Assessment to Estimate the Effect of Community-Wide Vector Control Initiatives on Zika Virus Transmission in Puerto Rico, 2016

Request for OMB Approval of a New Emergency Information Collection

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Supporting Statement A

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Goals:

1. Conduct household-based cluster investigations in areas of Puerto Rico with and without ongoing community-wide vector control (e.g., education, source reduction, targeted larviciding, and mosquito trap interventions) activities to:
    a. Conduct enhanced case finding to estimate the incidence of Zika Virus (ZIKV) infection in households around confirmed cases in areas with and without ongoing vector control activities;
    b. Identify risk factors for Zika virus infection;
    c. Estimate the frequency with which individuals with symptomatic ZIKV infection seek care;
    d. Estimate the frequency of accurate diagnosis and reporting to the Puerto Rico Department of Health (PRDH) of patients with ZIKV disease to estimate current rate of under-reporting of Zika virus disease cases;
    e. Describe the clinical spectrum of illness due to ZIKV infection, including age-or sex-specific symptoms of infection;
    f. Investigate the entomologic components of ZIKV transmission, including:
        i. Estimate vector densities in active foci of ZIKV transmission;
        ii. Estimate ZIKV infection rates in mosquitoes.
    g. Evaluate the effect of vector control activities on Zika transmission within the clusters that fall within vector control intervention areas.
2. Compare trends in ZIKV disease cases reported to the Passive Arboviral Diseases Surveillance System (PADSS) in areas with and without ongoing community-wide vector control activities (e.g., education, source reduction, targeted larviciding, and mosquito trap interventions).

Intended use of the resulting data: Findings will be used to develop or refine messaging to the public and medical communities to improve case-seeking behavior and case reporting, respectively, as well as evaluate the potential influence of vector control interventions on Zika virus transmission to inform vector control efforts in Puerto Rico during the Zika virus outbreak.

Methods: The assessment includes two parts: household-based cluster investigations and analytic review of passive surveillance data.

Subpopulation to be studied: Suspected Zika virus disease cases that have laboratory evidence of current or recent Zika virus infection in Puerto Rico.

How data will be analyzed: All data will be entered into RedCap and analyzed by SAS,

This is an emergency information collection request. It is not expected that this project will take longer than six months. If, in the course of conducting the assessment, it is determined that more than six months are necessary, a separate non-emergency ICR will be submitted to OMB for review.

1. Circumstances making the Collection of Information Necessary

Aedes aegypti mosquitos are endemic throughout the tropics and sub-tropics [1], and are responsible for the transmission of dengue (DENV), chikungunya (CHIKV), and Zika virus (ZIKV). Local transmission of ZIKV was first identified in the Americas in 2015 [2], and has since expanded across nearly all areas of the tropics and sub-tropics in the Americas and Caribbean [3]. Many individuals infected with ZIKV will experience either no symptoms of disease (i.e., asymptomatic infection) or a mild illness characterized by rash, fever, myalgia, and/or arthralgia, which will self-resolve within a week or less. However, ZIKV infection in pregnant women has recently been shown to cause microcephaly and other congenital anomalies [4], and has been associated with development of Guillain-Barré syndrome [5, 6] and severe thrombocytopenia [7, 8][Sharp et al., in review]. Hence, though initially perceived to be a relatively innocuous infection, the emergence of ZIKV in the Americas has revealed multiple associations with high-morbidity conditions and sequelae.

Traditional approaches to community-wide control of *Ae. aegypti* populations (e.g., fumigation, indoor/outdoor residual spraying, community education campaigns) have a long history of minimal to no success [9-13]. Novel approaches (e.g., genetically-modified mosquitos, *Wolbachia*-infected mosquitos, improved mosquito traps) show much promise, but have not yet been shown to be effective in reducing the incidence of disease caused by viruses that are transmitted by *Ae. aegypti* [10]. Therefore, a combination of approaches may be necessary to effectively reduce the impact of disease outbreaks caused by viruses transmitted by *Ae. aegypti*.

Passive surveillance for ZIKV disease commenced in the US territory of Puerto Rico in late 2015 by adapting the passive dengue and chikungunya surveillance systems to incorporate reporting of and diagnostic testing for suspected ZIKV disease. Local transmission of ZIKV was first detected in Puerto Rico in November, 2015 [14]. After expanding across much of the island, to date >5,500 laboratory-positive ZIKV disease cases have been reported to the Puerto Rico Department of Health (PRDH) via the Passive Arboviral Diseases Surveillance System (PADSS). In order to employ all possible approaches that are safe to humans and the flora and fauna of Puerto Rico to reduce the incidence of ZIKV infections in Puerto Rico, in early June 2016 the Director of the CDC recommended to PRDH and the Governor of Puerto Rico that a combination of aerial spraying, deployment of autocidal gravid ovitraps (AGO

traps), indoor/outdoor residual spraying, and/or intensive community education campaigns be utilized to attempt to reduce the burden of ZIKV infections in Puerto Rico. While aerial spraying is no longer being considered, community-wide vector control efforts with education and outreach, source reduction, larviciding and deployment of mosquito traps are in the final planning stages. Such efforts are currently slated to begin in September 2016.

Because *Aedes* species mosquitoes live in and around homes and other areas where humans congregate (e.g., schools) and do not typically fly more than a few hundred meters [15-17], the geographic distribution of both chikungunya and dengue virus infections tend to be highly focal [18-21]. Because *Aedes* species mosquitos are most active during the daytime, particularly at dusk and dawn, hours when most household members are at home, dengue and chikungunya cases frequently cluster within households [19, 22, 23]. Previous dengue cluster investigations demonstrated rates of DENV infection of 2.2–12.4% [24-27] among household members and neighbors residing within 10–100 meters of confirmed dengue cases. These studies enabled identification of household-level risk factors for DENV infection, such as uncovered water storage containers being a risk factor for DENV infection [24], and piped household water and use of mosquito nets as being protective against DENV infection [26, 27]. Dengue and chikungunya cluster investigations have also enabled identification of asymptomatic and sub-clinical infections that would not otherwise have been detected through traditional passive surveillance [27, 28][Bloch et al., in review], thereby providing additional information about the incidence and consequence health burden of infection.

2. Purpose and Use of Information Collection

Household-based cluster investigations have not yet been conducted during ZIKV outbreaks in Puerto Rico or elsewhere. Such investigations would enable enhanced case finding and subsequent estimation of current rates of under-reporting of ZIKV disease cases (due either to lack of presentation for care, clinical misdiagnosis, or failure for cases to be reported), description of the symptomatology of infected individuals, and elucidation of risk factors for infection among the individuals included in the investigation, which may or may not be the same as those amongst the larger population.

Simultaneously performing dengue, chikungunya, and Zika diagnostic testing may enable identification of differences in clinical and epidemiologic aspects of the three illnesses. More importantly, however, conducting such investigations in areas with and without intensive vector control efforts would provide the opportunity to extrapolate cluster-specific rates of ZIKV infection to then assess the effectiveness of vector control interventions. This information may be utilized to improve surveillance for and characterization of ZIKV disease in Puerto Rico, and provide ongoing feedback to public health partners regarding if the

various approaches to vector control are having an appreciable effect on reducing ZIKV infections.

If participants report that they sought care for a recent acute illness, the patients' medical records may be obtained and reviewed to better describe the patient's illness, clinical diagnosis, and if they were reported as a suspected ZIKV disease case to any surveillance system in operation in Puerto Rico. In addition, any specimens remaining from the patient's medical visit may be collected for ZIKV disease diagnostic testing. This activity directly supports Goals 1.c. and 1.d.

Entomologic investigations will be conducted in all cluster investigations. Field staff will deploy up to 20 surveillance mosquito traps (either BG-Sentinel traps or Autocidal Gravid Ovitraps) around homes, and/or perform aspiration inside all participating homes, within the 100 meter radius to evaluate the species and density of mosquitoes. Collected mosquitoes species will be pooled (10 specimens/pool) and tested by RT-PCR to estimate the minimum ZIKV infection rate. It is expected that some 100 pools of mosquitoes (*Aedes aegypti*) will be collected per cluster (approximately 1,000 female mosquitoes).

Utilization of both passive surveillance data and household-based cluster investigations are expected to be associated with limitations in interpretation of findings with regard to if and how well they represent the epidemiologic trends in ZIKV infection. Passive surveillance only captures infections that cause severe enough disease that the person seeks medical care. There physician that sees the patient must also correctly identify the symptoms, collect a specimen, and send the specimen for testing. All of these steps introduce bias into passive surveillance. Meanwhile, household-based cluster investigations have limitations because only people that are home at the time of the contact attempt have the opportunity to participate in the study. Additionally, many people offered participation refuse to participate because they are required to provide a blood sample. Also, parents may be reluctant to allow children to participate because they have to give a blood sample. Given this issue, we also want to collect demographics of refusing households in order to understand differences from participating households. Nonetheless, due to the urgent need for rapid assessment of the relationship between community-wide interventions and the concomitant incidence of ZIKV infections and/or ZIKV disease, such approaches are the only available methodology to rapidly gather such information. If findings from both passive surveillance data and household-based cluster investigations are considered together, they may provide a more informed interpretation of the community-wide patterns of ZIKV infections. Based on the results obtained, CDC may determine that these two efforts need to be further supplemented with a community-wide

serosurvey to better estimate the incidence of ZIKV infections in intervention and non-intervention community, thereby more fully characterizing the potential impact of community-wide vector control interventions. Should such an assessment be conducted in the future, it will be submitted as a separate information collection request to OMB.

Findings will be used to develop or refine messaging to the public and medical communities to improve case-seeking behavior and case reporting, respectively.

This information collection request is authorized by Section 301 of the Public Health Service Act (42 U.S.C. 241) (Attachment A).

3. Use of Improved Information Technology and Burden Reduction

Information will be collected on paper forms. Questionnaires will be entered into a database regularly or as a group at the close of data collection. Data will be organized in a REDCap database stored on a secure server at CDC. Data files will be restricted to study staff via a secure share folder. Paper forms and electronic devices will be kept locked when not in use.

4. Efforts to Identify Duplication and Use of Similar Information

Collection of data from passive surveillance systems and household-based cluster investigations in Puerto Rico is unique and is only able to be conducted by Puerto Rico Department of Health. Hence, duplication of data collection is unlikely to occur.

5. Impact on Small Businesses or Other Small Entities

The collection of information does not primarily involve small entities. However, for the small entities involved, the burden imposed by CDC's information collection requirements have been reduced to the minimum necessary for CDC to meet its regulatory and public health responsibilities.

6. Consequences of Collecting the Information Less Frequently

This is a one-time information collection.

Less frequent collection of data would result in a lessened ability to identify changes in the incidence of Zika virus infections that may result from community-wide vector control interventions. This could in turn result continuing such interventions in the absence of data demonstrating its effectiveness or lack thereof.

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

This request fully complies with the guidelines in 5 CFR 1320.5.

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

A. Since this is an emergency information collection request, we request to waive the 60-day public comment period. A 60-day notice for the Federal Register was drafted (Attachment B).

B. The Puerto Rico Department of Health will provide oversight, supervision, and directorship of this investigation. Representatives from the CDC will provide field support, as well as laboratory and subject matter expert (SME) support to PRDH, including on-the-ground field support during the activity.

9. Explanation of Any Payment or Gift to Respondents

There is no payment or gift to respondents.

10. Protection of the Privacy and Confidentiality of Information Provided by Respondents

The Privacy Act is applicable. Records are covered under CDC Privacy Act System of Records Notice (SORN) No. 0920-0136 “Epidemiologic Studies and Surveillance of Disease Problems” and SORN No. 09-20-0113, “Epidemic Investigation Case Records Systems Notice.”

This study will collect and record personal identifying information (e.g., name, contact information, GPS coordinates of residence). As in all studies involving human subjects, this study will involve people whose rights need to be safeguarded. A sticker with a study identifier will be placed on blood tubes and questionnaires and will be used to link all data collected during the study. All blood specimens will be securely transported to and stored at CDC Dengue Branch. All data will be entered into a survey database that will be secure; only personnel on the investigation team will have access to it. All personnel involved in this surveillance project will be required to adhere to an unwavering code of conduct regarding the confidentiality of patients’ information. Data will be kept as confidential as permitted by law. Hard copies of questionnaires will be stored in a locked cabinet in a room at CDC-DB that will be locked when not occupied. Access to these files will be limited to study personnel. Electronic copies of the data will be kept in the above-mentioned database, which will be password-protected and will only be accessible to relevant study personnel.

Paper copies of data collection instruments will be stored in a locked, secured filing cabinet in a locked room at the CDC and/or PRDH offices; only investigators directly involved in the investigation will have access to surveillance and investigation data. Information about sensitive topics such as sexual practices or drug use will not be collected. Names will be included in electronic databases to facilitate reporting of diagnostic test results to investigation participants that request it. No reports related to the findings of this study will include personal identifying information.

All written materials for investigations will be translated into Spanish, including consent and assent forms.

All residents of the household that are present at the time of visit will be oriented to the investigation and read a consent (Attachments D and E) or assent (Attachment F) script.

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

IRB Approval

The protocols and tools used to conduct this information collection request have been reviewed and approved by NCEZID's Human Subjects Advisor, who determined that this data collection meets the definition of research under 45 CFR 46.102(d). IRB approved the protocol on August 3, 2016 (Attachment C).

Justification for Sensitive Questions

No sensitive questions will be asked in the questionnaires.

12. Estimates of Annualized Burden Hours and Costs

A. Estimated Annualized Burden Hours

The total number of estimated annualized burden hours for this project is 560. This represents the amount of time for the household questionnaire (Attachment G) to be completed 200 times and for the individual questionnaire to be completed twice by 500 respondents. It is likely that the individual questionnaire will only be completed once by most respondents. However, if any participants have reported acute illness at the time of the interview or test positive for ZIKV infection in any specimens by RT-PCR in the absence of symptoms (which could be indicative of either asymptomatic or pre-symptomatic viremia), they will be contacted by telephone at least 14 days later to complete a follow-up interview to better characterize the individual's illness using the same questionnaire as was administered during the initial visit (Attachment H).

Based on previous household cluster investigation, we expect to recruit, interview, and collect blood from an average of 32 houses in each cluster. We expect that on average 2–3 persons per home will participate. Therefore, we expect about 3 participants in the target household and an additional 62–93 interviews in the homes within the 100 meter radius.

We expect that by recruiting 500 participants we will be able to accomplish goals 1.a–1.e. During the Chikungunya cluster investigation in Puerto Rico we found that only 8% of persons with symptomatic CHIKV infection sought healthcare and were identified as CHIKV+ through the surveillance system (this is related to Goal 1.d). Because Zika is a disease with less severe symptoms than Chikungunya, we expect this number to be even smaller. Therefore, we will need more people to be able to accurately estimate this number. We estimate that 500 participants would be sufficient to fulfill Goal 1.d. The exact number of participants will of course depend on exactly how many households per cluster and how many persons per household agree to participate).

Goal 1.e is to describe the clinical spectrum of illness due to ZIKV infection. During the Chikungunya cluster investigation we found that 30% of the participants had evidence of recent Chikungunya infection (5% positive by PCR and 25% positive by IgM ELISA). With 500 participants we would have approximately 150 Zika positive cases. We estimate that this will be sufficient to describe the clinical spectrum of illness by sex, age, and those that are symptomatic.

For homes that are offered enrollment and refuse to participate we will gather categorical demographic information on sex and age of the household inhabitants. This will allow us to compare demographic makeup of the participants to those that refuse. Based on a refusal rate of 32% during the Chikungunya cluster investigation, we expect roughly 100 homes will refuse participation.

Type of Respondent	Form Name	No. of Respondents	No. of Responses per Respondent	Average Burden per Response (in hours)	Total Burden Hours
General public	Household questionnaire	200	1	18/60	60
	Individual	500	2	30/60	500

	questionnaire				
	Individual specimen collection of blood, urine, and saliva	500	1	10/60	83.3
	Refusal demographic form	100	1	2/60	3.3
Total					646.9

There will be no anticipated costs to respondents other than time.

The mean hourly wage rate for general public ($22.71) was used. Information on mean wage rates is available at http://www.bls.gov/oes/current/oes_nat.htm.

B. Estimated Annualized Burden Costs

Type of Respondent	Form Name	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
General public	Household questionnaire	60	$22.71	$1,362.60
	Individual questionnaire	500	$22.71	$11,355.00
	Refusal demographic form	3.3	$22.71	$74.94
Total				$12,792.54

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

There are no known capital and maintenance costs incurred by respondents or record keepers.

14. Cost to the Government

The cost to the federal government is estimated at $8,052. This estimate represents the amount of time for the CDC staff to administer the survey, enter data, and conduct analysis. Hourly wage rates were used for step-1 FTEs for the Atlanta locality. These numbers are available at https://www.opm.gov/policy-data-oversight/pay-leave/salaries-wages/salary-tables/pdf/2015/ATL.pdf.

Grade	Hours	Hourly Wage	Total
GS-9	160	$24.40	$3,904
GS-11	80	$29.40	$2,352
GS-12	40	$35.20	$1,408
GS-13	20	$41.90	$838
Total			$8,502

15. Explanation for Program Changes or Adjustments

This is a new information collection. We are adding a short form to capture the basic demographic information for households that refuse, in order to try to understand if refusing households differ substantially from participating households.

16. Plans for Tabulation and Publication and Project Time Schedule

Once OMB approval is obtained, it is suspected that it will take roughly four weeks to complete testing and preliminary analysis for each weeks' household-based cluster investigations and passive surveillance data analysis.

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

The display of the OMB expiration date is appropriate.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.

Attachments

13

A. Public Health Service Act (42 USC 241)
B. Draft 60-day FRN
C. IRB Approval
D. Household & Individual Consent Form
E. Adult Consent Form
F. Assent for Children aged 5–14 Years
G. Household questionnaire
H. Individual questionnaire
I. Household tracking form
J. Refusal demographics form

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