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

New Request for OMB Review
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FoodNet Non-O157 Shiga Toxin-Producing *E. coli Study:*
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CDC is requesting OMB approval for a new data collection.

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 will be the first multistate investigation of non-outbreak-associated non-O157 STEC infections in the United States. It will investigate 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).[28, 29] 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 will purchase 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 will be included to facilitate socioeconomic comparisons between patients and controls. These lists will not contain any personal identifiers. To optimize efficiency in recruiting controls, every 12 months new telephone lists will be purchased from SSI. SSI will email these lists to CDC FoodNet and CDC will forward them to the FoodNet sites. To enroll controls, study coordinators will call telephone numbers from the appropriate county and age-group specific sublists, starting from the top and moving down. Every phone call attempt will be logged directly in a spreadsheet. If a control is recruited, the telephone number will be marked as completed and successful. The second time controls of a specific age group/county combination

need to be recruited, study coordinators will 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 will 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 will be marked as completed and unsuccessful. Calls to enroll controls will be 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 will be used as the preferred method of selecting controls for case-patients in this age group. Controls will be identified from birth registries within the county in which the matched case-patient resides. FoodNet sites will sort these lists by date of birth and will attempt to enroll those with the closest birth dates before and after the matched case-patient's birth date. Extensive efforts will be 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 will be 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 will use sequential digit dialing to recruit controls aged less than two years. First, a list of telephone numbers will be 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 will contain 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 will be 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 will interview case-patients by telephone. Case-patients will be identified through routine FoodNet active laboratory-based surveillance. As part of routine surveillance activities required by states' reporting rules, clinical laboratories will 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 will attempt to enroll every patient with a probable or confirmed non-O157 STEC infection that comes to their attention. FoodNet or local health department staff will contact patients to determine eligibility and, for those who are eligible, offer participation in the study. The study subject will be read the consent form and asked to participate. Verbal consent will be 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 will be obtained after verbal consent from a parent or guardian is obtained. With parental permission, the adolescent should preferably be 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 will be excluded from the main case-control analyses and all efforts to enroll matched controls will cease. Information from these possible cases may be summarized in a separate analysis. Additionally, some patients might be 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 will not be included in the analysis to identify risk factors and matched controls will not be 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 will not be 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 will be 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 will be recruited from the study population in participating sites as outlined above in the control selection section. FoodNet staff or local health department staff will read the consent form to the control or legal guardian by telephone. Verbal consent will be 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 will be obtained after verbal consent from a parent or guardian is obtained. With parental permission, the adolescent should be interviewed directly.

Items of Information to be Collected

Questionnaires

The case questionnaire covers demographic characteristics, clinical history, and specific food, water, animal, person-to-person, and environmental exposures (Attachment 2). 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 will be the 7 days before illness onset. The questionnaire administered to controls will include the same questions as that administered to cases, with the exception of questions about features of the illness (Attachment 3). The exposure period of interest for controls will be the 7 days before the date that the matched case-patient's illness began. Questionnaires will be translated into Spanish. Interviews will be conducted in English or Spanish, depending on the preference of the person being interviewed. Interviews will take approximately 25 minutes.

Microbiologic investigation

Isolates of non-O157 STEC from all cases enrolled into the study will be 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 will be streaked onto tryptose blood plates with washed sheep blood and incubated at 35C for 18–24 hours. The plates will be examined at 4 and 18 hours for production of enterohemolysin. Individual colonies, both hemolytic and nonhemolytic, will 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 will serologically be 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 will not be transmitted to CDC. CDC will only have access to coded information.

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

No websites will be 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 will be reviewed and coded by FoodNet staff at each study site, and the information will be entered into a secure Microsoft Access database. De-identified data will be transmitted to CDC FoodNet on a regular basis through PHINMS. For each case-patient, three sets of data will be 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. Analysis will be conducted by an analytic team comprising epidemiologists and statisticians from the investigators and collaborators identified previously. This study will abide by the Data Quality Act in ensuring and maximizing the quality, objectivity, utility, and integrity of information, including statistical information.

Preliminary analyses will be conducted as each site completes six months of enrollment. These analyses are intended to assess if the distributions of days of the week and time of day of enrollment are similar between case-patients and controls. If substantial differences are observed, additional specification regarding the process of contacting potential controls may be considered.

Descriptive analyses will be conducted to evaluate how patient demographic and clinical features vary by non-O157 STEC serogroup and by virulence factor profiles. Potential behavioral, environmental, dietary, and medical risk factors will be assessed through calculation of odds ratios and population attributable fraction (PAF); risk factors will be evaluated for all non-O157 STEC collectively as a single group, and individually 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 will 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 will not receive identifiable information.

Participants will 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 will be used by site personnel when interviewing cases and controls. Completed forms will be coded by FoodNet staff at each study site, and the information entered into a secure Microsoft Access database. De-identified data will be transmitted to CDC on a regular basis 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 will be 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 will 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 will begin 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 4), 75 Federal Register 248 (28 December 2010), pp. 81613-81614. Dane Bernard, Vice President of Food Safety and Quality at Keystone Foods, requested a copy of the data collection plans and instrument. A copy was provided.

Dr. David Plunkett, Senior Staff Attorney for the Center for Science in the Public Interest, sent a comment in support of the study to the CDC in a letter data April 5, 2011.

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 will handled will be read to each potential participant as part of the process of obtaining informed consent for participation in the study. Only the databases will be forwarded to CDC. Protected health information (e.g., name, address) will not be 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 will

be 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 CDC's Information Collection Review Office (ICRO) that has determined that the Privacy Act does not apply.

B. All information and identifiers will be 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 will be stored in a secure location to which only study investigators at FoodNet sites will have access.

C. Informed consent will be obtained from all study participants. For persons ≥18 years of age, verbal consent will be obtained from all participants (Attachment 6). For persons <18 years of age, verbal consent will be obtained from parents or legal guardians, and verbal assent will be 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, will be 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 will be 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.

Bcause the success of this study requires that participants be interviewed as soon as possible after the case-patient's illness onset, all participants will be 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 estimate an enrollment of 161 patients each year ([230][0.70]= 161) across all 10 sites. We estimate an enrollment of 483 controls each year ([161][3]= 483). Epidemiologists at the 10 FoodNet sites will record one response for each patient and control respondent. It will take 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 will typically be 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 hours][$28.47/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
Total				**268**		**$7,639.36**

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
Total	**800**		**$24,278.67**

15. Explanations for Program Changes or Adjustments

This is a new data collection.

16. Plans for Tabulation and Publication and Project Time Schedule

Data collection will begin as soon as OMB clearance and all site IRB approvals have been obtained (CDC IRB clearance is already in place). Data collection is estimated to continue for three years or until the projected study enrollment estimate is reached (whichever comes first). Descriptive statistics will be used to summarize the data. The results will be published in peer reviewed journals by project officers and scientists from CDC.

Table A.16 Project Time Schedule

Activity	Timeframe
Data collection	To begin as soon as OMB approval obtained and continue for 3 years
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.

B. Collections of Information Employing Statistical Methods

This data collection does not use statistical methods to select cases or controls.

A possible case is defined as identification of Shiga toxin (or the gene that encodes it) in a specimen, from which E. coli O157 was not isolated, taken from an ill person residing in a FoodNet site catchment area during that site's 36 month study period. A definite case for analyses will be defined as isolation of a non-O157 STEC and no isolation of *E. coli* O157 from a clinical specimen collected from an ill person residing in a FoodNet site catchment area during that site's 36 month study period.

Exclusion criteria: a case will be excluded from the case-control study if the patient or surrogate:

1. did not have a sample from which non-O157 STEC was eventually isolated and obtained by a state public health laboratory or CDC;
2. is not reachable after 10 unsolicited telephone attempts; if time permits, these calls should be made over no fewer than five days (including at least three attempts on a weekend [Saturday 10am–9pm, Sunday 1pm–9pm] and at least three during 5-9 pm on a weekday, the remainder can be made 9am-5pm on weekdays), all within 45 days of culture date (see Appendix E for case-patient call log form);
3. does not have a telephone number available;
4. does not speak either English or Spanish;
5. does not report illness associated with the submission of the clinical specimen from which non-O157 STEC was isolated;
6. was not a resident of the FoodNet catchment area at the time of specimen collection;
7. is part of an outbreak that has been investigated by public health officials, unless he or she is the outbreak patient with earliest known onset date;
8. lives in the same household as a confirmed case-patient who has an earlier onset date;
9. is unable to remember the date of illness onset, or the illness began more than 45 days before specimen collection date;
10. does not provide informed consent (and assent, when appropriate) to participating in the study;
11. is an inmate in a prison or other correctional facility.

Three age- and county-matched controls will be recruited for each enrolled case. Age matching will be by the following six age strata: 0 to <2 years, 2 to <6 years, 6 to <18 years, 18 to <40 years, 40 to <60 years, and 60 years or older. Controls in all except the youngest age group will primarily be selected from commercially available lists of residential telephone numbers, by county, that include age information on household members, allowing for the rapid identification of households at which an age-matched control might be available for a given case. Controls less than two years old will primarily be selected from birth registries.

Exclusion criteria: a person will not be included as a control in the case-control study if he or she:

1. resides outside the FoodNet catchment area;
2. does not speak English or Spanish;
3. is an inmate in a prison or other correctional facility;
4. does not provide informed consent (and assent, when appropriate) to participating in the

study.

List of Attachments

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