HLA Genotyping Laboratories. To the extent possible, the laboratory will be blinded to the pairing of the original and duplicate samples. The proportion of discordant allele calls will be assessed.

More detailed information regarding external and internal quality control procedures are contained in the laboratory-specific *T1DGC Laboratory Manual of Operations*.

C. Shipping and Data Collection Forms

1. Shipping Forms

The clinics will forward a copy of their shipping forms to the Regional Network Center as part of standard documentation. These forms include: (1) a copy of the shipping forms sent with the daily shipment of cell line and EDTA cell packs to the DNA

Repositories; and (2) a copy of shipping forms sent with the monthly shipment of blood samples to the Autoantibody and Storage Laboratories.

Upon receipt of the samples, laboratory staff completes the shipping forms with the necessary information and enters the data into the specimen tracking system. The laboratory staff makes a copy of the shipping forms for their records and sends the original shipping forms to the Regional Network Center. The Regional Network Center staff verifies that data entry of the forms was performed accurately.

2. Data Collection Forms Review

Each Regional Network Center is required to submit a 5% random sample of form sets to the Coordinating Center on a quarterly basis for a manual quality control review. A list of randomly generated ID numbers for each clinic will be supplied by the Coordinating Center. The manual review of forms by staff of the Coordinating Center will entail a page-by-page review of the following items:

1. form completion;
2. affixed T1DGC ID and quality control labels, when applicable;
3. interviewer IDs;
4. skip patterns observed;
5. data collection errors corrected according to study protocol;
6. ethnicity and study coding; and
7. overall form consistency and preparedness for data entry.

A report of errors and/or recommendations for improvement will be sent to the Regional Network Center and the Deputy Director of the Coordinating Center following each review.

3. Duplicate Data Entry

All study forms are entered at the Regional Network Centers. Following manual review, the 5% random sample of participant form sets sent by the Regional Network Center on a quarterly basis will be data entered at the Coordinating Center to estimate the data entry error rate. A field-by-field comparison will be made between the original and the re-entered record at the Coordinating Center. A report that indicates which fields were

discordant and form-specific error rates will be generated. The first-pass error rates will be adjudicated (via the hard-copy of the form) for data entry errors before final reports are sent to the Regional Network Center.

The resulting error rates will be summarized and forwarded to the Regional Network Center for review. **All** forms from the time period being evaluated where the random sample error rate is 0.50% or greater will be re-entered. The double entry of the 5% sample will be an ongoing process so that the Coordinating Center can identify specific problems. Double entry analysis initially will occur quarterly; however, this will be reassessed in view of the volume of re-entry required in the Regional Network Centers.

D. Query System

The T1DGC Query System was created to resolve data editing questions. It is to be used as a tool for the Regional Network Centers to record and identify sources of action taken to correct data collection or data entry errors or to correct or verify out-of-range or unexpected database values at either the Regional Network Center or clinic level. The responses that the Regional Network Centers enter into this system are used to create reports for the Forms Data Quality Control Committee, the Steering Committee and the External Advisory Board.

The Query System is dynamic, allowing the Regional Network Centers to identify at one time the entire list of queries for each family ID. Queries are created from the warning messages seen at the time of data entry, as well as cross-form validation checks that appear on the Irregularities Report.

The Regional Network Center first determines that the query is not a data entry error. Once this is confirmed, the Regional Network Center marks the query as “RNC – Data to be reviewed.” All queries marked as “RNC – Data to be reviewed” create the Query System Report, a clinic-specific report that can be sent, either electronically or via the post, to the clinic for resolution.

The clinic and the Regional Network Center can either verify or edit queries.

Queries that have been verified will no longer appear in the Query System and will be removed from other reports (*i.e.,* the Irregularities Report). The Project Managers at the Coordinating Center are responsible for reviewing queries that have been verified on a monthly basis. If a query has been verified and it is considered pertinent information for the T1DGC, the Project Manager changes the status of the query and notifies the Regional Network Center that verification of this query is unacceptable. See Appendix D of **Chapter XI**, *Data Entry System,* for detailed instructions in the use of the T1DGC Query System.

APPENDIX A
QUALITY CONTROL COMMITTEE

ALL SUB-COMMITTEES

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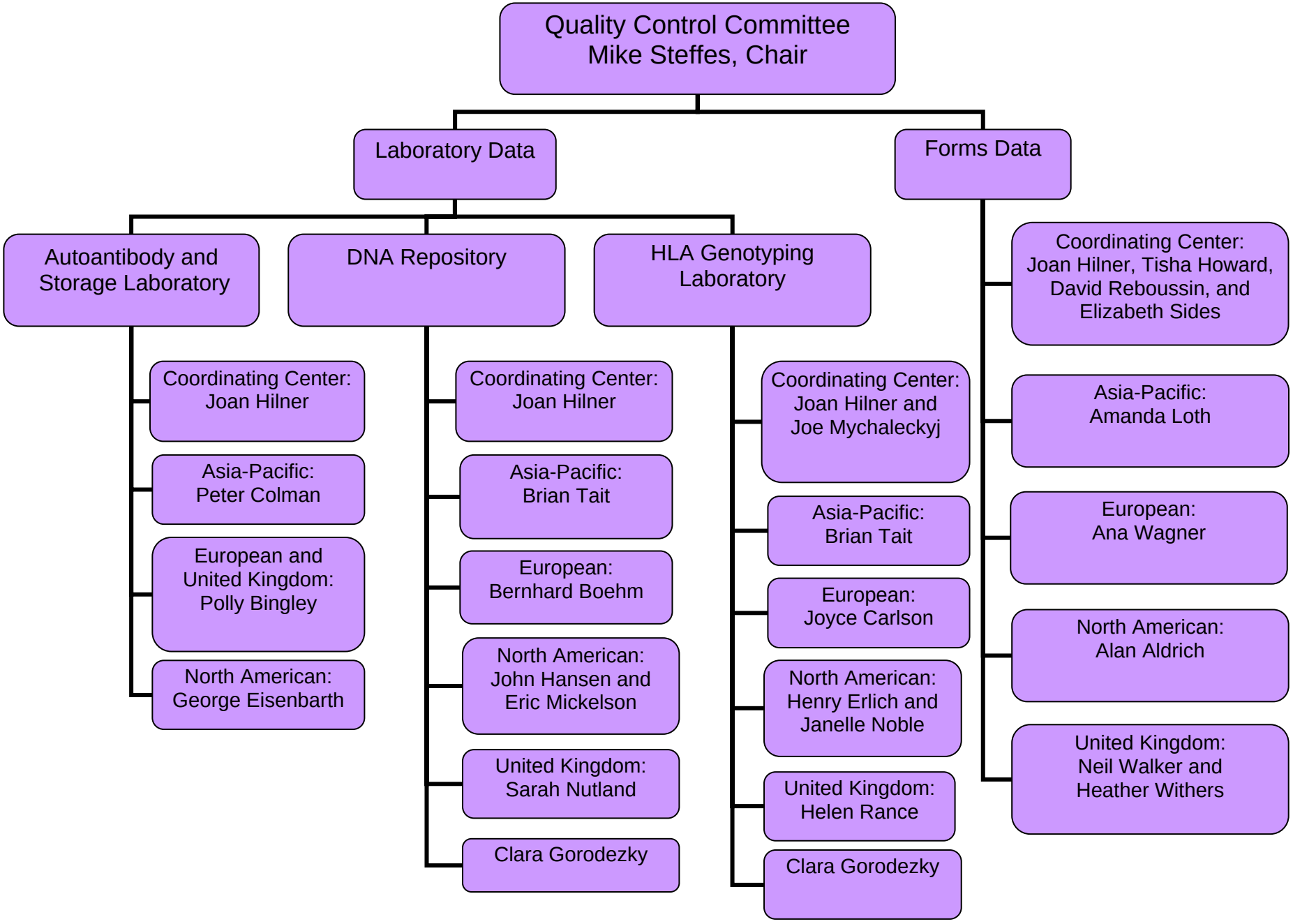
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Forms Data
Autoantibody and Storage Laboratory
DNA Repository
HLA Genotyping Laboratory
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Asia-Pacific: Amanda Loth
European: Ana Wagner
North American: Alan Aldrich
United Kingdom: Neil Walker and Heather Withers
Coordinating Center: Joan Hilner
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Asia-Pacific: Brian Tait
European: Bernhard Boehm
North American: John Hansen and Eric Mickelson
United Kingdom: Sarah Nutland
Clara Gorodezky
Coordinating Center: Joan Hilner and Joe Mychaleckyj
Asia-Pacific: Brian Tait
European: Joyce Carlson
North American: Henry Erlich and Janelle Noble
United Kingdom: Helen Rance
Clara Gorodezky

APPENDIX B

SITE VISIT AGENDAS

AGENDA
REGIONAL NETWORK CENTER
SITE VISITS

I. Observation of Family Collection (if possible)

II. Review of Recruitment
- A. Goals
- B. Recruitment Strategies and Materials
- C. Changes to Projections (through current fiscal period)

III. Review of Data Entry/ Edits
- A. Missing Data
- B. Errors
- C. Data Entry Flow (time from collection to entry)

IV. Review of Logs
- A. Daily Freezer Temperature Log
- B. Discarded ID Log
- C. Participant and QC Selection Log/ Adequacy of QC Sampling
- D. Data Editing Log
- E. Other Network Center or Clinic Logs (e.g., Staff IDs, Clinic IDs, etc)

V. Storage of Forms
- A. Data Collection Forms from Clinics
- B. Shipping Forms from Laboratories
- C. Layered Portion of Informed Consent Forms from Clinics
- D. IRB Approvals/Informed Consents

VI. Study Documents
- A. Manual of Operations
- B. Protocol

VII. T1DGC Label Sets
- A. Label Storage at Network Center
- B. Systems for Distribution to Clinic and Tracking
- C. Estimated Need for Additional Label Sets

VIII. Miscellaneous
- A. Communication with Clinics
- B. Communication with Coordinating Center
- C. “Problem Clinics”
- D. Reimbursement/ Invoicing
- E. Adverse Events
- F. Application to Eligibility Committee

Agenda for the Site Visit to the DNA Repository for the North American Regional Network (Eric Mickelson, Principal Investigator): Thursday, May 13, 2004

Visitors: Beena Akolkar, PhD, NIDDK
Joan Hilner, MPH, MA, RD, Wake Forest University
Michael Steffes, MD, PhD, University of Minnesota

Local Participants: Eric Mickelson, Ji Pei and Emily Villegas

8:00 Introductions

8:05 Review the Agenda

8:10 Review Plan of the Consortium – Transformation of Peripheral Blood Cells, Isolation of DNA

Several laboratories throughout the world will be transforming peripheral blood mononuclear cells for the Consortium, extracting DNA from transformed cells, storing DNA and (in some cases) shipping to other locations for analyses (including HLA genotyping).

Current plan for North America includes samples from clinical centers affiliated with the North American Regional Network.

Expected Numbers of Samples from Affected Sib-Pairs: 1,100 families with an average of 5/family: 5,500 samples transformed over 3 years. DNA to be extracted from a maximum 5,500 EDTA cell packs.

Shipments

What are the expected times for transport from distant sites (e.g., Canada)?
Shipments completed to date (specific issues to be discussed, if necessary).

9:00 Method for Transformation of Peripheral Blood Mononuclear Cells
Method used in Seattle – Overview
Proposed Workflow – Overview
Cost structures for several services: transforming cells, storing transformed cells, extracting DNA, storing DNA and shipping DNA or transformed cells to other locations (repositories or investigators)
Use of fetal calf serum (supplied from the USA)
Capacity to complete transformations with other current and future obligations

10:30 Tour of the Cell Transformation Facility, including Receiving Area

11:30 Discussions among all participants

Agenda for the Site Visit to the Autoantibody and Storage Laboratory for North American Network (Dr. George Eisenbarth, Principal Investigator): May 20, 2004

Visitors: Beena Akolkar, PhD, NIDDK
Joan Hilner, MPH, MA, RD, Wake Forest University
Michael Steffes, MD, PhD, University of Minnesota
Dustin Williams, Wake Forest University

Local Participants: George Eisenbarth, MD, PhD and Liping Yu, MD

8:00 Introductions

8:05 Review the Agenda

8:10 Review Plan of the Consortium – Measurements of Islet Antibodies
Three laboratories in Europe, Australia and North America will be measuring antibodies to GAD and IA-2_{ic}. Current plan for North America includes samples from clinical centers affiliated with the North American Network. Expected numbers of samples from affected individuals (type 1 diabetes) to be analyzed for the Consortium: a minimum of 2,200 samples (1,100 families with 2 members on average expected from each family).

Shipments
Well established protocols from shipping samples from the clinics.
Costs of shipping containers back to the clinics.

8:30 Methods for Measuring Islet Antibodies
Methods proposed in Denver – Overview, similarities of the revised method to methods in Bristol and Melbourne. Please present (preferably in tabular form) the similarities and differences between the method in Denver and those in Bristol and Melbourne. Review the radioactive labels used in each assay. Demonstrate that using double label assays in Denver will yield identical assays among the three laboratories. Do you calculate values for the unknowns using a single calibrator -- thereby calculating a ratio for each unknown, which can then be used to infer WHO units? If so, please document how similarly this assay produces results similar to those from the standard curves (with several points on a curve) used in Bristol and Melbourne.

10:00 Review results from the DASP surveys -- Please present the results with the assay which produces results closest to those in Bristol and Melbourne.
Overview of proposed workflow
Cost structures for shipping samples to other locations.

11:00 Tour of the Laboratory, including Receiving Area

11:30 Review of T1DGC Specimen Tracking System (Liping Yu and Dustin Williams)

Agenda for the Site Visit to the HLA Genotyping Laboratory for the Asia-Pacific Regional Network (Dr. Brian Tait, Principal Investigator), March 11, 2004

Visitors: Joan Hilner, MPH, MA, RD, Wake Forest University
Michael Steffes, MD, PhD, University of Minnesota

Local Participants: Brian Tait, Mike Varney, Anthony Louey, others as deemed appropriate

13:30 Introductions

13:35 Review the Agenda

13:40 Review Plan of the Consortium – Isolation of DNA and Completion of HLA Typing

Several laboratories throughout the world will complete HLA genotyping using kits from Roche Molecular Systems in Alameda, CA (i.e., everyone will be using the same method). The DNA extracted from collected blood or transformed cells will be analyzed in an identical manner using 96-well plates with consistent reporting protocols to the Coordinating Center at Wake Forest University. To provide DNA promptly, the Melbourne HLA Genotyping Laboratory will be extracting and utilizing DNA from EDTA-anti-coagulated blood (frozen cell pack).

Expected Numbers of Samples in the Asia-Pacific Regional Network: 200 affected sib-pair families with an average of 5/family plus up to 2,160 trios with 3/family over 2 year data collection period; 7,480 samples forwarded to the HLA Genotyping Laboratory in Melbourne, Australia

14:00 Tour of HLA Genotyping Facility, including Storage Area

14:30 Methods and resources
Method used currently in Melbourne – Overview
Specific items for discussion include the following:
- Methods used and volume of samples genotyped in past three years
- Experience of personnel in using various methods for HLA genotyping
- Participation in HLA workshops and verification of results by third-party laboratories
- Success in using DNA provided by other laboratories for HLA genotyping or for other techniques or procedures
- Systems used to receive and track the inventory of samples
- Turnaround time to complete HLA analyses

Specific items for discussion include the following (cont.):

Experience with SCORE to interpret results and determine HLA genotypes
Procedures utilized to report results to other entities, including coordinating centers for clinical studies or trials
Progress of certification studies to demonstrate proficiency of the laboratory in the methods of the Consortium
Facilities available for the method of the Consortium

16:00 Progress and preparation for assaying samples sent in the first quarter of 2004

Demonstration that the laboratory has the facilities and trained personnel to complete the assays in a timely manner.
Summary of the experience of the laboratory to complete similar work in an efficient manner from receipt of samples to reporting results to the Coordinating Center.

16:30 Adjourn

APPENDIX C

SITE VISIT CHECK SHEETS

- **Blood Collection**
- **Blood Handling, Storage and Shipping**
- **Interviewing**

T1DGC

BLOOD COLLECTION CHECK SHEET

CLINIC ID_____ DATE_____

OBSERVER(S)_____ TECHNICIAN ID_____

		S	U
A.	**Equipment, environment**		
1.	Isolated room, professional environment.	☐	☐
2.	Equipment, forms, supplies adequate (needles, vacutainers, bandaids, alcohol swabs, gauze, tourniquet, ice bath, ammonia, inhalants, butterfly needles, butterfly adapter, syringes).	☐	☐
B.	**Procedure**		
1.	Label checked.	☐	☐
2.	Participant prepared, procedure explained.	☐	☐
3.	Bleeding disorders queried and recorded.	☐	☐
4.	Needle, adapter, vacutainer prepared.	☐	☐
5.	Tourniquet applied properly.	☐	☐
6.	Vein palpated, cleansed, and dried.	☐	☐
7.	Venipuncture technique.	☐	☐
8.	Tubes filled in proper order and inverted.	☐	☐

		S	U
9.	Tourniquet released as soon as flow starts in last tube.	☐	☐
10.	Total tourniquet time within 2 minute limit.	☐	☐
11.	Vacutainers filled.	☐	☐
12.	Stasis obtained.	☐	☐
13.	Needle disposed properly.	☐	☐
14.	Tubes labeled properly.	☐	☐
15.	Form completed accurately.	☐	☐
16.	Other_____	☐	☐

COMMENTS:

S = Satisfactory
U = Unsatisfactory

T1DGC

BLOOD HANDLING, STORAGE, SHIPPING

CHECK SHEET

CLINIC ID_____ DATE_____

OBSERVER(S)_____ TECHNICIAN ID_____

		S	U
A.	**Equipment**		
1.	Equipment, supplies adequate.	☐	☐
2.	Equipment working correctly, centrifuge at 4°C.	☐	☐
3.	Daily record of freezer temperature up-to-date.	☐	☐
4.	Biohazard labels available.	☐	☐
5.	Other _____	☐	☐
B.	**Procedure**		
1.	Tubes labeled accurately.	☐	☐
2.	Tubes:		
	Red top tube to rack at room temperature 30-60 minutes.	☐	☐
	Purple top tube to ice water 30-60 minutes.	☐	☐
	Green/yellow top tube(s) at room temperature until shipped (daily).	☐	☐
3.	Centrifuge balanced.	☐	☐

		S	U
4.	Centrifuge operation.	☐	☐
5.	Aliquoting equipment ready, vials labeled and organized, biohazard labels available.	☐	☐
6.	Proper specimen volumes in respective vials.	☐	☐
7.	Vial filling priority observed.	☐	☐
8.	Sealing of vials.	☐	☐
9.	Cell pack in purple top tube saved for shipment with green top tube; purple top tube re-labeled, if needed	☐	☐
10.	Completion of blood collection form.	☐	☐
11.	Freezer organization and storage.	☐	☐
12.	Time constraints observed throughout procedure (90 minute maximum from drawing to freezing).	☐	☐
13.	Disposal of red top tubes and contaminated equipment.	☐	☐
14.	Other _____	☐	☐

C. Shipping

1.	Knowledge of shipping schedule for the laboratory.	☐	☐

		S	U
2.	Dry ice available.	☐	☐
3.	Shipping supplies adequate (for daily ambient and monthly frozen shipments).	☐	☐
4.	Specimens for labs packed properly (for daily ambient and monthly frozen shipments); adherence to IATA regulations.	☐	☐
5.	Serum and plasma specimens remain frozen while being packed.	☐	☐
6.	Shipping forms complete properly.	☐	☐
7.	Other _____	☐	☐

COMMENTS:

S = Satisfactory
U = Unsatisfactory

T1DGC
INTERVIEWING
CHECK SHEET

CLINIC ID _____ DATE _____

OBSERVER(S) _____ INTERVIEWER ID _____

	RATING Circle one: 1 = Yes (satisfactory) 2 = No (unsatisfactory)		**COMMENTS** Continue on reverse if necessary
I. Communication Skills			
Maintained:			
A. Adequate eye contact with participant	1	2	_____
B. Neutral attitude	1	2	_____
C. Non-judgmental voice tone and manner	1	2	_____
D. Good rapport with participant	1	2	_____
E. Professional, confident, competent manner	1	2	_____
II. Interviewing Techniques			
A. Good pacing and tempo; maintained pace while allowing the participant time to answer	1	2	_____
B. Probes			
1. Appropriate use of repetition and neutral probes	1	2	_____
2. Appropriate verification of responses	1	2	_____
C. Phrasing and pronunciation			
1. Clear, easily understood phrasing of sentences	1	2	_____
2. Proper pronunciation of medical terminology	1	2	_____

T1DGC
INTERVIEWING
CHECK SHEET

CLINIC ID _____ DATE _____

OBSERVER(S) _____ INTERVIEWER ID _____

	RATING Circle one: 1 = Yes (satisfactory) 2 = No (unsatisfactory)		**COMMENTS** Continue on reverse if necessary
III. Interviewing Procedures			
A. Recorded responses correctly	1	2	_____
B. Made notations in margin as appropriate	1	2	_____
C. Skip patterns followed correctly	1	2	_____
D. Other interviewer instructions followed correctly:			
1. Interviewer instruction not read aloud	1	2	_____
2. Response categories read correctly, where appropriate	1	2	_____
3. Cue cards used appropriately	1	2	_____
4. When two alternate phrasings are given, appropriate one chosen	1	2	_____

APPENDIX D

DUPLICATE BLOOD COLLECTION SAMPLING SCHEME AND CONTENTS OF BLOOD COLLECTION QUALITY CONTROL LABEL SETS

Duplicate Blood Collection Sampling Scheme

Quality Control – Red (Serum):
Age-or Size-Eligible Affected Siblings

	Total QC-Red collected
Pilot Study	
NO QC-Red sample collected	0 QC-Red samples for pilot study
Study Families	
Affected siblings from first two families will have a QC-Red sample collected; affecteds should not be in the same family	2 QC-Red samples on study families
After first 2 QC-Red samples collected, every 10th affected sibling will have a QC-Red sample collected	7 QC-Red samples on study families
After a **total** of 7 QC-Red samples have been collected, every 20th affected sibling will have a QC-Red sample collected	Until study is complete

Quality Control – Purple (Plasma and Cell Pack):
Age-or Size-Eligible Participants

	Total QC-Purple collected
Pilot Study	
QC-Purple sample collected on one participant during pilot study	1 QC-Purple sample for pilot study
Study Families	
First 2 families will have a QC-Purple sample collected from each; participants should not be in the same family	2 QC-Purple samples on study families
After first 2 QC-Purple samples collected, every 10th participant will have a QC-Purple sample collected	7 QC-Purple samples on study families
After a **total** of 7 QC-Purple samples have been collected, every 20th participant will have a QC-Purple sample collected	Until study is complete

Note: All QC participants must be age- or size-eligible.

CONTENTS OF BLOOD COLLECTION
QUALITY CONTROL LABEL SETS

QC-Red (Proband/Affected Sibling ONLY)

Large ID Labels
3 for proband (purple–striped)
3 for affected sibling (green–striped)
(1 label for blood tube, 1 for blood collection form and 1 for shipping form)

Small ID Labels
6 for proband (purple-striped)
6 for affected (green-striped)
(1 label for autoantibodies, 4 for storage and 1 for top of storage box)

QC-Purple (Any family member)

Large ID Labels
6 for every family member
(2 labels for blood tube, 1 for blood collection form and 2 for shipping forms)

Small ID Labels
5 for every family member
(4 for storage and 1 for top of storage box)