# Persistence of Zika virus in semen and urine of adult men in the United States with confirmed Zika virus infection

Request for OMB approval of a New ICR

**Supporting Statement A**
**January 23, 2021**

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- 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)

This is a request for a new ICR to continue the emergency information collection approved by OMB in March, 2016 (OMB Control No. 0920-1109). This emergency clearance expires on September 31, 2016. CDC requests an additional one-year of clearance to complete this investigation. OMB Control No. 0920-1109 covered the same project. However, since this ICR is now undergoing formal, non-emergency OMB review, it is being submitted as a new ICR.

## 1. Circumstances Making the Collection of Information Necessary

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 301 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.

*Update on progress since receiving emergency clearance*

As of June 21, 2016, we have contacted 26 jurisdictions (state and metropolitan health departments) to request help with identification and contact of eligible men. Of these, 19 are actively contacting potential participants in regards to this study. The remainder will begin contacting potential participants pending local ethics and/or leadership approval.

Study enrollment activities have picked up greatly since Mid-May. As of September 28, 2016, we have enrolled 170 participants from 21 states plus New York City. Three males have declined participation and three have withdrawn after enrollment. We have received over 700 specimens from the enrolled individuals.

**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, although the situations are quite different. 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.

During the 6 month Emergency clearance ICR period for this study, we reached over 50% of our target enrollment. At this pace, we anticipate meeting our enrollment goal by December 2016. Given this enrollment timeline and the fact that participants may provide data and specimens for up to 6 months after onset of their Zika virus illness, data collection for this study is anticipated to continue through June 2017.

**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**

Collecting multiple samples from each participant will increase the robustness of the scientific conclusions..

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. A 60-day Federal Register Notice was published in the Federal Register on Monday, May 2, 2016, Volume 81, No. 84, p. 26231 (Attachment B). One non-substantive public comment was received (Attachment B1).

B. There was no consultation outside of the Agency.

**9. Explanation of Any Payment or Gift to Respondents**

Participants will be provided compensation 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. This gift card value is consistent with the $50 compensation approved in the initial Emergency Clearance OMB Control No. 0920-1109. Samples will be submitted every 2 weeks for up to 6 months after each participant became ill with Zika virus. The maximum number of times a participant can submit specimens is 12, and the maximum compensation they could receive would be $600. It is expected that participants will submit an average of 5 specimen kits (range 1-11). They will receive the gift card in the next kit (or with the thank you letter at the end of the study) whether they provide both samples in the return kit or just one. 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 applies 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.

As part of the consent form for this study, we ask each participant for permission to store any unused portions of their samples and any samples of Zika virus found in their samples for future testing. We advise them that we will not test their samples for HIV, or use their samples for human genetic testing. If we share samples with other researchers, those researchers will not be able to find out who the participants are. However, because we will not have a link to the participant name, we will not be able to remove their sample from storage if they change their mind later. If they agree to long term storage, we will remove the link between their specimen and their name/ID at the end of this study (when the IRB protocol is closed). There is no limit on the number of times these banked specimens can be used.

## 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 134 hours. This represents the time it will take 250 respondents to each complete the twenty-minute introductory survey (Attachment C) once, and the one-minute follow-up surveys (Attachments D1 and D2) twelve times. The introductory survey also serves as documentation of consent. Answering questions will not take more than 3 minutes, but it will take approximately 20 minutes to listen to information about the study and give consent.

There are two Follow-Up surveys: one for the first time and one for all subsequent responses. They are identical aside from slight wording differences. For example, the first follow-up survey (Attachment D1) reads "Since you became ill…" while the regular follow-up survey (Attachment D2) reads "Since the last survey…"

| 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 | 20/60 | 84 |
| | Follow-up survey | 250 | 12 | 1/60 | 50 |
| **Total** | | | | | 134 |

*B) Estimated Annualized Burden Costs*

The average annual response burden cost is estimated to be $3,043.14. 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 survey | 84 | $22.71 | $1,907.64 |
| | Follow-up survey | 50 | $22.71 | $1,135.50 |
| **Total** | | | | $3,043.14 |

### 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 $94,003.20. 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 are based on Step 1 employees for the Denver-Aurora (Fort Collins) 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-11 | 2 | $30.52 | 50 | 720 | $43,948.80 |
| GS-13 | 1 | $43.50 | 50 | 720 | $31,320 |
| GS-14 | 1 | $51.40 | 5 | 72 | $3,700.80 |
| GS-14 | 1 | $51.40 | 10 | 144 | $7,401.60 |
| O-6 | 1 | $53.00 | 10 | 144 | $7,632.00 |
| **Total** | | | | | $94,003.20 |

### 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. OMB Control No. 0920-1109 covered the same project. However, since this ICR is undergoing formal, non-emergency OMB review, it is being submitted as a new ICR.

### 16. Plans for Tabulation and Publication and Project Time Schedule

Estimated dates for implementing and completing key activities. It is expected that the activities shaded in grey below will be completed by the time the emergency clearance for OMB Control No. 0920-1109 expires at the end of September, 2016.

| | **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 301 of the Public Health Service Act (42 USC 241)
B1. 60-day FRN
B2. Public comment
C. Verbal Script for Consent and Introductory Survey
D1. First Follow-Up Survey
D2. 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
K. State health department letter
L. State health department phone script