

**SEARCH FOR DIABETES IN YOUTH STUDY**

**OMB SUPPORTING STATEMENT: PART A**

Submitted by:

Sharon Saydah, PhD MHS

Project Officer

Epidemiology and Statistics Branch

Division of Diabetes Translation

Centers for Disease Control and Prevention

University Office Park, Williams Bldg.

Atlanta, GA 30341

Telephone: (301) 458-4183

Fax: (301) 458-4025

e-mail: [ssaydah@cdc.gov](mailto:ssaydah@cdc.gov)

**November 2, 2011**

## TABLE OF CONTENTS

### A. JUSTIFICATION

1. Circumstances Making the Collection of Information Necessary
2. Purpose and Use of the Information Collection
3. Use of Information Technology and Burden Reduction
4. Efforts to Identify Duplication and Use of Similar Information
5. Impact on Small Businesses or Other Small Entities
6. Consequences of Collecting the Information Less Frequently
7. Special Circumstances Relating to the Guidelines of 5 CFR 1320
8. Comments in Response to the Federal Register Notice
9. Explanation of Any Payment or Gift to Respondents
10. Assurance of Confidentiality Provided to Respondents
11. Justification for Sensitive Questions
12. Estimates of Annualized Burden Hours and Costs
13. Estimate of Other Total Annual Cost Burden to Respondents
14. Annualized Cost to the Federal Government
15. Explanation for Program Change or Adjustment
16. Plans for Tabulation and Publication and Project Time Schedule
17. Reason Display of OMB Expiration is Inappropriate
18. Exceptions to Certification for Paperwork Reduction Act Submission

## Attachments to Supporting Statement A

- Attachment 1: Authorizing Legislation: PHSA
- Attachment 2: Federal Register Notice
- Attachment 2B: Summary of Public Comments and CDC Response
- Attachment 3: SEARCH Study Sites and Coordinating Center
- Attachment 4A1-4: Registry Data Collection
- Attachment 4B1-15: Cohort Study Data Collection
- Attachment 5: References
- Attachment 6: Experts Consulted During SEARCH Development
- Attachment 7: IRB Approvals
- Attachment 8: Certificate of Confidentiality
- Attachment 9: Clinical site consent forms including HIPAA waiver language
- Attachment 10: Data use agreements
- Attachment 11: Published article documenting SEARCH methods

## **Abstract**

CDC requests OMB approval to collect information in Phase 3 of a registry study and longitudinal research study known as SEARCH for Diabetes in Youth. This is a new request. OMB approval is requested for the first three years of the five year project. Phase 3 builds upon activities initiated in 2000 through a multi-center collaborative research project that involved six clinical sites and a data coordinating center, all funded through cooperative agreements. Information collected in previous phases of SEARCH was not provided directly to the CDC.

A number of changes will be implemented during Phase 3. Respondents will be youth < 20 years of age who have been diagnosed with diabetes. Information will be collected from the study participants by five clinical sites, each funded through a cooperative agreement, and transmitted to CDC via a data collection contractor, which will serve as the Coordinating Center for the study. Information collection will support 1) a case registry that can be used to estimate the incidence of diabetes in youth in the U.S., and 2) a cohort study of youth with diabetes to estimate the prevalence and incidence of risk factors and complications, including chronic microvascular (retinopathy, nephropathy, and autonomic neuropathy) and selected markers of macrovascular complications (hypertension, arterial stiffness) of diabetes.

### **A. JUSTIFICATION**

#### **1. Circumstances Making the Collection of Information Necessary**

Diabetes is one of the most common chronic diseases among children in the United States. When diabetes strikes during childhood, it is routinely assumed to be type 1, or juvenile-onset, diabetes. Type 1 diabetes develops when the body's immune system destroys pancreatic cells that make the hormone insulin that regulates blood sugar. It normally strikes children and young adults. People with type 1 diabetes must have daily insulin injections to survive. In the last two decades, type 2 diabetes, formerly known as adult-onset diabetes, has been reported among U.S. children and adolescents with increasing frequency. Type 2 diabetes begins when the body develops a resistance to insulin and no longer uses the insulin properly. As the need for insulin rises, the pancreas gradually loses its ability to produce sufficient amounts of insulin to regulate blood sugar.

Reports of increasing frequency of both type 1 and type 2 diabetes in youth have been among the most concerning aspects of the evolving diabetes epidemic. Unfortunately, there was very limited data on how diabetes among children in the U.S. may have changed over time, or even how many children in the U.S. had type 1 or type 2 diabetes. There was no survey or study large enough to document either the change in incidence and prevalence of diabetes among youth or to distinguish between different types of diabetes. In response to this growing public health concern, the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH) funded the SEARCH for Diabetes in Youth study.

The SEARCH for Diabetes in Youth study began in 2000 as a multi-center, epidemiological study, conducted in six geographically dispersed Study Centers (Kaiser Permanente of Southern

California, Pasadena, California; Cincinnati Children's Medical Center, Cincinnati, Ohio; University of Colorado Denver, Denver, Colorado; Seattle Children's Hospital, Seattle, Washington; South Carolina coordinated at University of North Carolina, Chapel Hill, North Carolina; Kaukuni Medical Center, Hawaii) that reflected the racial and ethnic diversity of the U.S. Phases 1 (2000-2005) and 2 (2005-2010) were designed collaboratively by the research sites to produce estimates of the prevalence and incidence of diabetes among youth age < 20 years, according to diabetes type, age, sex, and race/ethnicity, and to characterize selected acute and chronic complications of diabetes and their risk factors, as well as the quality of life and quality of health care. During Phases 1 and 2, a Coordinating Center, funded through a cooperative agreement, worked collaboratively with clinical sites to conduct data collection and analysis. Major strengths of SEARCH include: 1) race/ethnic diversity within the large cohort of youth with type 1 diabetes; and 2) size and diversity of the cohort of youth with type 2 diabetes. In addition, SEARCH has substantially contributed to the understanding of the etiologic and clinical dimensions of childhood diabetes that relate to classification of diabetes. The SEARCH study brings together major and timely facets of childhood diabetes research: an epidemiologic component that assesses temporal trends in the incidence of diabetes in youth; a pathophysiologic component addressing the natural history of diabetes in youth; a health services research component to evaluate the processes and quality of care for youth with diabetes; and a public health perspective on case classification of diabetes in youth.

Critical questions remain regarding ongoing trends in incidence of childhood diabetes, as well as the rationale and sustainability of public health surveillance systems for diabetes in youth. SEARCH is exceptionally strongly positioned to address these questions through its established infrastructure and surveillance system, and its highly experienced, collaborative and multi-disciplinary investigative team.

Phase 3 of the SEARCH for Diabetes in Youth study will build on previous efforts, with some changes to the data collection and management procedures developed during Phases 1 and 2. As in the initial phases, clinical and observational protocols will be determined collaboratively by the principal investigators from five study sites, and guided by experience gained during Phases 1 and 2. De-identified information collected from the participants at each study site will be transmitted to a Coordinating Center, funded by CDC through a contract mechanism, for aggregation and analysis. CDC will receive a de-identified analysis data set from the Coordinating Center. These activities are authorized by section 301 of the Public Health Service Act (42 USC 241, Part A, Research and Investigation; see **Attachment 1**).

## **1.1 Privacy Impact Assessment**

### **Overview of the Data Collection**

Phase 3 will involve five geographically dispersed study sites and a Coordinating Center (see **Attachment 3**). Data collection will consist of two components:

1. The Registry Study will collect information on newly diagnosed incident diabetes cases in youth age < 20 years.
2. The Phase 3 Cohort Study will collect information about SEARCH participants whose diabetes was incident in 2002 or later, with duration of diabetes > 5 years, who completed a baseline study visit (expected n=3550) in a previous phase of SEARCH. The Phase 3 Cohort Study is based on a previous epidemiological study consisting of the largest and most culturally diverse population of youth with diabetes ever assembled.

De-identified, encrypted study data will be transmitted to the Coordinating Center via the study webpage. Personal health information will not be transmitted to the Coordinating Center or to CDC, but will be kept locally at the clinical sites. All study personnel will be trained in the appropriate management and security of study data.

#### Items of Information to be Collected

The information collected from the participants will include information about diabetes type, date of diabetes diagnosis, physical examination, and measurements of risk factors for micro and macro vascular diabetes complications. The data collection forms related to the Registry Study are included in **Attachments 4a1-4a4**. The data collection forms for the Cohort Study are included in **Attachments 4b1-4b15**.

#### Identification of Website(s) and Website Content Directed at Children under 13 Years of Age

There is no website content directed at children under 13.

### **A.2. Purpose and Use of Information Collection**

SEARCH provides the foundation for childhood diabetes surveillance efforts in public health, clinic, and research settings. SEARCH data will be used to design and implement public health efforts to prevent both type 1 and type 2 diabetes in youth. The data that are acquired by SEARCH regarding the natural history of the disease in youth including age of onset, risk factors of diabetes complications, quality of care and quality of life will also be used to assist with the design and implementation of interventions that can reduce the risk for both acute and chronic diabetes complications. De-identified information will also be made available to researchers for additional analyses.

In Phase 3, the specific aims of the SEARCH Registry Study are:

**Aim 1:** To ascertain newly diagnosed (2010 - 2014) incident diabetes cases in youth age < 20 years in order to assess temporal trends in diabetes incidence and temporal trends in presentation of diabetes for the period 2002-2014, by age, sex, race/ethnicity, and diabetes type.

**Aim 2:** To provide consultation and support to inform the development of low-cost sustainable public health surveillance systems of childhood diabetes in the U.S., with a focus on challenges in ascertainment and classification of cases with type 2 diabetes and cases among older youth (ages 15 years or older) with any form of non-gestational diabetes.

**Aim 3:** To conduct surveillance of mortality including cause of death on the incident cases from September 30, 2010 to September 29, 2015.

In Phase 3, the specific aims of the SEARCH Cohort Study are:

**Aim 4:** To assess the prevalence and incidence of, and risk factors for chronic microvascular degeneration (retinopathy, nephropathy, and autonomic neuropathy) and selected markers of macrovascular complications (hypertension, arterial stiffness) of diabetes.

**Aim 5:** To assess the incidence of, and risk factors for, serious acute complications of diabetes including severe hypoglycemia and diabetic ketoacidosis (DKA).

**Aim 6:** To determine the degree to which barriers to health care, quality of care, and the process of transition from pediatric to adult health care impact disease factors, including dimensions of diabetes type, and diabetes-related outcomes (acute and chronic complications, quality of life, diabetes-related mortality).

**Aim 7:** To maintain and supplement the SEARCH repository for biological specimens, and promote access to SEARCH for the conduct of scientifically and logistically appropriate ancillary studies.

Examples of information generated through previous phases of SEARCH include:

- SEARCH prevalence data indicate that in the U.S., at least 154,000 children/youth have diabetes. Diabetes prevalence varies across major racial/ethnic groups:
  - o In children 0–9 years of age non-Hispanic whites have the highest prevalence (about 1/1,000). In this age group across all race/ethnic groups, type 1 diabetes is the most common form of the disease. The study found that type 2 diabetes is extremely rare in children of all races younger than 10 years of age.
  - o Among adolescents and young adults (age 10–19 years), African American and non-Hispanic white youth have the highest burden of diabetes (about 1 of 315) and Asian/Pacific Islanders have the lowest (about 1 of 746). Type 1 diabetes prevalence is 2.3/1,000 and it is the most common form of diabetes in all racial/ethnic groups except in American Indian youth. Type 2 diabetes prevalence is 0.4/1,000 and it represented 6% of the cases of diabetes in Non-Hispanic White, 33% in African American, 40% in Asian/Pacific Islander, and 76% among American Indian youth.

- Based on 2002 and 2003 data, the overall incidence is estimated to be 24.3 per 100,000 per year. Annually, an estimated 15,000 youth are diagnosed with type 1 diabetes, and about 3,700 youth are diagnosed with type 2.
  - Among youth aged <10 years, most diabetes cases are type 1, regardless of race/ethnicity. In this age group the highest incidence of type 1 diabetes is observed in non-Hispanic whites (19/100,000 for 0- to 4- years-old and 28/100,000 for 5- to 9- years-old)
  - Among older youth (ages 10-14 and 15-19 years), the highest incidence of type 1 diabetes is in non-Hispanic white youth (33/100,000 per year for 10- to 14- years-old and 15/100,000 for 15- to 19- year olds), followed by African American (19.2 and 11.1) and Hispanic (17.6 and 12.1), and lowest among American Indian (7.1 and 4.8) and Asian/Pacific Islanders (8.3 and 6.8).
  - The incidence of type 2 diabetes is the highest among American Indians (25.3 and 49.4 for ages 10-14 and 15-19 years, respectively), followed by African Americans (22.3 and 19.4), Asian/Pacific Islanders (11.8 and 22.7) and Hispanics (8.9 and 17.0), and is low (3.0 and 5.6) among non-Hispanic whites.
  
- SEARCH has shown that nutritional intake in adolescents with diabetes is poor and does not follow current recommendations. Recommendations for total dietary fat intake are met by only 10 percent of youth with diabetes and recommendations for saturated fat intake by only 7 percent.
  
- SEARCH found that about 9 percent of adolescents with diabetes have moderate or severely depressed mood symptoms, with more girls than boys being affected. Depressed mood is associated with poor glycemic control and a higher likelihood of emergency room visits.
  
- About half of the SEARCH participants had an LDL-Cholesterol concentration above the optimal level of 100 mg/dL. In older youth ( $\geq 10$  yrs of age), the prevalence of abnormal lipids was higher in those with type 2 (33%) than in those with type 1 diabetes (19%). Moreover, worse glycemic control was associated with a worse lipid profile, regardless of diabetes type.
  
- The prevalence of multiple cardiovascular disease (CVD) risk factors is high in children and adolescents with diabetes. CVD risk factors are present in both youth with type 1 or type 2 DM, but were more common in adolescents with type2.
  
- Higher Body Mass Index (BMI) is associated with younger age at diagnosis of type 1 diabetes, but only in children with reduced beta cell function. These data suggest that, only among individuals with already compromised beta-cell function or high rate of beta cell loss, obesity accelerates type 1 diabetes onset. In addition, low birth weight may be a factor in accelerating the onset of type 1 diabetes. These data suggest that the intrauterine environment may be an important determinant of age of onset for type 1 diabetes.

Additional information about uses of SEARCH Phase 1 and Phase 2 data is provided in the References section of this Information Collection Request (see **Attachment 5**).

## **2.1 Privacy Impact Assessment**

The SEARCH clinical sites will collect information in identifiable form (IIF) on each registered diabetes case and cohort study participant (personal identifiers such as name, address, age, race/ethnicity) along with information about the youth's medical history and results of in-person visits. The collection of personal information is necessary in order for the clinical sites to contact registered cases for inclusion in the study and to conduct follow-up. While the SEARCH clinical sites will use a number of different methods to collect data (telephone and in-person interviews, medical record abstraction, laboratory and physical examination measurements, each collected on separate forms), all the data submitted to the Coordinating Center will be entered into a database. The data collection method for the Coordinating Center is the database that has been developed to capture the information collected by the SEARCH clinical sites. Each clinical site will enter the data collected on the forms into an Access database that is then transmitted to the Coordinating Center for compilation and analysis. Each SEARCH Clinical Site will maintain the data for 7 years after the end of the study. At the close out of SEARCH the Coordinating Center will provide CDC with a public use de-identified data set. This data will also be made publicly available through the NIH data repository or similar site to enable secondary, in-depth analyses.

Case-level information undergoes two levels of de-identification prior to transmission to CDC. First, each clinical site assigns a unique identifier (ID) code to each participant identified or followed at that site. The site-specific ID code is used to manage transmission of records from the clinical site to the Coordinating Center (data collection contractor). The information transmitted to the Coordinating Center does not include names or addresses of SEARCH participants. The Coordinating Center will not accept a method of record identification, such as social security number, that may be linked to other databases. The identifying information provided to the Coordinating Center will include a randomly generated site-specific patient ID code, state of residence, month and year of birth, and Hispanic origin and race. Details on the process to provide the Coordinating Center with a Limited Dataset under HIPPA are provided in Section 10.1 Privacy Impact Assessment information. The clinical site is solely responsible for maintaining the unique list linking the site-specific ID code with the participant's name, as well as the encryption information associating their unique ID codes with the personal identifiers maintained by the site. Neither the encryption scheme nor identifying information, other than the variables noted above, will ever be provided to the Coordinating Center or to CDC.

Upon receipt of the de-identified, coded data, the Coordinating Center will create a new, randomly generated ID code for each case. This randomly generated ID code will be used to manage and analyze the records in the de-identified data. The ID codes assigned by the Coordinating Center cannot be linked back to the ID codes assigned by the clinical sites, or the names of patients. Research entities such as the SEARCH clinical sites have successfully used

the two-step de-identification process to protect the identities of research participants and to guard against inadvertent disclosure of personal information in identifiable form.

The aggregate data provided to the Coordinating Center will be archived on secure network servers with user ID and password restricted access at the location of the Coordinating Center. Access rights and restrictions to network resources are determined by user ID. Network systems are maintained in a locked room with access strictly limited to essential employees. A public use de-identified dataset will be provided to CDC at the conclusion of the study.

**2.1.1.** . While the proposed data collection by CDC may impact the respondent's privacy, CDC has taken a number of steps to ensure the respondent's privacy is not impacted. CDC will not receive any identifying information. All identifying information will be maintained at the SEARCH Clinical Sites and will not be transmitted to the Coordinating Center or to the CDC. CDC has also obtained a Certificate of Confidentiality for each SEARCH Clinical Site. The current certificate is valid through August 2016 (**Attachment 8**). HIPAA waiver language is included in the consent form for each clinical site (**Attachment 9**).

### **A.3. Use of Information Technology and Burden Reduction**

Clinical sites will reduce the burden to the participants related to the data collected through surveys in several different ways to accommodate the participant a) by mailing the forms to the participant; b) by telephone; c) administered as an interview. Electronic information collection methods are not generally applicable to the participant-level data collection.

### **A.4. Efforts to Identify Duplication and Use of Similar Information**

These data are available exclusively from the SEARCH grantees, and no other source of data exists that would allow for national estimates of the incidence of diabetes in youth or for the incidence and prevalence of risk factors and complications among youth with diabetes. Although data-sets with questions and measures related to diabetes currently exist [e.g., the National Health and Nutrition Examination Survey [(NHANES), OMB No. 0920-0237, exp. 11/30/2012], the number of youth with diabetes from NHANES or other general-purpose information collections is too small to allow accurate estimates of diabetes burden in youth in the U.S. For example, in NHANES 1999 – 2004 there were only 41 youth under 20 who self reported diabetes and of those only 9 were less than 12 years old. This number is too small to examine any characteristics of the youth population with diabetes since it is stated in the NHANES Analytic Guidelines that a minimum sample size of 150 is needed. Further, the prevalence estimate based on NHANES 1999-2004 data for diabetes among youth under 20 years has a relative standard error of 24% and is considered unreliable based on the NHANES Analytic Guidelines. We are also unable to distinguish diabetes type in the NHANES sample. Since the estimates of the incidence or prevalence of diabetes among youth are not available from these data sets, SEARCH will supplement the existing information to provide this information. Further, the alternative data sources would only allow the tracking of prevalence

of diabetes and not estimates of incidence.

#### **A.5. Impact on Small Businesses or Other Small Entities**

No small businesses will be involved in this data collection.

#### **A.6. Consequences of Collecting Information Less Frequently**

Ongoing data collection is a necessary component of the SEARCH study in order to calculate incidence of diabetes among youth as it occurs in the study population and to obtain estimates of the prevalence and incidence of complications among youth with diabetes over time in the longitudinal study. Information will be collected for 5 years to allow for on-going monitoring of the study and estimates of the incidence of diabetes in youth. This allows the tracking of trends in the population. The reporting periods established for SEARCH are frequent enough to allow for ongoing evaluation, but not too frequent to be overly burdensome. The current reporting periods allow CDC and SEARCH grantees to assess performance at regular intervals, and to make adjustments as necessary. Less frequent data collection would compromise the ability to successfully conduct the SEARCH study.

#### **A.7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5**

This request fully complies with the regulation 5 CFR 1320.5.

#### **A.8. Comments to the Federal Register Notice and Efforts to Consult with Outside Agency**

- A. A 60-day Notice was published in the Federal Register on February 11, 2011, Vol. 76, No. 29, pp. 7859-7860 (Attachment 2). No comments were received in response to publication of the Notice.
- B. In 2006, CDC and NIH formed a working group of experts, the External Scientific Evaluation Committee (ESEC), to provide on-going outside consultation to the SEARCH Study. The ESEC meets annually. In 2009, the National Institutes of Health, National Institute for Diabetes, Digestive and Kidney Disease formed a group of experts (External Evaluation Committee) to advise NIH on recommendations for the future direction of SEARCH. There were no major problems that could not be resolved during the consultations. Members of both the ESEC and the NIH External Evaluation Committee, along with scientists at both the CDC and NIH, are listed in **Attachment 6**.

#### **A.9. Explanation of Any Payment or Gift to Respondents**

In general, the SEARCH cohort participants completing the in person visit will be offered \$120 token of appreciation in cash/gift cards. The SEARCH registry participants completing the initial participant survey will be offered \$10 token of appreciation in cash/gift cards and the SEARCH registry participants completing the in-person visit will be offered \$80 token of appreciation in cash/gift cards. Each clinical site is governed by a separate IRB and each site has unique characteristics, resulting in some differences across the sites. In Seattle, Washington, in addition to the tokens of appreciation mentioned above, participants also receive \$6 food voucher if they are fasting for the visit and an additional \$20 if blood draw or heart rate variability test needs to be repeated. At Kaiser Permanente of Southern California, in addition to the tokens of appreciation mentioned above, participants are provided with a gift card for gasoline if they have to travel more than 10 miles each way for the study visit (one \$10 gift card for 10-39 miles; two \$10 gift cards for 40-79 miles and three \$10 gift cards for more than 80 miles). In Cincinnati, Ohio, participants who are 18 years or older are offered \$100 gift card for the cohort study visit and \$20 gift card for the overnight urine collection and participants who are < 18 years old are offered \$60 gift card for the study, \$20 gift card for the overnight urine and the parent/guardian is offered \$40 gift card. In Carolina, cohort participants are offered \$80 Walmart gift card and the parent/guardian is offered \$40 Walmart gift card. In Carolina, registry participants are offered \$40 Walmart gift card and the parent/guardian is offered \$40 Walmart gift card. Because of long travel distances for the Carolina clinical site, if participants travel 80-120 miles round trip an additional \$20 Walmart gift card is offered and two \$20 Walmart gift cards are offered if round trip travel is more than 120 miles.

#### **A.10. Assurance of Confidentiality Provided to Respondents**

##### **10.1 Privacy Impact Assessment Information**

The SEARCH Phase 3 information collection has been approved by the IRB at each participating site and by IRB at the Coordinating Center (see **Attachment 7**). Each SEARCH Phase 3 participant signs an informed consent document that describes the voluntary nature of participation and states that the information they provide will be protected by a Certificate of Confidentiality (**Attachment 9**).

Data transmitted to the Coordinating Center qualifies as a HIPAA Limited Dataset. Each Center has a Limited Data Use Agreement with the Coordinating Center (**Attachment 10**) in compliance with the Standards of Privacy of Individually Identifiable Health Information as outlined by the HIPAA privacy rules. Access to study data is limited to the staff working on the study. Local access to the data is governed by the requirements of the local IRB. Additional safeguards include a two-step process of de-identification first at the clinical site and then at the Coordinating Center as detailed below in 10.1.A.

A. Privacy Act Determination. This submission has been reviewed by NCCDPHP and CDC's Information Collection Review Office, which determined that the Privacy Act applies to participant-level information collected by the clinical sites. The applicable System of Records

Notice is 09-20-0136, Epidemiologic Studies and Surveillance of Disease Problems. The Privacy Act does not apply to the de-identified information collected by the Coordinating Center and subsequently transmitted to CDC, as the coded information cannot be filed or retrieved by participant name. The two-step de-identification and re-coding process is described in more detail below.

In the first step, the clinical site removes patient name and other direct identifiers from the records, and assigns a randomly-generated, site-specific participant ID code to each record before transmitting participant-level information to the Coordinating Center. The clinical site maintains and protects the information that links direct patient identifiers to the site's participant ID codes. The Coordinating Center does not have the capacity to re-link the de-identified, coded information that it receives to direct patient identifiers such as name, SSN, or medical record number.

In the second step, the Coordinating Center replaces each record's site-specific ID code with a new, randomly generated participant ID code assigned by the Coordinating Center. Information reported to CDC includes only ID codes generated by the Coordinating Center. Patient names and other direct identifiers cannot be reconstructed from the ID code that is randomly generated by the Coordinating Center.

B. Administrative Safeguards. The information collected during prior phases of the SEARCH project was protected by a Certificate of Confidentiality at each site (**Attachment 8**). The 301(d) confidentiality certificates provide legally effective barriers to disclosure for individually identifiable data residing at the clinical sites and as needed, protection to data residing at laboratories, and other subcontractors with study data. These certificates will protect individual data from sources not connected with this study. CDC has updated Certificates of Confidentiality 301(d) for Phase 3 (**Attachment 8**). Sensitive individually identified patient data which require the continuous confidentiality protection granted under the earlier certificates will be covered under the updated certificates, as well as new data to be collected in Phase 3. All study personnel will be trained in the appropriate and sensitive means of data collection.

Physical and Electronic Safeguards. Information will be obtained from multiple sources: Medical Records, In Person Surveys, In Person Visits (including physical exam, questionnaires, laboratory studies of blood and urine). Forms used for data collection will be distributed to the clinical sites by the Coordinating Center. Data will be transmitted electronically via a password protected website to the Coordinating Center for data analysis. The Coordinating Center employs a digital server certificate from Verisign, Inc. This certificate allows the communications between the web server and the client system to be encrypted. This encryption is as advanced as is now allowable by the United States Government, and the mechanism is the same as is used by the banking industry and for electronic commerce. The Coordinating Center's web system is protected by a Cisco firewall that limits the source and type of traffic coming into the institution, and remains under constant monitoring and control. In addition, the institution is currently implementing a suite of Net Ranger products that will assist in the detection and circumvention of certain well-known attacks. Using attack

signatures, the products monitor incoming traffic, looking for data streams that match the signature of attacks. If found, information is collected about the attack and the transmission is terminated.

Restricted areas of the SEARCH web site are protected by user login. Prior to gaining access to the restricted area, the user is required to enter a username and password that are checked against a database of authorized system users. The organization of the SEARCH authorization database is such that it allows the Coordinating Center to restrict functions of an individual user by their login. The Coordinating Center can restrict their ability to view entire sections of the web site, reports, data elements and more. For security purposes, once a user has successfully logged into the system, inactivity for a period of 15 minutes will automatically force the user to re-authenticate prior to using the system again. Users are recommended to log out of the system before leaving their work area for any extended period.

C. Consent. The research at each clinical site is overseen by its Institutional Review Board. As required by 45 CFR 46, each site obtains assent from the youth who participate in the research, and permission from their parent(s) or guardian(s) (**Attachment 9**).

D. Nature of Response. Respondents are the study participants at each clinical site. Transmission of information to CDC via the Coordinating Center is required under the terms of the cooperative agreements that provide funding for the research.

#### **A.11. Justification for Sensitive Questions**

SEARCH grantees collect potentially sensitive information on baseline forms. Study aims cannot be achieved without the collection of sensitive, or potentially sensitive, information. The justification for each item is detailed below.

- Racial/ethnic group - necessary for subgroup analysis by ethnic group to evaluate differences in prevalence and incidence of diabetes and outcomes,
- Total family income, parental and participant education and finance questions - an important measure of socioeconomic status and predictor of disease development, medical care use, and longevity.
- Other medical issues - questions and measures pertaining to acute and chronic health conditions related to diabetes, such as diabetes ketoacidosis, severe hypoglycemia, retinopathy, nephropathy, neuropathy, vascular dysfunction, depressive symptoms, quality of life; necessary to determine the effects of diabetes on acute and chronic complications.
- Health behaviors - alcohol use, tobacco use, dietary intake; important for understanding the impact of these behaviors on diabetes complications.
- Quality of health care questions - adherence to standards of care for patients with diabetes; changes in diabetes care from adolescent to young adults; important to understanding the factors that affect health care for patients with diabetes during this vulnerable time period.

**A. 12. Estimates of Hour Burden Including Annualized Hourly Costs**

**A.12 Estimates of Annualized Burden and Costs**

Respondents will be the SEARCH for Diabetes in Youth Phase 3 study participants. All information will be transmitted to the Coordinating Center (CDC’s data collection contractor) for aggregation and analysis. Information will be transmitted electronically through a secure web site dedicated to the project. The information collection has two components:

- The Registry Study will collect information on newly diagnosed incident diabetes cases in youth age < 20 years. CDC estimates that each clinical site will identify and register an average of 255 cases per year, for a total of 1,275 cases across all sites. The items collected for each case include Medication Inventory, Inpatient Survey, Specimen Collection (Registry version), and Physical Exam (Registry version). Copies of the data collection instruments are included in **Attachments 4a1-4a4**. The total estimated annualized burden for this information collection is 2,444 hours.
- The Cohort Study is a longitudinal research study about SEARCH cases whose diabetes was incident in 2002 or later. CDC estimates that each clinical site will conduct follow-up on an average of 142 cases per year, for a total of 710 cases across all sites. The items collected for each case include a Health Questionnaire (Youth version), an additional Health Questionnaire (Parent version), Center for Epidemiologic Study-Depression, Quality of Care, Pediatric Quality of Life Survey (Peds QL), SEARCH Michigan Neuropathy Screening Instrument, Diabetes Eating Survey, Low Blood Sugar Survey, Supplemental Survey, Tanner Stage, Retinal Photo, and Family Conflict Survey, Pediatric Quality of Life Scale, Physical Exam, and Specimen Collection. Copies of the data collection instruments are included in **Attachments 4b1-4b15**. The total estimated annualized burden for this information collection is 3,691 hours.

The estimated annualized burden per participant respondent is 3.09 hours. The total estimated annualized burden for all sites is 6,135 hours, as shown in Table A.12-A.

**Table A.12-A. Estimated Annualized Burden Hours**

Type of Respondents	Number of Respondents	Number of Responses per Respondent	Information Collection	Form Name	Average Burden per Response	Total Burden (in hours)
SEARCH Participants	1,275	1	Registry Study	Medication Inventory	5/60	106
				Inpatient Survey	10/60	213
				Specimen Collection (Registry)	20/60	425
				Physical Exam	80/60	1,700

				(Registry)		
SEARCH Participants	710	1	Cohort Study	Health Questionnaire- Youth	15/60	178
				Health Questionnaire- Parent	15/60	178
				CES-Depression	4/60	47
				Quality of Care	13/60	154
				Peds QL	5/60	59
				SEARCH MNSI Neuropathy	10/60	118
				Diabetes Eating Survey	5/60	59
				Low Blood Sugar Survey	5/60	59
				Supplemental	10/60	118
				Tanner Stage	5/60	59
				Retinal Photo	15/60	178
				Family Conflict	5/60	59
				Pediatric Diabetes QOL Scale	5/60	59
				Physical Exam	180/60	2130
Specimen Collection	20/60	236				
					Total	6,135

The total estimated cost to study participants is \$130,984 as shown in Table A.12-B. The cost to respondents is based on an average hourly wage rate of \$21.35 (mean hourly wage for adults, 2010, U.S. Bureau of Labor Statistics). Some participants in the registry study and the cohort study are assumed to be employed. For younger patients who are not employed and would typically be dependent on a parent or guardian to enable their participation, the average hourly wage represents the value of the parent or guardian's time.

**Table A.12-B. Estimated Annualized Cost to Respondents**

Type of Respondents	Number of Respondents	Number of Responses per Respondent	Information Collection	Form Name	Total Burden (in hours)	Total Cost
SEARCH Participants	1,275	1	Registry Study	Medication Inventory	106	\$2,263
				Inpatient Survey	213	\$4,548
				Specimen Collection (Registry)	425	\$9,074
				Physical Exam (Registry)	1,700	\$36,295
SEARCH Participants	710	1	Cohort Study	Health Questionnaire- Youth	178	\$3,800
				Health Questionnaire- Parent	178	\$3,800

				CES-Depression	47	\$1,003
				Quality of Care	154	\$3,288
				Peds QL	59	\$1,260
				SEARCH MNSI Neuropathy	118	\$2,519
				Diabetes Eating Survey	59	\$1,260
				Low Blood Sugar Survey	59	\$1,260
				Supplemental	118	\$2,519
				Tanner Stage	59	\$1,260
				Retinal Photo	178	\$3,800
				Family Conflict	59	\$1,260
				Pediatric Diabetes QOL Scale	59	\$1,260
				Physical Exam	2130	\$45,476
				Specimen Collection	236	\$5,039
						\$130,984

**A.13. Estimate of Other Total Annual Cost Burden to Respondents or Recordkeepers**

There are no capital costs, operating costs or maintenance costs to report.

**A.14. Annualized Cost to the Federal Government**

For the SEARCH for Diabetes in Youth Study, the estimated average annual contract costs (including direct and indirect costs) in this 5 year submission for coordinating center are as follows:

<u>Cooperative Agreements</u>	
Clinical sites (\$675,045 for each site)	\$3,375,225
<u>Contract</u>	
Coordinating Center	\$1,469,580
Subcontractors	<u>\$729,364</u>
Annual Contract Costs	\$2,198,944
<u>CDC</u>	
Personnel	\$40,000
Total	\$5,614,169

Clinical sites are responsible for information collection from participants and transmitting data to the Coordinating Center. The Coordinating Center is responsible for coordinating data collection, data analysis, and providing general study support to the SEARCH clinical sites.

The Coordinating Center will identify subcontractors to complete the tasks of laboratory measurement, subclinical measurements, and development of recruitment materials.

CDC costs for staff time for project development, implementation and monitoring are estimated at 0.5 FTE for \$40,000 annually. The average annualized cost to the Federal Government for the SEARCH study in this submission period is estimated at \$5,614,169.

**A.15. Explanation for Program Changes or Adjustments**

This is a new data collection.

**A.16. Plans for Tabulation and Publication and Project Time Schedule**

CDC will continue to use the registry and cohort data reported by grantees to produce and provide national estimates on the incidence of diabetes among youth and the incidence and prevalence of micro and macro-vascular complications. This information will be included in CDC

reports such as the Diabetes Fact Sheet which is updated every two years and will also be reported in peer reviewed journals in collaboration with the SEARCH grantees and the contractor. The SEARCH Clinical Sites are funded under cooperative agreements, therefore decisions on specific publications and time tables is determined by the SEARCH Clinical Site Principal Investigators with input and suggestions by CDC. CDC and the Coordinating Center provide support to the SEARCH Clinical Sites in the efforts but do not develop specific timelines. The Coordinating Center will work with SEARCH Clinical Site investigators to develop detailed analysis plans and timelines for each publication. We are seeking OMB approval for the first three years of the five year study and plan to seek and plan to submit an Extension request to cover data collection for the remainder of the project period.

**A.17. Reason (s) Display of OMB Expiration Date is Inappropriate**

The OMB expiration date will be displayed.

**A.18. Exceptions to Certification for Paperwork Reduction Act Submissions**

There are no exceptions to the certification.