GUIDELINES

TABLE OF CONTENTS

I. INTRODUCTION

This chapter provides general guidelines for recruitment and data collection in the Type 1 Diabetes Genetic Consortium (T1DGC) study. This information serves as a general reference for questions that may arise in the conduct of this project. Refer to the *T1DGC Data Collection Flow Chart* (Appendix A) for the model containing the basic components of data collection; this may vary somewhat between networks or regions.

II. PARTICIPANT IDENTIFIERS

The T1DGC uses a consortium-wide scheme for unique participant identification. (See Appendix B for a complete description of this scheme.) For affected sibling pair (ASP) and trio families, the seven-digit ID structure includes 1 character for the network (*i.e.*, 1 for Asia-Pacific; 2 for European; 4 for North American; and 5 for United Kingdom). This network identifier is followed by 4 characters for the family (0001-9999) and 2 characters for the individual within a family (*i.e.*, 01 for father; 02 for mother; 03 for the proband or affected sibling 1; 04 for affected sibling 2; 05 for unaffected sibling 1; 06 for unaffected sibling 2; 07 for affected sibling 3; 08 for affected sibling 4; 09 for affected sibling 5). All IDs are bar-coded, with the numeric version of the ID (X-XXXX-XX) also on each label.

For the case-control collection, the unique participant identifier is also a seven-digit ID structure. The first character indicates the network (*i.e.*, 1 for Asia-Pacific; 2 for European; and 4 for North American). The second character identifies whether this is a case or a control (7 for case; 8 for control). The last five characters are the unique identifier for the participant. These IDs are also bar-coded with the numeric version on each label (X-X-XXXXX).

Another level of individual identifiers is recorded on all forms by clinic staff in the designated data field. These two or three character Secondary Identifiers are FA for father, MO for mother, AS1 for affected sibling 1 (proband), AS2 for affected sibling 2, UN1 for unaffected sibling 1, UN2 for unaffected sibling 2, AS3 for affected sibling 3;

AS4 for affected sibling 4; and AS5 for affected sibling 5. For the case-control collection there are two individual identifiers: CAS for the case and CON for the control participant.

III. FORM AND LABEL SETS

A. Data Collection Forms

Forms are created and revised at the Coordinating Center, with the most current version of each form posted on the T1DGC web site. Forms are printed by the clinic from the T1DGC web site as needed, or by the Regional Network Center for distribution to those clinics without Internet access.

A form set is composed of all required data forms necessary for an entire family recruited into the T1DGC study. An entire ASP form set consists of the following forms: one *T1DGC ASP Eligibility Form*, (either administered to the proband or administered to a guardian of the proband); one *T1DGC ASP Family Contact Sheet*; one *T1DGC ASP Consent Summary Form*; six *T1DGC ASP Exam Forms* (one for each potential member of the family); and six *T1DGC Blood Collection Form*s (one for each potential member of the family). For each ASP family, one *T1DGC ASP Eligibility Form* (proband or guardian version) and one *T1DGC Consent Summary Form* must be printed. For each member of the family, the appropriate *T1DGC ASP Exam Form* and *T1DGC Blood Collection Form* must be printed. A copy of the local informed consent must be completed.

Clinics in the Asia-Pacific, European and North American Networks are also collecting trio families (*i.e.*, proband, father and mother). Separate form sets exist for trios, comprised of the same types of forms as in the ASP families but for the proband, father and mother only. The *T1DGC North American Trio Pre-Eligibility Form* identifies eligible trios in the North American Network and **must** be completed in addition to the trio form set.

Three networks (Asia-Pacific, European and North American) are participating in the case-control collection. Separate form sets exist for this study, comprised of the

same types of forms as in the ASP and trio collections, but for the case (person with T1DGC-defined type 1 diabetes) and control (person without type 1 diabetes).

B. Label Sets

Label sets are produced at the Coordinating Center and are distributed to the Regional Network Centers in batches for data collection over an approximate three-month period. Regional Network Centers are responsible for subsequent distribution to individual clinics. The Regional Network Center staff must notify the Coordinating Center at least two weeks in advance when additional label sets are needed. An e-mail should be sent to the designated project manager.

For ASP and trio families, label sets are pre-packaged as a family unit for, at maximum, a six-member family. Each family is assigned a unique family ID with corresponding individual ID labels for each family member. A standard label set consists of all labels necessary for an entire family; a unique bar-coded family ID label appears on the outside of the envelope containing the label set. There are both large and small labels in each packet.

Label sets for the case-control collection are packaged individually. Each case and control is assigned a unique ID and a standard set of labels containing all labels necessary (both large and small labels) is contained in the packet.

1. Large Labels

The large labels are used on each page of the data forms and each of the blood collection tubes. The ASP and trio label packet includes the following sheets of large labels:

Family ID: 1 sheet of plain white labels

Father ID: 1 sheet of labels with a blue stripe at the top

Mother ID: 1 sheet of labels with a pink stripe at the top

Proband ID: 1 sheet of labels with a purple stripe at the top

Affected Sibling ID: 1 sheet of labels with a green stripe at the top

Unaffected Sibling IDs: 2 sheets of labels with a yellow stripe at the top (one for each of up to two unaffected siblings)

The case or control label packet will include one sheet of labels with an orange stripe at the top (case) or one sheet of labels with a gray stripe at the top (control).

Each large label sheet contains thirty labels; however, not all labels are used during the exam. Extra labels may be used for locally produced forms (*e.g.*, regional logs), and those not used are kept in the clinic file for each participant. These are used if a blood re-collection is necessary. Table 1 outlines the use and number of large labels to be used for data collection.

Table 1. Large Label Specifications for T1DGC Data Collection

Label Sheet (30/sheet)	Color	Number of Labels for Data Collection Forms and Samples	Total Number of Labels Needed
Family ID	White	ASP Eligibility Form – 8 ASP Consent Summary Form – 5 Trio Eligibility Form -- 4 or 5 Trio Consent Summary Form - 3 North American Trio Pre-Eligibility Form – 3 Participant Identification Form – 1 (ASP and trios)	14 (Trios: 8-9; dependent on the proband's age; 11-12 for North American Network trios)
Father ID	Blue	Informed Consent Form – 1 Consent Summary Form – 1 Exam Form – 7 Blood Collection Form – 5 One for each blood collection tube – 5 One for each shipping form – 2 Participant Identification Form – 1 Participant and QC Selection Log – 1	23
Mother ID	Pink	Informed Consent Form – 1 Consent Summary Form – 1 Exam Form – 7 Blood Collection Form – 5 One for each blood collection tube – 5 One for each shipping form – 2 Participant Identification Form – 1 Participant and QC Selection Log – 1	23

Label Sheet (30/sheet)	Color	Number of Labels for Data Collection Forms and Samples	Total Number of Labels Needed
Proband ID	Purple	Informed Consent Form – 1 Consent Summary Form – 1 Exam Form – 10 (Trios - 8) Blood Collection Form – 5 One for each blood collection tube – 4 or 5 One for each shipping form – 2 Participant Identification Form – 1 Participant and QC Selection Log – 1	25 – 26; dependent on the proband's age (Trios: 23-24; dependent on the proband's age)
Affected Sibling ID (ASP Family only)	Green	Informed Consent Form – 1 Consent Summary Form – 1 Exam Form – 4 Blood Collection Form – 5 One for each blood collection tube – 4 or 5 One for each shipping form – 2 Participant Identification Form – 1 Participant and QC Selection Log – 1	19 – 20; dependent on the affected sibling's age
Unaffected Sibling ID (ASP Family only)	Yellow	Informed Consent Form – 1 Consent Summary Form – 1 Exam Form – 5 Blood Collection Form – 5 One for each blood collection tube – 4 or 5 One for each shipping form – 2 Participant Identification Form – 1 Participant and QC Selection Log – 1	20 – 21; dependent on the unaffected sibling's age
Case ID	Orange	Eligibility Form - 4 Informed Consent Form – 1 Exam Form – 9 Blood Collection Form – 5 One for each blood collection tube – 4 or 5 One for each shipping form – 2 Participant and QC Selection Log – 1	26 – 27; dependent on the case's age
Control ID	Gray	Eligibility Form - 4 Informed Consent Form – 1 Blood Collection Form – 5 One for each blood collection tube – 4 or 5 One for each shipping form – 2 Participant and QC Selection Log – 1	17 – 18; dependent on the control's age

2. Small Labels

The small labels can tolerate -70°C and are used for the storage aliquots for each participant. The ASP and trio label packets contain one sheet of small labels for

each family; on each sheet, there is a column of 20 labels for each family member. These labels follow the same color scheme for each family member as the large labels (*i.e.,* blue for father, pink for mother, purple for proband, green for affected sibling, and yellow for unaffected sibling(s)). Each column contains more labels than needed. Case and control label packets contain only one sheet for the appropriate participant (orange for cases and grey for controls). Extra labels are kept in the participants' clinic file for future use if needed. Table 2 outlines the number and type of labels to be used for the individual aliquots.

Table 2. Small Label (Aliquot) Specifications for T1DGC Data Collection

Small Labels (20 / family member)			
	Color	Intended Use	Labels Needed
Father ID	Blue	Serum samples – 5 Plasma samples – 4 Top of storage box – 1 Potential re-collection – 10	20
Mother ID	Pink	Serum samples – 5 Plasma samples – 4 Top of storage box – 1 Potential re-collection – 10	20
Proband ID	Purple	Serum samples – 5 Plasma samples – 4 Top of storage box – 1 Potential re-collection – 10	20
Affected Sibling ID (ASP Family only)	Green	Serum samples – 5 Plasma samples – 4 Top of storage box – 1 Potential re-collection – 10	20
Unaffected Sibling(s) ID (ASP Family only)	Yellow	Serum samples – 5 Plasma samples – 4 Top of storage box – 1 Potential re-collection – 10	20
Case ID	Orange	Serum samples – 5 Plasma samples – 4 Top of storage box – 1 Potential re-collection – 10	20
Control ID	Gray	Serum samples – 5 Plasma samples – 4 Top of storage box – 1 Potential re-collection – 10	20

3. Labels for Trio Families

Special label sets are not produced for trio families. The standard label sets produced for the ASP families are used, discarding the labels for affected and unaffected siblings.

4. Labels for Case-Control Collection

Special label sets are produced for the cases and controls due to the unique ID structure. These can be distinguished from the ASP and trio label sets by the color striped label on the outside of the label set envelope.

5. Labels for Additional Affected Siblings

Under special circumstances, families with more than the standard number of members may be approved for study inclusion and the clinic will be sent the additional unique participant ID labels. The Coordinating Center will produce and send these label sets to the Regional Network Centers for shipment to the clinic.

6. Quality Control Labels

In addition to the pre-packaged label sets for family members, quality control (QC) labels are sent to the clinics. QC label sets are separate from the general exam label sets and are specified as “QC-Red” or “QC-Purple” on a label on the outside of the envelope. The QC label sets contain large labels for use on the *T1DGC Blood Collection Form* and QC blood collection tubes as well as small labels for laboratory (aliquot) use. The QC label sheets contain an additional row of labels printed with “Quality Control” to aid the clinics in identifying these labels and to prevent confusion. See **Chapter VIII,** *Quality Control*, for details regarding the QC scheme.

Table 3 outlines the use, number and type of labels (large and small) to be used for QC-Red and QC-Purple participants. For the case-control collection, separate sets of “QC-Red” and “QC-Purple” will be used. These can be distinguished by the label on the outside of the envelope, “Case QC-Red” or “Control QC-Purple.”

Table 3. Label Specifications for Quality Control Sample Collection

QC-Red	Number of Labels for Data Collection Forms and Samples	Total Number of Labels Needed
Large Label Sheet (3 labels/individual) Age Eligible Probands, Affected Siblings, Cases	Blood Collection Form – 1 Blood Collection Tube – 1 Shipping Form – 1	3/individual
Small Label Sheet (6 labels/individual)	Serum samples – 5 Top of Storage Box – 1	6/individual

QC-Purple	Number of Labels for Data Collection Forms and Samples	Total Number of Labels Needed
Large Label Sheet (6/family member) Any Age Eligible Family Member, Controls	Blood Collection Form – 1 Blood Collection Tube – 2 (1 for re-labeling EDTA tube after processing, if needed) Shipping Form – 1 for plasma sample shipment and 1 for cell pack shipment	5/individual
Small Label Sheet (5/individual)	Plasma samples – 4 Top of Storage Box – 1	5/individual

IV. RECRUITMENT

Chapter III, *Recruitment,* of the *Manual of Operations (MOO)* contains specific recruitment guidelines for this study. Participants are recruited based on individual network, regional and clinic strategies and goals. Recruitment strategies may include flyers, brochures and referrals from physicians or other healthcare professionals. Once an individual or family is contacted, eligibility of each individual and family must be ascertained.

V. ELIGIBILITY

An ASP family is deemed eligible if at least the proband **and** an affected full sibling are available and willing to participate; without these two individuals, the family itself is ineligible. The larger family unit is preferred, and the emphasis in the clinics must be to recruit and examine as many eligible family members as possible.

Trio families are eligible only if the affected child **and** both biological parents are available and willing to participate. No additional members of the trio family are eligible to participate. In the North American Network, trio families are eligible **only** if the biological parents self-identify as African American or Mexican American.

Case and control participants are eligible only in designated clinics in the Asia-Pacific, European and North American networks. In all networks, cases and controls are recruited from populations with a low prevalence of type 1 diabetes.

The *T1DGC Eligibility Form* identifies family members who are eligible and willing to participate in this study and is required to determine inclusion of a family and its members in the T1DGC. There are two versions of the eligibility form: one that is administered to the proband/case/control **OR** the other form for the parent/guardian of the proband/case/control if the proband/case/control is not old enough to consent. The appendices of **Chapter IV**, *Eligibility*, contain specific line-by-line instructions (Q x Qs) that guide the interviewer through each question of the eligibility form(s).

In the North American Network, the *T1DGC North American Trio Pre-Eligibility Form* is administered to the biological mother and father prior to the *T1DGC Eligibility Form.* This is to ascertain that the trio meets initial eligibility requirements. Appendix A of **Chapter IV**, *Eligibility*, contain specific line-by-line instructions (Q x Qs) that guide the interviewer through each question of the pre-eligibility form.

For ASP and trio families, once initial eligibility of the family is established, a family ID is assigned and contact with additional family members may proceed to determine other potential participants. The *T1DGC Family Contact Sheet* was developed to aid in tracking members of the family and provides room for contact information. It is intended for use by clinic personnel to help organize information as it is collected. This form is never data entered since it contains personal identifiers. Thus, this form is **never** forwarded to the Regional Network Center or to the Coordinating Center. In the case-control collection, only individuals are recruited, so there will be no

enrollment of other family members. Once eligibility of the individual is established, the case or control ID is assigned.

During completion of the *T1DGC Eligibility Form,* it is possible that the clinic will identify a participant whose type 1 diabetes status is questionable based on information obtained from this questionnaire (*e.g.*, type 1 diabetes not yet treated with insulin). At this point, eligibility is in question and a clinic staff member must complete the *T1DGC Application to Eligibility Committee*. (See **Chapter IV**, *Eligibility*, for detailed instructions in the use of this form.) All available information is included to aid the committee members in making a decision. If the application is for the proband and/or the affected sibling, only after the committee approves the application does the clinic continue the data collection with this family. The family is considered "PENDING" until that time. If a family is deemed ineligible, the clinic staff explains the reasons for ineligibility. **Chapter IV,** *Eligibility,* provides the interviewer with a response to questions regarding reasons for ineligibility that may arise during an interview. The same criteria apply to cases in the case-control collection in terms of completing an eligibility application. There is a separate *T1DGC Application to Eligibility Committee* for cases.

Up to three additional affected siblings may participate in an ASP family (for a total of five affected siblings). However, an *Application for Additional Affected Sibling* must be completed for approval of inclusion for each additional sibling. This form is completed at the clinic and forwarded to the Regional Network Center. Staff members at the Regional Network Center are responsible for approving inclusion of each sibling.

Upon approval, the Coordinating Center is notified and labels for the additional affected sibling are generated and sent to the Regional Network Center. Each Regional Network Center has also been provided several label packets that contain extra labels for families with additional affected siblings. If a clinic discovers that a family has potential additional affected siblings prior to assigning the family ID and label sets, they can request a set of labels that already include the additional labels and not have to wait for additional labels to be printed. The additional affected siblings are given participant

identifiers (*i.e.,* 07 for affected sibling 3; 08 for affected sibling 4; 09 for affected sibling 5), and secondary identifiers (*i.e.,* AS3 for affected sibling 3; AS4 for affected sibling 4; and AS5 for affected sibling 5).

In the event that a family ID, case ID or control ID has been assigned and the family, case or control subsequently is deemed ineligible or withdraws from the study before the exam, the assigned ID is discarded. The *T1DGC Discarded ID Log* was created to track such IDs and is located on the T1DGC web site. This log, in conjunction with other software, assists in tracking all IDs that have been sent to each network and clinic. The Regional Network Center or Coordinating Center may request to see the *Discarded ID Log* from individual clinics to verify missing IDs; however, it is not data entered. Once an ID (family, participant, case, or control) has been discarded, the remainder of the label set and any incomplete forms with those labels affixed must be destroyed. This will prevent that ID from being used mistakenly in the future.

VI. INFORMED CONSENT

A. Obtaining Consent

The following information contains guidelines for consenting individuals to participate in the T1DGC, and is set forth by the study investigators to ensure that good research practice is conducted and correct information is disseminated to the potential participant(s). Each institution's Internal Review Board (IRB) or Ethics Committee (EC) requires that the document being used by that particular clinic reflect the clinic-specific rules for written informed consent. Therefore, the following guidelines are general, and while they should be met to the best of each clinic's ability, there may be some variation among clinics and across networks.

The process of consenting individuals to participate in this study begins once potential participants have been asked if they are willing to participate in the T1DGC. For some institutions, this may be required prior to completing the *T1DGC Eligibility Form*, and for some this process begins once the participant is deemed eligible based

on the *T1DGC Eligibility Form*. Again, this is determined by the requirements of the local IRB or EC.

Once the participant agrees to participate, or to learn more about the study, a copy of the *Informed Consent* is provided to the potential participant or the parent/guardian of the participant. The most current version of the *Informed Consent* approved by the IRB or EC must be used. A template for each version of the informed consent (*i.e.*, adult, teenager, and child*)* for the T1DGC is maintained on the web site as a guide for the elements of consent required by the study. Separate consent forms for cases and controls are required and templates for each are maintained on the T1DGC web site. However, it is recognized that each clinic will need to modify the templates according to the specific requirements of the local IRB or EC.

Consent forms must be translated into the participant's native language. All translated forms must be back-translated into English.

A copy of the IRB or EC approval and the most current approved consent form must be provided to the Regional Network Center as soon as approval is obtained. The Regional Network Center will forward these on a monthly basis to the Coordinating Center. The approval documents should contain the date of approval and the date that the approval expires. Clinics will need to renew this approval prior to the expiration date for the years that the clinic is participating in the study.

A brief description of the study is written on a cue card and may be used to aid the interviewer in describing the study. However, the participant is required to read or have the *Informed Consent* read to him/her (if he/she is incapable of reading the document). The participant must be adequately informed of the purpose, methods, personal involvement in the study, direct benefit (or lack thereof), potential risks, and his/her rights. All questions that the potential participant/family has regarding the study must be answered thoroughly. Once the *Informed Consent* is provided to and read by

the participant and/or parent/guardian, it must be signed. In the case of a minor, the legal guardian signs the form. Once a signature is obtained, a unique individual ID is assigned.

Because this study involves children, special guidelines/considerations may be required by the institution's IRB or EC. Each clinic's study coordinators or recruiters must be familiar with all requirements that the institution has regarding the informed consent process with studies involving children. For example, certain institutions may require that young participants give their assent to participate in the study in addition to consent given by the parent or guardian of the child(ren). Assent is a child's oral or written affirmative agreement to participate in research (*i.e.*, a child says "yes" when asked if he/she would like to participate in the study). In addition, the age requirement for written consent may vary depending on the network, region and/or institution.

Once informed consent forms have been completed, copies are made. Certain local IRBs or ECs may require that the original be kept in the IRB/EC office. A copy must be maintained in the clinic and a copy **must** be provided to the participant.

A copy of the page on which the layered consent for various aspects of the exam is obtained is labeled with the participant's ID and sent to the Regional Network Center for entry into the informed consent database. Regional Network Centers and/or clinics may choose to include an ID label box on this layered portion of the consent form for the participant's ID label. The copy of the informed consent page that is forwarded to the Regional Network Center must be free of personal identifiers and participant signatures. In the event that a participant is re-consented or withdraws their consent, the Regional Network Center is notified and the informed consent database is updated.

For ASP and trio families, as informed consent forms for family members are signed and completed, the *T1DGC Consent Summary Form* is completed. Details on completion of this form are located in the Question by Question instructions (Q x Qs) in the appendices of **Chapter V**, *Interviewing Instructions*. No consent summary form is

completed for the case-control collection; however, there is an additional page to use with the layered consent [*T1DGC Consent Record (Addendum to Layered Consent)*] that records the type of consent and the consent date.

B. Withdrawing Consent

The consent form for the T1DGC study indicates that participants who change their mind about participating in the study may withdraw consent at any time by notifying the clinic/institution where they gave consent. Withdrawal of consent will require that their data be removed from the study database and that their data forms, blood samples and genetic material be destroyed.

As clinics begin to plan for close-out, the Clinic Coordinator should contact the local IRB/Ethics Committee to receive specific instructions and information about the local requirements for handling withdrawal of consent after the clinic, Regional Network Center and Coordinating Center are closed. The Clinic Coordinator and/or Clinic Principal Investigator should develop a long-term plan for handling withdrawal of consent. This may include providing the IRB/Ethics Committee with the list that contains the link of the participant and study IDs as well as the contact information for the network repositories.

Appropriate steps to be taken are outlined below, depending upon the family member(s) withdrawing their consent.

1. Withdrawal of Consent by ASP Family Participant

a. Proband or Affected Sibling Withdraws Consent

If either the proband (AS1, -03) or the affected sibling (AS2, -04) withdraws consent, the family is no longer eligible, unless there is an additional affected sibling (*i.e.,* there are still two siblings who have type 1 diabetes).

Clinic:

i. Notify the Regional Network Center (RNC) in writing that this participant has withdrawn consent and no longer wants to be enrolled in the study. The RNC should only be supplied participant ID; the participant's name should never be provided to the RNC. Include the participant IDs for all family members originally enrolled in the study.

ii. Place a statement in the family's file indicating the date that the clinic was contacted by the participant and the date that the RNC was notified that the participant had withdrawn consent and the family was no longer eligible.

iii. To ensure that this participant is not contacted again, clearly note the withdrawal of consent in a highly visible way in the participant's file and on the *ASP Family Contact Sheet*.

iv. Use the method that meets the local institution's IRB or Ethics Committee requirements to destroy the set of data forms collected for this participant and all family members. Retain only the statement regarding withdrawal of consent and RNC notification.

v. If needed, the Coordinating Center will send the *Notification to Destroy Samples* form(s) for each family member. If samples are still at the clinic, the clinic should complete the clinic section of the *Notification to Destroy Samples* form(s), send completed form(s) to the Coordinating Center and retain a copy of the form(s) in the clinic file.

Regional Network Center:

i. Notify the Coordinating Center of this participant's withdrawal of consent in writing and request that a *Notification to Destroy Samples* form be initiated, if needed. The form will need to be requested for each family member. Include participant IDs, the number and location of samples.

ii. Promptly complete the RNC portion of the *Notification to Destroy Samples* form when it is received from the Coordinating Center and forward it to the Coordinating Center.

iii. When a completed copy of the *Notification to Destroy Samples* form (if required) is received, place it in this participant's file.

iv. Using the method that meets the RNC's IRB or Ethics Committee requirements, destroy the set of data forms on file for this participant. Retain the statement from the clinic regarding withdrawal of consent and the RNC copy of the *Notification to Destroy Samples* form.

Coordinating Center:

i. Initiate the *Notification to Destroy Samples* for the participant and all family members.

ii. Send a copy of the completed *Notification to Destroy Samples* to the RNC for their files.

iii. Data previously entered into the study database will be marked as "withdrew consent," and these data will be deleted from the system and removed from reports.

iv. Determine if this family's forms were entered during double data entry; if so, these data should be deleted.

b. Father, Mother, Unaffected Sibling, and/or Additional Affected Sibling Withdraws Consent

If any other family member withdraws consent, the remaining family members' consents are valid and they are still eligible to participate in the study. If the father, mother, unaffected sibling, or an additional affected sibling notifies the Clinic Coordinator or Clinic Principal Investigator that they want to withdraw from the study, this does not affect the eligibility of the remaining family members. The following procedures should be implemented:

Clinic:

i. Notify the Regional Network Center in writing that this participant has withdrawn consent and no longer wants to be enrolled in the study. The

RNC should only be supplied participant ID; the participant's name should never be provided to the RNC.

ii. Place a statement in the family's file indicating the date that the clinic was contacted by the participant and the date that the RNC was notified.

iii. To ensure that this participant is not contacted again, clearly note the withdrawal of consent in a highly visible way in the participant's file and on the *ASP Family Contact Sheet.*

iv. If needed, the Coordinating Center will send the *Notification to Destroy Samples* form(s) for each family member. If samples are still at the clinic, the clinic should complete the clinic section of the *Notification to Destroy Samples* form(s), send completed form(s) to the Coordinating Center and retain a copy of the form(s) in the clinic file.

v. Use the method that meets the local institution's IRB or Ethics Committee requirements to destroy the set of data forms collected for this participant.

Regional Network Center:

i. Notify the Coordinating Center of this participant's withdrawal of consent in writing and request that a *Notification to Destroy Samples* form be initiated, if it is needed.

ii. Promptly complete the RNC portion of the *Notification to Destroy Samples* form when it is received from the Coordinating Center and forward it back to the Coordinating Center.

iii. When a completed copy of the *Notification to Destroy Samples* (if required) is received, place it in this participant's file.

iv. Using the method that meets the RNC's IRB or Ethics Committee requirements, destroy the set of data forms on file for this participant. Retain the statement from the clinic regarding withdrawal of consent and the RNC copy of the *Notification to Destroy Samples* form.

Coordinating Center:

i. Initiate the *Notification to Destroy Samples* for the participant, if needed.

ii. Send a copy of the completed *Notification to Destroy Samples* to the RNC for their files.

iii. Data previously entered into the study database will be marked as "withdrew consent," and these data will be deleted from the system and removed from reports.

iv. Determine if this participant's forms were entered during double data entry; if so, these data should be deleted from the study database.

2. Withdrawal of Consent by Proband in Trio Family

If the proband of a trio family withdraws consent, the trio is no longer eligible and the following procedures should be completed.

Clinic:

i. Notify the Regional Network Center in writing that the proband of this trio has withdrawn consent and no longer wants to be enrolled in the study. The RNC should only be supplied participant ID; they should never be given a participant's name. Include the participant IDs for all family members originally enrolled in the study

ii. Place a statement in the family's file indicating the date that the clinic was contacted by the proband and the date that the RNC was notified that proband had withdrawn consent and the trio was no longer eligible.

iii. To ensure that this proband is not contacted again, clearly note the withdrawal of consent in a highly visible way in the family's file and on the *Trio Family Contact Sheet*.

iv. If needed, the Coordinating Center will send the *Notification to Destroy Samples* form(s) for each family member. If samples are still at the clinic, the clinic should complete the clinic section of the *Notification to Destroy Samples* form(s), send completed form(s) to the Coordinating Center and retain a copy of the form(s) in the clinic file.

v. Use the method that meets the local institution's IRB or Ethics Committee requirements to destroy the set of data forms collected for this participant

and all family members. Retain only the statement regarding withdrawal of consent and RNC notification.

Regional Network Center:

i. Notify the Coordinating Center of this proband's withdrawal of consent in writing and request that a *Notification to Destroy Samples* form be initiated, if samples were collected. The form should be requested for each trio family member who had samples collected.

ii. Promptly complete the RNC portion of the *Notification to Destroy Samples* form when it is received from the Coordinating Center and forward it to the Coordinating Center.

iii. When a completed copy of the *Notification to Destroy Samples* form (if required) is received, place it in the family's file.

iv. Using the method that meets the RNC's IRB or Ethics Committee requirements, destroy the set of data forms on file for each member of the trio family. Retain the statement from the clinic regarding withdrawal of consent and the RNC copy of the *Notification to Destroy Samples* form.

Coordinating Center:

i. Initiate the *Notification to Destroy Samples* for any family member who had samples collected.

ii. Send a copy of the completed *Notification to Destroy Samples* to the RNC for their files.

iii. Data previously entered into the study database will be marked as "withdrew consent," and these data will be deleted from the system and removed from reports.

iv. Determine if this family's forms were entered during double data entry; if so, these data should be deleted from the study database.

3. Withdrawal of Consent by Mother and/or Father of Trio Family

If the mother or father of a trio family withdraws consent, the family is no longer eligible as a trio family and both the mother and father are considered ineligible. If the clinic is also recruiting case participants, the proband may be eligible for the study as a case participant. For more details on converting the proband to a case participant, see **Chapter XIV**, S*tudy Close-Out*. A *T1DGC Conversion to Case* form is completed for the proband and forwarded to the Regional Network Center along with the other data forms.

Clinic:

i. Notify the Regional Network Center (RNC) in writing that this mother or father has withdrawn consent and no longer wants to be enrolled in the study and thus both the mother and father are ineligible. The RNC should only be supplied the participants' ID; the participant's name should never be provided to the RNC. Include the participant IDs for both mother and father if either one withdraws.

ii. Place a statement in the family's file indicating the date that the clinic was contacted by the participant and the date that the RNC was notified that the participant had withdrawn consent and the family was no longer eligible. Note whether the proband was converted to a case participant.

iii. To ensure that these participants are not contacted again, clearly note the withdrawal of consent in a highly visible way in the participant's file and on the *Family Contact Sheet*.

iv. Use the method that meets the local institution's IRB or Ethics Committee requirements to destroy the set of data forms collected for the mother and the father. Retain only the statement regarding withdrawal of consent and RNC notification and the set of data forms for the proband.

v. If needed, the Coordinating Center will send the *Notification to Destroy Samples* form(s) for the mother and the father. If samples are still at the clinic, the clinic should complete the clinic section of the *Notification to*

Destroy Samples form(s), send completed form(s) to the Coordinating Center and retain a copy of the form(s) in the clinic file.

Regional Network Center:

i. Notify the Coordinating Center of the mother or father's withdrawal of consent in writing and request that a *Notification to Destroy Samples* form be initiated, if needed. The form will need to be requested both the mother and the father. Include participant IDs, the number and location of samples.

ii. Promptly complete the RNC portion of the *Notification to Destroy Samples* form when it is received from the Coordinating Center and forward it to the Coordinating Center.

iii. When a completed copy of the *Notification to Destroy Samples* form (if required) is received, place it in this family's file.

iv. Using the method that meets the RNC's IRB or Ethics Committee requirements, destroy the set of data forms on file for the mother and father. Retain the statement from the clinic regarding withdrawal of consent and the RNC copy of the *Notification to Destroy Samples* form as well as the proband's set of data forms if the proband is converted to a case participant.

Coordinating Center:

i. Initiate the *Notification to Destroy Samples* for the mother and father.

ii. Send a copy of the completed *Notification to Destroy Samples* to the RNC for their files.

iii. Data previously entered into the study database will be marked as "withdrew consent," and these data will be deleted from the system and removed from reports.

iv. Determine if this family's forms were entered during double data entry; if so, these data should be deleted from the study database.

4. Withdrawal of Consent by Case or Control Participant

If a case or control participant withdraws consent, the individual is no longer eligible and his/her data will be removed from the study database and data forms, blood samples and genetic material be destroyed.

Clinic:

i. Notify the Regional Network Center in writing that this participant has withdrawn consent and no longer wants to be enrolled in the study. The RNC should only be supplied participant ID; the participant's name should never be provided to the RNC.

ii. Place a statement in the individual's file indicating the date that the clinic was contacted by the participant and the date that the RNC was notified that the participant had withdrawn consent and was no longer eligible.

iii. To ensure that this participant is not contacted again, clearly note the withdrawal of consent in a highly visible way in the participant's file.

iv. If needed, the Coordinating Center will send the *Notification to Destroy Samples* form(s) for the participant. If samples are still at the clinic, the clinic should complete the clinic section of the *Notification to Destroy Samples* form, send the completed form to the Coordinating Center and retain a copy of the form in the clinic file.

v. Use the method that meets the local institution's IRB or Ethics Committee requirements to destroy the set of data forms collected for this participant. Retain only the statement regarding withdrawal of consent and RNC notification.

Regional Network Center:

i. Notify the Coordinating Center of this participant's withdrawal of consent in writing and request that a *Notification to Destroy Samples* form be initiated, if needed. Include participant ID, the number and location of samples.

ii. Promptly complete the RNC portion of the *Notification to Destroy Samples* form when it is received from the Coordinating Center and forward it to the Coordinating Center.

iii. When a completed copy of the *Notification to Destroy Samples* form (if required) is received, place it in this participant's file.

iv. Using the method that meets the RNC's IRB or Ethics Committee requirements, destroy the set of data forms on file for this participant. Retain the statement from the clinic regarding withdrawal of consent and the RNC copy of the *Notification to Destroy Samples* form.

Coordinating Center:

i. Initiate the *Notification to Destroy Samples* for the participant.

ii. Send a copy of the completed *Notification to Destroy Samples* to the RNC for their files.

iii. Data previously entered in the study database will be marked as "withdrew consent" and these data will be deleted from the system and removed from reports.

iv. Determine if this participant's forms were entered during double data entry; if so, these data should be deleted from the study database.

VII. HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY ACT OF 1996 (HIPAA)

The Health Insurance Portability and Accountability Act (HIPAA) was passed in 1996 as a means for the United States Congress to strive for incremental health care reform in the country. This act encompasses many components and is quite complex. For research purposes, we are concerned with a subsection called the Privacy Rule. This rule was established to protect individually identifiable health information by putting limits on the use and disclosure of an individual's protected health information (PHI).

On April 14, 2003, all institutions with access to PHI were required to be in compliance with these regulations. Health information included in this rule is anything

oral or recorded in any form that is created or received by a health care worker, health plan, public health authority, employer, life insurer, school, university or health care clearinghouse. The information can pertain to a person's physical or mental health or condition, health care provided to that person, or payment for the provision of health care in the past, present or future. Data collected from research is included as PHI, and thus is subject to the rules and regulations of HIPAA.

For research practice to continue within an entity that is covered by HIPAA, there are certain rules that must be followed. This includes the transmission of data within the T1DGC study. Under HIPAA regulations, data that are transmitted must be de-identified (*i.e.,* removal of eighteen identifiers from all forms of PHI). However, there are several ways in which PHI can be used and transmitted for research purposes that permit inclusion of certain data elements. For additional information regarding HIPPA regulations, visit http://www.hhs.gov/ocr/hipaa/.

For the T1DGC, a *Data Use Agreement for a Limited Data Set* is established by the Coordinating Center with each of the Regional Network Centers. This agreement essentially permits a limited number of identifiers to be released with health information including: age, full elements of dates (*e.g.,* birth date) and geocoding data to the level of city (*e.g.,* town/city, state, and full zip code). Copies of all data use agreements are maintained at the Coordinating Center and the Regional Network Centers.

All participants in the United States who sign an informed consent **must** sign a *Written Authorization* that authorizes the T1DGC to disclose certain elements of their PHI for research purposes. The *Written Authorization* is a document, either independent of the informed consent or embedded within the informed consent, that authorizes the entity to disclose that person's protected health information to other entities described in the document. Simply stated, this allows data/information to flow between all participating clinics, regions and networks to carry out the goals of the T1DGC. A potential participant who refuses to sign the *Written Authorization* cannot participate in the study. Refer to Appendix C for templates of the *Data Use Agreement* and *Written*

Authorization. The template for the *Written Authorization* is a guide for all elements important for this study.

In addition to the *Written Authorization*, each participant in the United States must be offered the Notice of Privacy Practices brochure. This brochure explains the privacy policy of the institution and is provided by the institution itself, and must be available for each potential participant of the T1DGC. Appendix C contains an example of this privacy notice, but this may not be used by any clinic. All clinics must obtain this material from their local IRB or EC.

For Regional Network Centers outside the United States, the rules of HIPAA apply only as it pertains to participant's data that are transmitted to the Coordinating Center at Wake Forest University School of Medicine. That is, all data must be de-identified, and contain only those few identifiers allowed by the terms of the *Data Use Agreement for a Limited Data Set*. Participants outside the United States sign only an informed consent and do **not** sign a *Written Authorization*.

The Coordinating Center at Wake Forest University practices strict procedures to maintain privacy and confidentiality of all research participants and the subsequent generated data. The Coordinating Center takes every precaution necessary to protect the privacy of all participants who have volunteered their time, and expects that all clinics, regions and networks uphold these same standards. It is expected that individual clinics maintain all participant files in locked cabinets accessible **only** to the study staff. In addition, information that is considered a personal identifier (*e.g.,* participant name) is kept only by the clinic staff and is **never** transmitted to the Regional Network Center or Coordinating Center.

VIII. EXAM (PARTICIPANT VISIT)

Once the participant has signed an informed consent, the exam consists of two required components: an interview to complete a brief questionnaire (the *T1DGC Exam Form*) and a blood collection for each consented participant (using the *Blood Collection*

Form). The exam form is completed before the blood is collected. (See **Chapter V**, *Interviewing Instructions,* for general interviewing guidelines and the Question by Question (QxQs) instructions for administering each form.) In the case-control collection, only the case completes the *T1DGC Exam Form*; there is no exam form for the control participant.

A. Scheduling Visits

Family members may attend a single clinic visit together or each member may come on a separate day. Thus, the length of time required to complete examination of an entire family varies. Clinics must be flexible in scheduling visits and every effort should be made to accommodate participants' schedules.

Family members may be seen at different clinics within the same network. The clinic IDs recorded on the forms must correspond to the clinic where the information was collected for that particular family member.

B. Identification Form, Participant and QC Selection Log

A *T1DGC Participant Identification Form* was created to establish a link between participant names and the T1DGC family and participant IDs. This form is available on the T1DGC web site, and it, or a similar one developed in the clinic, must be used for each unique ASP and trio family which participates in the T1DGC. The form is kept with the family's files, is **never** forwarded to the Regional Network Center or Coordinating Center, and is **never** data entered. If a problem arises and the participant must be identified (*e.g.,* the participant wishes to withdraw their blood sample) and the ID must be linked back to him/her, this form will provide a mechanism to do so. Each clinic is responsible for linking the family names and their respective IDs. There is no *Participant Identification Form* for the case-control collection. Clinics should be able to identify the participants in cases where the participant needs to be re-contacted.

In addition to the *T1DGC Participant Identification Form,* a *T1DGC Participant and QC Selection Log* was created as a method to track all participants seen in the

clinic and to determine when a QC sample needs to be collected and on which individual. The clinic staff member places a participant ID label on the log for each person participating in the study. Details on the use and completion of this form as well as quality control procedures are outlined in **Chapter VIII**, *Quality Control*. Although this form is not automatically sent to the Regional Network Center, the Regional Network Center may request these forms from a clinic.

C. Blood Collection

Once the exam form is completed (or the eligibility form for the control participant), the participant has blood collected. Prior to the exam, the participant should be informed of the procedures. This includes reiterating to the participant the amount of blood to be collected (approximately 2-3 tablespoons) and the importance of being well hydrated for the blood collection. Detailed procedures for blood collection, handling, and shipment to the various laboratories are outlined in **Chapter VI**, *Blood Collection and Processing*, and **Chapter VII**, *Sample Storage and Shipping*.

D. Completed Forms

Copies of the completed forms are sent weekly from the clinics to the Regional Network Center by regular postal service for data entry and subsequent transmission to the Coordinating Center. **Original forms are maintained at the clinics with copies forwarded to the Regional Network Center for data entry.**

1. ASP Families

For ASP families, forms are sent **only** when both the proband and affected sibling have been recruited and examined. When the ASP exams are completed, copies of the *T1DGC ASP Eligibility Form*, the *T1DGC ASP Consent Summary Form*, the layered portion of the consent form, the *T1DGC Blood Collection Form* for both individuals, and their respective *T1DGC ASP Exam Form* are sent to the Regional Network Center. As other members of the family are recruited, consented and blood collected, copies of the remainder of the *T1DGC ASP Exam Forms* and *T1DGC Blood Collection Forms* are sent. The most current version of the *T1DGC ASP Consent*

Summary Form is sent each time new members of a family are examined, and the exam and blood collection forms are sent to the Regional Network Center for entry. If desired, forms can be held until all family members are consented.

2. Trio Families

In trio families, all three members (*i.e.*, proband, father and mother) must be available and recruited for a family to participate. No forms are sent to the Regional Network Center unless all three are eligible, all have been interviewed, and all have had blood collected. When all are completed, the *T1DGC Trio Eligibility Form*, the *T1DGC Trio Consent Summary Form*, the layered portion of the consent form, the *T1DGC Trio Exam Forms*, and the *T1DGC Blood Collection Forms* are forwarded to the Regional Network Center.

In the North American Network, the *T1DGC North American Trio Pre-Eligibility Form* should be forwarded to the Regional Network Center with all other completed forms.

3. Case and Control Participants

In the case-control collection, forms are sent to the Regional Network Center as soon as eligibility has been determined and the participant has been interviewed, their blood has been collected, and the forms for that particular individual are completed. For cases, the *T1DGC Case Eligibility Form*, the layered portion of the consent form, the *T1DGC Consent Record (Addendum to Layered Consent)*, the T*1DGC Case Exam Form*, and the *T1DGC Blood Collection Form* are forwarded to the Regional Network Center on a weekly basis. For controls, the *T1DGC Control Eligibility form,* the layered portion of the consent form, the *T1DGC Consent Record (Addendum to Layered Consent)*, and the *T1DGC Blood Collection* Form are forwarded to the Regional Network Center.

E. Incomplete Forms/Data

Incomplete questionnaires/data are not sent to the Regional Network Centers. This includes a participant/family that is "PENDING" for varying reasons. Only at the time that the "PENDING" status is resolved and eligibility is confirmed can the completed forms be sent. No forms for an ASP family can be sent unless both the proband and affected sibling are recruited and examined. Likewise, forms for a family and/or participant deemed ineligible are **not** sent to the Regional Network Centers for data entry. Locally produced forms may be forwarded to the Regional Network Center for monitoring purposes, but are not entered into the primary T1DGC database. Figure 1 illustrates the sequence of events from distribution of label sets by the Coordinating Center through completion of exam and return of completed forms to the Regional Network Center for data entry.

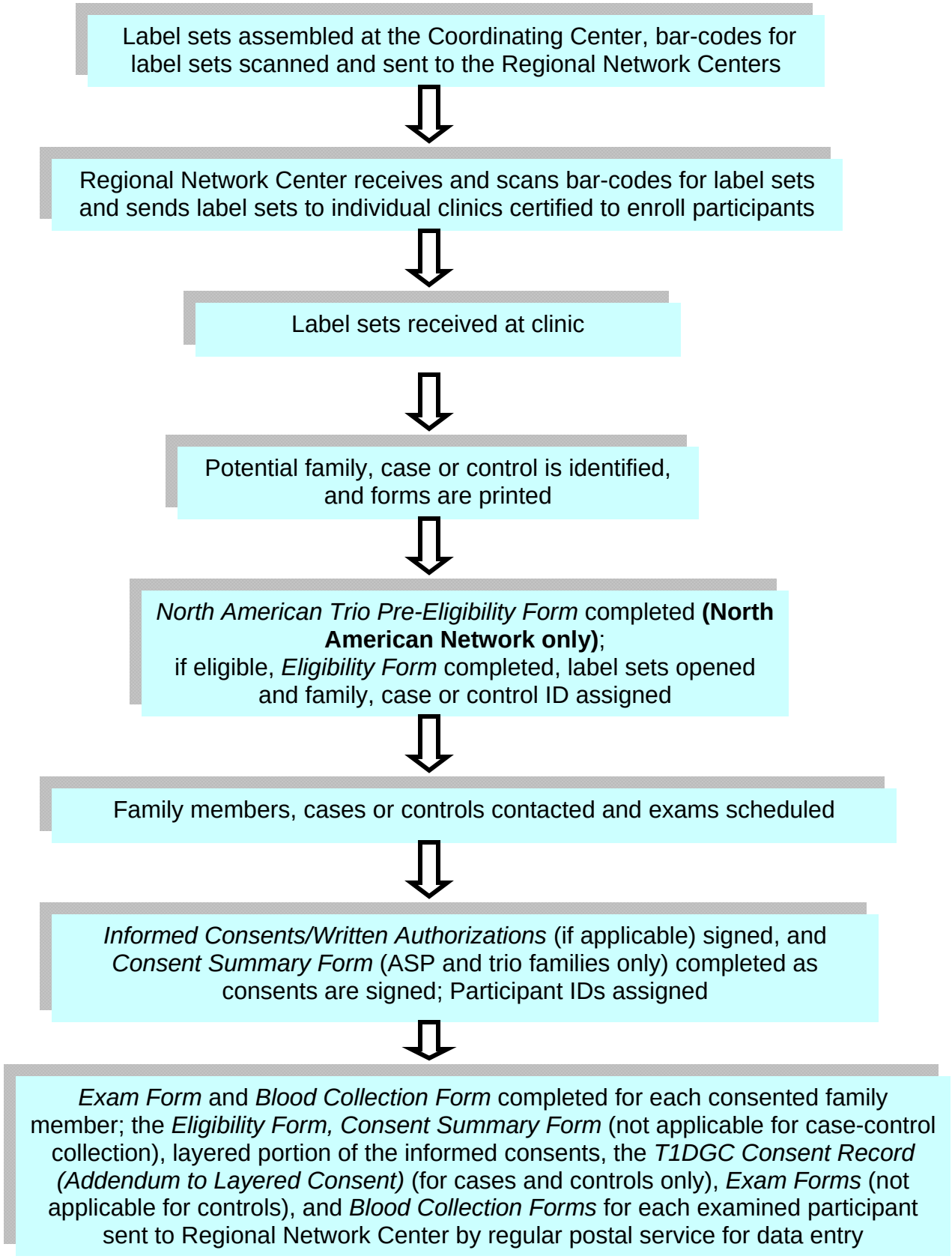
IX. POLICY FOR UNRELATED PARTICIPANTS

Throughout the course of the study, the T1DGC investigators may discover that a participant is unrelated to all other family members**. It is study policy that this information will not be shared with the family.** The Coordinating Center will notify the Regional Network Center of the suspected unrelatedness. If at all possible, a re-collection will be performed to confirm the familial relationship. If the study is unable to determine that the participant is related to the other family members, the participant's samples will be destroyed and the data removed from the database. Appendix D provides the complete *T1DGC Policy for Unrelated Participants*.

X. DESTRUCTION OF SAMPLES

All T1DGC samples should be retained until the clinic and/or laboratories receive a completed *T1DGC Notification to Destroy Samples* form from the Coordinating Center at Wake Forest University Health Sciences. The Coordinating Center will confirm the list of samples to be destroyed with the Regional Network Center prior to forwarding the form to the appropriate clinic or laboratory. Only after receipt of this form can the listed samples be destroyed. (See **Chapter VII**, *Sample Shipping and Storage,* for detailed instruction regarding destruction of samples.)

Figure 1. Sequence of Events in T1DGC Data Collection



XI. CLINIC PREPARATION, TRAINING AND CERTIFICATION

Prior to participant recruitment and data collection, each clinic must be formally trained by the Regional Network Center staff and certified by the Coordinating Center to begin the study. Clinics may not begin enrollment until they have received notification of successful completion of these requirements.

A. Clinic Preparation

Prior to the beginning of recruitment, there are requirements for conducting the study that must be made. First, the clinic's institution must have Office of Human Subjects Protections (OHRP) approval. This office is part of the US Department of Health and Human Services and has the responsibility of assuring that research with human subjects is done ethically and safely. If the institution already has approval, the clinic forwards the federal wide assurance (FWA) number to the Regional Network Center. If it does not, this process needs to begin immediately. The OHRP web site (http://www.hhs.gov/ohrp) provides detailed information on how to apply and obtain approval from this office for a clinic as well as a listing of the institutions that have this approval. Local IRB and EC offices are a good resource for determining if a clinic has an FWA number or for additional assistance in this process. As soon as approval is obtained, the clinic should notify the Regional Network Center of the FWA number.

The T1DGC study must be approved by the institution's IRB or EC. This includes the protocol, MOO, study forms, the informed consent document(s), and any posters or recruitment brochures. The informed consent templates are available on the T1DGC web site (https://www.t1dgc.org) and should be modified to satisfy the local institution's IRB or EC requirements and should include local contact information. If needed, the informed consent must be translated and then back-translated into English.

Once the IRB or EC has approved the study, a copy of the approved informed consent and the IRB/EC approval letter is forwarded to the Regional Network Center which forwards copies of each to the Coordinating Center. The approval letter must clearly state the date of the approval and the expiration date of the approval. For IRB or

EC approval letters in foreign languages, the clinic must provide these dates when the letter is forwarded to the Regional Network Center.

Clinics will need to order supplies for blood collection and shipping. The Regional Network Center can provide further guidance about this part of the clinic preparation.

B. Training

Training is provided by the Regional Network Center staff and can be conducted as centralized group training or with an individualized training session at the clinic site, depending on the needs and timing of the clinic joining the study. Training can occur while the clinic preparation is in process. It must occur prior to the certification and pilot study.

C. Certification

Certification consists of successful completion of a pilot study, including data forms, blood collection (including a QC sample for plasma) and laboratory shipments. The pilot study is intended to assess the readiness of the clinic to begin data collection for the T1DGC; as such, poor performance during the pilot signals a need to re-train prior to initiating data collection. Volunteers for the pilot study should not be T1DGC participants; use of "mock families," consisting of staff or family volunteers, is encouraged.

The Regional Network Center will work with the new clinic to ascertain that the pilot study was completed correctly by reviewing forms submitted and asking the clinic to correct any errors. The Regional Network Center will data enter the forms for the pilot study and notify the Coordinating Center that the pilot study is completed.

Once the data are entered, and the Regional Network Center has notified the Coordinating Center that the blood shipments arrived at the laboratories, the Coordinating Center will review the pilot study data and must indicate successful

completion of the pilot prior to a clinic beginning actual participant recruitment. This requires data entry of all forms at the Regional Network Center and successful specimen shipments to the Autoantibody and Storage Laboratory and the DNA Repository (including data entry of shipping forms at the laboratory).

The Coordinating Center will notify the Regional Network Center when a clinic has successfully completed the pilot study. If all other requirements are met, then the clinic can be certified to begin enrollment of participants.

BEFORE PARTICIPANT RECRUITMENT CAN BEGIN: In addition to the successful completion of the pilot study, all appropriate documentation (*i.e.*, copy of the clinic's approved informed consent, IRB/EC approval letter and OHRP approval) must be on file at the Regional Network Center and the Coordinating Center before actual data collection begins.

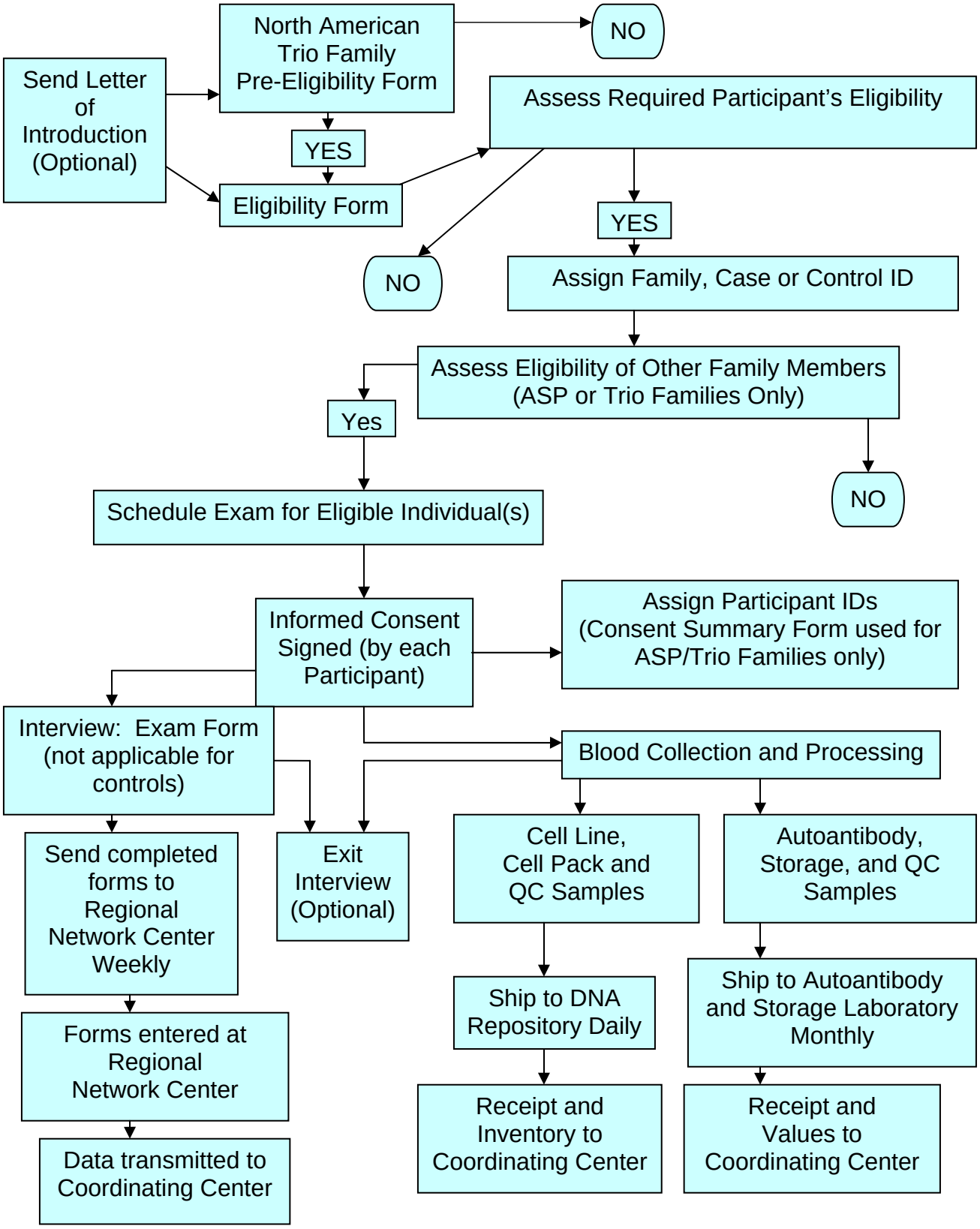
XII. SUMMARY OF STUDY FORMS

Table 4 summarizes the T1DGC forms, when each form is used and who is interviewed. The most current versions of the study forms are located on the T1DGC web site (http://www.t1dgc.org).

Table 4. Summary of T1DGC Study Forms

Form	Administered/ Used When	Participant Interviewed	Notes
North American Trio Pre-Eligibility	First contact with participant	Mother **AND** Father	One form completed per family; only for North American trios
Eligibility	First contact with participant	Proband/Case/ Control **OR** Guardian	One form completed per family/per case/per control
Family Contact Sheet	As eligibility is determined	Proband **OR** Guardian	Not data entered; ASP/trio families only
Consent Summary	As family members are consented	Each participating family member	One form per family ; ASP/trio families only
Layered Consent page	As family members are consented	Each participating family member	One form per individual
Addendum to Layered Consent	As cases or controls are consented	Each case or control	
Exam	Exam visit	Each participating individual	Administered to the guardian for children too young to complete for themselves. (Not applicable for Control)
Blood Collection (Original Collection)	Exam visit, at blood collection	Each participating individual	
Blood Collection (Re-collection)	As needed, at re-collection	Each participating individual	Only if errors or problems in the original collection or samples are lost or damaged during shipping
Application to Eligibility Committee	As needed, to determine eligibility	Proband, Affected Sibling, or Case	Only if type 1 diagnosis is in question
Application for Additional Affected Siblings	As needed	Proband **OR** Guardian	Only if more than 2 affected siblings in family; ASP families only. Sent to Regional Network Center for approval.
Adverse Event Report	As needed	Not applicable	If adverse event occurs
Clinic Shipping Form: Face Sheet and Contents Sheet	As needed	Not applicable	Completed with every shipment
Data Editing Log	As needed	Not applicable	Not data entered
Discarded ID Log	As needed	Not applicable	Not data entered
Daily Freezer Temperature Log	Recorded daily	Not applicable	Not data entered
Participant Identification	As needed	Not applicable	ASP/trio families only. Not data entered
Participant and QC Selection Log	As needed; each new participant added	Not applicable	Not data entered

APPENDIX A
T1DGC DATA COLLECTION FLOW CHART



APPENDIX B

IDENTIFIERS FOR T1DGC FAMILIES AND INDIVIDUALS

I. OVERVIEW

In a multi-center, international consortium that is as complex and diverse as the Type 1 Diabetes Genetics Consortium (T1DGC), there is great potential for confusion over participant specimens and forms. This confusion can compromise the integrity of data collected and overall study quality control. A consistent consortium-wide scheme for identification of participants and data that are collected from them can minimize these problems. While the consortium recognizes that it is highly unlikely that any clinic or laboratory currently uses the same identification scheme for clinical or research purposes, and, therefore an added burden is placed upon them, the benefits of a consortium-wide system outweighs the costs in familiarization and training.

II. REQUIREMENTS

The major requirements for the consortium identification scheme are:

A. Utilize a single identifier for all study data collected or derived for an individual participant in the consortium.

B. Ensure the identifier format chosen can be encoded within a bar-code label that can be attached to forms, large vacutainer tubes, or small 2-ml aliquot cryovials.

C. Identify any family within any network within the consortium.

D. Identify any individual within any network within the consortium.

E. Provide an easy mechanism for clinics or labs to identify forms or specimens that belong to the same individual, or the same family.

III. IDENTIFICATION SCHEME

A. Implementation

The requirements discussed above (Section II) are met by using a labeling system to label all paper forms and specimens. Each label has a bar-code and a numeric version of the identifier (ID) printed underneath the bar-code on the same label. Scanning the bar-code will show the numeric version of the ID on data entry screens. The numeric version of the bar-code ID (the participant ID) is the unique identifier for an individual participating in the T1DGC. All communications between clinics, Regional Network Centers, laboratories, and the Coordinating Center regarding the forms and specimens for individuals and families in the study will refer to the participant ID. Clinics use one set of bar-coded labels per family or individual, attaching them to paper copies of forms and blood collection tubes for each individual. Laboratories will scan the bar-codes on blood collection and storage tubes received from clinics or from the network laboratories.

After eligibility has been determined, the clinic staff selects a set of labels from the available sets, attaches these labels to forms and blood collection tubes; thus this family and/or participant ID is assigned to this specific individual. Labels not used at the initial visit are kept in the participant's files so that if a blood re-collection is necessary, the forms and blood collection tubes are labeled with the same participant ID as previous forms and tubes. Should the family (or participant) choose to withdraw from the study, the ID is **not** reassigned to another family or participant.

B. Technical Specifications

The specifications have been created using a Code 39 + mod 43 checksum bar-code format, with a numeric version of the ID printed underneath the bar-code on the same label. The vertical lines in the bar-code are the encoding of the ID that can be read by a bar-code scanner.

The separate components of the bar-code are discussed below. The actual bar-code lines do not encode the '-' (hyphen) separators; for example, the numeric ID 1-

1001-01 is actually read by a scanner as 1100101; the hyphens are automatically included in the numeric form on labels and in reports.

1. Network Code

Each network in the consortium has been assigned a single digit Regional Network Center code. The digits are assigned alphabetically:

Asia Pacific	1	
European	2	
North American	4	
United Kingdom	5	
Existing Samples	7	
Pilot Studies	8	(Reserved for pilot studies in all networks)
Coordinating Center	9	(Reserved for testing/Coordinating Center use)

2. ASP and Trio Participant IDs

a. Finalized bar-code format for ASP and trio families is:

Attribute	**Size**	**Allowed Value Range**
Network Code	char(1)	1 - 9
Family Code	char(4)	0001 – 9999
Individual Code	char(2)	01 – 99

The numeric version of the bar-code for the ASP and trio families, printed on labels will be:

X-XXXX-XX for example: 1-1001-01

b. Family Code

Within each network, the family code numbering begins at 0001 with a maximum of 9999; allowing for 9999 maximum families that can be recruited in a single network.

Since the same range of family codes is used within each network, the unique ID for a family in the study is a combination of network code + family code.

Family codes will not necessarily be sequential across families seen in a clinic. For example: family "A" is assigned family ID 2-0012 and then family "B" enters the clinic for their exam immediately after family "A," family "B" ***does not have to be assigned*** ID 2-0013. Available label sets may be split across multiple clinics in a network. Certain codes within each network will be reserved for special purposes such as quality control and internal checking. Clinics do not need to be concerned with these reserved family IDs and should use the next available label set as directed.

c. Participant Identifier

The individuals within an eligible participating family are assigned participant identifiers according to their relationship. The following list provides the standard codes for each family member:

Participant Identifier	**Relationship**
01	Father
02	Mother
03	Affected Sibling 1 (Proband)
04	Affected Sibling 2
05	Unaffected Sibling 1
06	Unaffected Sibling 2
07	Affected Sibling 3
08	Affected Sibling 4
09	Affected Sibling 5

Each father in every network will have a participant identifier of 01, each mother 02 and so on. ***The unique ID for an ASP or trio family individual in the study is a combination of network code + family code + individual code.***

In addition to the individual code within the overall bar-code, the individual members of a family can easily be identified from the colored stripes on the labels. The following list provides the standard bar-code color stripes for individual family members:

Bar-code Color Stripe	Relationship
Blue	Father
Pink	Mother
Purple	Affected Sibling 1 (Proband)
Green	Affected Sibling 2
Yellow	Unaffected Sibling 1
Yellow	Unaffected Sibling 2
Green	Affected Sibling 3
Green	Affected Sibling 4
Green	Affected Sibling 5

There will be some repetition in label stripe color. In these cases, such as multiple affected siblings or unaffected siblings, each individual will have a different participant identifier, but the same label color.

A third level of individual identifiers, the Secondary IDs, are recorded on forms by clinic staff. The corresponding Secondary IDs are shown below.

Secondary IDs	Relationship
FA	Father
MO	Mother
AS1	Affected Sibling 1 (Proband)
AS2	Affected Sibling 2
UN1	Unaffected Sibling 1
UN2	Unaffected Sibling 2
AS3	Affected Sibling 3
AS4	Affected Sibling 4
AS5	Affected Sibling 5

The Secondary IDs have two or three characters; for example, father is FA, while unaffected sibling 1 is UN1. When recording the Secondary ID on forms, for FA and MO, clinics leave one box blank in the three digit field.

The label's bar-code contains the full individual ID (X-XXXX-XX). The label also has the colored stripe and personal identifier that indicates the specific family member. The Secondary ID is recorded by clinic staff on all forms; except the *Eligibility Form* and the *Consent Summary Form,* which both require only the overall family ID.

3. Case and Control Participant IDs

a. Finalized bar-code format for cases and controls is:

Attribute	**Size**	**Allowed Value Range**
Network Code	char(1)	1 - 9
Participant Identifier	char(1)	7 (Case) or 8 (Control)
Individual Code	char(4)	0001 – 9999

The numeric version of the bar-code for the case-control collection, printed on labels will be:

X-X-XXXXX for example: 1-7-40001

b. Participant Code

Within each network, the case and control code numbering each begins at 0001 with a maximum of 9999; allowing for 9999 maximum cases and 9999 controls that can be recruited in a single network. ***Since the same range of individual codes is used within each network, the unique ID for a case or control participant in the study is a combination of the network code + the participant code.***

Codes for these individuals will not necessarily be sequential as assigned to each clinic because these label sets also may be split across multiple clinics in a

network. Clinics should use the next available label set for the case or control as directed.

c. Participant Identifier

Each case in every network will have a participant identifier of 7 and each control will have a participant identifier of 8. The unique ID for a case or control is a combination of network code + participant identifier + participant code.

In addition to the individual code within the overall bar-code, the individual can easily be identified from the colored stripes on the labels. The following list provides the standard bar-code color stripes for individuals in the case-control collection.

Bar-code Color Stripe	**Relationship**
Orange	Case
Gray	Control

A third level of individual identifiers, the Secondary IDs, are recorded on forms by clinic staff. The corresponding Secondary IDs are shown below.

Secondary IDs	**Relationship**
CAS	Case
CON	Control

In the case-control collection, all forms will include the individual participant ID in addition to the Secondary ID that will either be pre-recorded on the forms that are unique to the case and the control, or it will be completed by the clinic coordinator. The label's bar-code contains the full individual ID (X-X-XXXXX) as well as the colored stripe and the participant identifier that indicates that the person is a case or a control.

C. Examples

This section shows examples demonstrating the use of the identification scheme for different family (pedigree) structures.

Example 1:

ASP Family 0034 in Europe with participating father, mother, 2 affected siblings and 1 unaffected sibling.

Family ID = 2-0034

Individual	Full Bar-code ID	Secondary ID
Father	2-0034-01	FA
Mother	2-0034-02	MO
Affected Sibling 1 (Proband)	2-0034-03	AS1
Affected Sibling 2	2-0034-04	AS2
Unaffected Sibling 1	2-0034-05	UN1

Example 2:

*ASP Family 0034 in North America, participating father, mother, 4 affected siblings and 1 unaffected sibling.

Family ID = 4-0034

Individual	Full Bar-code ID	Secondary ID
Father	4-0034-01	FA
Mother	4-0034-02	MO
Affected Sibling 1 (Proband)	4-0034-03	AS1
Affected Sibling 2	4-0034-04	AS2
Unaffected Sibling 1	4-0034-05	UN1
Affected Sibling 3	4-0034-07	AS3
Affected Sibling 4	4-0034-08	AS4

* Notes:

1. 4-0034-06 is not used here since there is only 1 unaffected sibling in the family
2. Families in different networks may have the same family code, but the combination of network code + family code is unique study-wide, and constitutes the family ID.

Example 3:

Trio Family 0114 in Asia-Pacific, participating father, mother, 1 affected sibling.

Family ID = 1-0114

Individual	Full Bar-code ID	Secondary ID
Father	1-0114-01	FA
Mother	1-0114-02	MO
Affected Sibling 1 (Proband)	1-0114-03	AS1

Example 4:

*Case 00080 in the North American Network is an individual participating as a case.

Individual	Full Bar-code ID	Secondary ID
Case	4-7-00080	CAS

Note:

1. Cases and controls in different networks may have the same participant code, but the combination of network code + participant identifier + participant code is unique study-wide, and constitutes the individual's ID.

D. Rationale

The bar-code and participant ID format strikes a balance between having a long confusing string of redundantly encoded information with the need for being able to perform a quick visual check for source network and family on a blood sample or form. Since clinics generally manage and ship family specimens as a unit in the same box, this ID provides a quick way to identify and count family specimens without the need for constant cross-referencing of random single code identifiers. A visual check of family ID can help clinics prepare the boxes appropriately. Similarly, receiving laboratories will benefit from having a visual way to recognize family specimens since they will typically be stored in freezers, in boxes or racks with adjacent freezer addresses.

The network is encoded in the Participant ID to create the unique key for a family across all networks. This scheme of network code + family (or participant) code in the

identifier enables the Coordinating Center, Central Repositories, and other laboratories to quickly identify the source network for an individual/family.

APPENDIX C
HIPAA-RELATED DOCUMENTS

DATA USE AGREEMENT TEMPLATE

WRITTEN AUTHORIZATION TEMPLATE

EXAMPLE OF NOTICE OF PRIVACY PRACTICES

DATA USE AGREEMENT

This **DATA USE AGREEMENT ("the Agreement")** is effective the____day of _____, 2003, by and between **Wake Forest University Health Sciences** (**"Wake Forest"),** and _____ (**"Participant").**

R E C I T A L S:

WHEREAS, Wake Forest and Participant are part of the Type 1 Diabetes Genetics Consortium (the "**Consortium**"), whose general purpose is to identify genes that determine an individual's risk of type 1 diabetes;

WHEREAS, the Consortium requires the transfer, sharing, analysis, and other uses of various types of medical data among the many institutions that are participating internationally;

WHEREAS, medical data is regulated by various laws, regulations, protocols, and guidelines in both the United States and in other countries that are part of the Consortium, which the parties to this agreement wish to comply with;

NOW, THEREFORE, in consideration of the mutual agreements, covenants, terms and conditions herein contained, Wake Forest and Participant agree as follows:

I. TRANSFER AND USE OF LIMITED DATA

Section 1.1 **Activities.** Wake Forest and Participant will use and transfer data under this agreement only for the research purposes of the Consortium, specified in its Consortium Agreement, its Statement of Purposes, and its Specific Aims, as they may be modified from time to time.

Section 1.2 **Limited Data.** Wake Forest and Participant will transfer to each other data that is collected through the forms and protocols established by the Consortium, as they may be amended from time to time. Wake Forest and Participant acknowledge that these data elements are the minimum necessary for accomplishing the research purposes of the Consortium. Data that are transferred between Wake Forest and Participant will not contain any of the following information that can be used to identify the research participant or their relatives, household members or employers: names, telephone numbers, fax numbers, street addresses, electronic mail addresses, social security numbers, medical record numbers, insurance identification numbers, account numbers, certificate/license numbers, vehicle identifiers and serial numbers (including license plate numbers) device identifiers and serial numbers, Web Universal Resource Locators (URLs); Internet Protocol (IP) address numbers, biometric identifiers, full face photographic images and comparable images. Data without these personal identifiers shall be known as "**Limited Data**."

Section 1.3. **Use of Limited Data.** Wake Forest and Participant may use and disclose the Limited Data only as permitted under the terms of this Agreement or required by law, but shall not otherwise use or disclose the Limited Data and shall ensure that its directors, officers, employees, contractors and agents do not use or disclose the Limited Data in any manner that would constitute a violation of this Agreement or applicable law. Wake Forest and Participant agree not to use the Limited Data in such a way as to identify any individual and further agree not to contact any individual who might be identified using this data. Data User shall limit the use or receipt of the Limited Data to the individuals who reasonably need the Limited Data for the performance of the Consortium's Activities. Wake Forest and Participant shall use appropriate safeguards to prevent use or disclosure of the Limited Data other than as permitted under this Agreement.

Section 1.4. **Reporting of Disclosures of Protected Health Information.** Wake Forest or Participant shall, within thirty (30) days of becoming aware of any use or disclosure of the Limited Data in violation of this Agreement, report any such use or disclosure to the other party to this Agreement.

Section 1.5. **Notice of Request for Data**. Wake Forest and Participant agree to notify the other party within (7) business days if it receives an official request or legal subpoena for any Limited Data. To the extent that one party decides to challenge the validity of such request, the other party shall cooperate fully in such challenge.

Section 1.6. **Agreements by Third Parties.** Wake Forest and Participant shall obtain and maintain an agreement with each agent or subcontractor that has or will have access to the Limited Data, which requires such agent or subcontractor to be bound by the same restrictions, terms and conditions that apply to the Limited Data under this Agreement.

II. GENERAL PROVISIONS

Section 2.1. **Termination Upon Breach.** Any other provision of this Agreement notwithstanding, this Agreement may be terminated by either party upon fifteen (15) days written notice (including e-mail) to the other party in the event that the second party breaches any provision contained in this Agreement and such breach is not cured within such fifteen (15) day period. Wake Forest and Participant acknowledge and agree that in the event the other's efforts to cure any breach are unsuccessful, the first party has a duty to discontinue use of the Limited Data, notwithstanding any other provision of this Agreement to the contrary.

Section 2.2. **Return or Destruction of Data upon Termination.** If this Agreement is terminated due to breach of the Agreement, the breaching party shall either return or destroy all data received from the other party that the breaching party maintains in any form. The breaching party shall not retain any copies of such data. Notwithstanding the foregoing, to the extent that the non-breaching party agrees that it is not feasible to return or destroy such data, the terms and provisions of this Agreement shall survive termination of the Agreement and such data shall be used or disclosed solely as required by the reasons that prevented their return or destruction.

Section 2.3 **Injunction.** Wake Forest and Participant each acknowledge and agree that the other party will suffer irreparable damage if it breaches this Agreement and that damages from such breach shall be difficult to quantify. Therefore, Wake Forest and Participant acknowledge and agree that an action for an injunction may be filed to enforce the terms of this Agreement, in addition to any other remedy the law may provide.

Section 2.4. **Effect.** The terms and provisions of this Agreement shall supercede any other conflicting or inconsistent agreements between Wake Forest and Participant, including all exhibits or other attachments thereto and all documents incorporated therein by reference.

IN WITNESS WHEREOF, the parties have caused this Agreement to be executed as of the day and year first written above.

Wake Forest:	**Participant:**
By: _____	By: _____
Title: _____	Title: _____
Date: _____	Date: _____

Wake Forest University Health Sciences
North Carolina Baptist Hospital
Authorization for Use or Disclosure of Protected Health Information for Research

Study Title
First Name Last Name, Degree, Principle Investigator

You have already agreed to take part in the research study with the title listed above. The purpose of this study is *[insert purpose of study as it appears in the informed consent]*. In deciding whether or not to take part you have read the informed consent, been able to ask questions about this research study, have had your questions answered, signed the informed consent and been given a copy. This form gives you some more information about how health information collected about you for this research study will be used by the researchers and disclosed to others involved in the research study.

Taking part in this research study may involve collecting health information that you consider confidential or private and that directly identifies you. As described in the research informed consent for this study, information from study-related visits, procedures, test, interventions, interactions, questionnaires, or surveys will be collected. In addition, information in your medical/health records may be reviewed and collected. The researchers may also need to discuss your health information with individuals responsible for treating you such as your physician. All the collected information will be used and possible disclosed and re-disclosed to monitor your health status, to measure effects of drugs/devices/procedures/interventions, to determine research results and outcomes, and possibly to develop new drugs/devices/tests/procedures and commercial products.

Your health information may be used by, disclosed to and re-disclosed for research, quality assurance, or regulatory purposes by members, agents or successors of the research team such as the principal investigator, co-investigators, and members of their research staff; other researchers and their staff involved with this study at other medical centers, institutions, hospitals, central laboratories or study related sites such as data monitoring committees, coordinating centers, data management centers, or data reading centers; the sponsor of the study, [Insert Sponsor Name]; the U.S. Food and Drug Administration (FDA) and similar governmental agencies in other countries; the Department of Health and Human Services (DHHS) agencies; the Federal Office of Human Research Protection; North Carolina Baptist Hospitals;, and Wake Forest University Health Sciences. *[Add any other individuals, organizations, agencies, etc. to this list as applicable for the particular study]* All or part of your research related health information may be used or disclosed for treatment, operations or payment related to providing you healthcare. If this research study involves the treatment or diagnosis of a medical condition research related health information may be placed in your medical record and discussed with individual not involved with the study that are caring for you. This will allow the individuals caring for you to have information about what drugs, tests or procedures you are receiving in the study and treat you appropriately, if you have other health problems or needs. Your research related health information may be disclosed if required by state or federal law. The results of this research study may be presented at meetings or in publications. Your identity will not be disclosed in those presentations.

Although every effort will be made to keep your research-related information private, absolute confidentiality and protection of your information cannot be guaranteed. If your information is disclosed to a person or entity that is not covered by the federal privacy regulations it may be re-disclosed. Your research-related information may be used or disclosed until the end of the research study. If your research-related information is included in a research database or repository there is no scheduled date at which this information will be destroyed or no longer used. This is because research information continues to be analyzed for many years and it is not possible to determine when this will be complete. You agree to waive access to or review of your research-related information for the period of the conduct of the research and of the use of the research findings for regulatory purposes. You can access or review your information after this time.

Taking part in this research study is voluntary and you have the right to choose to not sign this form. If you decide not to sign, you cannot participate in this study. You may decide to revoke this authorization at any time by providing written notification of your decision. If you decide at any time to revoke your authorization any information already collected will continue to be used to the extent that it has already been relied on for the study, as necessary to maintain the integrity of the research study or as required by law. You will also not be able to continue to take part in the study if you revoke this authorization. Refusing to sign this authorization or deciding to revoke this authorization will not affect you ability to obtain treatment, or payment or eligibility for benefits to which you are entitled. This Authorization has no expiration date.

You will be given a signed copy of this authorization form.

Signatures

I agree to authorize the use and disclosure of my health information as described above. By signing this form I have not given up any legal rights that I am entitled to. If I have not already received a copy of the Privacy Notice, I may request one. If I have any question or concerns about my privacy or for information about where to write to revoke this Authorization I should contact the Privacy Officer at (336) 713-2320.

_____

Subject Name (Printed)

_____ _____

Subject Signature Date

_____

Legally Authorized Representative Name (Print)

The above named Legally Authorized Representative has authority to act for the research subject based upon:

[ ] The Legally Authorized Representative holds the subject's health care power of attorney

[ ] The Legally Authorized Representative is the subject's spouse

[ ] The subject is a minor and the Legally Authorized Representative is the subject's parent

[ ] The subject is a minor and the Legally Authorized Representative is the subject's guardian who is authorized under North Carolina state law to consent on behalf of the minor for general medical care.

[ ] Other: (specify) _____

_____ _____

Legally Authorized Representative Signature Date

Wake Forest University Health Sciences
North Carolina Baptist Hospital
Authorization for Use or Disclosure of Protected Health Information for Research

Study Title
BG# ____-_____
First Name Last Name, Degree, Principle Investigator

You have already agreed to take part in the research study with the title listed above. The purpose of this study is *[insert purpose of study as it appears in the informed consent]*. In deciding whether or not to take part, you have read the informed consent, been able to ask questions about this research study, have had your questions answered, signed the informed consent and been given a copy. This form gives you additional information about how health information collected about you for this research study will be used by the researchers and disclosed to others involved in the research study.

Taking part in this research study may involve collecting health information that you consider confidential or private and that directly identifies you. As described in the research informed consent for this study, information from study-related visits, procedures, test, interventions, interactions, questionnaires, or surveys will be collected. In addition, information in your medical/health records may be reviewed and collected. The researchers may also need to discuss your health information with individuals responsible for treating you such as your physician. All the collected information will be used and possibly disclosed and re-disclosed to monitor your health status, to measure effects of drugs/devices/procedures/interventions, to determine research results and outcomes, and possibly to develop new drugs/devices/tests/procedures and commercial products.

Your health information may be used by, disclosed to and re-disclosed for research, quality assurance, or regulatory purposes by members, agents or successors of the research team such as the principal investigator, co-investigators, and members of their research staff; other researchers and their staff involved with this study at other medical centers, institutions, hospitals, central laboratories or study related sites such as data monitoring committees, coordinating centers, data management centers, or data reading centers; the sponsor of the study, [Insert Sponsor Name]; the U.S. Food and Drug Administration (FDA) and similar governmental agencies in other countries; the Department of Health and Human Services (DHHS) agencies; the Federal Office of Human Research Protection; North Carolina Baptist Hospitals;, and Wake Forest University Health Sciences. *[Add any other individuals, organizations, agencies, etc. to this list as applicable for the particular study]* All or part of your research related health information may be used or disclosed for treatment, operations or payment related to providing you healthcare. If this research study involves the treatment or diagnosis of a medical condition, research related health information may be placed in your medical record and discussed with individuals not involved with the study who are caring for you. This will allow the individuals caring for you to have information about what drugs, tests, or procedures you are receiving in the study and treat you appropriately if you have other health problems or needs. Your research related health information may be disclosed if required by state or federal law. The results of this research

study may be presented at meetings or in publications. Your identity will not be disclosed in those presentations.

Although every effort will be made to keep your research-related information private, absolute confidentiality and protection of your information cannot be guaranteed. If your information is disclosed to a person or entity that is not covered by the federal privacy regulations, it may be re-disclosed. Your research-related information may be used or disclosed until the end of the research study. If your research-related information is included in a research database or repository there is no scheduled date at which this information will be destroyed or no longer used. This is because research information continues to be analyzed for many years and it is not possible to determine when this will be complete. You agree to waive access to or review of your research-related information for the period of the conduct of the research and of the use of the research findings for regulatory purposes. You can access or review your information after this time.

Taking part in this research study is voluntary and you have the right to choose not to sign this form. If you decide not to sign, you cannot participate in this study. You may decide to revoke this authorization at any time by providing written notification of your decision. If you decide at any time to revoke your authorization, any information already collected will continue to be used to the extent that it has already been relied on for the study, as necessary to maintain the integrity of the research study, or as required by law. You will also not be able to continue to take part in the study if you revoke this authorization. Refusing to sign this authorization or deciding to revoke this authorization will not affect your ability to obtain treatment, or payment, or eligibility for benefits to which you are entitled. This Authorization has no expiration date.

You will be given a signed copy of this authorization form.

Signatures

I agree to authorize the use and disclosure of my health information as described above. By signing this form, I have not given up any legal rights that I am entitled to. If I have not already received a copy of the Privacy Notice, I may request one. If I have any question or concerns about my privacy or for information about where to write to revoke this Authorization, I should contact the Privacy Officer at (336) 713-2320.

_____

Subject Name (Printed)

_____ _____

Subject Signature Date

_____

Legally Authorized Representative Name (Print)

The above named Legally Authorized Representative has authority to act for the research subject based upon:

[ ] The Legally Authorized Representative holds the subject's health care power of attorney

[ ] The Legally Authorized Representative is the subject's spouse

[ ] The subject is a minor and the Legally Authorized Representative is the subject's parent

[ ] The subject is a minor and the Legally Authorized Representative is the subject's guardian who is authorized under North Carolina state law to consent on behalf of the minor for general medical care.

[ ] Other: (specify) _____

_____ _____

Legally Authorized Representative Signature Date

NORTH CAROLINA BAPTIST HOSPITAL
WAKE FOREST UNIVERSITY HEALTH SCIENCES

PRIVACY NOTICE

THIS NOTICE DESCRIBES HOW MEDICAL INFORMATION ABOUT YOU MAY BE USED AND DISCLOSED AND HOW YOU CAN GET ACCESS TO THIS INFORMATION.

PLEASE REVIEW IT CAREFULLY.

WHO WILL FOLLOW THIS NOTICE
This Notice describes the privacy practices of North Carolina Baptist Hospital (Hospital) and Wake Forest University Health Sciences, which includes Wake Forest University Physicians (Clinic) and:

- Any health care professional authorized to enter information into your Hospital and/or Clinic chart;
- All departments and units of the Hospital or Clinic (including the pharmacy);
- Any member of a volunteer group we allow to help you while you are in the Hospital or Clinic; and
- All employees, staff and other Hospital and/or Clinic personnel.

These entities, sites and locations will follow the terms of this Notice. In addition, these entities, sites and locations may share medical information with each other for treatment, payment or Hospital operations purposes described in this Notice.

OUR PLEDGE REGARDING MEDICAL INFORMATION
We understand that medical information about you and your health is personal. We are committed to protecting medical information about you. We create a record of the care and services you receive at the Hospital and/or Clinic. We need this record to provide you with quality care and to comply with certain legal requirements. This Notice applies to all of your health information communicated by you or generated by the Hospital and/or the Clinic, whether made by Hospital personnel or your personal doctor. A doctor or Hospital not associated with our facilities may have different policies or notices regarding the doctor's use and disclosure of your medical information created in the doctor's office or Clinic. A notice of their privacy practices may be obtained directly from them.

This Notice will tell you about the ways in which we may use and disclose medical information about you. This Notice also describes your rights and certain obligations we have regarding the use and disclosure of medical information.

We are required by law to:

- make sure that medical information that identifies you is kept private;
- give you this Notice of our legal duties and privacy practices with respect to medical information about you; and
- follow the terms of the Notice that is currently in effect.

HOW WE MAY USE AND DISCLOSE MEDICAL INFORMATION ABOUT YOU

The following categories describe different ways that we use and disclose medical information. For each category of uses or disclosures we will explain what we mean and try to give some examples. Not every use or disclosure in a category will be listed. However, all of the ways we are permitted to use and disclose information will fall within one of the categories.

For Treatment: We may use your medical information to provide you with medical treatment or services. We may disclose your medical information to doctors, nurses, technicians, medical students, or other Hospital personnel who are involved in taking care of you. For example, a doctor treating you for a broken leg may need to know if you have diabetes because diabetes may slow the healing process. In addition, the doctor may need to tell the dietitian if you have diabetes so that we can arrange for appropriate meals. Different departments of the Hospital and/or Clinics also may share medical information about you in order to coordinate the different things you need, such as prescriptions, lab work and x-rays. We also may disclose medical information about you to people outside the Hospital or Clinic who will be involved in your medical care after you leave the Hospital or Clinic, such as caregivers or others we use to provide services that are part of your care.

For Payment: We may use and disclose medical information about you so that the treatment and services you receive at the Hospital and/or Clinic may be billed to and payment may be collected from you, an insurance company or a third party (including collection agencies). For example, we may need to give your health plan information about surgery you received at the Hospital so your health plan will pay us or reimburse you for the surgery. We may also tell your health plan about a treatment you are going to receive to obtain prior approval or to determine whether your plan will cover the treatment.

For Health Care Operations: We may use and disclose medical information about you for Hospital and/or Clinic operations. We may disclose medical information to "business associates" who provide business services on behalf of the Hospital and/or Clinic. These uses and disclosures are necessary to run the Hospital and Clinics and make sure that all of our patients receive quality care. For example, we may use medical information to review our treatment and services and to evaluate the performance of our staff in caring for you. We may also combine medical information about many Hospital patients to decide what additional services the Hospital or Clinic should offer, what services are not needed, and whether certain new treatments are effective. We may also disclose information to doctors, nurses, technicians, medical students, and other Hospital or Clinic personnel for review and learning purposes. We may also combine the medical information we have with medical information

from other health care entities to compare how we are doing and see where we can make improvements in the care and services we offer. We may remove information that identifies you from this set of medical information so others may use it to study health care and health care delivery without learning who you are. For example, your information may be used for purposes of quality assurance and quality improvement by either/or the Hospital or its physicians.

Appointment Reminders: We may use and disclose medical information to contact you as a reminder that you have an appointment for treatment or medical care at the Hospital or Clinic.

Treatment Alternatives: We may use and disclose medical information to tell you about or recommend possible treatment options or alternatives that may be of interest to you.

Health-Related Benefits and Services: We may use and disclose medical information to tell you about health-related benefits or services that may be of interest to you.

Fundraising Activities: We may use certain information (such as your name, address, telephone number, dates of service) to contact you in the future to seek donations for community service programs, patient care, medical research, and education.

Hospital Directory: We may include certain limited information about you in the Hospital directory while you are a patient at the Hospital. This information may include your name, location in the Hospital, your general condition (e.g., fair, stable, etc.) and your religious affiliation. The directory information, except for your religious affiliation, may also be released to people who ask for you by name. Your religious affiliation may be given to a member of the clergy, such as a priest or rabbi, even if they don't ask for you by name. This is so your family, friends, and clergy can visit you in the Hospital and generally know how you are doing.

Individuals Involved in Your Care or Payment for Your Care: We may release medical information about you to a friend or family member who is involved in your medical care. We may also give information to someone who helps pay for your care. We may also tell your family or friends your condition and that you are in the Hospital. In addition, we may disclose medical information about you to an entity assisting in a disaster relief effort so that your family can be notified about your condition, status and location.

Research: Under certain circumstances, we may use and disclose medical information about you for research purposes. For example, a research project may involve comparing the health and recovery of all patients who received one medication to those who received another, for the same condition. All research projects, however, are subject to a special approval process. This process evaluates a proposed research project and the use of medical information pursuant to the project, trying to balance the research needs with patients' need for privacy of their medical information. Before we use or disclose medical information for research, the project will have been approved through this research approval process; however, we may disclose medical information about you to people preparing to conduct a research project, for example, to help them look for patients with specific medical needs, so long as the medical information they review does not leave the facility, and so long as the information sought is necessary for the research purpose. We will almost always ask for your specific permission if the research involves treatment. If you are asked for such permission, you have the right to refuse.

As Required by Law: We will disclose medical information about you when required to do so by federal, state or local law.

To Avert a Serious Threat to Health or Safety: We may use and disclose medical information about you when necessary to prevent a serious threat to your health and safety or the health and safety of the public or another person.

SPECIAL SITUATIONS

As Required by State or Federal Law: We will disclose medical information about you when necessary to do so by federal, state, or local law or other judicial or administrative proceeding.

Organ and Tissue Donation: If you are an organ donor, we may release medical information to organizations that handle organ procurement or organ, eye or tissue transplantation or to an organ donation bank, as necessary to facilitate organ or tissue donation and transplantation.

Military and Veterans: If you are a member of the armed forces, we may release medical information about you as required by military command authorities. We may also release medical information about foreign military personnel to the appropriate foreign military authority.

Workers' Compensation: We may release medical information about you for workers' compensation or similar programs. These programs provide benefits for work-related injuries or illness.

Public Health Risks: We may disclose medical information about you for public health activities. These activities generally include the following:

- to prevent or control disease, injury or disability;
- to report births and deaths;
- to report child abuse or neglect;
- to report reactions to medications or problems with products;

- to notify people of recalls of products they may be using;
- to notify a person who may have been exposed to a disease or may be at risk for contracting or spreading a disease or condition; and
- to notify the appropriate government authority if we believe a patient has been the victim of abuse, neglect or domestic violence. We will only make this disclosure if you agree or when required or authorized by law.

Health Oversight Activities: We may disclose medical information to a health oversight agency for activities authorized by law. These oversight activities include, for example, audits, investigations, inspections, and licensure. These activities are necessary for the government to monitor the health care system, government programs, and compliance with civil rights laws.

Lawsuits and Disputes: If you are involved in a lawsuit or a dispute, we may disclose medical information about you in response to a court or administrative order. We may also disclose medical information about you in response to a subpoena, discovery request, or other lawful process by someone else involved in the dispute, but only if efforts have been made to tell you about the request or to obtain an order protecting the information requested.

Law Enforcement: We may release medical information if asked to do so by a law enforcement official:

- in response to a court order, subpoena, warrant, summons or similar process;
- to identify or locate a suspect, fugitive, material witness, or missing person;
- about the victim of a crime if, under certain limited circumstances, we are unable to obtain the person's agreement;
- about a death we believe may be the result of criminal conduct;
- about criminal conduct at the Hospital or Clinic or on medical center property; and
- in emergency circumstances to report a crime; the location of the crime or victims; or the identity, description or location of the person who committed the crime.

Coroners, Medical Examiners and Funeral Directors: We may release medical information to a coroner or medical examiners. This may be necessary, for example, to identify a deceased person or determine the cause of death. We may also release medical information about patients of the Hospital to funeral directors as necessary to carry out their duties.

National Security and Intelligence Activities: We may release medical information about you to authorized federal officials for intelligence, counterintelligence, and other national security activities authorized by law.

Protective Services for the President and Others: We may disclose medical information about you to authorized federal officials so they may provide protection to the President, other authorized persons or foreign heads of state, or to conduct special investigations.

Inmates: If you are an inmate of a correctional institution or under the custody of a law enforcement official, we may release medical information about you to the correctional institution or law enforcement official. This release would be necessary (1) for the institution to provide you with health care; (2) to protect your health and safety or the health and safety of others; or (3) for the safety and security of the correctional institution.

YOUR RIGHTS REGARDING MEDICAL INFORMATION ABOUT YOU
You have the following rights regarding medical information we maintain about you:

Right to Inspect and Copy: You have the right to inspect and copy medical information that may be used to make decisions about your care. Usually, this includes medical and billing records, but does not include psychotherapy notes.

If you request a copy of the information, we may charge a fee for the costs of copying, mailing or other supplies associated with your request.

We may deny your request to inspect and copy in certain very limited circumstances. If you are denied access to medical information, you may request that the denial be reviewed. Another licensed health care professional chosen by the Hospital or Clinic, as applicable, will review your request and the denial. The person conducting the review will not be the person who denied your request. We will comply with the outcome of the review.

Right to Amend: If you feel that medical information we have about you is incorrect or incomplete, you may ask us to amend the information. You have the right to request an amendment for as long as the information is kept by or for the Hospital or Clinic.

We may deny your request for an amendment if it is not in writing or does not include a reason to support the request. In addition, we may deny your request if you ask us to amend information that:

- was not created by us, unless the person or entity that created the information is no longer available to make the amendment;
- is not part of the medical information kept by or for the Hospital or Clinic;
- is not part of the information which you would be permitted to inspect and copy; or
- is accurate and complete.

Right to an Accounting of Disclosures: You have the right to request an "accounting of disclosures." This is a list of certain disclosures we made of medical information about you. This accounting does not include disclosures that are made to carry out treatment, payment, or health care operations, or information that has already been delivered to you or your health care representative, or information disclosed pursuant to an authorization.

Your request must state a time period which may not be longer than six years and may not include dates before April 14, 2003. Your request should indicate in what form you want the list (for example, on paper, electronically). The first list you request within a 12 month period will be free. For additional lists, we may charge you for the costs of providing the list. We will notify you of the cost involved and you may choose to withdraw or modify your request at that time before any costs are incurred.

Right to Request Restrictions: You have the right to request a restriction or limitation on the medical information we use or disclose about you for treatment, payment or health care operations. You also have the right to request a limit on the medical information we disclose about you to someone who is involved in your care or the payment for your care, like a family member or friend.
We are not required to agree to your request. If we do agree, we will comply with your request unless the information is needed to provide you emergency treatment.

In your request, you must tell us (1) what information you want to limit; (2) whether you want to limit our use, disclosure or both; and (3) to whom you want the limits to apply, for example, disclosures to your spouse.

Right to Request Confidential Communications: You have the right to request that we communicate with you about medical matters in a certain way or at a certain location. For example, you can ask that we only contact you at work or by mail.

We will not ask you the reason for your request. We will accommodate all reasonable requests. Your request must specify how and where you wish to be contacted.

Right to a Paper Copy of This Notice: You have the right to a paper copy of this Notice. You may ask us to give you a copy of this Notice at any time. Even if you have agreed to receive this Notice electronically, you are still entitled to a paper copy of this Notice.

You may obtain a copy of this Notice at our web site, www.Privacy@wfubmc.edu.
To obtain a paper copy of this Notice, contact (336) 713-HIPA (4472) (Privacy Office).

CHANGES TO THIS NOTICE

We reserve the right to change this Notice. We reserve the right to make the revised or changed Notice effective for medical information we already have about you as well as any information we receive in the future. We will post a copy of the current Notice in the Hospital and Clinics. The Notice will contain the effective date. In addition, each time you register at or are admitted to the Hospital or Clinic for treatment or health care services as an inpatient or outpatient, we will make best efforts to make available a copy of the current Notice in effect.

COMPLAINTS

If you believe your privacy rights have been violated, you may file a complaint with the Hospital, Clinic, or with the Secretary of the Department of Health and Human Services. To file a complaint with the Hospital or Clinic, contact the Privacy Office at (336) 713-HIPA (4472).

You will not be penalized for filing a complaint.

OTHER USES OF MEDICAL INFORMATION

Other uses and disclosures of medical information not covered by this Notice or the laws that apply to us (for example, treatment, payment, and health care operations) will be made only with your written authorization. If you provide us with an authorization to use or disclose medical information about you, you may revoke that authorization, in writing, at any time. If you revoke your authorization, we will no longer use or disclose medical information about you for the reasons covered by your written authorization. We are unable to protect disclosures that were made with your authorization. We are required to retain our records of the care that we provided to you.

OPT-OUT INFORMATION

To not have this Hospital or Clinic contact you for fundraising efforts, disclose directory information about you, disclose medical information about you to a friend or family member, you must notify the Privacy Office in writing.

To request inspection and copying of medical information about you, an amendment, an accounting of disclosures, restrictions, or confidential communication, you must notify the Privacy Office in writing. WFUBMC Medical Center Boulevard Winston-Salem, NC 27157

If you have any questions about this Notice, please contact the Privacy Office at (336) 713-HIPA (4472).

EFFECTIVE DATE: April 14, 2003

NCBH Department of Legal Affairs Review Date: April 1, 2003
WFUHS University Counsel Review Date: April 1, 2003

Reference: AHA Regulatory Advisory (2/13/01) 42 C.F.R. Parts 160 and 164 (2003)

APPENDIX D
T1DGC POLICY FOR UNRELATED PARTICIPANTS

If a participant is found to be unrelated to all other family members through various T1DGC genotyping projects, the policy will be to:

- request a replacement sample be sent to the genotyping facility for re-testing, if possible (depending on the genotyping facility) ;
- request the Network DNA Repository to confirm that the cell line and cell pack DNA are the same; and
- request the clinic to complete a re-collection sample, if possible.

Affected Sibling Pair (ASP) Families

- If an unrelated participant is confirmed in an ASP family (father, mother, unaffected sibling), the unrelated participant's samples will be destroyed and the participant will be marked as ineligible.
- If the unrelated participant in the ASP family is a proband or affected sibling, and there is not another affected sibling OR the family is not one of the minority populations where trios/cases are being collected, all family members will be destroyed and this family will be marked as ineligible.
- If there is another affected sibling, the unrelated proband or affected sibling's samples will be destroyed and the participant will be marked as ineligible; this family will still be an ASP family.
- If the ASP was collected in a clinic where trios are being collected and both parents are participating, this family will be converted to a trio family. This will involve transferring the information on the ASP forms to trio forms.
- If both parents are not participating and the clinic is recruiting cases, the other affected sibling (not the unrelated one) will be converted to a case using the "T1DGC Conversion to Case Form." All other family members will have their samples destroyed and will be marked as ineligible.
- If both parents are not participating and the clinic is not recruiting cases, all family members will be destroyed and the family will be marked as ineligible.

Trio Families

- If an unrelated participant is determined in a trio family, and the clinic is collecting case participants, the proband will be converted to a case sample and the mother and father's samples will be destroyed and they will be marked as ineligible participants.
- If the clinic is not collecting case participants, all samples from the family will be destroyed and the family will be marked as ineligible.
- Probands will be able to be converted to cases in Asia-Pacific (Cuttack), Europe (Cameroon) and North America (those clinics recruiting cases). All unrelated participants found in other clinics will have samples from the entire family destroyed.
- If the proband is being converted to a case participant, the clinic and Regional Network Center will complete the "T1DGC Conversion to Case Form."

Notification to Clinics

- Clinics will be notified of confirmed unrelated participants. Clinics will be instructed **not** to notify the families of the relationships discovered by the T1DGC.