Pediatric Hepatitis-Adenovirus Case Control Evaluation, United States, 2022 – 2026

CSTLTS Generic Information Collection Request
OMB No. 0920-0879

Supporting Statement – Section A

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- **Purpose of the data collection:** This information collection is for the State and Local Health Departments (SLHD) to evaluate persons under investigation (PUIs) for pediatric hepatitis of unknown etiology and matched controls without hepatitis. The information is needed to assess why children with hepatitis of unknown etiology continue to be identified by jurisdictions and determine if adenovirus is associated with acute pediatric hepatitis and whether exposures, pathogens, or risk factors other than adenovirus infection may contribute to risk of pediatric hepatitis, either independently or in conjunction with adenovirus.

- **Intended use of the resulting data:** The data collected will fill CDC gaps in knowledge of pediatric hepatitis of unknown etiology and improve CDC's support and technical assistance to states and communities in decision making that affects planning, response, and recovery activities of outbreaks of pediatric hepatitis of unknown etiology. Specifically, results will be used to develop guidance for state, tribal, local, and territorial health departments and delegates of health departments (i.e. clinicians) on the association of adenovirus or other potential exposures with pediatric hepatitis.

  Methods to be used to collect data: Public health officials will conduct medical chart abstractions among controls matched to persons under investigation (PUIs) for pediatric hepatitis of unknown etiology, using a standardized data collection instrument. Public health officials will also work with parents and/or caregivers of PUIs to complete an exposure questionnaire on demographics, health history, and potential risk factors and exposures. Specimens from both PUIs and matched controls will be tested for adenovirus and other potential pathogens of interest.

- **Respondent Universe:** State, tribal, local, and territorial public health officials are in a unique position to provide CDC with these data because they represent the jurisdictions where this public health threat exists. Data collection will be conducted by up to 52 public health officials from up to 52 state, tribal, local, and territorial jurisdictions in the United States. Data will include up to 520 responses from three data collection instruments.

- **How data will be analyzed:** Specimens from PUIs and controls will be tested at CDC. Statistical analyses will be conducted to analyze data collected from the medical chart abstraction and exposure questionnaires. Analyses may include, but are not limited to, descriptive statistics and estimation of odds ratios for potential associations between exposures and outcomes.

Section A – Justification

1. Circumstances Making the Collection of Information Necessary

Background

This information collection is to evaluate persons under investigation (PUIs) for pediatric hepatitis of unknown etiology and matched controls without hepatitis. This information collection is being conducted using OMB No. 0920-0879 "Information Collections to Advance State, Tribal, Local and Territorial Governmental Agency System Performance, Capacity, and Program Delivery" nicknamed the "CSTLTS Generic." This information was conducted under OMB No. 09290-0879 from 03/07/2023-01/31/2024 and an extension is requested through 08/31/2026.
The respondent universe for this information collection aligns with that of the CSTLTS Generic. Data will include up to 10 responses from 52 respondents across state, local, tribal and territorial jurisdictions. Public health officials from all state, local, tribal, and territorial jurisdictions are invited to participate in this voluntary evaluation. Respondents acting in their official capacities include public health officials from state, local, tribal, and territorial health departments, and have identified at least one Patient Under Investigation (PUI) for pediatric hepatitis of unknown etiology.

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

☒ **1. Assess and monitor population health status, factors that influence health, and community needs and assets**
☒ **2. Investigate, diagnose, and address health problems and hazards affecting the population**
☐ 3. Communicate effectively to inform and educate people about health, factors that influence it, and how to improve it
☐ 4. Strengthen, support, and mobilize communities and partnerships to improve health
☐ 5. Create, champion, and implement policies, plans, and laws that impact health
☐ 6. Utilize legal and regulatory actions designed to improve and protect the public's health ☐ 7. Assure an effective system that enables equitable access to the individual services and care needed to be healthy
☐ 8. Build and support a diverse and skilled public health workforce
☐ 9. Improve and innovate public health functions through ongoing evaluation, research, and continuous quality improvement
☐ 10. Build and maintain a strong organizational infrastructure for public health[1]

Adenovirus is recognized as a cause of hepatitis among immunocompromised children; however, it is not known to cause severe disease among immunocompetent children. Following the identification of a cluster of pediatric patients with hepatitis of unknown etiology in the United States and similar clusters identified internationally, CDC, in collaboration with Council of State and Territorial Epidemiologists (CSTE) and State and local health departments (SLHD), initiated an investigation in the United States in April 2022. CDC also issued a Health Alert Network (HAN)

Health Advisory encouraging U.S. clinicians to report and test all patients aged <10 years with hepatitis of unknown etiology to public health authorities.

During the emergency response investigation, the evaluation of PUIs and matched controls was coordinated with state, local, tribal, and territorial health departments to assess the potential association between adenovirus infection and hepatitis of unknown etiology. The activities for the emergency response investigation were approved by OMB on April 28, 2022 under the Emergency Epidemic Investigations (EEI) Generic ICR (OMB No. 0920-1011).

The purpose of the evaluation is to determine if adenovirus infection may be associated with acute pediatric hepatitis and if exposures, pathogens, or risk factors other than adenovirus infection may contribute to risk, independently or in conjunction with adenovirus. Therefore, CDC is seeking approval to continue the collaboration with jurisdictions in this current CSTLTS Generic submission because children with hepatitis of unknown etiology continue to be identified by jurisdictions and the cause of these severe cases of hepatitis remains unknown. The questions included in this data collection have been developed to assess and monitor health status related to pediatric hepatitis of unknown etiology to identify the health problems associated with this illness. The data collected will fill CDC gaps in knowledge of pediatric hepatitis of unknown etiology, improve CDC's support and technical assistance to states and communities through guidance development that currently does not exist, and assist in decision making that affects planning, response, and recovery activities of subsequent outbreaks such as testing recommendations and prevention guidance. As of January 2024, CDC continues to receive reports from jurisdictions on patients with acute hepatitis of unknown etiology. CDC is seeking an extension of this approval to continue collaboration with jurisdictions and to increase the sample size of PUIs and controls for analyses to appropriately inform the evidence base and decision-making policies.

Overview of the Information Collection System

Medical chart data on matched controls will be collected from all participating jurisdictions via the medical chart abstraction form (**see Attachment A— "Pediatric Hepatitis of Unknown Etiology Medical Record Abstraction Form: Controls"**). The medical record abstraction form (Attachment A) will only be completed in English and does not need a Spanish translation. Public health officials will also administer the exposure questionnaires to parents/caregivers of PUIs (**see Attachment B — Pediatric Hepatitis of Unknown Etiology - Exposures Questionnaire [Parental Interview])** and matched controls **(see Attachment C "Pediatric Hepatitis of Unknown Etiology - Exposures Questionnaire CONTROL [Parental Interview]"**). The exposure questionnaires have also been translated into Spanish to facilitate administration of the interviews to Spanish speakers **(see Attachment D— "Hepatitis pediátrica de etiología desconocida - Cuestionario sobre exposiciones [entrevista a los padres]" and Attachment E— Hepatitis pediátrica de etiología desconocida. CONTROL del cuestionario sobre exposiciones [Entrevista a los padres]").**

The instruments will be used to gather information from medical records and parents/caregivers regarding clinical characteristics for controls (medical abstraction) and demographics, health

history, and potential risk factors and exposures for both PUIs and matched controls (exposure questionnaire). These information collection instruments are based on input from jurisdictional health departments and analysis results from the data collected during the initial emergency investigation to ensure accurate programming, skip patterns and the estimated time required to complete the information collections. Medical chart abstraction of PUIs has been submitted under National Disease Surveillance Program II—Disease Summaries (OMB Control No. 0920-0004).

Items of Information to be Collected

1. Medical chart abstraction for controls (**see Attachment A— "Pediatric Hepatitis of Unknown Etiology Medical Record Abstraction Form: Controls"**): This data collection instrument consists of approximately 270 main questions of various types, including dichotomous (yes/no), multiple response, and a limited number of open-ended questions. The instrument will collect data on the following:
   - Signs and symptoms
   - Clinical information
   - Underlying health conditions
   - Testing for adenoviruses, gastrointestinal or respiratory pathogens and any other viruses
   - History of COVID-19
   - Laboratory markers
   - Vaccination information

2. Exposure questionnaire for PUIs (**see Attachment B— Pediatric Hepatitis of Unknown Etiology - Exposures Questionnaire [Parental Interview])**: This data collection instrument consists of approximately 200 main questions of various types, including dichotomous (yes/no), multiple response, and a limited number of open-ended questions with prompts that were intended to identify novel exposures or risk factors that might not have been previously considered. **Attachment D— "Hepatitis pediátrica de etiología desconocida - Cuestionario sobre exposiciones [entrevista a los padres]"** is an identical version of this form translated into Spanish. The instrument will collect data on the following:
   - Demographics, household structure, and general health information
   - Medications and patient history of hepatitis illness and previous illnesses
   - Exposures, including school/daycare, illness among close contacts, travel, animals/insects, food, water, and other environmental exposures
   - Socioeconomic status

3. Exposure questionnaire for controls **(see Attachment C "Pediatric Hepatitis of Unknown Etiology - Exposures Questionnaire CONTROL [Parental Interview]"**): This data collection instrument consists of approximately 200 main questions of various types, including dichotomous (yes/no), multiple response, and a limited number of open-ended questions with prompts that were designed to identify novel exposures or risk factors that might not have been previously considered. The content of this form is identical to the Exposure questionnaire for PUIs (see **Attachment B— Pediatric Hepatitis of Unknown Etiology - Exposures Questionnaire [Parental Interview]**). **Attachment E— Hepatitis**

pediátrica de etiología desconocida. CONTROL del cuestionario sobre exposiciones [Entrevista a los padres]") is an identical version of this form translated into Spanish. The instrument will collect data on the following:

- Demographics, household structure, and general health information
- Medications and patient history of previous illnesses
- Exposures, including school/daycare, illness among close contacts, travel, animals/insects, food, water, and other environmental exposures
- Socioeconomic status

2. Purpose and Use of the Information Collection

The purpose of this information collection is to determine if adenovirus may be associated with acute pediatric hepatitis and if exposures, pathogens, or risk factors other than adenovirus infection may contribute to risk of pediatric hepatitis, either independently or in conjunction with adenovirus.

CDC does not expect these collections to yield data that can be generalized, but it is expected to build capacity within the health departments and produce needed information that affect state and local public health issues related to pediatric hepatitis of unknown etiology. Results from this evaluation will help inform guidance to state, tribal, local, and territorial health departments and delegates of health departments (i.e., clinicians) on the association of adenovirus or other potential exposures with pediatric hepatitis.

3. Use of Improved Information Technology and Burden Reduction

Data will be collected from all participating jurisdictions via the medical chart abstraction form for controls and the exposure questionnaires for PUIs and controls. Forms will be transmitted to CDC via secure ShareFile after which data will be entered by CDC staff into an established REDCap database. ShareFile is a file sharing and uploading service for CDC staff to securely share files and folders with each other and external partners. Alternatively, jurisdiction public health officials may enter data directly into the REDCap database should they choose to do so. This method was chosen to reduce the overall burden on respondents by allowing for data entry to be completed at CDC or by the jurisdiction, if preferred. The data collection instruments were designed to collect the minimum information necessary for the purposes of this project (i.e., limited to approximately 270 questions for the medical chart abstraction and approximately 200 questions each for the PUI and control exposure questionnaires). Skip patterns are indicated on the forms where applicable and have been programmed into the REDCap database to guide data entry.

4. Efforts to Identify Duplication and Use of Similar Information

Prior to that approval of 0920-1011, no collection activities or data existed on pediatric hepatitis of unknown etiology and what is causing these severe cases of hepatitis.

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 an extension of one-time data collection. There are no legal obstacles to reduce the burden. The purpose of CDC's request for this generic clearance is to ensure the collection of data that is currently unavailable and is time sensitive given the need to determine the cause of this severe pediatric illness to inform guidance to state, tribal, local, and territorial health departments on evaluating pediatric hepatitis of unknown etiology. If no data are collected, CDC will be unable to:

- Address gaps in knowledge of pediatric hepatitis of unknown etiology that will strengthen surveillance, epidemiology, and laboratory science. Specifically, CDC will be unable to assess the potential epidemiologic association between adenovirus infection (or other risk factors) and pediatric hepatitis.
- Provide timely support and technical assistance to states and communities, and assist in decision making that affects planning, response, and recovery activities of subsequent outbreaks of pediatric hepatitis of unknown etiology.
- Provide guidance to state, tribal, local, and territorial health departments and delegates of health departments (i.e., clinicians) on the association of adenovirus or other potential exposures with pediatric hepatitis
- Build capacity and improve programs for surveillance of pediatric hepatitis

Children with hepatitis of unknown etiology continue to be identified by jurisdictions, though the cause of these severe cases of hepatitis continues to remain unknown. There is currently no guidance to assist state, tribal, local, and territorial health departments in evaluating pediatric hepatitis of unknown etiology nor are there existing data collections that include data that is needed to evaluate this unique problem.

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

There are no special circumstances with this data 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 data collection is being conducted using the Generic Information Collection mechanism of the CSTLTS Generic Information Collection Service (CSTLTS Generic) – OMB No. 0920-0879. A 60-day Federal Register Notice was published in the Federal Register on May 21, 2020, Vol. 85, No. 99, pp 30962-30963. 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. Protection of the Privacy and Confidentiality of Information Provided by Respondents

The Privacy Act does not apply to this data collection. STLT governmental staff and / or delegates will be speaking from their official roles.

11. Institutional Review Board (IRB) and Justification for Sensitive Questions

No information will be collected that are of personal or sensitive nature. This data collection is not research involving human subjects.

12. Estimates of Annualized Burden Hours and Costs

The total burden hours for this submission is 375 burden hours. The medical chart abstraction and exposure questionnaires are based on the forms used in the initial investigation and refined based on feedback from jurisdictions.

(Attachment A – Pediatric Hepatitis of Unknown Etiology Medical Record Abstraction Form: Controls): The average time to complete the medical chart abstraction for PUIs, including time for reviewing instructions, gathering needed information and completing the instrument, was

approximately 45 minutes. Given the similarities between the forms for PUIs and controls, completion of the medical chart abstraction for controls is approximately 45 minutes total.

(Attachment B – Pediatric Hepatitis of Unknown Etiology - Exposures Questionnaire [Parental Interview]) and **Attachment D -** Hepatitis pediátrica de etiología desconocida - Cuestionario sobre exposiciones (entrevista a los padres), *Spanish translation of Exposures Questionnaire for PUIs*. The average time to administer and complete the exposure questionnaire for PUIs, including time for reviewing instructions, gathering needed information and completing the instrument is approximately 45 minutes.

(Attachment C –Pediatric Hepatitis of Unknown Etiology - Exposures Questionnaire CONTROL [Parental Interview])and **Attachment E -** Hepatitis pediátrica de etiología desconocida. CONTROL del cuestionario sobre exposiciones (Entrevista a los padres), *Spanish translation of Exposures Questionnaire for controls*. The average time to administer and complete the exposure questionnaire for PUIs, including time for reviewing instructions, gathering needed information and completing the instrument, was approximately 45 minutes. Given the similarities between the forms for PUIs and controls, completion of the exposure questionnaires for controls is approximately 45 minutes total.

Estimates for the average hourly wage for respondents are based on the Department of Labor (DOL) Bureau of Labor Statistics for occupational employment for epidemiologists http://www.bls.gov/oes/current/oes_nat.htm. Based on DOL data, an average hourly wage of $41.70 is estimated for all respondents. Table A-12 shows estimated burden and cost information.

Participation is voluntary for the health departments.

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**
Attachment A – Pediatric Hepatitis of Unknown Etiology Medical Record Abstraction Form: Controls	Public Health Officials	50	4	45 / 60	150	$41.70	$6,255.00
Attachment B – Pediatric Hepatitis of	Public Health Officials	50	2	45 / 60	75	$41.70	$3,127.50

Unknown Etiology - Exposures Questionnaire [Parental Interview]							
Attachment C – Pediatric Hepatitis of Unknown Etiology - Exposures Questionnaire CONTROL [Parental Interview]	Public Health Officials	50	4	45 / 60	150	$41.70	$6, 255.00
	TOTALS	**50**	**10**		**375**		**$15,637.5**

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 data 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 a contractor to develop the data collection instrument, enter data, and perform data analysis. The total estimated cost to the federal government is $56,591.60. 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	Total Average Cost
Principal Investigator – GS-14, Step 1 Staff Role: Advise development of data collection instrument and data analysis	260	$56.58 /hour	$14,710.80
Epidemiologist – GS-12, Step 1 Staff role: develop data collection instrument, enter data, and perform data analysis	260	$40.27/hour	$10,470.20
Epidemiologist – GS-12, Step 1 Staff role: develop data collection instrument, enter data, and perform data analysis	260	$40.27/hour	$10,470.20
Epidemiologist – GS-12, Step 1 Staff role: develop data collection	260	$40.27/hour	$10,470.20

instrument, enter data, and perform data analysis			
Epidemiologist – GS-12, Step 1 Staff role: develop data collection instrument, enter data, and perform data analysis	260	$40.27/hour	$10,470.20
Estimated Total Cost of Information Collection			**$56,591.60**

15. Explanation for Program Changes or Adjustments

This is a new data collection.

16. Plans for Tabulation and Publication and Project Time Schedule

All data will be submitted to CDC via secure ShareFile or via direct entry into the CDC instance of REDCap, which is behind the SAMS authenticated firewall and only accessible to project team members via SmartCard. Data collected during the assessment will be tabulated and shared only in aggregated form; no personally identifiable information will be collected or shared. Analysis results from these data will be published in peer-reviewed journals and presented to public health partners and others in medical and public health fields (e.g., conferences).

Project Time Schedule

- ✓ Design instrument ..... (COMPLETE)
- ✓ Develop protocol, instructions, and analysis plan ..... (COMPLETE)
- ✓ Pilot test instrument ..... (COMPLETE)
- ✓ Prepare OMB package ..... (COMPLETE)
- ✓ Submit OMB package ..... (COMPLETE)
- ❑ OMB approval ..... (Open 32 months)
- ❑ Conduct data collection ..... (Open 32 months)
- ❑ Code data, conduct quality control, and analyze data..... (6 months)
- ❑ Prepare summary report(s) ..... (6 months)
- ❑ Disseminate results/reports ..... (6 months)

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. Attachment A –** Pediatric Hepatitis of Unknown Etiology Medical Record Abstraction Form: Controls
- **B. Attachment B –** Pediatric Hepatitis of Unknown Etiology - Exposures Questionnaire [Parental Interview]
- **C. Attachment C –**Pediatric Hepatitis of Unknown Etiology - Exposures Questionnaire CONTROL [Parental Interview]
- **D. Attachment D -** Hepatitis pediátrica de etiología desconocida - Cuestionario sobre exposiciones (entrevista a los padres). *Spanish translation of Exposures Questionnaire for PUIs*
- **E. Attachment E -** Hepatitis pediátrica de etiología desconocida. CONTROL del cuestionario sobre exposiciones (Entrevista a los padres). *Spanish translation of Exposures Questionnaire for controls*

REFERENCE LIST

1. Centers for Disease Control and Prevention (CDC). "National Public Health Performance Standards Program (NPHPSP): 10 Essential Public Health Services." Available at http://www.cdc.gov/nphpsp/essentialservices.html. Accessed on 8/14/14.
2. Baker JM, Buchfellner M, Britt W, et al. Acute hepatitis and adenovirus infection among children—Alabama, October 2021–February 2022. MMWR Morb Mortal Wkly Rep 2022;71:638–40. https://doi.org/10.15585/mmwr.mm7118e1 PMID:35511732
3. Centers for Disease Control and Prevention (CDC). "Children with Acute Hepatitis of Unknown Cause" Available at: https://www.cdc.gov/ncird/investigation/hepatitis-unknown-cause/index.html. Accessed on 9/8/2022
4. Kambhampati AK, Burke RM, Dietz S, et al. Trends in Acute Hepatitis of Unspecified Etiology and Adenovirus Stool Testing Results in Children — United States, 2017–2022. MMWR Morbidity and mortality weekly report. 2022; 71(24);797–802.