DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
National Institutes of Health

National Institute of Diabetes and
Digestive and Kidney Diseases
Bethesda, Maryland 20892

March 25, 2016

Ralph B. D'Agostino, Ph.D.
Professor
Biostatistical Sciences
525 at Vine, 4th floor
Medical Center Boulevard
Winston-Salem, NC 27157

Dear Dr. D'Agostino:

Enclosed is the Certificate of Confidentiality (DK-16-014) protecting the identity of research subjects in your project entitled, "SEARCH for Diabetes in Youth Study." Please note that the Certificate expires on September 29, 2020.

Please be sure that the consent form given to research participants accurately states the intended uses of personally identifiable information (including matters subject to reporting) and the confidentiality protections, including the protection provided by the Certificate of Confidentiality with its limits and exceptions.

If you determine that the research project will not be completed by the expiration date, September 29, 2020, you must submit a written request for an extension of the Certificate **three months** prior to the expiration date. If you make any changes to the protocol for this study, you should contact me regarding modification of this Certificate. Any requests for modifications of this Certificate must include the reason for the request, documentation of the most recent IRB approval, and the expected date for completion of the research project. Please note that IRB approval must be maintained throughout the length of the study. Approval must be current and unconditional, or conditioned only upon the issuance of a Certificate of Confidentiality and documented by a letter or form signed by an authorized IRB representative.

Please advise me of any situation in which the Certificate is employed to resist disclosure of information in legal proceedings. Should attorneys for the project wish to discuss the use of the certificate, they may contact the Office of the NIH Legal Advisor, National Institutes of Health, at (301) 496-6043.

Correspondence should be sent to:

Francisco O. Calvo, Ph.D.
Chief, Review Branch
NIDDK, National Institutes of Health
6707 Democracy Blvd, Room 752
Bethesda, MD 20892-5452
FC15Y@nih.gov

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Sincerely,

Gregory G. Germino, MD
Deputy Director

CONFIDENTIALITY CERTIFICATE

DK-16-014

Issued to

Wake Forest Scholl of Medicine

conducting research known as

"SEARCH for Diabetes in Youth Study"

In accordance with the provisions of section 301(d) of the Public Health Service Act 42 U.S.C. 241(d), this Certificate is issued in response to the request of the Principal Investigator, Dr. Ralph D'Agostino, to protect the privacy of research subjects by withholding their identities from all persons not connected with this research. Dr. Agostino is primarily responsible for the conduct of this research, which is supported by the NIH.

Under the authority vested in the Secretary of Health and Human Services by section 301(d), all persons who:

1. are enrolled in, employed by, or associated with Wake Forest School of Medicine and its contractors or cooperating agencies operating in multiple centers worldwide, and
2. have in the course of their employment or association access to information that would identify individuals who are subjects of the research pertaining to the project known as "SEARCH for Diabetes in Youth Study."

are hereby authorized to protect the privacy of the individuals who are the subjects of that research by withholding their names and other identifying characteristics from all persons not connected with the conduct of that research. In addition, IRB approval must be maintained throughout the length of the study. Approval must be current and unconditional, or conditioned only upon the issuance of a Certificate of Confidentiality and documented by a letter or form signed by an authorized IRB representative.

From Applicant's Petition:

SEARCH 4: Executive Summary of the Protocol

The SEARCH for Diabetes in Youth Study has been ongoing since 2000. It includes two components: a surveillance component and a cohort component. SEARCH has documented a 31% increase in the prevalence of type 2 diabetes (T2D) between 2001 and 2009, as well as an increase of 21 % in the prevalence of type 1 diabetes (T1D). Increases occurred across most but not all major subgroups of age, sex and race/ethnicity. Further, we documented an annual increase in the incidence of T1D among non-Hispanic

White (NHW) youth of approximately 2.7% per year. In contrast, studies from Europe suggest that incidence of T1D may be stabilizing. SEARCH has also reported that many youth with diabetes are at risk for acute and subclinical chronic complications, with the greatest risk in racial/ethnic minorities and those with T2D. Also, while many youth with diabetes are receiving quality care, a significant proportion of minority youth and young adults are not. These findings suggest that a substantial number of such youth will develop debilitating complications early in life adversely affecting their quality of life and life expectancy.

With funding awarded in 2015-2020, the SEARCH surveillance component will continue to ascertain newly diagnosed incident cases of diabetes throughout the study period and one additional prevalent cohort (index year 2017) for youth age < 20 years across our five geographically dispersed Study Centers. Specific Aims of the surveillance component are: 1) To ascertain cases of prevalent diabetes in calendar year 2017 among youth age < 20 years at diagnosis; 2) To continue to ascertain newly diagnosed (2015-2020) incident diabetes cases in youth age < 20 years; 3) To confirm classification of diabetes type using biochemical markers, to describe selected clinical characteristics at diagnosis, and to maintain an infrastructure that facilitates the development of more detailed ancillary studies by storing biological samples and preserving contact with potential study participants; and 4) To optimize efficiency of the SEARCH Surveillance activities through targeted development and validation projects designed to utilize relevant electronic health data to operationalize each of the aims above.

Beginning in 2002, SEARCH recruited a series of incident cohorts representative of the diverse racial/ethnic, socioeconomic and geographic base population, who were well-characterized through a variety of surveys, physical and laboratory assessments soon after diagnosis and followed them longitudinally (SEARCH Cohort Study). With funding awarded in 2015-2020, the SEARCH cohort component will continue longitudinal follow-up of the cohort participants to examine four specific aims: 1) To establish, compare and contrast the burden (prevalence, incidence, progression and clustering) of acute and chronic complications of diabetes, and explore the responsible risk factors and pathways among youth and young adults with T1D and T2D; 2) To explore, compare and contrast processes of care (including barriers to care and quality of care) and their influence on quality of life among youth T1D and T2D, as they transition from pediatric to adult care; 3) To conduct surveillance of mortality including cause of death in the SEARCH cohort; and 4) To maintain, supplement and promote access to the SEARCH Cohort repository for biological specimens to conduct scientifically and logistically appropriate ancillary studies.

These studies will provide critical information on the prevalence, incidence and early clinical course of diabetes in youth and will assist in understanding the factors and pathways that contribute to the burden of diabetes in youth, providing the foundation to develop strategic interventions to limit individual morbidity and mortality and promote an effective, sustainable national health policy.

A Certificate of Confidentiality is requested since as in previous phases of the SEARCH Study, we can offer further protection of privacy for study participants. This will protect

our investigators and institutions from being compelled to disclose identifying characteristics of study participants in response to legal demands at the federal, state, or local level.

Data from each site is obtained, managed, and protected according to a standard study protocol that has been developed and vetted by the Steering Committee and approved by all participating IRBs and by the NIDDK Observational Studies Monitoring Board (OSMB). Clinic sites use a standard informed consent template, modified as needed by local IRB requirements. All clinic staff is trained and certified, operate under a single Manual of Procedures (MOP), and follow a standard set of data collection procedures. Clinic staff participates in both central and local training as needed. Clinical Center investigators and staff participate in ongoing working groups and established study committees to ensure that identical procedures are followed at each site for the purpose of recruitment, retention, and ensuring the highest quality of study data.

The SEARCH 4 Study utilizes a study-wide case registration data management system that is technically advanced and utilizes electronic health records, mobile platforms, and direct access by study participants to the website. The system requires that Protected Health Information (PHI) is entered into the registration database in order to successfully accomplish the following tasks: directly obtaining the IPS by the participant, deduplication, scheduling study visits, and tracking. PHI is blinded to Coordinating Center personnel throughout both the web systems and the database. This is accomplished through both client-side and Microsoft SQL Server level encryption methods.

As in previous phases of SEARCH, every precaution is taken to maintain the confidentiality of all study participants. For both the Cohort and Registry Studies, confidentiality of data is maintained by using research identification (ID) numbers that uniquely identify each individual. Hardcopies of individual participants' research records will be retained and secured by each SEARCH Clinical Center. The file that links participants' names and demographic information with their research ID numbers is retained separately from the study data, using an approach consistent with local IRB requirements. After the study is completed, local data are stored with that of other completed studies in a secure storage area following all applicable local regulations for the storage, maintenance, and destruction of research data.

This research is expected to begin on September 30, 2015 and is expected to end on September 29, 2020.

As provided in section 301 (d) of the Public Health Service Act 42 U.S.C. 241(d):

> "Persons so authorized to protect the privacy of such individuals may not be compelled in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings to identify such individuals."

This Certificate does not protect you from being compelled to make disclosures that: (1) have been consented to in writing by the research subject or the subject's legally authorized representative; (2) are required by the Federal Food, Drug, and Cosmetic Act (21. U.S.C.301 et seq.) or regulations issued under that Act; or (3) have been requested from a research project funded by NIH or DHHS by authorized representatives of those agencies for the purpose of audit or program review.

This Certificate does not represent an endorsement of the research project by the Department of Health and Human Services. This Certificate is now in effect and will expire on September 29, 2020. The protection afforded by this Confidentiality Certificate is permanent with respect to subjects who participate in the research during the time the Certificate is in effect.

Gregory G. Germino -S

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Gregory G. Germino, MD
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