

Cryptosporidiosis: Diagnostic Laboratory and Reporting Practices in the United States

OSTLTS Generic Information Collection Request

OMB No. 0920-0879

SUPPORTING STATEMENT – Section A

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Program Official/Project Officers

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Section A. JUSTIFICATION

1. Circumstances Making the Collection of Information Necessary

Background

This information collection is being conducted using the Generic Information Collection mechanism of the OSTLTS OMB Clearance Center (O2C2) – OMB No. 0920-0879. The respondent universe for this information collection aligns with that of the O2C2. Data will be collected from 52 waterborne disease coordinators in each of the 50 state, New York City, and Washington, DC health departments, acting in their official capacities.

Cryptosporidiosis, a gastrointestinal illness caused by protozoa of the genus *Cryptosporidium*, is a major source of human illness and the leading etiology of all waterborne outbreaks in the United States (2001–2010).^{1,2} Approximately 748,000 cryptosporidiosis cases occur annually, and hospitalizations resulting from cryptosporidiosis cost an estimated \$45.8 million per year.^{3,4}

Cryptosporidiosis is typically characterized by profuse, watery, usually non-bloody diarrhea. Other symptoms can include weight loss, abdominal pain, anorexia, fatigue, joint pain, headache, fever, and vomiting.⁵ Asymptomatic infection can also occur.^{6–9} Recurrence of symptoms after seeming resolution has been frequently reported; however, illness is self-limiting in immunocompetent patients, and symptoms often completely resolve within 2–3 weeks.⁵ Cryptosporidiosis can be treated with nitazoxanide, approved by the U.S. Food and Drug Administration for immunocompetent children aged 1–11 years in 2004 and immunocompetent persons aged ≥ 1 years in 2005.^{10,11}

Historically, cryptosporidiosis was considered a relatively common opportunistic infection in HIV-infected patients,¹² with the ability to cause profuse, watery diarrhea and life-threatening wasting and malabsorption.¹³ However, the incidence of cryptosporidiosis among HIV-infected persons has decreased since the introduction of highly active antiretroviral therapy for HIV infection.^{14,15} Extra-intestinal cryptosporidiosis (i.e., in the biliary or respiratory tract or rarely the pancreas) has also been documented in immunocompromised persons.

Most cases of cryptosporidiosis in humans are caused by *C. hominis* and *C. parvum*.^{16,17} Human infections caused by *C. meleagridis*, *C. canis*, *C. felis*, *C. ubiquitum*, *C. cuniculus*, *C. suis*, *C. muris*, and several other species and genotypes have also been documented. Species distribution might vary by geographic areas (e.g., urban versus rural).¹⁸ Infections caused by the different *Cryptosporidium* species, and subtypes within species, can clinically differ.^{19,20} To enhance cryptosporidiosis surveillance, CDC plans to launch CryptoNet – a DNA sequence-based surveillance system for cryptosporidiosis. CDC has developed a package of molecular characterization methods and database for this system. These molecular tools are crucial to understanding national transmission patterns and developing targeted prevention guidance.

Cryptosporidium is transmitted by the fecal-oral route. *Cryptosporidium* oocysts are infectious immediately upon being excreted in feces. Infection results from the ingestion of oocysts through fecally contaminated food or water, or through contact with an infected person or animal. The infectious dose is low; feeding studies have demonstrated that the ingestion of ≤ 10 *C. hominis* or *C. parvum* oocysts can cause infection in healthy persons.^{21,22} Infected persons have been reported to shed 10^7 – 10^8 oocysts in a single bowel movement,²³ and can excrete infectious oocysts for up to 60 days after cessation of gastrointestinal symptoms.²⁴ *Cryptosporidium* oocysts are extremely chlorine tolerant and can survive

for 3.5–10.6 days in water where free chlorine levels are maintained at CDC-recommended levels (1–3 mg/L) for treated recreational water venues, such as pools and interactive fountains.²⁵

Risk factors for cryptosporidiosis include ingestion of recreational water;^{26,27} ingestion of untreated drinking water;²⁸ contact with livestock, particularly pre-weaned calves;^{26,28,29} recent international travel;^{26,29} or contact with infected persons (e.g., caregivers of young children).^{26,27,29} Risk factors might vary by geographic setting (e.g., urban versus rural).^{18,30} Although cryptosporidiosis cases can occur sporadically, waterborne outbreaks have been documented since the first reported U.S. drinking water-associated outbreak in 1984³¹ and the first reported U.S. recreational water-associated outbreak in 1988.^{32,33} Outbreaks resulting from foodborne, person-to-person, and animal-to-person transmission also have been reported.³⁴⁻³⁸

Given the public health impact and healthcare expenditure for cryptosporidiosis, combined with *Cryptosporidium*'s ability to cause community-wide outbreaks, surveillance is a national priority. In 1994, the Council of State and Territorial Epidemiologists (CSTE) called for the reporting of cryptosporidiosis as a nationally notifiable disease; 1995 marked the first full year of reporting from state and local health departments.

National surveillance data for 1995–2010 have been previously published,^{1,39-43} and analysis of the national cryptosporidiosis surveillance data for 2011–2012 has recently been completed. The annual rate of reported cryptosporidiosis cases was relatively stable during 1995–2004, ranging from 0.9–1.4 per 100,000 person-years, with very few non-confirmed cases (see **Attachment A—Figure 1. Rate of cryptosporidiosis**). During 2005–2012, rates of confirmed cases ranged from 2.2 to 3.9 per 100,000 person-years with rates of non-confirmed cases ranging from 0.1 to 1.0 per 100,000 person-years. The increase in annual rates of cryptosporidiosis from 2005–2008 can be explained by large community-wide outbreaks in 2005, 2007, and 2008, which each affected thousands of persons. From 2009–2010, annual rates of cryptosporidiosis in the United States remained elevated at the 2005–2008 levels; however, there were no large outbreaks during 2009–2010. CDC speculated that perhaps those were aberrant years in terms of cryptosporidiosis reporting. Upon recent completion of the 2011–2012 cryptosporidiosis surveillance data, it is clear that cryptosporidiosis rates continue to be elevated (around 8,000–9,000 cases per year), similar to the elevated 2005–2008 levels (i.e., up from the pre-2005 baseline of 2,500–3,500 cases per year). Thus, for 4 consecutive years, there has been an unexplained increase in cryptosporidiosis rates.

To that end, CDC recognizes the need to elucidate factors contributing to the ongoing, persistent increase in cryptosporidiosis incidence rates from 2009–2012 in the United States. Potential factors contributing to the increase include changes in the ordering of diagnostic tests by healthcare providers; testing and reporting patterns among laboratories and health departments; changes in transmission of *Cryptosporidium*; FDA licensure of nitazoxanide for persons aged ≥ 1 years in 2005; or a combination of these factors. One major contributing factor might be a recent major revision of the case definition. Historically, all cases with laboratory-confirmed evidence of *Cryptosporidium* oocysts or DNA were classified as confirmed, regardless of type of diagnostic test used.⁴⁴ In 2011, responding to concerns about false-positive results, the cryptosporidiosis confirmed case definition was revised to include only those cases diagnosed using laboratory methods with a high positive predictive value and redefined cases diagnosed by immunochromatographic card tests as “probable”.⁴⁵ A better understanding of the degree to which each of these factors, particularly those related to the change in case definition, has

contributed to increased cryptosporidiosis rates is critical to understanding state and local public health needs and informing development of recommendations and resources for state and local public health partners. For this data collection, CDC plans to investigate factors associated with cryptosporidiosis testing and reporting among 52 state and local waterborne disease coordinators.

This information collection is authorized by Section 301 of the Public Health Service Act (42 U.S.C. 241).⁴⁶ This information collection falls under the essential public health service of:

1. Diagnosing and investigating health problems and health hazards in the community
2. Informing, educating, and empowering people about health issues
3. Mobilizing community partnerships to identify and solve health problems
4. Assuring a competent public health and personal health care workforce

Overview of the Data Collection System

The information collection system consists of a web-based questionnaire (see **Attachment B – Crypto Instrument: Word version** and **Attachment C – Crypto Instrument: Web version** designed to assess cryptosporidiosis diagnostic laboratory and reporting practices in reporting jurisdictions in the United States. The information collection instrument will be administered as a web-based instrument. Examples of questions that will be asked include what type of laboratory tests are used to diagnose cryptosporidiosis in the jurisdiction, how cryptosporidiosis cases are reported in the jurisdiction, and whether follow-up interviews are conducted with case-patients. The information collection instrument was pilot tested by 7 public health professionals at CDC. Feedback from this group was used to refine questions as needed, ensure accurate programming and skip patterns, and establish the estimated time required to complete the information collection instrument.

Items of Information to be Collected

The data collection instrument consists of 4 main sections, totaling 29 questions. The sections include: 1. Reporting to the state or city (3 questions); 2. Laboratory information (17 questions); 3. Follow-up with case-patients (5 questions); 4. Reporting to CDC's National Notifiable Diseases Surveillance System (NNDSS) (4 questions). All questions are closed-ended questions, with the exception of the last question which asks the respondent to provide a web-link to their jurisdiction's definition of cryptosporidiosis cases.

2. Purpose and Use of the Information Collection

The objectives of the data collection are to:

- Elucidate factors contributing to the ongoing, persistent increase in cryptosporidiosis incidence rates from 2009–2012 in the United States.
- Assess cryptosporidiosis-related diagnostic laboratory testing and reporting practices in U.S. state and local jurisdictions.
- Assess the extent to which state and territorial health laboratories are using immunochromatographic card tests for cryptosporidiosis diagnosis.
- Determine the extent to which states classify cryptosporidiosis cases as confirmed based on laboratory test type.

At CDC, the results of the data collection will be used to:

- Improve cryptosporidiosis surveillance at the national level by identifying reporting gaps in and limitations of current data collection.
- Inform development of cryptosporidiosis surveillance recommendations and resources to address identified state and local needs.
- Inform development of recommendations or other resources regarding the use of immunochromatographic card tests for cryptosporidiosis diagnosis and reporting.

The results of the data collection will be shared with state and local health departments via email and written report. The results will also be incorporated into a scientific publication describing cryptosporidiosis surveillance in the United States.

3. Use of Improved Information Technology and Burden Reduction

Data will be collected via a web-based instrument, using the IBM SPSS Data Collection (version 7.0) platform and allowing respondents to complete and submit their responses electronically. This method was chosen to reduce the overall burden on respondents (e.g., IBM SPSS Data Collection will cut questions based on programmed skip patterns). The data will be stored in a secured SQL Server Database at CDC hosted by the Information Technology Services Office (ITSO). Only limited technical support personnel and individuals authorized by the Principal Investigator will have access to the database. The information-collection instrument was designed to collect the minimum information necessary for the purposes of this project.

4. Efforts to Identify Duplication and Use of Similar Information

The proposed data collection is unique. Although cryptosporidiosis is a nationally notifiable disease, states are not required to report information about reporting or diagnostic laboratory practices to CDC. Therefore, CDC has not collected information on reporting and diagnostic laboratory practices for cryptosporidiosis from state and local public health partners.

5. Impact on Small Businesses or Other Small Entities

No small businesses will be involved in this information collection.

6. Consequences of Collecting the Information Less Frequently

This request is for a one-time information collection. There are no legal obstacles to reduce the burden. The purpose of this collection is to gather information that is not otherwise available. Specifically, without this information there would be:

- Incomplete understanding of current practices regarding cryptosporidiosis reporting and diagnostic laboratory practices at the state and local level, potentially leading to misinterpretation of national surveillance data analysis, interpretation of findings, and consequently public health decision making.
- Gap in information on current diagnostic testing practices for cryptosporidiosis and lack of ability to inform recommendations for use of immunochromatographic card tests.
- No information on the impact of previous recommendations to consider cryptosporidiosis cases as confirmed only if they have been diagnosed with laboratory methods with a high positive predictive value.
- Incomplete understanding of the capacity for and gaps in cryptosporidiosis speciation and molecular sub-typing at state health departments.

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

There are no special circumstances with this information collection package. This request fully complies with the regulation 5 CFR 1320.5 and will be voluntary.

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

This information collection is being conducted using the Generic Information Collection mechanism of the OSTLTS OMB Clearance Center (O2C2) – OMB No. 0920-0879. A 60-day Federal Register Notice was published in the Federal Register on October 31, 2013, Vol. 78, No. 211; pp. 653 25-26. No comments were received.

CDC partners with professional STLT organizations, such as the Association of State and Territorial Health Officials (ASTHO), the National Association of County and City Health Officials (NACCHO), and the National Association of Local Boards of Health (NALBOH) along with the National Center for Health Statistics (NCHS) to ensure that the collection requests under individual ICs are not in conflict with collections they have or will have in the field within the same timeframe.

9. Explanation of Any Payment or Gift to Respondents

CDC will not provide payments or gifts to respondents.

10. Assurance of Confidentiality Provided to Respondents

The Privacy Act does not apply to this data collection. Employees of state and local public health agencies will be speaking from their official roles and will not be asked, nor will they provide individually identifiable information.

This data collection is not research involving human subjects.

10.1 Privacy Impact Assessment Information

No individually identifiable information (IIF) will be collected.

11. Justification for Sensitive Questions

No information will be collected that are of personal or sensitive nature.

12. Estimates of Annualized Burden Hours and Costs

The estimate for burden hours is based on a pilot test of the information collection instrument by 7 public health professionals. In the pilot test, the average time to complete the instrument including time for reading introductory email and instructions and completing the instrument, was approximately 7.86 minutes. Based on these results, the estimated time range for actual respondents to complete the instrument is 5–15 minutes. For the purposes of estimating burden hours, the upper limit of this range (i.e., 15 minutes) is used.

Estimates for the average hourly wage for respondents are based on the Department of Labor (DOL) National Compensation Survey estimate for management occupations – medical and health services managers in state government (<http://www.bls.gov/ncs/ocs/sp/nctbl349.pdf>). Based on DOL data, an average hourly wage of \$24.22 is estimated for life scientists, which could include state waterborne disease coordinators. Table A-12 shows estimated burden and cost information.

Table A-12: Estimated Annualized Burden Hours and Costs to Respondents

| Data Collection Instrument: Form Name | Type of Respondent | No. of Respondents | No. of Responses per Respondent | Average Burden per Response (in hours) | Total Burden Hours | Hourly Wage Rate | Total Respondent Costs |
|---------------------------------------|--|--------------------|---------------------------------|--|--------------------|------------------|------------------------|
| Crypto Instrument | State Waterborne Disease Prevention Coordinators | 52 | 1 | 15/60 | 13 | \$24.22 | \$315 |
| | TOTALS | 52 | 1 | | 13 | | \$315 |

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

There will be no direct costs to the respondents other than their time to participate in each information collection

14. Annualized Cost to the Government

There are no equipment or overhead costs. The only cost to the federal government would be the salary of CDC staff and contractors. The total estimated cost to the federal government is \$12,102. Table A-14 describes how this cost estimate was calculated.

Table A-14: Estimated Annualized Cost to the Federal Government

| Staff (FTE) | Average Hours per Collection | Average Hourly Rate | Average Cost |
|---|------------------------------|---------------------|--------------|
| Senior Epidemiologist(GS-13): Development of instrument, pilot testing, OMB package preparation, data collection, data analysis, report preparation | 60 | \$49.65 | \$2979 |
| EIS Officer (GS-12): Development of instrument, pilot testing, OMB package preparation, data collection, data analysis, report preparation | 60 | \$35.96 | \$2158 |
| Senior Epidemiologist (GS-13): Development of instrument, data collection, data analysis, report preparation | 20 | \$48.27 | \$965 |
| Senior Survey Methodologist (Contractor) | 40 | \$150 | \$6000 |
| Estimated Total Cost of Information Collection | | | \$12,102 |

15. Explanation for Program Changes or Adjustments

This is a new data collection.

16. Plans for Tabulation and Publication and Project Time Schedule

The results of this information collection project will be shared with state and local health departments via email and written report. Results will also be included as part of a manuscript describing cryptosporidiosis surveillance in the United States and is currently in the planning phase.

Analysis Plan

Analysis will begin upon completion of information collection. CDC FTEs and an EIS officer will perform the analysis using SAS 9.3. The analysis will consist of simple descriptive and stratified statistics to understand current reporting and laboratory practices.

Project Time Schedule

- ✓ Design questionnaire.....(COMPLETE)
- ✓ Develop protocol, instructions, and analysis plan..... (COMPLETE)
- ✓ Pilot test questionnaire.....(COMPLETE)
- ✓ Prepare OMB package.....(COMPLETE)
- ✓ Submit OMB package.....(COMPLETE)
- OMB approval.....(TBD)
- Gather responses.....(questionnaire available online for 4 weeks)
 - Reminder email at 7 and 20 days
- Collect, code, quality control, and analyze data.....(3 weeks)

- Prepare report.....(3 weeks)
- Disseminate results/publication of findings.....(4 weeks)

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

We are requesting no exemption.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification. These activities comply with the requirements in 5 CFR 1320.9.

LIST OF ATTACHMENTS – Section A

Note: Attachments are included as separate files as instructed.

- A. Figure 1. Rate of cryptosporidiosis
- B. Crypto Instrument (Word version)
- C. Crypto Instrument (Web version)

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