Request for Approval Under the Generic Clearance for
Emergency Epidemic Investigation Data Collections
(0920-1011)

Instruction: This form should be completed by the primary contact person from the CDC CIO that will be sponsoring the investigation.

Determine if your investigation is appropriate for this Generic mechanism: *Instruction: Before completing and submitting this form, determine first if the proposed investigation is appropriate for the EEI Generic ICR mechanism. Complete the checklist below. If you select "yes" to all criteria in Column A, the EEI Generic IR mechanism <u>can</u> be used. If you select "yes" to any criterion in Column B, the EEI Generic ICR mechanism <u>cannot</u> be used.*

Column A	**Column B**
CDC epidemiological assistance is requested by one or more external partners (e.g., local, state, tribal, military, port, other federal agency, or international health authority or other partner organization). ☒ Yes ☐ No	The Investigation is initiated by CDC, without request from an external partner. ☐ Yes ☒ No
The investigation is urgent in nature (i.e., timely data are needed to inform rapid public health action to prevent or reduce injury, disease, or death). ☒ Yes ☐ No	The investigation is not urgent in nature. ☐ Yes ☒ No
The investigation is characterized by undetermined agent, undetermined source, undetermined mode of transmission, or undetermined risk factors. ☒ Yes ☐ No	The investigation is conducted for the primary purpose of program evaluation, surveillance, needs assessment, or research to contribute to generalizable knowledge. ☐ Yes ☒ No
One or more CDC staff (including trainees and fellows) will be deployed to the field. ☒ Yes ☐ No	CDC staff (including trainees or fellows) are not deployed to the field. ☐ Yes ☒ No
Data collection will be completed in 90 days or less. ☒ Yes ☐ No	Data collection expected to require greater than 90 days. ☐ Yes ☒ No

Did you select "Yes" to ***all*** criteria in Column A?

If yes, the EEI Generic ICR may be appropriate for your investigation. → You may proceed with this form.

Did you select "Yes" to ***any*** criterion in Column B?

If yes, the EEI Generic ICR is not appropriate for your investigation. → Stop completing this form now.

GenIC # 2019003 - XXX **Date** 6/12/2019

Title of Investigation: *Instruction: Provide the title of the investigation in the following format: [Undetermined agent, undetermined source, undetermined mode of transmission, undetermined risk factor] for [disease/problem] among [subpopulation]—[State], [Year]*

Undetermined cause of Acute Flaccid Myelitis, multiple states, United States, 2018

Location of Investigation: *Instruction: Indicate location where investigation will occur. If multiple locations, specify each one.*

State:	39 US state health department and large city jurisdictions: AL, AZ, AR, CA, Chicago, CO, GA, Houston, IL, IN, IA, KS, KY, MD, MA, MI, MS, MO, MT, MN, NE, NV, NH, NJ, NYC, NY, NC, ND, OK, PA, RI, SC, SD, TN, TX, UT, VA, WA, WI
City/County (if applicable)	
Country	USA

Requesting Agency: *Instruction: Indicate name of agency requesting epidemiological assistance and the name and position title of the requestor*

Agency:	Minnesota Department of Health
Name and Position Title:	Ruth Lynfield MD, State Epidemiologist and Medical Director

Note: Attach the Letter of Invitation requesting support. The letter should include the following information: 1) background on the outbreak or event; 2) steps already taken toward prevention and control, if any; 3) request for CDC assistance, including objectives of the investigation; and 4) how data will be used to inform prevention and control measures. Sensitive information in the Letter of Invitation not appropriate for public dissemination should be redacted.

Description of Investigation

1. Problem to be Investigated: *Instruction: Provide a summary of the outbreak or event. The summary should include all the information you know at this time about the outbreak or event and the investigation that is planned. At a minimum, please provide the following information: 1) background necessary to understand the importance of the outbreak or event, including a justification of the need for an investigation and why this issue requires an urgent response; 2) the objectives of the investigation, including how the information collected will be used to inform prevention and control measures; and 3) a brief overview of the investigation planned, including study design, respondents, mode of data collection. In the description, indicate whether a data collection instrument is attached with the GenIC request (refer to as Appendix 1, etc) and what instruments will be developed in the field. (suggested length: 250-500 words).*

Acute flaccid myelitis (AFM) is a rare condition characterized by rapid onset of flaccid weakness in one or more limbs and spinal cord gray matter lesions, for which no specific treatment or prevention exists. In fall 2018, Minnesota experienced an increase in the number of AFM cases. To date, there have been 11 confirmed AFM cases in Minnesota with onset during 2018 compared with 4 during 2014-2017. No common exposures have been identified among the cases and although the majority of patients with AFM have reported signs and symptoms consistent with viral illness in the weeks preceding limb weakness, the risk factors for this disease are not well understood.

The pathogenic mechanisms for AFM are unclear, and it is unknown why some people go from

having a mild respiratory illness or fever to developing AFM while others recover. Although the clinical presentation of AFM may resemble poliomyelitis, these AFM cases are not caused by poliovirus and all stool specimens from AFM patients have tested negative for poliovirus. A number of other viral infections have been recognized to cause acute flaccid limb weakness, including enteroviruses (coxsackievirus A16, EV-D68 and EV-A71), flaviviruses (i.e. West Nile Virus), and herpesviruses (cytomegalovirus and Epstein-Barr virus). However, direct evidence of a viral etiology, specifically detection of virus in the cerebral spinal fluid of AFM patients, has been limited. Non-infectious and post-infectious causes of AFM have also been hypothesized. Identifying risk factors for AFM is a crucial step for understanding the causes and pathogenic mechanisms of AFM, establishing prevention measures, and developing effective treatments. Additionally, there have been reports that diagnosis might have been delayed in some cases, perhaps due to a lack of awareness about AFM by healthcare providers.

Most 2018 AFM cases occurred beginning in the fall. However, case confirmation is a lengthy process which can take weeks to months. Before an illness can be classified as a confirmed case, the health departments must be notified by the providers of the illness, gather the required medical records (including any lab, radiologic records, and MRI images), and then send them to CDC for review and chart abstraction. Every report received at CDC is then further reviewed by a panel of external neurologists (two neurologists review the records independently and if there is disagreement the case and records are discussed with a 3rd neurologist) to provide the final classification of confirmed case. To date, as of June 12, 2019, approximately 10 cases reported to CDC in late 2018 are still pending case classification.

By spring 2019, a sufficient number of 2018 illnesses were classified as confirmed cases to verify an upsurge in cases in 2018 compared to prior years. At this time, the Minnesota Department of Health notified CDC they intended to request epidemiologic technical assistance to create a comprehensive hypothesis-generating questionnaire to investigate more broadly the AFM cases. In an effort to better understand common exposures among AFM patients, other state and local health jurisdictions with AFM cases indicated to CDC that they also wished to collaborate in a case investigation which involves administering a hypothesis-generating questionnaire to all patients with a 2018 confirmed AFM case in their jurisdiction.

During April and May 2019, the Minnesota Department of Health, with concurrence from 35 states and 3 large city jurisdictions with AFM cases in 2018, formally requested CDC assistance with a coordinated investigation of 2018 AFM cases to identify exposures that are potentially associated with developing AFM or disease severity.

The 39 jurisdictions, with technical assistance from CDC, have worked collaboratively during the last few months to develop a common questionnaire (Appendix 1 – English version; Appendix 2 – Spanish version) to collect data from 2018 patients with a confirmed AFM case. Because the number of cases in any one jurisdiction is small, the participating jurisdictions will aggregate data to provide sufficient power for detecting significant associations.

Objectives of this investigation are:

1. Assist the state and local health department with the investigation to better characterize potential exposures common to AFM patients; evaluate potential non-infectious and infectious etiologies.
2. Describe the healthcare seeking behaviors of AFM patients and their families prior to the AFM diagnosis.

To date in the United States, a total of 232 AFM cases from 2018 have been confirmed in 41 states, compared with 35 cases in 16 states in 2017. This response is urgent since timely data are needed to inform rapid public health action to prevent and reduce disease in children. As detailed

above, most 2018 AFM cases occurred beginning in the fall of 2018. By spring 2019, class classification (which can take months) was completed for a sufficient number of patients with illness to confirm a concerning upsurge in confirmed cases in 2018 compared to prior years. In response to this upsurge, 39 state and local jurisdictions requested CDC technical assistance with a case investigation and have been working collaboratively during the past few months to develop a questionnaire to identify risk factors.

Data will be collected by interview with the patients or the primary caregiver of patients using a common questionnaire (Appendix 1 – English version; Appendix 2 – Spanish version). Interviews will be conducted via telephone. One state (CO), plans to conduct the interviews in-person. Although a total of 232 cases have been classified in 41 states from 2018, not all states are participating in this investigation. This GenIC requests approval to collect data from the 210 confirmed cases in the 39 collaborating jurisdictions.

2. Characteristics of Outbreak or Event (Check all that Apply):

- ☒ Undetermined agent
- ☐ Undetermined source
- ☒ Undetermined mode of transmission
- ☒ Undetermined risk factor

3. Respondents: *Instruction: Select all that apply. For each respondent type selected, provide a brief description. Be sure to include a description of control respondents, if applicable. Use as much space as necessary for each description.*

- ☐ General public (describe):
- ☐ Healthcare staff (describe):
- ☐ Laboratory staff (describe):
- ☒ Patients (describe):
  AFM patients 18 years and older or the primary caregiver of AFM patients aged <18 years will be interviewed using a standardized questionnaire.
- ☐ Restaurant staff (describe):
- ☐ Other (describe):

4. Selection of Respondents: *Instruction: Provide a brief description of how respondents will be identified and selected. Use as much space as necessary for the description.*

As part of AFM surveillance, providers who diagnose a patient with AFM report the case to the state or local health department who then reports it to CDC for case confirmation. State and local health departments have information on the AFM patients in their jurisdiction. Telephone (or, for one state, in-person) interviews will be conducted with primary caregivers of confirmed AFM patients or the patients (if 18 years of age or older).

5. Study Design: *Instruction: Select all that apply. For each study design planned, provide a brief description. Use as much space as necessary for the description.*

☒ Epidemiologic Study (indicate which type(s) below)

☒ Descriptive Study (describe):

This is a descriptive study of patients confirmed with AFM to systematically collect information about potential exposures associated with AFM to identify common exposures as potential risk factors and describe the healthcare seeking behaviors of AFM patients and their families prior to the AFM diagnosis.

☐ Cross-sectional Study (describe):

☐ Cohort Study (describe):

☐ Case-Control Study (describe):

☐ Other (describe):

☐ Environmental Assessment (describe):

☐ Laboratory Testing (describe):

☐ Other (describe):

6. Data Collection Mode: *Instruction: Select all that apply. For each data collection mode planned, provide a brief description. Use as much space as necessary for the description.*

☒ Survey Mode (indicate which mode(s) below):

☒ Face-to-face Interview (describe):

The primary caregiver of patients or the patients (if 18 years of age or older) might be interviewed in-person in one state (Appendix 1).

☒ Telephone Interview (describe):

The primary caregiver of patients or the patients (if 18 years of age or older) will be contacted by telephone for interview. (Appendix 1, Appendix 2)

☐ Self-administered Paper-and-Pencil Questionnaire (describe):

☐ Self-administered Internet Questionnaire (describe):

☐ Other (describe):

☐ Medical Record Abstraction (describe):

☐ Biological Specimen Sample

☐ Environmental Sample:

☐ Other (describe):

7. Type of Information to be Collected: *Instruction: Select all that apply. For each type of information to be collected, provide a brief description. Use as much space as necessary for the description.*

☒ Behaviors (describe):
Attendance at daycare, schools, visits to doctors' offices and hospitals.

☒ Clinical information/symptoms (describe):
Symptoms/illnesses of AFM patients and their household contacts within 30 days before the limb weakness onset.

☐ Contact information (describe):

☒ Demographic information (describe):
Name, Sex, Date of Birth, Race, Ethnicity.

☐ Environmental factors (describe):

☒ Exposures (describe):
Information regarding exposures to potentially infected people will be collected.

☒ Medical history (describe):
Past medical history and medication history of AFM patients will be collected.

☒ Risk factors (describe):
Risk factors for this illness are currently unknown. The questions are broad in order to formulate hypotheses regarding risk factors. We will ask about relevant past medical history of 1st and 2nd degree blood relatives, exposure to vectors, exposure to pets, contact with pesticides/fertilizers, or special diet in the 30 days before limb weakness onset.

☐ Specimen/lab information (describe):

☒ Travel history (describe):
Travel in the US and outside US of the patients in the 30 days before limb weakness.

☐ Other (describe):

8. Duration of Data Collection (number of weeks):
Up to 12 weeks

Research Determination: *Instruction: Indicate the research determination decision. If the decision is research, provide the research determination letter and IRB approval, if required.*

☐ Research ☒ Not Research

CDC Investigation Lead: *Instruction: Indicate the name, title, and affiliation of the person who will serve as the CDC lead for this investigation.*

Name: Mona Marin, MD

Title: Medical Epidemiologist

Affiliation:	CDC - National Center for Immunization and Respiratory Diseases/Division of Viral Diseases/Viral Vaccine Preventable Diseases Branch (NCIRD/DVD/VVPDB)

CDC Sponsoring Program and Primary Contact Person: *Instruction: Indicate the sponsoring CIO/Division/Branch for this investigation. Indicate the name, title, and contact information of the CDC Primary Contact Person for this investigation. Indicate the preferred method of contact during the OMB approval process. Note, contact person or a designee must be available during the OMB approval process in case questions arise.*

CIO/Division/Branch:	NCIRD/DVD/EB
Name:	Mona Marin, MD
Title:	Medical Epidemiologist, NCIRD/DVD/VVPDB

zsn8@cdc.gov; 404-639-8791

Certification: *Please read the certification carefully. Type your name to validate that you are providing certification. Note: If you incorrectly certify, the collection will be returned as improperly submitted or it will be disapproved. Certification should be signed by the CDC Primary Contact Person for this Investigation.*

I, [insert name of CDC sponsoring program contact], certify the following to be true:
1. The collection is voluntary.
2. Respondents will not be personally identified in any published reports of the study.
3. Information gathered will be primarily used to inform effective prevention and control measures.

CDC Sponsoring Program Primary Contact Name:	Mona Marin, MD
Date of Certification:	6/11/2019

Requested Approval Date (mm/dd/yyyy): *Instruction: Indicate the date by which approval is needed.*
6/15/2019

E-mail the completed form to the Information Collection Request Liaison (ICRL) or EIS program ICRL designee.

EEI Information Collection Request Liaison:
Danice Eaton, PhD, MPH
EIS Program Staff Epidemiologist
EWB/DSEPD/CDC
2400 Century Center, MS E-92
Office: 404.498.6389
Deaton@cdc.gov