Zika Emergency Package III:
Persistence of Zika virus in semen and urine of adult men with confirmed Zika virus infection

Request for OMB approval of a New ICR

Supporting Statement A
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Contact:
Lee Samuel
National Center for Emerging and Zoonotic Infectious Diseases
Centers for Disease Control and Prevention
1600 Clifton Road, NE
Atlanta, Georgia 30333
Phone: (404) 718-1616
Email: llj3@cdc.gov

Table of Contents

- The objectives of this study are:
    - Determine the frequency and duration of Zika virus RNA in semen and urine of infected adult men as determined by quantitative reverse transcriptase polymerase chain reaction assay (RT PCR)
    - Determine the correlation between RT PCR results and ability to recover replicative virus from semen and urine of infected adult men

1. Circumstances Making the Collection of Information Necessary

This is an emergency request for a new information collection for six months. This investigation will need more than six months, though, so after getting emergency approval, an ICR will be formally submitted to OMB for non-emergency review following the publication of broad 60- and 30-day FRNs.

Zika virus is an arthropod-borne flavivirus that has recently emerged in the Americas. Maternal infection has been linked to congenital microcephaly, fetal loss, and other adverse reproductive health outcomes. Although spread primarily by mosquitoes, recent reports have highlighted the potential for sexual transmission of Zika virus through the semen of infected men. Detection of viral RNA in semen 62 days after illness onset has been reported; however the frequency and duration of virus shedding is largely unknown. Information on these parameters is needed urgently to better inform public health recommendations, particularly for couples contemplating pregnancy.

Authorizing legislation is Section 361 of the Public Health Service Act (42 USC 241) (Attachment A).

2. Purpose and Use of Information Collection

This study will fill gaps in the scientific knowledge base for Zika virus regarding the persistence and transmissibility of Zika virus in body fluids.

The purpose of this study is to determine the frequency and duration of Zika virus shedding in semen and urine of infected men. Minimal health information and specimens from consenting men with recent Zika virus infection will be collected once every two weeks for up to 6 months post onset of symptoms (or up to 12 collections). Specimens will be tested for Zika RNA by reverse transcriptase polymerase chain reaction assay (RT-PCR) at CDC; those testing positive may be further evaluated by virus isolation techniques. Zika virus disease is a nationally notifiable condition, and participants will be recruited through contact with CDC personnel. Urine and semen specimens will be self-collected using home collection kits, a short questionnaire will be self-administered, and participants will be compensated for their time. Results of testing will be provided to participants at the conclusion of testing. The results of this study are expected to have immediate implications for public health recommendations and disease prevention.

This is a prospective, descriptive cohort study. The prospective nature of the proposed cohort study allows for determining the persistence of shedding Zika virus in semen and urine through serial specimen collection from individuals with confirmed Zika virus.

The results of this study will be of great relevance to provide evidence-based information to circumvent Zika virus transmission. They will inform the development of recommendations used in the current epidemic setting, as well as in future Zika virus situations. Results and analysis will be used to update and refine relevant counseling messages and recommendations. Potential products include scientific abstracts and manuscripts, presentations, and guidance documents.

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

The CDC is carrying out a similar study in Puerto Rico. While the studies are similar, the situations are quite difference. In the continental United States, cases to date have only been from traveling abroad as no local transmission cases have been recorded. Additionally, residents of Puerto Rico are exposed to dengue, another flavivirus similar to Zika which is regularly monitored through a sentinel surveillance system.

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 burdens 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

CDC activities pertaining to the Zika virus response would be significantly hindered if it were not able to collect the information at the frequency necessary to prohibit the spread of this disease.

Collecting information less frequently than the CDC recommendations would interfere with the public health actions required to contain and respond to Zika virus transmission and to do everything possible to limit, if not stop, deaths and birth defects due to this disease.

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

The activities outlined in this package fully comply with all guidelines of 5 CFR 1320.5.

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

A) Because this is a request for an emergency clearance, CDC asks that the 60-day comment period be waived.

B) There was no consultation outside of the Agency.

9. Explanation of Any Payment or Gift to Respondents

Participants will be provided a token of appreciation for the time and effort needed to complete study procedures (i.e., sample collection and packaging, survey completion, and initiation of shipping process). Specifically, participants will receive a $50 gift card for each study kit returned to CDC Fort Collins. They will receive the gift card in the next kit (or with the thank you letter and the end of the study) whether they provide both samples in the return kit or just one. It would be unjust to withhold payment for time and effort based on an inability or unwillingness to provide both samples, and it would constitute a penalty for the voluntary refusal of study procedures, which is prohibited by the regulation. From similar studies, we expect that the gift cards will help minimize attrition.

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

This information collection request has been reviewed by the CDC National Center for Emerging and Zoonotic Diseases (NCEZID). NCEZID has determined that the Privacy Act does apply to this information collection request. The applicable System of Records Notice is 09-20-0136.

All participant information contained on study forms, in laboratory records and reports, and in electronic files will be kept confidential. Specimens and study forms will be linked through a unique study number only.

Only the study staff will have access to the participants' information. Physical documents containing study data will be stored in a locked file cabinet in the CDC study coordinator's office. These data collection forms will be destroyed at the time the study protocol is closed with the IRB office. At that same time, all PII will be deleted from the study database and any separate specimen data will be de-identified. All electronic files will subsequently be stored in a password protected database on a CDC secure network. The results from this study will be published or presented for scientific purposes in aggregate form only so that individuals cannot be identified.

Verbal informed consent will be sought over the telephone using a standardized script that includes all required consent elements (Attachment C). A paper copy of the consent form will be sent to participants for their reference with their first specimen collection kit (Attachment F). This study presents no more

than minimal risk to subjects, and the study includes no procedures for which written informed consent is ordinarily required outside the research context.

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

IRB Approval

The protocols and tools used to conduct both of these information collection requests have been reviewed and approved by NCEZID's Human Subjects Advisor, who determined that the data collections meet the definition of research under 45 CFR 46.102(d). IRB approved the protocol and the information collection tools (Attachment J).

Justification for Sensitive Questions

There is some risk of embarrassment or anxiety for the participant associated with provision of semen samples. However, the study staff will be professional and compassionate when speaking with participants. They will assure the participant that they can stop or withdraw from the study at any time.

The topics included in the questionnaires include asking for information that may be perceived as sensitive, however, participants will answer questions individually and submit the forms securely with their specimens. Participants will be instructed during consent that they may skip any question they choose.

12. Estimates of Annualized Burden Hours and Costs

A) Estimated Annualized Burden Hours

The total estimated burden is 58.5 hours. This represents the time it will take 250 respondents to each complete the two-minute baseline questionnaire (Attachment C) once, and the one-minute follow-up survey (Attachment D) twelve times.

Type of Respondent	Form Name	No. of Respondents	No. of Responses per Respondent	Average Burden per Response (in Hours)	Total Burden Hours
General public	Introductory survey	250	1	2/60	8
	Follow-up survey	250	12	1/60	50
Total					58

B) Estimated Annualized Burden Costs

The average annual response burden cost is estimated to be $1,328.54. The hourly wage estimates are based on the Bureau of Labor Statistics May 2014 National Occupational Employment and Wage Estimates (http://www.bls.gov/oes/current/oes_nat.htm). The mean hourly wage rate for all occupations ($22.71) was used.

Type of Respondent	Form Name	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
General public	Introductory	8.5	$22.71	$193.04

	survey			
	Follow-up survey	50	$22.71	$1,135.50
Total				$1,328.54

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

There are no costs to respondents other than their time to participate.

14. Annualized Cost to the Government

The total estimated cost to the government is $36,396.73. The table below breaks down how many CDC employees will be working on this project, what percentage of their time will be devoted to this project, and how much they will make during this time. Information collection is expected to last nine months. Hourly wages were based on Step 1 employees for the Atlanta locality available here: https://www.opm.gov/policy-data-oversight/pay-leave/salaries-wages/salary-tables/pdf/2016/ATL_h.pdf.

Grade	# of FTEs	Hourly Wage	% time devoted to project	Total Hours	Total
GS-12	2	$35.58	2	42	$1,494.36
GS-13	2	$42.31	25	522	$22,085.82
GS-13	2	$42.31	5	105	$4,442.55
O-6	1	$53.00	10	105	$5,565.00
O-6	1	$53.00	5	53	$2,809.00
Total					$36,396.73

15. Explanation for Program Changes or Adjustments

This is a new information collection request, therefore program changes and adjustments do not apply at this time.

16. Plans for Tabulation and Publication and Project Time Schedule

Estimated dates for implementing and completing key activities.

	Study Timeline in Months											
	1	2	3	4	5	6	7	8	9	10	11	12
Local Ethics Committee Review	**X**											
Investigator Coordination Meeting	**X**											
Questionnaire Development	**X**											
Study Training	**X**											
Recruitment	**X**	**X**	**X**	**X**								
Data Collection		**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**		
Data Management		**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Data Analysis		**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Laboratory Analysis		**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Results interpretation					**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**

Interim Project Report				**X**	**X**							
Final Project Reports											**X**	**X**
Final Project Review Process											**X**	**X**
Dissemination of Project Outcomes												**X**

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

The OMB Expiration Date will be displayed.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.

Attachments

A. Section 361 of the Public Health Service Act (42 USC 241)
B. 60-day FRN
C. Verbal Script for Consent and Introductory Survey
D. Follow-up Survey
E. Instructions for Sample Collection
F. Copy of Consent Form
G. General Questions
H. FAQs Sheet
I. Thank You and Test Results Letter
J. IRB Approval