

**FoodNet Non-O157 Shiga Toxin-Producing *E. coli* Study:  
Assessment of Risk Factors for Laboratory-Confirmed Infections and Characterization of  
Illnesses by Microbiological Characteristics (0920-0905)**

**Request for Extension**

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**FoodNet Non-O157 Shiga Toxin-Producing *E. coli* Study:  
Assessment of Risk Factors for Laboratory-Confirmed Infections and Characterization of  
Illnesses by Microbiological Characteristics**

CDC is requesting OMB approval for extension of an existing data collection.

**Summary/Update:**

Persons are enrolled in the study based on a positive Shiga toxin result and a culture that is negative for STEC O157. If a non-O157 STEC is isolated, then the patient will be included in the analytical definition. If not, then they remain in the enrollment case definition. As of July 2014, enrollment was attempted for 1,331 cases; 611 were enrolled, 38 are pending, and 685 were not enrolled. We have an overall enrollment rate (i.e. all enrolled (including mixed infections)/all enrolled+refused+unable to interview <45 days) of 75% ranging from 56% in Maryland to 90% in Minnesota. The time between identification of a case and enrollment ranged from an average of 4 days in MN to 18 days in GA.

A total of 1,149 cases met the analytical case definition. Of these, 602 were enrolled, 39 are pending, and 515 were not enrolled. We enrolled a total of 1,482 controls. Seventy-eight percent of cases have three controls, 4% have two controls, 5% have 1 control, 11% are pending or have 0 controls and 3% have mixed infections (and therefore do not get controls).

Cases and controls were distributed geographically as follows: CA (22; 57), CO (44; 88), CT (34; 80), GA (72; 184), MD (25; 53), MN (185; 499), NM (36; 91), NY (41; 99), OR (62; 146), and TN (81; 185). Demographics of cases and controls are included in the table below.

	Cases	Controls
Female	239	516
Male	192	331
Unknown	171	635
Hispanic	66	149
Non-Hisp	524	1166
Unknown	12	167
Am Ind	3	8
Asian	12	27
Black	42	101
Nat Haw	2	4
White	506	1126
Multiple	5	11
Unknown	32	205

Reasons for non-enrollment included: refusal (28%), unable to interview <45 days of ill onset/specimen collection date (9%), >10 attempts (30%), onset unknown or not within 45 days of specimen collection (10%), secondary case (4%), part of an outbreak (8%), not ill (2%), wrong/no phone number (2%), language barrier (2%), did not provide consent/assent (1%), and 4% for other reasons.

No changes have been made to the study questionnaire or other documents.

## **A. Justification**

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

#### **Background**

Each year many Shiga toxin-producing *E. coli* (STEC) infections occur in the United States, ranging in severity from mild diarrhea, to hemorrhagic colitis and in some cases, life-threatening hemolytic uremic syndrome (HUS). HUS occurs most frequently following infection with serogroup O157; 6% of patients with this type of STEC infection develop HUS, with highest occurrence in children aged < 5 years. HUS has a fatality rate of approximately 5%; up to 25% of HUS survivors are left with chronic kidney damage. Animals, especially ruminants, carry STEC in their intestinal tract. Consumption of food or water containing animal feces and direct contact with infected animals or persons are important routes of transmission.

STEC are broadly categorized into two groups by their O antigens, O157 STEC and non-O157 STEC. The serogroup O157 is most frequently isolated and most strongly associated with HUS. Risk factors for STEC O157 infections in the United States and internationally have been intensely studied. Epidemiological studies of O157 STEC infections identified risk factors such as consumption of ground beef that facilitated implementation of control efforts that have reduced the incidence O157 STEC infections. Non-O157 STEC are a diverse group that includes all Shiga toxin-producing *E. coli* of serogroups other than O157. Over 50 STEC serogroups are known to have caused human illness; in the United States, over 70% of strains isolated from humans belong to one of six serogroups (O26, O111, O103, O121, O45, and O145); each serogroup may contain several serotypes. Little is known about the specific risk factors for infections due to non-O157 STEC serogroups. Better identification of exposures that lead to these infections could assist in designing effective control and prevention measures.

Although they have been studied less than O157 STEC, non-O157 STEC are of public health importance. Numerous non-O157 outbreaks have been reported from throughout the world and clinical outcomes in some patients can be as severe as those seen with STEC O157 infections. The clinical severity of non-O157 STEC infections appears to vary considerably by serotype or by the profile of virulence genes carried by specific strains.

Until 1995, a major obstacle to the study of non-O157 STEC was the lack of practical laboratory diagnostic methods to detect these pathogens in clinical specimens. *E. coli* O157 are more easily detected because of their inability to rapidly ferment sorbitol within 24h of growth. Most non-O157 STEC, on the other hand, typically readily ferment sorbitol and, therefore, cannot be easily distinguished from ubiquitous non-pathogenic *E. coli* when cultured. Therefore, cases of non-O157 STEC infection have traditionally been under-diagnosed.

In 1995, the first enzyme immunoassays (EIA) to detect Shiga toxin became available. Some public health labs now use polymerase chain reaction (PCR) tests to detect STEC and a few clinical labs have begun adopting PCR testing. These non-culture tests have facilitated diagnosis of non-O157 STEC infections. Public health authorities responded by designating non-O157 STEC infection as a nationally notifiable condition in 2000. Several studies conducted after the availability of non-culture tests indicate that, collectively, non-O157 STEC cause a similar or slightly higher number of infections, as O157 STEC in many parts of the United States; similar findings have been documented internationally.

Recent clinical laboratory guidelines aim to maximize detection and identification of STEC infections. These guidelines recommend that, upon receipt of stool specimens from patients with acute community-acquired diarrhea, clinical laboratories should rapidly and simultaneously perform non-culture tests (EIA or PCR) to detect Shiga toxin (or the genes that encode the toxins) and culture the specimen on both routine agar (to detect *Salmonella*, *Shigella*, and *Campylobacter* species) and a sorbitol-containing agar to detect O157 STEC. Samples that test positive for Shiga toxin should be sent to public health laboratories so that STEC isolates can be identified and characterized for epidemiological purposes. As adoption of these guidelines grows, the number of non-O157 STEC infections reported to surveillance is expected to increase.

Two state-level studies have been conducted to identify risk factors for non-O157 STEC infections. These studies compared exposures among patients with sporadic non-O157 STEC infections with those among patients with sporadic O157 STEC infection in New Mexico and Minnesota and found that recent international travel, urban residence, and non-white race might be more common in persons with non-O157 STEC infection than in persons with O157 infection. In Minnesota, no significant exposure differences were seen between the two groups for several well characterized STEC O157 risk factors such as a history of consuming raw milk, living on a farm, or visiting a petting zoo in the week before illness onset.

More comprehensive understanding of risk factors for sporadic non-O157 STEC infections is needed to inform prevention and control efforts. A few small case-control studies have been undertaken in other countries in which exposures were compared between non-O157 STEC patients and population controls. However, these studies were limited by small sample size (29 to 71 non-O157 STEC cases) and have uncertain relevance to the United States. Risk factors identified in Australia were eating sliced chicken and corned beef from delicatessens, camping, catered meals, and having a family member with occupational exposure to animals during the 10 days before illnesses began. Risk factors identified in Argentina were drinking from a bottle left at room temperature, drinking infant formula, eating beef outside of home, teething on undercooked beef, contact with a child < 5 years of age, wearing diapers, and living in an overcrowded setting during the seven days before illness began.

Preliminary analysis of a case-control study of non-O157 STEC infections with 45 cases enrolled suggests that international travel, travel within the state, drinking untreated water, living on a farm, having a family member who was ill with diarrhea, and attending daycare during the seven days before illness might be risk factors. (Personal communication, Minnesota Department of Health).

The FoodNet case-control study is the first multistate investigation of non-outbreak-associated non-O157 STEC infections in the United States. It investigates risk factors for non-O157 STEC infections, both as a group and individually for the most common non-O157 STEC serogroups. In addition, the study will characterize the major known virulence factors of non-O157 STEC to assess how risk factors and clinical features vary by virulence factor profiles. As the largest, most comprehensive, and most powerful study of its kind, it could make an important contribution towards better understanding of non-O157 STEC infections and to providing science-based recommendations for interventions to prevent these infections.

This study is authorized under the Public Health Service Act, (42 USC 241) Section 301. A copy is included in the attachments (Attachment 1).

### Privacy Impact Assessment

The Privacy Act is not applicable to this data collection. While the state health department will have access to personal identifiers as part of their routine public health follow up, no identifiable information will be transmitted to CDC.

### Overview of the Data Collection System

FoodNet is an active surveillance network for infections transmitted commonly through food that consists of all or part of 10 states in the United States: California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee. The total population of the 10 FoodNet sites is approximately 46 million persons (15 percent of the U.S. population).<sup>28, 29</sup> The FoodNet and U.S. populations are similar in age, sex, and race distributions, but the Hispanic/Latino population is slightly under-represented in FoodNet. Because relatively few non-O157 STEC cases are reported annually from the counties in the

California FoodNet site, additional counties within California might be added to the study catchment area at a later date, pending all necessary approvals. This study is a prospective, population-based, multi-center, individually matched case-control study of sporadic illness. The cases will be identified through FoodNet over a 36-month period within each site.

Survey Sample International (SSI) is a company that uses various data sources to determine the ages of persons living in households with landline telephone phone numbers listed in the White Pages. For this study, CDC FoodNet purchased from SSI lists of telephone numbers for each of the study's age strata for every county in the FoodNet catchment area. For each telephone number, census block is included to facilitate socioeconomic comparisons between patients and controls. These lists do not contain any personal identifiers. To optimize efficiency in recruiting controls, every 12 months new telephone lists are purchased from SSI. SSI emails these lists to CDC FoodNet and CDC forwards them to the FoodNet sites. To enroll controls, study coordinators call telephone numbers from the appropriate county and age-group specific sublists, starting from the top and moving down. Every phone call attempt is logged directly in a spreadsheet. If a control is recruited, the telephone number is marked as completed and successful. The second time controls of a specific age group/county combination need to be recruited, study coordinators start with the next phone number on the sublist where they had last left off. When the end of a sublist is reached, study coordinators cycle back to the top of the sublist and begin calling phone numbers on the sublist a second time. Up to 10 unsolicited telephone attempts may be made to given telephone number during the course of the study. More than 10 total calls can be made if someone in the household asks to be called back. After completing 10 unsuccessful unsolicited calls, or after learning that a person of the relevant age stratum does not live in the household, or after someone in the household asks to not be called back or hangs up, that telephone number is marked as completed and unsuccessful. Calls to enroll controls are made during weekdays (9am-5pm), weeknights (5-9pm), and weekends (Saturday 10am-9pm, Sunday 1-9pm).

Because SSI is unable to provide reliable age information for persons aged less than 2 years, birth registries are used as the preferred method of selecting controls for case-patients in this age group. Controls are identified from birth registries within the county in which the matched case-patient resides. FoodNet sites sort these lists by date of birth and attempt to enroll those with the closest birth dates before and after the matched case-patient's birth date. Extensive efforts are made to enroll these potential controls, including 10 unsolicited phone calls over at least 5 days including attempts on weekends weekday evenings, during the time periods mentioned above. This procedure is continued by progressively moving further from the matched case's birth date until three qualifying controls are successfully interviewed for each case-patient. As specified by the local IRBs, there might be some variation from site to site on how birth registry data is accessed by their respective vital records departments and some vital records departments might require parents of potential controls to be sent letters by mail allowing them to call the health department to opt out of being called.

Sites that do not have access to birth registries use sequential digit dialing to recruit controls aged less than two years. First, a list of telephone numbers are generated using the case-patient's primary residence phone number as an anchor for the list. If the patient's primary phone number is a cell phone, the phone list will be anchored to the landline phone number of the residence that

is closest to the patient's address. The list contains 100 phone numbers generated by repeatedly adding one to the anchor phone number and 100 phone numbers generated by repeatedly subtracting one from the anchor phone number. Each number on the list is called once until a number is reached at which someone of the appropriate age agrees to be a control. This same approach may be used to recruit older controls if the SSI lists become unavailable during the course of the study. No voice messages will be left.

### **Enrollment: Case-patients**

A FoodNet staff member or local health department staff in each site interviews case-patients by telephone. Case-patients are identified through routine FoodNet active laboratory-based surveillance. As part of routine surveillance activities required by states' reporting rules, clinical laboratories send STEC positive broths or specimens that tested positive for Shiga toxin by EIA or PCR to the state public health laboratory for confirmation and serogrouping. Characterization of STEC strains is a multistep process. Often the first evidence of a probable non-O157 STEC infection is a positive EIA or PCR test for Shiga toxin from a specimen that yielded no colonies suggestive of STEC O157. FoodNet staff members are usually notified of infections with these test results even before a specific non-O157 STEC has been identified. Alternatively, FoodNet staff members are first notified when the public health laboratory identifies non-O157 STEC. Each site attempts to enroll every patient with a probable or confirmed non-O157 STEC infection that comes to their attention. FoodNet or local health department staff contact patients to determine eligibility and, for those who are eligible, offer participation in the study. The study subject is read the consent form and asked to participate. Verbal consent is obtained and documented by the interviewer on the consent form. For children 12–17 years of age (or as specified by a local IRB), verbal assent to be interviewed is obtained after verbal consent from a parent or guardian is obtained. With parental permission, the adolescent is interviewed directly. However, the parent or guardian can be the respondent. Case-patients may be enrolled up to 45 days after specimen collection date, but every effort will be made to enroll them as soon as possible after their infection is identified.

If after enrolling a possible case, a non-O157 STEC is not isolated, that case and any matched controls is excluded from the main case-control analyses and all efforts to enroll matched controls cease. Information from these possible cases may be summarized in a separate analysis. Additionally, some patients have been identified with mixed infections, defined as the isolation non-O157 STEC and one or more additional enteric pathogens. In mixed infections uncertainty exists as to which pathogen(s) caused the patient's illness. Therefore, patients with mixed infections are not included in the analysis to identify risk factors and matched controls are not enrolled. However, information from cases of mixed infections will still be analyzed for other purposes, e.g., to define the clinical spectrum of infection and to compare exposures between patients with mixed infections and patients with infections in which only non-O157 STEC was isolated.

Sera has not been solicited for the purpose of this study; however, information on the results of any test for antibodies to *Escherichia coli* lipopolysaccharide (LPS) will be collected when available by linking data collected specifically for this study to data collected as part of routine public health surveillance in FoodNet for the hemolytic uremic syndrome. Cases with antibodies to O157 LPS are considered to have a mixed infection. Cases with strong serologic evidence of



non-O157 STEC, other than the one isolated will be excluded from analyses of individual serogroups.

### **Enrollment: Controls**

Controls are recruited from the study population in participating sites as outlined above in the control selection section. FoodNet staff or local health department staff read the consent form to the control or legal guardian by telephone. Verbal consent is obtained and documented on the consent form. For children 12–17 years of age (or as specified by a local IRB), verbal assent to be interviewed is obtained after verbal consent from a parent or guardian is obtained. With parental permission, the adolescent is interviewed directly.

### Items of Information that are Collected

#### **Questionnaires**

The case questionnaire covers demographic characteristics, clinical history, and specific food, water, animal, person-to-person, and environmental exposures (Attachment 3). It does not include name, address or contact information, or questions about sensitive subjects, such as sexual activity or use of illegal substances. The exposure period of interest for case-patients is the 7 days before illness onset. The questionnaire administered to controls includes the same questions as that administered to cases, with the exception of questions about features of the illness (Attachment 4). The exposure period of interest for controls is the 7 days before the date that the matched case-patient's illness began. Questionnaires have been translated into Spanish. Interviews are conducted in English or Spanish, depending on the preference of the person being interviewed. Interviews take approximately 25 minutes.

#### **Microbiologic investigation**

Isolates of non-O157 STEC from all cases enrolled into the study are sent from participating state health department laboratories to CDC *E. coli* Reference laboratory for additional characterization including complete serotyping and assessment of virulence factors. This process of isolate submission and characterization is a component of routine public health surveillance.

Submitted isolates are streaked onto tryptose blood plates with washed sheep blood and incubated at 35C for 18–24 hours. The plates are examined at 4 and 18 hours for production of enterohemolysin. Individual colonies, both hemolytic and nonhemolytic, are then plated on trypticase soy agar with 5% sheep blood, incubated for 18–24 h, and tested by polymerase chain reaction for gene sequences encoding the following virulence factors: Shiga toxins 1 and 2 (stx1 and stx2), intimin (eae), and enterohemolysin (E-hly). Isolates that are positive for either or both Shiga toxins are serologically characterized for O and H antigens. Additional isolate characterization may be included if additional methods become available. At completion of this study these isolates will be stored at CDC and may be used for approved research at CDC or at a requesting organization.

Although the site health departments will have access to identifiable information as part of routine public health case follow-up, this information is not be transmitted to CDC. CDC only has access to coded information.

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

No websites are used for data collection in this study.

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

This multi-center, population-based, case-control study of persons with laboratory-confirmed non-O157 STEC infections and individually matched controls will address two specific aims.

1. The case-control analysis will:
  - a. Identify behavioral, environmental, dietary, and medical risk factors for sporadic non-O157 STEC infections, both as a group and for at least the three most common individual serogroups, and by the most common virulence profiles;
  - b. Estimate the proportion of disease risk attributable to specific risk factors (population attributable fraction or PAF).
2. Laboratory characterization of non-O157 STEC isolates in combination with clinical information collected through the study questionnaire and through routine public health surveillance will:
  - a. determine the serotypes and virulence factor profiles, including at least intimin (encoded by the *eaeA* gene), enterohemolysin (encoded by the *Ehx* gene), Shiga toxin 1 (encoded by the *stx1* gene), Shiga toxin 2 (encoded by the *stx2* gene, and *stx2* subtypes of non-O157 STEC strains isolated from symptomatic patients;
  - b. characterize the spectrum and severity of illnesses associated with different virulence factor profiles, different serogroups, and possibly different serotypes of non-O157 STEC;
  - c. determine features (e.g., serogroup, virulence factors, and symptoms) associated with isolation of additional enteric pathogens other than non-O157 STEC; additional pathogens will be identified through routine FoodNet surveillance.

### **Data handling/Analysis**

Completed case and control questionnaires are reviewed and coded by FoodNet staff at each study site, and the information entered into a secure Microsoft Access database. De-identified data is transmitted to CDC FoodNet bi-annually or upon request through PHINMS. For each case-patient, three sets of data are linked; these include data collected through the study questionnaire, routine public health case-investigations, and routine public health microbiological analysis of the patient's sample. Analyses are conducted by an analytic team comprising epidemiologists and statisticians from the investigators and collaborators identified previously. This study abides by the Data Quality Act in ensuring and maximizing the quality, objectivity, utility, and integrity of information, including statistical information.

Descriptive analysis was conducted in February 2014 to evaluate how patient demographic and clinical features vary by non-O157 STEC serogroup and by virulence factor profiles. Behavioral, environmental, dietary, and medical risk factors were assessed through calculation of odds ratios and population attributable fractions (PAF) for all non-O157 STEC collectively as a single

group. Future analysis will examine factors for the most common serogroups and virulence factor profiles. Multivariate modeling of potential risk factors, confounders and effect modifiers may be performed. Finally, we will compare demographic characteristics, clinical features, and reported exposures between patients with and without landline telephones in their primary residence and between patients with mixed infections and patients with single etiology infections.

### Privacy Impact Assessment Information

No Information in Identifiable Form (IIF) is being collected as part of this study; however, sites review identifiable information that is already being collected as part of routine public health surveillance information in order to determine a person's eligibility for inclusion in this study. CDC does not receive identifiable information.

Participants receive no direct benefit from the study other than the satisfaction of contributing to science. There is no penalty for not participating. There is also no risk to the subject beyond the unlikely risk of loss of confidentiality regarding non-sensitive questions. Participants may refuse to answer any of the questions or stop at any time.

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

Hardcopy forms are used by site personnel when interviewing cases and controls. Completed forms are coded by FoodNet staff at each study site, and the information entered into a secure Microsoft Access database. De-identified data is transmitted to CDC bi-annually or upon request through PHINMS.

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

FoodNet is a program coordinated within the Enteric Disease Epidemiology Branch (EDEB) at CDC. EDEB is responsible for surveillance of non-O157 STEC infections. No other groups at CDC collect the type and level of detailed epidemiologic information on non-O157 STEC infection that is proposed in this study. While state health departments do collect basic demographic and limited symptom and outcome information from patients with non-O157 STEC infections using state-specific public health case investigation forms, they do not collect the detailed epidemiologic information proposed in this study.

However, this does not mean a patient or their guardian necessarily needs to be contacted more than once or be asked similar questions more than once. It is incumbent upon participating state departments of health to minimize burden by contacting respondents as few times as possible. Whenever possible FoodNet staff in the participating states abstract data collected study questionnaire to complete state case investigation forms.

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

No small businesses are included in this study. To minimize the burden on health department and SSI staff, we have streamlined the data collection instruments to keep the number of questions to the minimum required for the intended use of the data.

## **6. Consequences if Information Collected Less Frequently**

Data collection begins as soon as a case is identified through routine public health surveillance. Due to the type of information that is being collected (e.g. 7 day food history), it is essential that cases and controls be interviewed promptly to increase the chances of accurate information recall. If information collection were to be performed less frequently, there is a potential for recall bias resulting in inaccurate information for analysis.

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

The information collection activity fully complies with the Guidelines 5 CFR 1320.5. There are no special circumstances related to the proposed surveys.

## **8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency**

A. A 60-day Federal Register notice was published in the *Federal Register* (Attachment 2) on 04/10/14, p. 19914, vol. 79, No. 69. No comments were received.

B. In revising the surveys and planning for this project, CDC solicited the advice and help of the following internal CDC experts:

The development of this study was a collaborative effort of all agencies in the FoodNet program; 3 Federal agencies and 10 state agencies. Federal agencies in FoodNet include CDC, the U.S. Food and Drug Administration (FDA), and the U.S. Department of Agriculture's Food Safety and Inspection Service (FSIS). State agencies in FoodNet include California Department of Health Services, California EIP, Colorado Department of Public Health and Environment, Connecticut Department of Public Health, Connecticut Emerging Infections Program, Georgia Division of Public Health, Georgia Emerging Infections Program, Maryland Department of Health and Mental Hygiene, Minnesota Department of Health, New Mexico Department of Health, New Mexico Emerging Infections Program, New York State Department of Health, Oregon Department of Human Services and the Tennessee Department of Health.

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

No remuneration is to be provided to respondents.

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

A statement of how data is handled is read to each potential participant as part of the process of obtaining informed consent for participation in the study. Only the databases are forwarded to CDC. Protected health information (e.g., name, address) is not forwarded to CDC or included in any published materials relating to this study. The primary unique identifiers attached to each isolate are the state laboratory ID number (already an established practice for identifying specimens sent to the CDC) and a case-control study ID number. These numbers are used to merge laboratory, questionnaire, and routine public health data. The assignment of a unique state lab ID and case-control study ID number permits the removal of all personal identifiers and ensures data security.

This study has been approved by IRB at CDC (Attachment 5).

#### Privacy Impact Assessment Information

A. This information collection request has been reviewed by NCEZID and it has determined that the Privacy Act does not apply.

B. All information and identifiers are kept secure in locked cabinets in locked offices with limited access and electronic information on password-protected computers in a password-protected database. All written questionnaires containing patient identifiers are stored in a secure location to which only study investigators at FoodNet sites will have access.

C. Informed consent is obtained from all study participants. For persons  $\geq 18$  years of age, verbal consent is obtained from all participants (Attachment 6). For persons  $< 18$  years of age, verbal consent is obtained from parents or legal guardians, and verbal assent is obtained from participants aged 12–17 years unless specifically noted otherwise by a FoodNet site local IRB (Attachment 6). A copy of the consent form (and assent form, as appropriate) read to the patient, with his or her response noted and signed by the interviewer, is kept with each completed questionnaire. Throughout this protocol we refer to the study subject and/or the subject's parent or legal guardian as simply the study subject. Consent and assent forms were translated into Spanish. If a patient is deceased any next of kin, that is at least 18 years old, may provide consent and answer questions as a surrogate.

Because the success of this study requires that participants be interviewed as soon as possible after the case-patient's illness onset; all participants are interviewed by telephone. The research could not be performed without a waiver of written documentation of informed consent because the amount of time needed to document consent would seriously impair the quality of the information collected. This research presents no more than minimal risk of harm to patients. Only non-sensitive questionnaire data and existing isolates are involved. No procedure for which written consent is normally required outside of the research context is involved. This waiver of written documentation of informed consent will not adversely affect the rights and welfare of participants.

D. Participants are informed that study participation is completely voluntary and they may choose to decline study enrollment or to not answer any questions that they consider to be of a

sensitive nature. There are no penalties for not participating. There is also no risk to the subject beyond the unlikely risk of loss of confidentiality regarding non-sensitive questions. Participants may refuse to answer any of the questions or to discontinue the survey at any time.

**11. Justification for Sensitive Questions**

CDC does not feel that the proposed questions are sensitive in nature and that all requested information is necessary for the study objectives. Study participants may choose to decline study enrollment or to not answer any questions that they consider to be of a sensitive nature.

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

A. The average annual number of non-O157 STEC cases reported by the 10 FoodNet sites from 2006 through 2008 was 230. Assuming a 70% participation rate, we estimated an enrollment of 161 patients each year ( $[230][0.70]= 161$ ) across all 10 sites. We estimated an enrollment of 483 controls each year ( $[161][3]= 483$ ). Epidemiologists at the 10 FoodNet sites record one response for each patient and control respondent. It takes approximately 25 minutes (or  $25/60=0.417$  hrs) to record each response through administration of the study questionnaire. These estimates result in an annualized burden of 268.33 hours (67.08 hours for cases patients and 201.33 hours for controls).

B. Case and control interviews are conducted by epidemiologists at state or local health departments. According to the U.S. Department of Labor, Bureau of Labor Statistics, the mean hourly rate for epidemiologists at state health departments is \$28.47 per hour (<http://www.bls.gov/oes/2009/may/oes191041.htm>). The total estimated annualized cost to the 10 FoodNet state health departments will be \$7,639 ( $[268.33 \text{ hours}][\$28.47/\text{hour}]= \$7,639.36$ )

Respondents	Number of Respondents	Number of Responses per Respondent	Average Burden per Response (in hours)	Total Burden (in hours)	Hourly wage	Total cost
Patients	161	1	25/60	67	\$28.47	\$1,909.77
Controls	483	1	25/60	201	\$28.47	\$5,729.59
<b>Total</b>				<b>268</b>		<b>\$7,639.36</b>

**13. Estimates of Other Total Annual Cost Burden to Respondents or Record Keepers**

None

**14. Annualized Cost to the Government**

The estimated cost to the Government is shown in the following table. This cost includes wages for staff hours involved in formatting, printing, mailing, emailing, data collection, data input, data analysis, and overhead expenses.

Table A.14 Annualized Cost to the Federal Government

Expense item	Burden hours	Hourly Wage Rate	Cost
Control call lists (quote from SSI contractor)	n/a	n/a	\$1,658.67
CDC Project Officer	400 (8 hrs/wk – assumes 50 weeks per year)	\$32.00	\$12,800
Surveillance epidemiologist (GS 9 Step 2)	400 (8 hrs/wk – assumes 50 weeks per year)	\$24.55	\$9,820
<b>Total</b>	<b>800</b>		<b>\$24,278.67</b>

### 15. Explanations for Program Changes or Adjustments

This is an extension. We have made no changes to any study documents (including the protocol and study questionnaire).

### 16. Plans for Tabulation and Publication and Project Time Schedule

Data collection began 2012 and is estimated to continue until each site has collected data for 36 months. Descriptive statistics will be used to summarize the data. A preliminary analysis of study data was conducted and shared with study sites in February 2014. Final results will be published in peer reviewed journals by project officers and scientists from CDC.

Table A.16 Project Time Schedule

<u>Activity</u>	<u>Timeframe</u>
Data collection	Ongoing or a total of 3 years in each study site
Interim analysis	Half way through data collection
Final data cleaning/analysis	7 months after completion of data collection
Final report	12 months after completion of data collection

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

Exemption is not being sought.

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

There are no exceptions to certification.



## **List of Attachments**

1. Authorizing Legislation
2. 60 Day Federal Register Notice
3. Case questionnaire
4. Control questionnaire
5. IRB approval letter
6. Consent and assent forms for cases and controls