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 can be used. If you select "yes" to any criterion in Column B, the EEI Generic ICR mechanism cannot 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 # 2016009 - XXX **Date** 02/11/2016

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 sources, modes of transmission, risk factors, and health outcomes for Zika virus infection — Brazil, 2016

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

State:	
City/County (if applicable)	
Country	Brazil

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

Agency:	Brazil Ministry of Health
Name and Position Title:	Giovanini Evelim Coelho, MD, PhD, Director, National Dengue Control Program

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).*

Zika virus is a mosquito-borne flavivirus transmitted by Aedes species mosquitoes. Around 1 in 5 people infected with Zika virus become symptomatic, and the most common symptoms include fever, rash, joint pain, and conjunctivitis. The illness is usually mild and self-limited with symptoms lasting for several days to a week. No vaccine is available and treatment is supportive. However, Zika virus infection could potentially lead to severe health outcomes, including microcephaly in babies born to infected mothers and Guillain-Barre syndrome.

Prior to 2015, Zika virus outbreaks had been identified in Africa, Southeast Asia, and the Pacific Islands. In May 2015, the World Health Organization reported an outbreak of Zika in Brazil, with an estimated 440,000–1,300,000 suspected cases of Zika virus disease having occurred through the end of 2015. Locally-acquired cases of Zika virus disease have since been identified in 27 countries and territories in the Americas.

On January 13, 2016 a GenIC request was submitted under the Emergency Epidemic Investigations (EEI) Generic ICR (OMB No. 0920-10-11; exp: 3/31/2017) to respond to a request for assistance from the Brazil Ministry of Health to identify risk factors for Guillain-Barré Syndrome, including Zika virus. This data collection was approved by OMB on January 13 (GenIC 2016007-XXX, expires: 4/12/2016). As the Zika virus outbreak expands, there is increasing concern that the full spectrum of potential health consequences of Zika virus infection are not well understood. Because infection could potentially lead to severe health outcomes, there is an urgent public health need to better understand the epidemiology of and risk factors for Zika virus infection in affected areas.

In October 2015, the Secretary of Health of Pernambuco State was alerted by clinicians to a potential increase in the number of cases of microcephaly; an investigation was launched. On 22 October, the Secretariat confirmed the finding and alerted the national authorities. The following day, the Brazil Ministry of Health sent a notification through International Health Regulations of the occurrence of 26 cases of microcephaly in Pernambuco. On November 11, Brazil declared a national public health emergency and engaged in discussion with international partners.

As of January 16, 2016, a total of 3,893 cases of microcephaly had been reported to national authorities from 21 Brazilian States. Although Zika virus RNA has been identified in specimens (i.e., brain tissue, placenta, and amniotic fluid) from several infants with microcephaly and from fetal losses in women infected with Zika virus during pregnancy, it is not currently known how many of the cases of microcephaly being reported in Brazil are associated with Zika virus infection.

The Brazil Ministry of Health (MOH) has requested CDC's assistance to respond to the Zika virus outbreak in Brazil. The results will be used to identify prevention and control measures for Zika virus infection and its sequelae.

The objectives of the investigation include:

1) to describe the potential association of Zika virus infection and microcephaly and other negative outcomes.
2) to describe the clinical characteristics and current outcome of children with microcephaly associated with Zika virus infection.
3) to provide guidance on public messaging and support with additional aspects of outbreak response.

This GenIC requests approval for urgent data collection necessary for prevention and control of Zika virus and negative health outcomes associated with infection, including:

1. Appendix 1: Questionnaire
2. Appendix 2: Chart Abstraction

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

☒ Undetermined agent

☒ Undetermined source

☒ Undetermined mode of transmission

☒ Undetermined risk factor

4. 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):

Face-to-face interviews with mothers of children with microcephaly (cases) and without microcephaly (matched controls) regarding exposure history. Controls will be matched on location of residence and age restricted. Interviews will be conducted in either English or Portuguese as appropriate (Appendix 1).

☒ Healthcare staff (describe):

For incomplete medical records, information will be obtained from healthcare and laboratory staff (Appendix 2)

☒ Laboratory staff (describe):

For incomplete medical records, information will be obtained from healthcare and laboratory staff (Appendix 2)

☐ Patients (describe):

☐ Restaurant staff (describe):

☒ Other (describe):

Public health personnel from the CDC and Brazil MOH investigation team will perform medical chart reviews from case infant medical charts (Appendix 2)

5. 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.*

Cases will be identified from a list of microcephaly cases reported to the Brazil Ministry of Health. A case will be defined as a live born infant whose head circumference is less than the third percentile based on sex and gestational age and whose head circumference (in centimeters) to length (in centimeters) ratio is less than or equal to 0.65. Information from the Secretary of Health database will be reviewed to ensure that the case meets the case definition. Once a complete list of cases is finalized, a simple random selection will be performed to select cases for potential enrollment in the investigation.

Vital birth records will be used to identify potential controls. A control is a live born infant whose head circumference is greater than the twenty-fifth percentile based on sex and gestational age or current age, if birth measurements are not available.

Cases will be matched to controls whose mother lived in the same neighborhood or an immediately adjoining neighborhood for at least 80% of her pregnancy and subsequent to the delivery. If there are no control infants in the immediate geographic vicinity, the cases will be matched to control infants that are the shortest distance from the case. Eligible controls will be randomly selected from those meeting the geographic and age restrictions until 3 controls are enrolled for each case.

6. 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):

☐ Cross-sectional Study (describe):

☐ Cohort Study (describe):

☒ Case-Control Study (describe):

After consent has been obtained, the investigation team will ask mothers of case and control infants a series of questions related to her familial history of birth defects, pregnancy history (e.g., any complications, gestational age of infant when born) and potential exposures and illnesses during pregnancy (Appendix 1). Basic demographic as well as information on the infant as to any medical problems the infant might have and some basic developmental questions will also be collected.

After information has been collected, a blood sample will be collected from both the mother and infant. Trained phlebotomists will draw the blood samples using standard sterile technique. One serum separator sample will be collected from the infant and their mother. Up to 7.5 mLs will be collected for the mothers and up to 3 mLs will be collected from the infants. A minimum of 500 microliters of whole blood will be needed to perform the tests. Specimen collection, storage, and transport will be performed according to local procedures and protocols.

For all cases, a chart review will be conducted, as long as the mother or guardian provides their consent, to determine test results for congenital infectious diseases as well as obtain imaging and clinical laboratory findings (Appendix 2).

☒ Other (describe):

Other ancillary response efforts to provide data leading to outbreak control will also be carried out.

☐ Environmental Assessment (describe):

☒ Laboratory Testing (describe):

Acute blood specimens will be tested at CDC for Zika virus and dengue virus (a closely related virus that elicit antibodies that can cross-react on Zika virus assays) IgM antibodies using an enzyme-linked immunosorbent assay (ELISA) per methods described elsewhere. For samples testing positive for Zika or dengue virus IgM antibodies, plaque reduction neutralization test using a 90% cut-off (PRNT90) will be performed using Vero cells for Zika and dengue viruses. For infants who test negative for IgM antibodies against Zika virus, their serum sample will be tested by RT-PCR for Zika viral RNA. Specimen collection, storage, and transport will be performed according to local procedures and protocols.

☐ Other (describe):

7. 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):

Questionnaire related to the maternal familial history of birth defects, pregnancy history (e.g., any complications, gestational age of infant when born) and potential exposures and illnesses during pregnancy (Appendix 1)

☐ Telephone Interview (describe):

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

☐ Self-administered Internet Questionnaire (describe):

☐ Other (describe):

☒ Medical Record Abstraction (describe):

Public health personnel from the CDC and Brazil MOH investigation team will perform medical chart reviews to determine test results for congenital infectious diseases as well as obtain imaging and clinical laboratory findings (Appendix 2).

☐ Biological Specimen Sample

☐ Environmental Sample:

☐ Other (describe):

8. 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):

☒ Clinical information/symptoms (describe):

Illnesses during pregnancy including potential signs and symptoms of Zika virus disease (Appendices 1-2); any signs or symptoms infants have experienced since birth (Appendices 1-2); maternal medications, and results of imaging and infectious disease testing for case mothers and infants (Appendix 2).

☐ Contact information (describe):

☒ Demographic information (describe):

Basic demographic information (e.g., DOB, age sex, height, weight, residence, education level) (Appendices 1-2)

☐ Environmental factors (describe):

☒ Exposures (describe):

Exposures during pregnancy that have been associated with microcephaly, such as infectious diseases, mosquito exposure and prevent measures, smoking and alcohol use, water sources, exposure to pesticides, travel (Appendices 1-2)

☒ Medical history (describe):
History of illnesses during pregnancy (Appendices 1-2)

☒ Risk factors (describe):
(See exposures)

☒ Specimen/lab information (describe):
Whether a blood sample or not was obtained (Appendix 2)

☒ Travel history (describe):
History of travel to other locations in the month before and during pregnancy (Appendix 2)

☐ Other (describe):

8. Duration of Data Collection (number of weeks):
6-7 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:	J. Erin Staples
Title:	Medical Epidemiologist
Affiliation:	NCEZID/DVBD/ADB

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:	J. Erin Staples
Name:	Medical Epidemiologist
Title:	NCEZID/DVBD/ADB

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, J. Erin Staples, 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:	J. Erin Staples

Date of Certification: 2/4/2016

Requested Approval Date (mm/dd/yyyy): *Instruction: Indicate the date by which approval is needed.*
2/14/2016

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
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