WAKE FOREST
UNIVERSITY
HEALTH SCIENCES

Office of Research
INSTITUTIONAL REVIEW BOARD.

MEMORANDUM

To: Ronny Bell, Ph.D.
PHS - Epidemiology

From: Chair, IRB # 2
Institutional Review Board

Date: 4/13/2011

Subject: Human Protocol: IRB00015926
SEARCH for Diabetes in Youth - Phase 3 - Coordinating Center

Study Documents:
Protocol Version: SEARCH 3 Protocol; Other Documents: CES-D form, Colorado IRB Approval Letter, Contact Information - Participant, Contact Information Form - Parent version, Diabetes Eating Problem Survey - age 10 and older, Diabetes Related Family Conflict Survey - Parent version, Diabetes Related Family Conflict Survey - Participant age 10 and older, Extended Core Information form, Family Medical History form, Food Frequency Questionnaire, Health Questionnaire - Parent version, Health Questionnaire - Participant version, Initial Participant Survey - Parent version, Initial Participant Survey - Participant version, Kaiser Permanente IRB Approval Letter, Low Blood Sugar Survey - Adult age 18 and over, Low Blood Sugar Survey - Child Teen age 10-17 version, Low Blood Sugar Survey - Parent, Medical Record Validation of Self-Report, Medication Inventory form, Neuropathy form, Pediatric Diabetes Quality of Life - Parent version, Pediatric Quality of Life - Participant version, PedsQL Child Report (ages 5-7), PedsQL Child Report (ages 5-7) Diabetes module, PedsQL Child Report (ages 8-12), PedsQL Child Report (ages 8-12) Diabetes module, PedsQL Parent Report for Children (ages 8-12), PedsQL Parent Report for Children (ages 8-12) Diabetes module, PedsQL Parent Report for Teens (ages 13-18), PedsQL Parent Report for Teens (ages 13-18) Diabetes module, PedsQL Parent Report for Toddlers (ages 2-4), PedsQL Parent Report for Toddlers (ages 2-4) Diabetes module, PedsQL Parent Report for Young Children (ages 5-7), PedsQL Parent Report for Young Children (ages 5-7) Diabetes module, PedsQL Teen Report (ages 13-18), PedsQL Teen Report (ages 13-18) Diabetes module, PedsQL Young Adult (ages 19 and over), PedsQL Young Adult (ages 19 and over) Diabetes module, Physical Examination form, Quality of Care - Parent version, Quality of Care - Participant version, Specimen Collection form, Supplemental Questionnaire for age 10 and older, Tanner Stage - Female, Tanner Stage - Male, Unanticipated Occurrence Condition Reporting form, Unregistration form

The Institutional Review Board (IRB) has approved the above-named protocol and study documents, after review at a convened meeting on 4/12/2011. A submission requesting renewal together with a summary progress report must be submitted to the Board at least one month prior to 4/12/2012.

This research meets the criteria for a waiver of consent entirely according to 45 CFR 46(d).

This research meets the criteria for a waiver of assent according to 45 CFR 46.116(d).

This research meets the criteria for a waiver of HIPAA authorization according to 45 CFR 164.512.

Based on the information provided, the IRB has determined that HIPAA does not apply to this study.

This research, which involves children, meets the criteria at 45 CFR 46.404 (research involving no greater than minimal risk). Permission of one parent or guardian is sufficient.

Federal regulations and Board policy require that you promptly report to the Board for review/approval:

- Proposed changes in the research activity (e.g., protocol amendments; consent form revision; advertisements). Changes may not be initiated without IRB review and approval, unless necessary to eliminate an immediate hazard to subjects.

- Serious adverse events and unanticipated problems involving risks must be reported to the Board, institutional officials, FDA, sponsor and other regulatory agencies as required by the protocol, local policy and state or federal regulation.

Please provide a final report to the Board when the project is completed and Board approval can be terminated.

This IRB is in compliance with the requirements in Part 56, Subchapter D, Part 312 of the 21 Code of Federal Regulations published January 27, 1981 and Part 46, Subpart A of 45 CFR published January 26, 1981.

Gregory Hawkins, Ph.D.

Medical Center Boulevard, Winston-Salem, NC 27157-1023 (336) 716-4542 / fax (336) 716-4480

KAISER PERMANENTE®
Medical Care Program
Southern California Region

Institutional Review Board
Kaiser Permanente Southern California

Approval Notice

December 22, 2010

KPSC Principal Investigator

Jean M. Lawrence, ScD, MPH, MSSA
Research and Evaluation
100 S Los Robles Ave, 4th Floor
Pasadena, CA 91101

KPSC Approved Performance Site(s)

Kaiser Permanente Southern California
(Except San Diego)

KPSC Sub-Investigator(s)

Kristi Reynolds, PhD
Ann K. Kershnar, MD

Study Title: SEARCH for Diabetes in Youth, Phase 3: California Center (#5836)

Approved Materials:

Centers for Epidemiologic Study Depression Scale Protocol; SEARCH for Diabetes in Youth Phase 3 Protocol, Version 11/09/2010; Blood Test Results Letter for Registry and Cohort English/Spanish; Blood Test Results with Error Message Registry and Cohort 110510 English/Spanish; Centers for Epidemiologic Study Mental Health Referral Letter; Immediate Retinal Pathology Participant Letter; IPS Introductory Letter-Young Adults 110810; IPS Last Chance Letter- Parent; IPS Last Chance Letter-Young Adult; Physician Cover letter for Lab Results; Business Reply Envelope; Opt-out and Information Request Post Card Eng/Spanish; Basic Guidelines for Scheduling Study Visits by Telephone; Appointment Reminder Card Spanish/English; Birthday Card English/Spanish; Birthday Card Envelope; Behavioral Health Care Declined Referral Form; Cohort Visit Invitation Card Parents 110510; Cohort Visit Invitation Card Young Adults 110510; Contact Information -Parent Spanish/English 020106; Contact Information- Participant Spanish/English 020106; Documentation of Receipt of Gift Cards for Search Study Participation; Explanation of SEARCH Laboratory Test Results Spanish/English; Family Medical History Form Spanish/English; Lab Fresh Specimen Shipment Form; Lab Frozen Specimen Shipment Form; SEARCH physical examination form (3 and older); Case Validation Form; SEARCH IPS Thank You Card Registry Visit Parent; SEARCH IPS Thank You Card Registry Visit Young Adult; SEARCH Phase 3 List of Forms Submitted; Retinal Eye Photography Report; SEARCH 3 Extended Core Information Form; Medical Record Validation of Self Report; Specimen Collection Form; Unanticipated Occurrence Condition Reporting Form; Un-registration Form

Approved Questionnaires:

SEARCH CES-D Survey English/Spanish; Diabetes Eating Problem Survey (DEPS-R) for Age 10 and Older Eng/Span; Diabtes Related Family Conflict Survey -Parent Version Cohort Study (Spanish); Diabetes Related Family Conflict Survey-Participant Version (Age 10-17)Eng/Spanish; Food Frequency Questionnaire Spanish/Engl
Health Questionnaire Young Adult Cohort Study Spanish; Health Questionnaire-Parent Version Eng/Span
Health Questionnaie-Young Adult Version (Age 18 and Older) Eng/Span; Initial Patient Survey-Parent/Gurdian Version Eng/Span; Initial Patient Survey-Young Adult Version; Eng/Span; Low Blood Sugar Survey-Children/Teen Version (age 10-17) Eng/Span; Low Blood Sugar Survey-Adult Version (Age 18 and over) Eng/Span; Low Blood Sugar Survey-Parent Version; Medication Inventory Form Eng/Span; Pediatric Quality of Life Scale-Parent Version Eng/Span; Pediatric Quality of Life Scale- Young Child Report (ages 5-7) Eng/Span; Peds-QL-Pediatric Quality of Life Inventory- Young Child Report (ages 5-7) Eng/Span; Peds-QL- Diabetes Module, Version 3.0-Young Child Report (Ages 5-7) Eng/Span; Peds-QL Child Report (Ages 5-7) Eng/Span; Peds-QL Diabetes Module Young Child Report (Ages 5-7) Eng/Span; Peds-QL Child Report (Ages 8-12) Eng/Span; Peds-QL Diabetes Module Child Report (Ages 8-12)Eng/Span; Peds-QL Parent Report for Children (ages 8-12) Eng/Span; Peds-QL Diabetes Module Parent Report for Children (ages 8-12) Eng/Span; Peds-QL Parent Report for

Teens (ages 13-18) Eng/Spanish; Peds-QL Diabetes Parent Report for Teens (ages 13-18) Eng/Span; Peds-QL Parent Report for Toodlers (ages 2-4) Eng/Span; Peds-QL Diabetes Parent Report for Toodlers (ages 2-4) Eng/Span; Peds-QL Parent Report for Young Children (ages 5-7) Eng/Span; Peds-QL Diabetes Parent Report for Young Children (ages 5-7) Eng/Span; Peds-QL Teen Report (ages 13-18) Eng/Span; Peds-QL Diabetes Teen Report (ages 13-18) Eng/Span; Peds-QL Young Adult (ages 19+) Eng/Span; Peds-QL Diabetes Young Adult (ages 19+) Eng/Span; Quality of Care Survey Parent/Guardian Version Cohort Study Eng/Span; Quality of Care Survey Young Adult Version Eng/Spanish; Michigan Neuropathy Screening Instrument and 10-gram Filament Exam; Diabetes Related Family Conflict Survey-Parent Version for those who have a 10-17 year old child; SEARCH Medication Inventory; Supplemental Questionnaire for age 10 and older English/Spanish; SEARCH Tanner Stage Female for age 10-17 English/Spanish; SEARCH Tanner Stage Male for age 10-17 English/Spanish

Accepted Documents:
Award Letter and two CDC funding Applications included

Study Expiration Date: **11/25/2011**

On **December 21, 2010**, the convened Kaiser Permanente Southern California (KPSC) Institutional Review Board (IRB) reviewed and **approved** your new study for one year.

The IRB determined that this study satisfies the requirements of 45 CFR 46.404, research/clinical investigations not involving greater than minimal risk. The permission, including signed informed consent, of one parent is required. In accordance with 45 CFR 46.408 , the KPSC IRB has determined that assent of children age 7 and older is a necessary condition for proceeding with this research/clinical investigation.

The IRB granted a waiver of written HIPAA authorization to use of Protected Health Information for the eligibility screening component of the study.

The IRB also **approved** the informed consent form(s) as submitted.

The finalized informed consent form[s], which includes the HIPAA Authorization section, will be sent to you via e-mail in an Acrobat PDF file. If you have any questions or need any information regarding the consent form[s], please contact Daria Galindo at (626) 405-5972 (tie line 8/335-5972).

The KPSC Principal Investigator (PI) is required to:

- Review the document entitled HIPAA Privacy Rule Instructions for Researchers (attached).
- Submit a complete progress or final report of research activities.

And if applicable,

- Submit for IRB review modifications to the research and/or IRB approved research documents.
- Submit Adverse Event report(s) according to IRB policies and procedures and consistent with federal regulations.
- Submit Protocol Violation report(s) according to IRB policies and procedures and consistent with federal regulations.

Sincerely,

Armida Ayala, MHA, PhD
Director, KPSC Research Subjects Protections
Office/Institutional Review Board (IRB)

Cc
Sharon Figgins
Area Research Chairperson

Academic Affairs
Pharmacy Service Director

InterOffice Memorandum

December 22, 2010

KAISER PERMANENTE®
Medical Care Program
Southern California Region

Institutional Review Board
Kaiser Permanente Southern California

Steven J. Jacobsen, MD, PhD
Director, Research & Evaluation

Eric Macy, M.D.
Chair, Institutional Review Board

Walnut/2
Telephone 626.405-3665
Telefax 626.405.5186
Tie Line 335

To
Distribution

Disposition of Pharmaceutical Company Funds After Completion of Research Project

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Congratulations on the approval of your research project. We want to inform you at the beginning of your study that there is an SCPMG Board of Directors policy on the disposition of account balances at the conclusion of pharmaceutical/ manufacturing company funded research projects. If applicable, this policy calls for any remaining balance at the completion of a study to be transferred to a general research fund which is administered by the Regional Research Department.

Consistent with this SCPMG policy, we want you to be informed that any funds remaining at the completion of your project will revert to the general research account to supplement Community Service research funds allocated for studies approved by the Regional Research Committee and the Institutional Review Board.

We wish you success in your research endeavors. Please do not hesitate to call Dr. Jacobsen (8-338-3460) or Dr. Macy (8-291-5410) if you have any questions.

Cc
Sharon Figgins
Area Research Chairperson

Academic Affairs
Pharmacy Service Director

Consent Form Approval

Approved

Date: FEB 04 2011 Valid For Use Through: 10.21.2011

COMIRB B2

Study Title: SEARCH for Diabetes in Youth Registry Study
Principal Investigator: Dana Dabelea, MD, PhD
COMIRB No: Protocol 01-934
Version Date: 01/24/2011
Version No: 1.0

You (in this form 'you' refers to you and/or your child) are being asked to participate in a research study. This form provides you with information about the study. A member of the research team will describe this study to you and answer all of your questions. Please read the information below and ask questions about anything you don't understand before deciding whether or not to take part.

Why is this study being done?
You are being asked to take part in a research study called the SEARCH for Diabetes in Youth Registry Study because you have diabetes and were diagnosed under the age of 20. The study's aims are to count how many children have diabetes and determine whether diabetes is increasing in children and adolescents, to more accurately determine what type of diabetes you have, and to identify how diabetes affects the lives of youth with diabetes.

Diabetes is the third most common chronic disease in individuals under 20 years of age. The total number of cases of diabetes in this age group is increasing. Also, types of diabetes not seen previously in young people are now being seen. We do not know how many cases and types of diabetes in children and adolescents there are in the United States and whether diabetes is increasing. We also do not know the type of care young people with diabetes receive, or the effect of diabetes on their lives. Specifically, this project is interested in studying the following questions.

a. How many cases of diabetes are there in the United States in people under 20 years old?
b. How many new cases of diabetes develop every year?
c. What can we learn about each type of diabetes?
d. What medical care is given to youth with diabetes?
e. How does diabetes affect the lives of youth with diabetes?

Other people in this study
Up to 1200 youth less than 20 years old will be enrolled locally, and up to 4000 youth less than 20 years old will be invited to participate nationally in this study.

What happens if I join this study?
If you agree to participate in this study you will be asked to come to an in-person visit. If you haven't already completed the Initial Participant Survey (IPS), you will be asked to complete the IPS at the visit. The IPS is a brief survey that asks questions about demographic information (name, address, date of birth, data of diagnosis, education), as well as information about family history, symptoms you may have experienced at the time of diagnosis, your health care and health insurance. The IPS also collects contact information so we know the best way to reach you. A brief survey will also be sent to you each year in order to maintain contact information, no matter what parts of the study you choose to participate in.

All aspects of this study are for research purposes only and are in addition to regular health care. You may choose not to take part in any part of the study. If you join the study, you will be in it until the end of SEARCH in September 2015.

In-person Visit

1.) Collection of Blood and Urine:

You will be scheduled for a morning appointment. You will come to the visit after not having anything to eat or drink other than water for 8-12 hours. Please do not take your morning insulin prior to arrival, unless you must control your blood sugars. Upon arrival, blood will be drawn from your arm to measure blood sugar, hemoglobin A1c, c-peptide (a measure of your own insulin production), different types of cholesterol (blood fats), and islet cell antibodies (markers in the blood for type 1 diabetes). A genetic marker for diabetes risk (HLA genes) will also be tested. The total amount of blood drawn for these tests will be based on weight tables and will not exceed 1.5 tablespoons.

A urine sample will also be collected and tested to see if diabetes is affecting your kidneys. After these tests are obtained, you can take your pills or insulin and you will be given a snack.

2.) **Physical Examination and Questionnaire:**

After eating, you will have your medicines recorded and a physical examination will be performed by trained study personnel. The physical examination will include height, weight, waist measurement, blood pressure, and examination of the skin on the neck. Thereafter a brief questionnaire will be administered to update your contact information.

The time to complete the in-person is approximately 40 minutes. If you need numbing cream applied before the blood draw, it will add about 30 minutes to the visit.

Research Data and Specimens

Blood and urine samples will be labeled with a study number code and sent to the Central Laboratory at University of Washington Seattle to be tested. The research team will inform you of your test results that may affect your health or healthcare. With your permission, the test results will also be shared with your healthcare provider.

The SEARCH study would like to keep some of the blood and urine that is taken during the study but is not used for other tests. If you agree, an additional sample of blood (1.5 tablespoons) will be taken, and the excess urine sample will be saved. Whenever possible, blood for storage will be drawn at the same time as the samples for the in-person visit tests. If it is not possible, an additional needle stick will be required with your permission. The blood and urine samples will be kept and may be used in future research to learn more about diabetes. The research that is done with your blood and urine samples is not designed to specifically help you. It might help people who have diabetes and other diseases in the future. Reports about research done with your samples will not be given to you or your doctor. These reports will not be put in your health records. The research using your stored blood and urine samples will not affect your care.

The choice to let SEARCH study investigators keep the blood and urine samples for future research is up to you. No matter what you decide to do, it will not affect the care that you will receive as part of the study. If you decide now that your blood and urine samples can be kept for research, you can change your mind at any time and contact your study doctor to let him or her know that you do not want the SEARCH study to use your blood and urine samples any longer, and they will no longer be used for research. Otherwise, they may be kept until they are used up, or until the SEARCH study investigators decide to destroy them.

In the future, people who do research with your blood and tissue samples may need to know more about your health. While the SEARCH study may provide reports about your health, they will not give them your name, address, phone number or any other information that will let the researcher know who you are.

DNA (Genes) Blood Sample

You are also being asked for permission to use your blood to have genetic material (DNA) stored for possible use in genetic research about diseases that are passed on in families. If you agree to this request, no more than one additional tablespoon (15ml) of blood will be drawn. DNA is found in all of your cells. DNA makes up your genes. Your genes control how tall you are, what color hair you have, and all other body traits. The DNA in each person's body is different from every other person's DNA (except identical twins or triplets who have the same DNA). The differences in DNA may explain why some people are more likely to get certain diseases like diabetes.

We know that diabetes runs in families, but we don't know all the genes that are involved in the development of diabetes and its complications. In addition, there are specific types of diabetes that can only be diagnosed by genetic tests. By studying the DNA in your blood sample, researchers may be able to find the genes that carry the risk factors for problems such as diabetes, heart disease, complications such as eye and kidney trouble, and related conditions (high cholesterol, etc.).

Even if your blood samples are used for this kind of research, the results will not be told to you and will not be put in your health records.

Blood and Urine Storage

Your blood and urine samples will only be used for research and will not be sold. The research done with your samples may help to develop new products in the future, but there is no plan for you to be paid. The possible benefits of research from your blood and urine include learning more about what causes diabetes and other diseases, how to prevent them and how to treat them. The greatest risk to you is the release of information from your health records. The SEARCH study research team will protect your records so that your name, address and phone number will be kept private. The chance that this information will be given to someone else is very small. There will be no cost to you for any blood or urine collected and stored by the SEARCH study.

Your stored blood, urine and DNA samples will be kept in storage indefinitely or until the sample is no longer usable. A code number identifies samples and the link between the code and your personal information is stored in a secure location at the University of Colorado. Thus, your sample will not be directly identified with your name. Your samples would be released to a SEARCH investigator (or other investigator authorized by the SEARCH) only after determination of the scientific usefulness of a proposed study and would be reviewed for compliance with human research safety and protection guidelines before approval.

Participation in this study is voluntary and you may choose to withdraw from the study at any time. You may request that your stored samples be permanently removed from the Central Laboratory if you choose to withdraw consent. To request that your sample be permanently removed from the central laboratory, contact:

Dr. Dana Dabelea
UCD Colorado School of Public Health
Dept. of Epidemiology
Bldg 500, Box B-119
Aurora, CO 80045
Ph. (303) 724-4414 FAX (303) 724-4491

We will send a request to the central laboratory and they will then destroy the samples and send us a letter certifying that the sample has been destroyed. We will send you a copy of this letter.

Please read each sentence below and think about your choice. After reading each sentence, check "Yes" or "No" and write your initials. If you have questions, please talk to the SEARCH study staff, Dr. Dabelea or your healthcare provider. Remember, no matter what you decide to do about the storage and future use of your blood and urine samples, you may still take part in the study.

1. I wish to have the results of my blood and urine tests given to my doctor or diabetes care provider.

☐ Yes ☐ No _____Initials

2. I give my permission for my blood and urine samples to be stored in a central laboratory at the University of Washington, Seattle for future use by study investigators in studies of diabetes and diabetes risk factors and complications.

☐ Yes ☐ No _____Initials

3. I give my permission for my DNA (genes) blood sample to be tested for inherited factors in the development of diabetes, diabetes risk factors and complications.

☐ Yes ☐ No _____Initials

4. I give my permission for my DNA (genes) blood sample to be stored in a central laboratory at the University of Washington, Seattle for future use in diabetes and diabetes-related studies.

☐ Yes ☐ No _____Initials

5. I give my permission for my study doctor (or someone he or she chooses) to contact me in the future to ask me to take part in more research.

☐ Yes ☐ No _____Initials

What are the possible discomforts or risks?

Discomforts you may experience while in this study include those related to the collection of blood for laboratory studies, the disclosure of laboratory results to participants, and breaches of confidentiality of research data.

In this study we may need to get a maximum of 3 tablespoons (1.5 tablespoons for testing and 1.5 tablespoons for storage) of blood from you. We will get blood by putting a needle into a vein and letting the blood flow into a glass tube. You may feel some pain when the needle goes into your vein. To reduce the pain, a local skin numbing cream or spray (EMLA or Ethyl Chloride) may be applied to the skin before blood is drawn. On rare occasions EMLA cream may cause slight short-lived skin irritation. A day or two later, you may have a small bruise where the needle went under the skin.

You might worry about whether results of a blood test will lead to discrimination, for example denial of health insurance or employment. Laws exist to protect against discrimination, and these vary from state to state. While it is theoretically possible that information about you could lead to this sort of discrimination, this is very unlikely. Information about you will not be given to insurance companies, employers, or other parties without your permission. Results of this testing will be reported to your healthcare provider with your permission, and therefore will go into your medical record.

The central laboratory receives only number coded information that does not have your name on it and will make every effort to protect your privacy, although no guarantee of confidentiality can be absolute.

Some of the tests will look for the presence of risk factors for complications of diabetes. If these tests identify complications of diabetes, the results may raise anxiety about the complications. If this happens, you will be referred to a local mental health professional for evaluation and treatment.

Sample Storage Risks: You, your family, or your doctor will not receive the results of tests from the storage samples and the results will not become a part of your medical record because this research is not expected to affect your medical care. The study investigators will make every effort to maintain confidentiality by labeling your samples with a number rather than with your name or other personal information. However, in the unlikely circumstance that your test results are unintentionally made known to a third party, or revealed to you because they are deemed to be important to your medical care, you will need to consider the risks associated with having this information. First, as with any medical study, there is a risk that the result may be in error. Also, having information that you are at risk for a condition related to that disease might be emotionally stressful.

The study may include risks that are unknown at this time.

What are the possible benefits of the study?
This study is designed for the researchers to learn more about children and youth diagnosed with diabetes. This study is not designed to treat any illness or to improve your health. You will receive no health benefit from participating in this research study and there are risks as mentioned in the Risk section.

Sometimes, research results in findings or inventions that have value if they are made or sold. These findings or inventions may be patented or licensed, which could give a company the sole right to make and sell products or offer testing based on the discovery. Some of the profits from this may be paid back to the researchers and the organizations doing this study, but there are no plans for you to receive any financial benefits.

Are there alternative treatments?
There are no treatments proposed in this study, and the decision to participate in this study will not affect your treatment. Blood and urine test results will be available approximately 3 months after the samples are collected. Someone from the study will explain the results to you if you wish. Your diabetes provider will also receive the results, if you have given your permission.

Who is paying for this study?
This research is being paid for by the Centers for Disease Control and Prevention (CDC) and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) (PA number 00097 and DP-05-069).

Will I be paid for being in the study?

You will be given a gift card worth $10 for completing the Initial Participant Survey. You will be given a gift card worth $40 for having a blood draw and an additional $40 in gift cards for completing the questionnaires and physical measurements. It is important for you to know that payment for participation in the study is taxable income. If needed, we can offer assistance with transportation to the visit.

Will I have to pay for anything?

It will not cost you anything to be in the study.

Is my participation voluntary?
Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you choose to take part, you have the right to stop at any time. If you refuse or decide to withdraw later, you will not lose any benefits or rights to which you are entitled.

If you leave this study, you will still receive your normal medical care. The only medical care that you will lose is the medical care you are getting as part of this study. You might be able to get that same kind of medical care outside of the study.

Your doctor may also choose to withdraw you from the study at any time if he/she feels that it would be harmful to your health for you to continue or the side effects are too severe. If you drop out of the research study you can request that all blood or DNA samples that have been collected be destroyed. Withdrawal from this research study will have no effect on access to medical care nor will it have any effect on the standard of care your health care professionals are providing. If there are any new findings during the study that may affect whether you want to continue to take part, you will be told about them. Significant new findings that relate to your participation in this study will be discussed with you and/or your health care provider with your permission.

Can I be removed from this study?
You may be taken out of this study if the study doctor thinks it is not safe for you to be in the study. You can be taken out of the study even if you do not want to leave the study. The study doctor may decide to stop your participation without your permission if the study doctor thinks that being in the study may cause you harm, or for any other reason.

What happens if I am injured or hurt during the study?
If you are hurt by this research, you should call Dr. Dana Dabelea immediately at (303) 724-4414. We will arrange to get you medical care if you have an injury that is caused by this research. However, you or your insurance company will have to pay for the care that is needed. You should inform your health care providers if you decide to participate in this research study. If you have questions about injury related to the research, you may call Dr. Dabelea and/or your private physician.

Who do I call if I have questions?
If you have questions right now, you can ask the person who is talking to you about this consent form. The researcher carrying out this study is Dr. Dana Dabelea. If you have questions, concerns or complaints later, you may call Dr. Dana Dabelea at (303) 724-4414. You will be given a copy of this form to keep. If you have questions about your rights as a subject in this study, you can call the Colorado Multiple Institutional Review Board (COMIRB) office at (303) 724-1055.

Who will see my research information?
The University of Colorado Denver has rules to protect information about you. Federal and state laws including the Health Insurance Portability and Accountability Act (HIPAA) also protect your privacy. This part of the consent form tells you what information about you may be collected in this study and who might see or use it.

The institution involved in this study is the University of Colorado Denver. We cannot do this study without your permission to see, use and give out your information. You do not have to give us this permission. If you do not, then you may not join this study.

We will see, use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside the University of Colorado Denver and its affiliate hospitals may not be covered by this promise.

We will do everything we can to keep your records a secret. It cannot be guaranteed.

The use and disclosure of your information has no time limit. You can cancel your permission to use and disclose your information at any time by writing to the study's Primary Investigator, at the name and address listed below. If you do cancel your permission to use and disclose your information, your part in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected in this study.

Dr. Dana Dabelea
UCD Colorado School of Public Health
Dept. of Epidemiology
Bldg 500, Box B-119
Aurora, CO 80045
Ph. (303) 724-4414 FAX (303) 724-4491

Both the records that identify you and the consent form signed by you may be looked at by the following people:

- The Centers for Disease Control and Prevention (CDC)
- Department of Health and Human Services (DHHS) agencies
- National Institutes of Health (NIH) – NIDDK
- Colorado Multiple Institutional Review Board
- Officials at the institution where the research is being conducted and officials at other institutions involved in this study who are in charge of making sure that we follow all of the rules for research.

The researchers might talk about this research study at meetings. We might also print the results of this research study in relevant journals. But we will always keep the names of the research subjects, like you, private.

You have the right to request access to your personal health information from the Investigator. To ensure proper evaluation of test results, your access to these study results may not be allowed until after the study has been completed.

The investigator (or staff acting on behalf of the investigator) will also make *all or some* of the following health information about you available to: Wake Forest University Coordinating Center and Northwest Lipid Metabolism and Diabetes Research Laboratory

Information about you that will be seen, collected, used and disclosed in this study:

- Age, sex, race/ethnicity
- Date of birth
- Date of diabetes diagnosis
- Portions of your previous and current Medical Records that are relevant to this study, including but not limited to Diagnoses, History and Physical, or laboratory studies,
- Research visit records
- Blood and urine samples
-

All information gathered during this study will be held in strict confidence. Once you decide to join the research study, a unique number, called a research study number, will be assigned to you. The unique identifying number will be used instead of your name. The list linking the number assigned to you to your name will be kept in a locked file at the clinic site in Denver, Colorado. Thus, no one other than Dr. Dana Dabelea and her research team will be able to connect any of the research study information to you.

All answers that you give will be kept private. This is so because this study has been given a certificate of confidentiality. This means that anything you tell us will not have to be given to anyone even if a court orders us to do so unless you give permission. However, under the law we must report to the state suspected cases of child abuse or if you tell us you are planning to cause serious damage to yourself or others.

Agreement to be in this study

I have read this paper about the study or it was read to me. I understand the possible risks and benefits of this study. I know that being in this study is voluntary. I choose to be in this study. I will get a copy of this consent form.

In addition, if I agree to the questions regarding blood, urine and DNA storage, I understand that I might not be asked again for consent and that I may or may not be informed of the results of future studies that may be done with stored blood and urine samples. I realize I can withdraw my consent to use stored samples at any time and still participate in the SEARCH for Diabetes in Youth study (initial all previous pages of the consent form).

Signature: _____ Print Name: _____ Date: _____
Parent or guardian if subject < 18 years

Signature: _____ Print Name _____ Date: _____
Subject >18 years

Consent form explained by: _____ Date:_____
Signature Print Name

Investigator's Signature: _____ Date: _____

For children ages 14-18 who can read this form:

_____ Date_____
Child's Name

Approved

Date: FEB 04 2011 Valid For Use Through: 10.21.2011

COMIRB B2

Study Title: SEARCH for Diabetes in Youth Registry Study
Principal Investigator: Dana Dabelea, MD, PhD
COMIRB No: Protocol 01-934
Version Date: 01/24/2011
Version No: 1.0

Assent Format for participants 8 -13 years of age

What is this study about?
I am being asked to decide if I want to be in this research study. The goal of this study is to know more about diabetes in children and how it affects my life.

Why are you asking me?
I am being asked to be in the study because I have diabetes.

What do I have to do?
I know that to be in the study I will come to the clinic for one visit, for approximately 1 hour, which includes a questionnaire, blood draw and body measurements.

Will this hurt?
The blood draw might hurt but we can use a numbing cream so that you do not feel the pain.

Can I ask questions?
I asked any questions I have now about the study. All my questions were answered. I know that I can ask any questions about this study at any time. If I want to, I can call Dr. Dana Dabelea at (303) 724-4414.

Do I have to do this?
I know that I do not have to be in this study. No one will be mad at me if I say no.

I want to be in the study at this time. YES NO

I will get a copy of this form to keep.

Child's Printed Name: _____

Child's Signature: _____ Date: _____

Witness or Mediator: _____ Date: _____

I have explained the research at a level that is understandable by the child and believe that the child understands what is expected during this study.

Signature of person obtaining assent: _____ Date: _____

Consent Form Approval

Approved

FEB 04 2011

Date: COMIRB 62 Valid For Use Through: 10.21.2011

Study Title: SEARCH for Diabetes in Youth Cohort Study
Principal Investigator: Dana Dabelea, MD, PhD
COMIRB No: Protocol 01-934
Version Date: 01/24/2011
Version No: 1.0

You (in this form 'you' refers to you and/or your child) are being asked to participate in a research study. This form provides you with information about the study. A member of the research team will describe this study to you and answer all of your questions. Please read the information below and ask questions about anything you don't understand before deciding whether or not to take part.

Why is this study being done?
You are being asked to take part in a research study called the SEARCH for Diabetes in Youth Cohort Study because you have diabetes and were diagnosed under the age of 20 and you have previously completed an in person visit with the SEARCH study.

Diabetes is the third most common chronic disease in individuals under 20 years of age. The total number of cases of diabetes in this age group is increasing. Also, types of diabetes not seen previously in young people are now present. Specifically, this project is interested in studying the following questions.

a. How common are long-term complications related to diabetes, including: retinopathy (damage to back of the eye), nephropathy (kidney damage), neuropathy (nerve damage), and damage to the heart and blood vessels?
b. How common are short-term complications, including hypoglycemia (low blood sugar) and diabetic ketoacidosis (DKA)?
c. What type of medical care are young people with diabetes receiving and how does diabetes affect the lives of these individuals?

Other people in this study
Up to 1250 youth will be enrolled locally, and up to 3900 youth will be invited to participate nationally in this study.

What happens if I join this study?
If you agree to participate in this study you will be asked to come in for an in-person visit at the SEARCH clinic that lasts about 3 1/2 hours. A brief survey will be sent to you each year in order to update your contact information, no matter what other parts of the study you choose to participate in. You may be asked whether you agree to have your medical records released to get more information about your diabetes. All aspects of this study are for research purposes only and are in addition to regular health care. Participation in this study is voluntary and you may refuse to take part in any procedure in the study.

In-person Visit
1.) Collection of Blood and Urine:
Blood Draw: You will be scheduled for a morning appointment. You will come to the visit after not having anything to eat or drink other than water for 8-12 hours. Please do not take your morning insulin prior to

arrival, unless you must control your blood sugars. Upon arrival, blood will be drawn from your arm or hand to measure blood sugar, hemoglobin A1c (a measure of long-term blood sugar control), c-peptide (a measure of insulin production), different types of cholesterol (blood fats), islet cell antibodies (markers in the blood for type 1 diabetes), serum creatinine (a measure of kidney function), and several new blood markers associated with risk for developing heart disease or stroke (apolipoprotein B, C-reactive protein, interleukin-6, leptin, and adiponectin).

The total amount of blood drawn for these tests will be based on weight tables and will not exceed 4 tablespoons (20ml). The blood draw takes about 10 minutes. If you need numbing cream for the blood draw, it will add about 30 minutes to this part.

Urine Collection: Two weeks before your scheduled appointment, you will be mailed a container with detailed instructions to collect an overnight, timed urine sample 2 -7 days before your visit. You will be asked to bring this urine container with you on the day of your visit.

A urine sample will also be collected at the visit after the blood draw. You will mark the time that you give this urine sample on a sheet of paper. After the blood and urine samples are obtained, you can take your pills or insulin and you will be given a snack. If you need to urinate again during the visit, you will be asked to collect that urine in a container and leave it with the study personnel at the end of your visit. You will mark the time you last gave a urine sample.

Your urine will be tested for albumin and creatinine (small particles of protein) to see how well your kidneys are working.

2.) Physical Examination:

The physical examination will include height, weight, waist measurement, blood pressure, and examination of your feet and of the skin on your neck. The time to complete this section of the visit is approximately 30 minutes.

3.) Questionnaires:

The questionnaires can be completed either at home before the visit or at the visit. If you prefer, a separate visit may be scheduled to complete the forms. Several questionnaires will be administered that gather information about the following areas:

- personal and family medical history
- stage of puberty (if you are over 8 years of age)
- the effect that diabetes has had on your life
- your strategies to prevent low blood sugar
- your family's income and education
- types of diabetes education you have received
- your diabetes self-care habits
- symptoms of diabetes complications
- types of food you eat
- who provides your diabetes and general medical care, and,
- costs for care

The estimated time to complete the questionnaires is 70 minutes.

If you are over 10 years of age, you will be asked to complete questions dealing with the following health issues – physical activity, smoking, eating and sleeping patterns, depression, and how many children you may have had. This information will not be shared with parents unless health issues are identified that need to be treated. The reason why the information will not be shared with parents is to increase the chance that you will answer the questions more honestly. A description of the types of questions asked will be shared with your parents if you are under 18 but your parent must agree NOT to see your answers and let you do the questionnaire by yourself by initialing here:

_____Yes, my child can participate in the questionnaire and I agree to NOT see the answers.
Initial

The estimated time to complete these questions is about 15 minutes.

4.) Photographs of Your Eyes:

Diabetic retinopathy is a complication of diabetes that results from damage to the blood vessels at the back of the eye (retina). We will take 2 photographs of each of your eyes using a camera with a bright flash. These pictures will be sent to the Ocular Epidemiology Reading Center in Madison, Wisconsin to be read by trained eye specialists who will study the blood vessels and look for any unusual changes.

You will be asked to sit in a darkened room before a special eye camera with your chin in a chin rest. After your pupils have dilated (opened) naturally, we will take 2 photographs of the back of each of your eyes (retinas). No drops will be put in your eyes and the camera will not touch your eyes. After each picture is taken, you may see a blue or red spot which will disappear within 5 to 7 minutes and cause no damage to the eye. We will pause for approximately 3-5 minutes between photographs to allow your eyes time to re-adjust to the darkened room so the pupils will open once again.

You will also be asked for the name and phone number of your eye doctor, and whether or not you have ever had laser treatments on the back of your eyes. Doing the eye photographs will take about 20 minutes. We will send you the results of your eye photographs.

5.) Nerve and Heart Function Tests:

Nerve Test: Diabetic neuropathy is a complication of diabetes that results from damage to the nerves. We will be looking for signs of early nerve damage by asking you to complete a short questionnaire, doing a physical examination of your feet, and doing an electrocardiogram (EKG) test of your heart.

We will ask you to answer a brief questionnaire about foot sensation including pain, numbness, and temperature sensitivity. We will examine your feet to measure your ability to feel vibrations, your reflexes, and your ability to feel light touches to your feet. The examiner will test your vibration sense by placing a tuning fork (vibrating instrument) on your big toe. The examiner will use a rubber "hammer" to test the reflexes at your ankle. To test your sense of touch, the examiner will touch your big toe several times with a thin piece of flexible plastic, similar to fishing line. Doing the foot nerve tests will take about 10 minutes. The results of the tests will be sent to the University of Michigan for analysis.

In order to check the accuracy of our measurements, the foot test will be repeated for approximately 5% (1 in 20) of participants. Participants will be randomly selected to receive the repeat measurements. If you are selected for repeat measurements of the feet and you agree to have the measurements performed, your visit will last about 10 minutes longer. You may refuse to have the repeat measures, but still complete the foot examination.

_____ You **have** been selected for the repeat measurements of the feet.

_____ You **have not** been selected for repeat measurements of the feet.

Heart Rate Variability: Heart Rate Variability (HRV) is a measurement to assess the health of nerves in your heart. The test uses an ECG, or electrocardiogram. This is a machine that doctors routinely use to study the heart; your doctor may have used it with you before. It involves placing three electrodes (sticky pads) on your chest and abdomen. The electrodes will record your heartbeat. The examiner will also take your blood pressure with a blood pressure cuff at least once during the test. During the ECG test, you will simply breathe normally for five minutes while the machine records your heartbeat and blood pressure. Then you will breathe deeply for one minute. The ECG machine will also record your heartbeat and blood

pressure during this minute and compare it to your heartbeat and blood pressure at rest. This test should take about 10 minutes total.

Blood Vessel Test: We will perform a test to measure how your blood vessels function. The test is called an arterial stiffness test. You will be asked to wear loose shorts or to put on a patient gown. A trained member of the research team will measure your pulse in your groin area, but will not expose your private parts. At your request a chaperone will be present during these procedures.
The following test will then be performed:

After a 5-minute rest period, your blood pressure and heart rate will be measured using a blood pressure cuff placed on your upper arm. This test will be repeated 3 times.

A staff member will then measure the distance from your neck to the bottom of your sternum (breast bone), from your sternum to your wrist, from your sternum to the top of your thigh, and from your thigh to your foot. Electrodes (sticky pads) will then be placed on your chest.

Your wrist will be touched with a small instrument shaped like a pen and the stiffness of your blood vessels will be measured. The pen instrument detects pressure changes with a tiny, highly-sensitive pressure sensor in the flat end of the device that is shaped like a pencil eraser. It does not use radiation (X-rays), sound waves (ultrasound), or needles. This test is painless and will be repeated 3 times.

Then the same pen-shaped instrument will be touched on the side of your neck, the top of your thigh, and your foot to measure the speed at which blood travels from your heart to that area of the body. This test will be repeated 3 times. The blood vessel tests will take about one hour.

This test is designed to be short, simple, and painless. This is a test that doctors use every day, and they are not dangerous. But if you feel uncomfortable at any time during any of these tests, just tell the examiner and he/she will immediately stop the tests.

In order to check the accuracy of our measurements, the blood vessel tests will be repeated for approximately 5% (1 in 20) of participants. Participants will be randomly selected to receive repeat measurements. If you are selected for repeat measurements of the blood vessel tests and you agree to have the measurements performed, your visit will last about 30 minutes longer. You may refuse to have the repeat measures, but still complete the blood vessel testing. You will receive additional compensation for your time if you have the repeat measures done.

____ You **have** been selected for repeat measurements of the blood vessels.

____ You **have not** been selected for repeat measurements of the blood vessels.

What happens to lab samples collected in this study?
Blood and urine samples will labeled with a study number code and will be sent to the Central Laboratory at University of Washington, Seattle to be tested. Your name and other identifying information will not be on the samples. The research team will inform you of your test results that may affect your health or healthcare. With your permission, the test results will also be shared with your healthcare provider.

The SEARCH study would like to keep some of the blood and urine that is taken during the study but is not used for other tests. If you agree, an additional sample of blood (1 tablespoon) will be taken, and the excess urine sample will be saved. Whenever possible, blood for storage will be drawn at the same time as the samples for the in-person visit tests. If it is not possible, an additional needle stick will be required with your permission. The blood and urine samples will be kept and may be used in future research to learn more about diabetes. The research that is done with your blood and urine samples is not designed to specifically help you. It might help people who have diabetes and other diseases in the future. Reports about research done with your samples will not be given to you or your doctor. These reports will not be put in your health records. The research using your stored blood and urine samples will not affect your care.

The choice to let SEARCH study investigators keep the blood and urine samples for future research is up to you. No matter what you decide to do, it will not affect the care that you will receive as part of the study. If you decide now that your blood and urine samples can be kept for research, you can change your mind at any time and contact your study doctor to let him or her know that you do not want the study to use your blood and urine samples any longer, and they will be destroyed. Otherwise, they may be kept until they are used up, or until the SEARCH study investigators decide to destroy them.

In the future, people who do research with your blood and urine samples may need to know more about your health. While the SEARCH study may provide reports about your health, they will not give them your name, address, phone number or any other information that will let the researcher know who you are.

DNA (Genes) Blood Sample

You are also being asked for permission to use your blood to have genetic material (DNA) stored for possible use in genetic research about diseases that are passed on in families. If you did not previously provide SEARCH a DNA sample or if the amount of the DNA sample drawn was too little, we may ask you to provide another blood sample. If you agree to this request, no more than one additional tablespoon (15ml) of blood will be drawn.

DNA is found in all of your cells. DNA makes up your genes. Your genes control how tall you are, what color hair you have, and all other body traits. The DNA in each person's body is different from every other person's DNA (except identical twins or triplets who have the same DNA). The differences in DNA may explain why some people are more likely to get certain diseases like diabetes.

We know that diabetes runs in families, but we don't know all the genes that are involved in the development of diabetes and its complications. In addition, there are specific types of diabetes that can only be diagnosed by genetic tests. By studying the DNA in your blood sample, researchers may be able to find the genes that carry the risk factors for problems such as diabetes, heart disease, and complications such as eye and kidney trouble, and related conditions (high cholesterol, etc.).

Even if your blood samples are used for this kind of research, the results will not be told to you and will not be put in your health records.

Blood and Urine Storage

Your blood and urine samples will only be used for research and will not be sold. The research done with your samples may help to develop new products in the future, but there is no plan for you to be paid. The possible benefits of research from your blood and urine include learning more about what causes diabetes and other diseases, how to prevent them and how to treat them. The greatest risk to you is the release of information from your health records. The SEARCH study research team will protect your records so that your name, address and phone number will be kept private. The chance that this information will be given to someone else is very small. There will be no cost to you for any blood or urine collected and stored by the SEARCH study.

Your stored blood, urine and DNA samples will be kept in storage indefinitely or until the sample is no longer usable. A code number identifies samples and the link between the code and your personal information is stored in a secure location at the University of Colorado. Thus, your sample will not be directly identified with your name. Your samples would be released to a SEARCH investigator (or other investigator authorized by the SEARCH) only after determination of the scientific usefulness of a proposed study and would be reviewed for compliance with human research safety and protection guidelines before approval.

Participation in this study is voluntary and you may choose to withdraw from the study at any time. You may request that your stored samples be permanently removed from the Central Laboratory if you choose

to withdraw consent. To request that your sample be permanently removed from the central laboratory, contact:

Dr. Dana Dabelea
UCD Colorado School of Public Health
Dept. of Epidemiology
Bldg 500, Box B-119
Aurora, CO 80045
Ph. (303) 724-4414 FAX (303) 724-4491

We will send a request to the central laboratory and they will then destroy the samples and send us a letter certifying that the sample has been destroyed. We will send you a copy of this letter.

Medical Record Review

A medical record review will be conducted for a small number (~25 people) who give us permission to check that the information you gave us regarding key medical events and markers of healthcare quality were remembered correctly.

Please read each sentence below and think about your choice. After reading each sentence, check "Yes" or "No" and write your initials. If you have questions, please talk to the SEARCH study staff, Dr Dabelea or your healthcare provider. Remember, no matter what you decide to do about the storage and future use of your blood and urine samples, you may still take part in the study.

1. I wish to have the results of my tests given to my doctor or diabetes care provider.

☐ Yes ☐ No _____Initials

2. I give my permission for my blood and urine samples to be stored in a central laboratory at the University of Washington, Seattle for future use by study investigators in studies of diabetes and diabetes risk factors and complications:

☐ Yes ☐ No _____Initials

3. I give my permission for my DNA (genes) blood sample to be tested for inherited factors in the development of diabetes, diabetes risk factors and complications.

☐ Yes ☐ No _____Initials

4. I give my permission for my DNA (genes) blood sample to be stored in a central laboratory at the University of Washington, Seattle for future use in diabetes and diabetes-related studies.

☐ Yes ☐ No _____Initials

5. I give my permission for my study doctor (or someone he or she chooses) to contact me in the future to ask me to take part in more research.

☐ Yes ☐ No _____Initials

6. I give permission for my medical records to be reviewed to check that the information I remembered was correct.

☐ Yes ☐ No _____Initials

What are the possible discomforts or risks?

Discomforts you may experience while in this study include those related to the collection of blood for laboratory studies, the disclosure of laboratory results to participants, and breaches of confidentiality of research data.

In this study we will need to get a maximum of 4 tablespoons (3 tablespoons for testing and 1 tablespoon for storage) of blood from you. We will get blood by putting a needle into a vein and letting the blood flow into a glass tube. You may feel some pain when the needle goes into your vein. To reduce the pain, a local skin numbing cream or spray (EMLA or Ethyl Chloride) can be applied to the skin before blood is drawn. On rare occasions EMLA cream may cause slight short-lived skin irritation. A day or two later, you may have a small bruise where the needle went under the skin.

You might worry about whether results of a blood test will lead to discrimination, for example denial of health insurance or employment. Laws exist to protect against discrimination, and these vary from state to state. While it is theoretically possible that information about you could lead to this sort of discrimination, this is very unlikely. Information about you will not be given to insurance companies, employers, or other parties without your permission. Results of this testing will be reported to your healthcare provider with your permission, and therefore will go into your medical record.

The central laboratory receives only coded information that does not have your name on it and will make every effort to protect your privacy, although no guarantee of confidentiality can be absolute.

There are no known risks associated with taking a photograph of the eye. Although you will see a flash of light when the picture is taken, this flash is not harmful. People who are light sensitive may experience some minor discomfort from the camera flash, but the discomfort will not last for longer than a few minutes.

There are no majors risks associated with the nerve tests on the feet. All of the devices used (a reflex hammer, a tuning fork, and a monofilament) are used daily in doctors' offices; your doctor has probably used them with you before. They are non-invasive instruments. They may, however, cause a slight agitation or discomfort in some patients.

There are no major risks associated with the heart function tests. ECGs are performed daily in hospitals; you may have had one before. No electrical current is sent through the body, so there is no risk of electrical shock. Application of the sticky pads may feel cold, and in very rare cases, a patient may develop a skin rash or irritation where the patches were applied. You may feel some pressure for a few seconds when the pen-shaped device is placed on your skin. Some participants may feel discomfort when the arm cuff is inflated for the blood pressure measurements.

Some of the tests will look for the presence of risk factors for complications of diabetes. If these tests identify complications of diabetes, the results may raise anxiety about the complications. If this happens, you will be referred to a local mental health professional for evaluation and treatment.

Sample Storage Risks: You, your family, or your doctor will not receive the results of tests from the storage samples and the results will not become a part of your medical record because this research is not expected to affect your medical care. The study investigators will make every effort to maintain confidentiality by labeling your samples with a number rather than with your name or other personal information. However, in the unlikely circumstance that your test results are unintentionally made known to a third party or revealed to you because they are deemed to be important to your medical care, you will need to consider the risks associated with having this information. First, as with any medical study, there is

a risk that the result may be in error. Also, having information that you are at risk for a condition related to that disease might be emotionally stressful.

The study may include risks that are unknown at this time.

What are the possible benefits of the study?

This study is designed for the researchers to learn more about children and youth diagnosed with diabetes. This study is not designed to treat any illness or to improve your health. You will receive no direct health benefit from participating in this research study and there are risks as mentioned in the discomfort and risk section.

Sometimes, research results in findings or inventions that have value if they are made or sold. These findings or inventions may be patented or licensed, which could give a company the sole right to make and sell products or offer testing based on the discovery. Some of the profits from this may be paid back to the researchers and the organizations doing this study, but there are no plans for you to receive any financial benefits.

Are there alternative treatments?

There are no treatments proposed in this study, and the decision to participate in this study will not affect your treatment. Blood and urine test results will be available approximately 3 months after it is collected. Eye photography results will be available approximately 6 months after your visit. Someone from the study will explain the results to you if you wish. Your diabetes provider will also receive the results, if you have given your permission.

Who is paying for this study?

This research is being paid for by the Centers for Disease Control and Prevention (CDC) and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) (PA number 00097 and DP-05-069).

Will I be paid for being in the study?

You will be given gift cards worth $60 for having the blood draw. If you complete the physical measurements and the questionnaires, you will given an additional $60 in gift cards. If you are selected to repeat the blood vessel measurements you will receive an additional $20 gift card. It is important for you to know that payment for participation in the study is taxable income. If needed, we can offer assistance with transportation to the visit.

Will I have to pay for anything?

It will not cost you anything to be in the study.

Is my participation voluntary?

Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you choose to take part, you have the right to stop at any time. If you refuse or decide to withdraw later, you will not lose any benefits or rights to which you are entitled.

If you leave this study, you will still receive your normal medical care. The only medical care that you will lose is the medical care you are getting as part of this study. You might be able to get that same kind of medical care outside of the study.

Your doctor may also choose to withdraw you from the study at any time if he/she feels that it would be harmful to your health for you to continue or the side effects are too severe. If you drop out of the research study you can request that all blood, urine or DNA samples that have been collected be destroyed. Withdrawal from this research study will have no effect on access to medical care nor will it have any effect on the standard of care your health care professionals are providing. If there are any new findings during the study that may affect whether you want to continue to take part, you will be told about them. Significant

new findings that relate to your participation in this study will be discussed with you and/or your health care provider with your permission.

Can I be removed from this study?
You may be taken out of this study if the study doctor thinks it is not safe for you to be in the study. You can be taken out of the study even if you do not want to leave the study. The study doctor may decide to stop your participation without your permission if the study doctor thinks that being in the study may cause you harm, or for any other reason.

What happens if I am injured or hurt during the study?
If you are hurt by this research, you should call Dr. Dana Dabelea immediately at (303) 724-4414. We will arrange to get you medical care if you have an injury that is caused by this research. However, you or your insurance company will have to pay for the care that is needed. You should inform your health care providers if you decide to participate in this research study. If you have questions about injury related to the research, you may call Dr. Dabelea and/or your private physician.

Who do I call if I have questions?
If you have questions right now, you can ask the person who is talking to you about this consent form. The researcher carrying out this study is Dr. Dana Dabelea. If you have questions, concerns or complaints later, you may call Dr. Dana Dabelea at (303) 724-4414. You will be given a copy of this form to keep. If you have questions about your rights as a subject in this study, you can call the Colorado Multiple Institutional Review Board (COMIRB) office at (303) 724-1055.

Who will see my research information?
The University of Colorado Denver has rules to protect information about you. Federal and state laws including the Health Insurance Portability and Accountability Act (HIPAA) also protect your privacy. This part of the consent form tells you what information about you may be collected in this study and who might see or use it.

The institution involved in this study is the University of Colorado Denver. We cannot do this study without your permission to see, use and give out your information. You do not have to give us this permission. If you do not, then you may not join this study.

We will see, use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside the University of Colorado Denver and its affiliate hospitals may not be covered by this promise.

We will do everything we can to keep your records a secret. It cannot be guaranteed.

The use and disclosure of your information has no time limit. You can cancel your permission to use and disclose your information at any time by writing to the study's Primary Investigator, at the name and address listed below. If you do cancel your permission to use and disclose your information, your part in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected in this study.

Dr. Dana Dabelea
UCD Colorado School of Public Health
Dept. of Epidemiology
Bldg 500, Box B-119
Aurora, CO 80045
TEL (303) 724-4414 FAX (303) 724-4491

Both the records that identify you and the consent form signed by you may be looked at by the following people:

- The Centers for Disease Control and Prevention (CDC)

- Department of Health and Human Services (DHHS) agencies
- National Institutes of Health (NIH) – NIDDK
- Colorado Multiple Institutional Review Board
- Officials at the institution where the research is being conducted and officials at other institutions involved in this study who are in charge of making sure that we follow all of the rules for research.

The researchers might talk about this research study at meetings. We might also print the results of this research study in relevant journals. But we will always keep the names of the research subjects, like you, private.

You have the right to request access to your personal health information from the Investigator. To ensure proper evaluation of test results, your access to these study results may not be allowed until after the study has been completed.

The investigator (or staff acting on behalf of the investigator) will also make *all or some* **of the following health information about you available to:**

- Wake Forest University
- Northwest Lipid Metabolism and Diabetes Research Laboratory
- University of Wisconsin Madison Eye Photography Reading Center
- University of Michigan

Information about you that will be seen, collected, used and disclosed in this study:

- Age, sex, race/ethnicity
- Date of birth
- Date of diabetes diagnosis
- Portions of your previous and current medical records that are relevant to this study, including but not limited to diagnoses, history and physical, or laboratory studies,
- Research visit records including questionnaires and physical examinations
- Blood and urine samples
- Eye photographs
- Heart and blood vessel tests

All information gathered during this study will be held in strict confidence. Once you decide to join the research study, a unique number, called a research study number, will be assigned to you. The unique identifying number will be used instead of your name. The list linking the number assigned to you to your name will be kept in a locked file at the clinic site in Denver, Colorado. Thus, no one other than Dr. Dana Dabelea and her research team will be able to connect any of the research study information to you.

All answers that you give will be kept private. This is so because this study has been given a certificate of confidentiality. This means that anything you tell us will not have to be given to anyone even if a court orders us to do so unless you give permission. However, under the law we must report to the state suspected cases of child abuse or if you tell us you are planning to cause serious damage to yourself or others.

Agreement to be in this study

I have read this paper about the study or it was read to me. I understand the possible risks and benefits of this study. I know that being in this study is voluntary. I choose to be in this study. I will get a copy of this consent form.

In addition, if I agree to the questions regarding blood, urine and DNA storage, I understand that I might not be asked again for consent and that I may or may not be informed of the results of future studies that may be done with stored blood or urine samples. I realize I can withdraw my consent to use stored samples at any time and still participate in the SEARCH for Diabetes in Youth Study (initial all previous pages of the consent form).

Signature: _____ Print Name: _____ Date: _____
Parent or guardian if subject < 18 years

Signature: _____ Print Name _____ Date: _____
Subject >18 years

Consent form explained by: _____ Date:_____
Signature Print Name

Investigator's Signature: _____ Date: _____

For children ages 14-18 who can read this form:

_____ Date_____
Child's Name

Approved

FEB 04 2011

COMIRB

Date: _____ 02 Valid For Use Through: 10 21 2011

Study Title: SEARCH for Diabetes in Youth Cohort Study

Principal Investigator: Dana Dabelea, MD, PhD
COMIRB No: Protocol 01-934
Version Date: 01/24/11
Version No: 1.0

Assent Format for participants 8 -13 years of age

What is this study about?
I am being asked to decide if I want to be in this research study. The goal of this study is to know more about diabetes in children and how it affects my life.

Why are you asking me?
I am being asked to be in the study because I have diabetes.

What do I have to do?
I know that to be in the study I will come to the clinic for one visit for approximately 3-4 hours, which includes questionnaires, blood draw, body measurements, eye photos and a heart test.

Will this hurt?
The blood draw might hurt but we will use a numbing cream so that you do not feel the pain. The eye photos have a bright light and may cause me to blink or to see spots.

Can I ask questions?
I asked any questions I have now about the study. All my questions were answered.
I know that I can ask any questions about this study at any time. If I want to, I can call Dr. Dana Dabelea at (303) 724-4414.

Do I have to do this?
I know that I do not have to be in this study. No one will be mad at me if I say no.

I want to be in the study at this time. ☐ YES ☐ NO

I will get a copy of this form to keep.

Child's Printed Name: _____

Child's Signature: _____ Date: _____

Witness or Mediator: _____ Date: _____

I have explained the research at a level that is understandable by the child and believe that the child understands what is expected during this study.

Signature of person obtaining assent: _____ Date: _____

Institutional Review Board - Federalwide Assurance #00002988
Cincinnati Children's Hospital Medical Center

Date: 3/16/2011 2:03 PM

From: IRB Committee

To: Principal Investigator: Lawrence Dolan
Division: Endocrinology

Re: Study ID: 2011-0407
Study Title: SEARCH for Diabetes in Youth

The above referenced protocol and all applicable additional documentation provided to the CCHMC IRB were reviewed and **APPROVED** using an **EXPEDITED** review procedure in accordance with 45 CFR 46.110(b)(1)(see below) on **3/16/2011** .

This study will be due for continuing review at least 30 days before: 3/15/2012.

The following documents were reviewed and approved:

Name
CES-D | History
Cohort description 10-17 years | History
Cohort description 5-10 years | History
Cohort description adult | History
Cohort instructions | History
Cohort intro letter | History
cohort lab result description | History
Cohort reminder letter | History
Consent for 2012 visits | History
Consent for Single Follow-up Visit | History
Consent for volunteers | History
Contact information | History
Eating Problems | History
Family conflict | History
Family medical history | History
Food Frequency | History
Health Questionnaire | History
IPS | History
IPS letter | History
IPS thank you letter | History
Low blood sugar | History
Medical record review | History
Medication inventory | History
MNSI | History
PDQ | History
PedsQL - diabetes-specific | History
PedsQL - generic | History
Protocol - version 1 | History
Quality of Care | History
Registry description | History
Registry instructions | History
Registry lab result description | History
Registry reminder letter | History
Result letter - participant | History
Result letter - provider | History

Supplemental | History
Tanner - female | History
Tanner - male | History
Urine collection instructions | History

Please note the following requirements:

Per 45 CFR 46.116 (21 CFR 50.20) the CCHMC IRB has determined that informed consent must be obtained from all adult participants and that this consent must be documented by signature on the IRB approval consent form.

Per 45 CFR 46.408 the CCHMC IRB has determined that at least 1 parent(s) (or guardian) must give permission for the inclusion of a child in this research and that permission must be documented by signature on the IRB approved parental permission form.

Per 45 CFR 46.408 the CCHMC IRB has determined that documented assent must also be obtained from all child participants between 11 and 17 years of age.
Per 45 CFR 164.508 the CCHMC IRB has determined that all adult participants and/or the legally authorized representative of child participants must provide authorization for the use and/or disclosure of the protected health information in the conduct of this research.

OTHER APPROVALS: Principal investigators are responsible for assuring final approval from other applicable review committees and performance sites prior to study initiation. This includes, but is not limited to, Divisional Scientific Review committee, General Clinical Research Center (GCRC), Radiation Safety, Institutional Biosafety Committee (IBC), Conflict of Interest (COI) Committee, and any sites (i.e. schools, hospitals) where the research may be conducted. Principal investigators are also responsible for obtaining final approval from the FDA and a valid contract between the sponsor and CCHMC, as applicable. If any of these entities require changes to the IRB-approved protocol and/or informed consent/assent document(s), the changes must be submitted to and approved by the IRB prior to implementation.

AMENDMENTS: The principal investigator is responsible for notifying the IRB of any changes in the protocol, participating investigators, procedures, recruitment, consent forms, FDA status, or conflicts of interest. Approval is based on the information as submitted. New procedures cannot be initiated until IRB approval has been given. If you wish to change any aspect of this study, please submit an Amendment via ePAS to the IRB, providing a justification for each requested change.

CONTINUING REVIEW: The investigator is responsible for submitting a Continuing Review via ePAS to the IRB at least 30 days prior to the expiration date listed above. Please note that study procedures may only continue into the next cycle if the IRB has reviewed and granted re-approval prior to the expiration date.

UNANTICIPATED PROBLEMS: The investigator is responsible for reporting **unanticipated problems** promptly to the CCHMC IRB via ePAS according to current CCHMC reporting policy found on CenterLink.

STUDY COMPLETION: The investigator is responsible for notifying the IRB by submitting a Request to Close via ePAS when the research, including data analysis, has completed.

If you have any questions about the information in this letter, please contact the Institutional Review Board office at 513-636-8039.

Thank you for your cooperation during the review process.

Research Categories

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition

assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

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5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

From: IRB [mailto:irb_no_reply@mailserv.grad.unc.edu]

Sent: Friday, April 15, 2011 12:44 PM

To: Mayer-Davis, Elizabeth Jane

Cc: Thomas, Joan M; Ruehl, Jennifer

Subject: IRB Notice

A paper copy of the approval memo and any relevant documents are being mailed today.

To: Elizabeth Mayer-Davis

Nutrition CB:7461

From: Public Health-Nursing IRB

Approval Date: 4/13/2011
Expiration Date of Approval: 4/11/2012
RE: Notice of IRB Approval by Full Board Review
Submission Type: Initial
Study #: 10-2341
Study Title: SEARCH for Diabetes in Youth: Carolina Site (SEARCH 3)
Sponsors: Centers for Disease Control and Prevention (CDC); National Institutes of Health (NIH); National Institute of Diabetes, Digestive and Kidney Diseases

This submission has been approved by the above IRB for the period indicated.

Study Description:

This application includes two distinct aspects of SEARCH 3 (Continuation of SEARCH 2, IRB # 08-0909 and sustainable surveillance effort, IRB #10-0169.

Purpose: SEARCH for Diabetes in Youth is a multi-center study designed with a two-fold purpose of: (1) developing a uniform population based approach to finding and understanding rates and types of diabetes mellitus in youth including the development of a sustainable surveillance effort. (Registry study) and (2) Monitoring development of complications of diabetes in youth that were previously identified and participated in a SEARCH study baseline visit (Cohort Study). Participants: Children and youth from 0-19 years of age with newly diagnosed diabetes living in South Carolina (Registry study) and individuals diagnosed with diabetes between 2002 and 2008 that previously completed a SEARCH study baseline visit and have had diabetes for at least five years(Cohort study). Also, for the sustainable surveillance effort, existing medical records from the UNC system will be used.

Regulatory and other findings:

This research, which involves children, meets criteria at 45 CFR 46.404 and/or 21 CFR 50.51 (research involving no greater than minimal risk). Permission of one parent or guardian is sufficient.

This research meets criteria for a waiver of written (signed) consent according to 45 CFR 46.117(c)(2) for completion of the IPS survey and for the collection of the overnight urine sample. Written consent will be collected before the urine is given to the research staff the next day.

This research meets criteria for waiver of informed consent for research [45 CFR 46.116(d)] and waiver of HIPAA authorization [45 CFR 164.512(i)(2)(ii)] for the case ascertainment and validation portion of the study.

This approval includes a limited waiver of HIPAA authorization to identify potential subjects for recruitment into this research study (Registry Study only), as allowed under 45 CFR 164.512. This temporary waiver provides access to protected health information (PHI) to confirm eligibility and facilitate initial contact, after which consent and HIPAA authorization will be sought. Access and use is limited to the minimum amount of PHI necessary to review eligibility criteria and to contact potential subjects.

Investigator's Responsibilities:

Federal regulations require that all research be reviewed at least annually. It is the Principal Investigator's responsibility to submit for renewal and obtain approval before the expiration date. You may not continue any research activity beyond the expiration date without IRB approval. Failure to receive approval for continuation before the expiration date will result in automatic termination of the approval for this study on the expiration date.

Enclosed are stamped copies of approved consent documents and other recruitment materials (when applicable). You must copy the stamped consent forms for use with subjects unless you have approval to do otherwise.

You are required to obtain IRB approval for any changes to any aspect of this study before they can be implemented (use the modification form at ohre.unc.edu/forms). Any unanticipated problem involving risks to subjects or others (including adverse events reportable under UNC-Chapel Hill policy) should be reported to the IRB using the web portal at https://irbis.unc.edu/irb.

Researchers are reminded that additional approvals may be needed from relevant "gatekeepers" to access subjects (e.g., principals, facility directors, healthcare system).

This study was reviewed in accordance with federal regulations governing human subjects research, including those found at 45 CFR 46 (Common Rule), 45 CFR 164 (HIPAA), 21 CFR 50 & 56 (FDA), and 40 CFR 26 (EPA), where applicable.

CC: Joan Thomas, Nutrition; Jennifer Ruehl, Nutrition

IRB Informational Message—please do not use email REPLY to this address

Seattle Children's
HOSPITAL • RESEARCH • FOUNDATION

INSTITUTIONAL REVIEW BOARD
FWA00002443

March 23, 2011

Catherine Pihoker, MD

Re: IRB Application Number 12074, entitled "SEARCH for Diabetes in Youth 3"

Dear Dr. Pihoker,

The Institutional Review Board (IRB) Chair reviewed the contingency response to the requested modification(s) on March 16, 2011. The IRB Chair determined that you sufficiently addressed the contingencies, and approved the modification(s) to begin SEARCH 3. The approval period for this modification is March 3, 2011 through February 2, 2012 (with the exception of the "Patient Instructions for Collecting Overnight Urines" document). Attached is a copy of the approved modification form for your records.

The Institutional Review Board (IRB) Subcommittee reviewed the "Patient Instructions for Collecting Overnight Urines" document on March 23, 2011, after it was discovered the document was accidentally omitted from review with the other SEARCH 3 documents. The Subcommittee determined this modification qualifies for expedited review as a minor change in previously approved research during the period for which approval is authorized. (*45 CFR 46.110(b)(2)*). The Subcommittee approved the "Patient Instructions for Collecting Overnight Urines" document. The approval period for this modification is March 23, 2011 through February 12, 2012.

IRB Findings and Determinations
Category of Research with Children: The IRB determined this research remains open under the following category of research involving children as subjects:

Research not involving greater than minimal risk (**45 CFR 46.404** and **21 CFR 50.51**).

(Note, now that the C-peptide portion of the study has been eliminated, the 45 CFR 46.405 risk category no longer applies.)

Alteration of Limited Elements of Informed Consent: The IRB understands that many participants were enrolled in the Initial Participant Survey (IPS) portion of the research under a waiver of documentation of consent (45 CFR 46.117(c)(2)). The IRB noted the cover letters to the surveys were to serve in lieu of a consent form or consent discussion. The letters did not contain all required elements of consent under 45 CFR 46.116(a). The missing elements include:

1. a statement regarding benefits,
2. risks,
3. alternatives, and
4. who to contact in the event of an injury

The IRB determined this research meets the criteria for an alteration of the above outlined elements of consent (45 CFR 46.116(d)) for subjects already enrolled with an IPS cover letter that did not contain all required elements of consent. This waiver is not intended to be retrospective in nature. It is, however, intended so that you do not have to obtain "re-consent" from all prior participants utilizing a method with all required elements of consent to use their data.

You will be required to use cover letters for the IPS portion of the research which contain all required elements under 45 CFR 46.116(a) going forward.

Alteration of HIPAA Authorization: The IRB determined the IPS portion of the research meets the criteria for an alteration of authorization under HIPAA (45 CFR 164.512(i)) for the signature requirement. This means that you are no longer required to obtain a signed authorization form for IPS participants. You are still required to provide an authorization form in the materials sent to potential IPS participants, which they may choose to return. This alteration means that for participants that forget to return the authorization form with the survey, or participants that take the survey online, you will not be required to attempt to contact participants to obtain a signed authorization.

If you would like to further modify your study, please submit the Modification Request Form and relevant documents to the IRB at irb@seattlechildrens.org.

Sincerely,

Douglas S. Diekema, M.D., M.P.H., Chair
Institutional Review Board

Tori Lallemont, J.D., MPH, Human Subjects Protection Analyst
Human Subjects Protection Program

Medical School Institutional Review Board (IRBMED) • 2800 Plymouth Rd., Building 200, Room 2086, Ann Arbor, MI 48109-2800 • phone (734) 763 4768 • fax (734) 763 9603 • irbmed@umich.edu

To: Rodica Pop-Busui

From:
There are no items to display

Cc:

Catherine	Martin
Mitali	Mehta
Eva	Feldman
Rodica	Pop-Busui

Subject: Notice of Exemption for [HUM00040643]

SUBMISSION INFORMATION:
Title: SEARCH - CAN READING CENTER
Full Study Title (if applicable): SEARCH for Diabetes in Youth Study
Study eResearch ID: HUM00040643
Date of this Notification from IRB: 8/23/2010
Date of IRB Exempt Determination: 8/23/2010
UM Federalwide Assurance: FWA00004969 expiring on 11/17/2011
OHRP IRB Registration Number(s):

IRB EXEMPTION STATUS:
The IRBMED has reviewed the study referenced above and determined that, as currently described, it is exempt from ongoing IRB review, per the following federal exemption category:

> **EXEMPTION #4 of the 45 CFR 46.101.(b):**
> Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

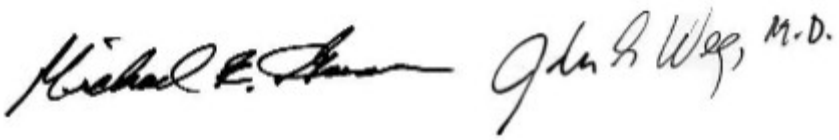
Note that the study is considered exempt as long as any changes to the use of human subjects (including their data) remain within the scope of the exemption category above. Any proposed changes that may exceed the scope of this category, or the approval conditions of any other non-IRB reviewing committees, must be submitted as an amendment through eResearch.

Although an exemption determination eliminates the need for ongoing IRB review and approval, you still have an obligation to understand and abide by generally accepted principles of responsible and ethical conduct of research. Examples of these principles can be found in the Belmont Report as well as in guidance from professional societies and scientific organizations.

SUBMITTING AMENDMENTS VIA eRESEARCH:
You can access the online forms for amendments in the eResearch workspace for this exempt study, referenced above.

ACCESSING EXEMPT STUDIES IN eRESEARCH:

Click the "Exempt and Not Regulated" tab in your eResearch home workspace to access this exempt study.



Michael Geisser
Co-chair, IRBMED

John Weg
Co-chair, IRBMED
