

Long-term sequela of Rocky Mountain spotted fever (RMSF)

Request for OMB approval of a New Information Collection

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Supporting Statement A

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- **Goal of the study:** Describe persistent neurological damage in patients who were hospitalized with Rocky Mountain spotted fever (RMSF).
- **Intended use of the resulting data:** Provide information to healthcare providers, patients, and policy makers about the long term consequences of severe RMSF, including length of time to recovery, and risk factors during acute illness which may be associated with long term impairment.
- **Methods to be used to collect:** Cross sectional survey of patients about their recovery, and neurological exam in a subset of hospitalized cases of RMSF.
- **The subpopulation to be studied:** Hospitalized cases of RMSF in Arizona between 2002-2017.
- **How data will be analyzed:** Univariate and bivariate analysis comparing observed values to validated norms.

Data collection for this investigation was initiated in July 2018 following OMB approval on 7/22/2018, with a second approval on 11/15/2018 under the Emergency Epidemic Investigations (EEI) Generic ICR (OMB Control Number 0920-1011, exp 1/31/2020). A full OMB package is being submitted to allow for continuation of the project.

Between 7/23/2018 and 10/19/2018, data were collected from 22 patients (Attachment 3 Patient Screening Questionnaire) and 9 neurological exams (Attachment 4. Neurological Exam Form) were completed at one site. A second request was approved in order to complete data collection between 11/14/2018-2/13/2019 at the second and third sites; however, local approvals were unable to be obtained due to the partial government shutdown and no data collection occurred during the second approval period.

Data collected to date under the previous ICRs have been entered into secured databases as per the study protocol.

1. Circumstances Making the Collection of Information Necessary

The Centers for Disease Control and Prevention (CDC), National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of Vector-Borne Diseases (DVBD), Rickettsial Zoonoses Branch (RZB), requests a 3-year approval of a new information request “Long-term sequela of Rocky Mountain spotted fever.” Extended time is requested to ensure adequate time for tribal approvals at the remaining sites, data collection, analysis and reporting.

Rocky Mountain spotted fever (RMSF), a life-threatening and rapidly progressive tickborne disease, is caused by infection with the bacterium *Rickettsia rickettsii*. Infection begins with non-specific symptoms like fever, headache, and muscle pain, but when left untreated the bacteria can cause damage to blood vessels throughout the body leading to organ and tissue damage. Delay in recognition and treatment of RMSF can result in irreparable damage leading to amputation of extremities, neurological deficits (such as hearing loss, paralysis, and encephalopathy), and death.

RMSF is an emerging threat to Arizona tribal communities. In 2018, cases have more than doubled in number compared to what was reported last year at this time (25 cases between January and October

2017 compared to 43 cases in 2018 to-date, including two deaths). In addition, family members and providers in the area are reporting that patients, even those who have been treated, are experiencing long-term neurological dysfunction and severe outcomes leading to long-term disability following their discharge. The reason for these negative outcomes are unclear. There is growing concern among physicians and patients that we have an incomplete understanding of the risk factors that lead to severe disease and neurologic sequela, impeding their ability to provide anticipatory guidance and timely access to appropriate follow-up services. Two deaths in 2017, followed by two additional deaths thus far in 2018, in addition to numerous hospitalizations, point to the striking need for better understanding of risk factors to prevent death and disability.

Authorizing Legislation comes from Section 301 of the Public Health Service Act (42 U.S.C. 241) (Attachment 1).

2. Purpose and Use of Information Collection

There are two components of the data collection:

1. Patient screening questionnaire (attachment 3)
2. Neurological exam (attachment 4)

The multiple data collection pieces in this study are designed to capture evidence at multiple stages in the disease process. As of March 18, 2019, patient medical charts have already been abstracted by federal staff for information about potential risk factors for severe disease progression, including RMSF testing history, their illness progression, previous medical conditions, type and timing of treatment for RMSF, length of hospital stay, neurologic signs and symptoms during hospitalization, sequelae observed at the time of discharge, recommended follow-up care, and other relevant clinical characteristics (Chart Abstraction Form - attachment 5). [Medical chart abstractions were undertaken only for hospitalized cases of RMSF which were reported to the Arizona Department of Health Services as part of a notifiable disease process between 2002-2017. Additional medical information was obtained according to HIPAA privacy rules, for each tribe as determined by their Institutional Review Board or tribal health department for public health purposes.](#)

The patient screening questionnaire (attachment 3) asks about experiences since original illness in order to document if individuals subjectively believe they fully recovered following their RMSF episode and if they have any identifiable neurological experiences since their RMSF diagnosis. The questionnaire will be given by members of the study team to individual patients. The questionnaire takes less than 10 minutes to complete. The screening questionnaire allows us to identify individuals who are still experiencing reported (subjective) neurological impairment at the present time. If symptoms have resolved completely, a neurological assessment (attachment 3) for long-term sequela will not be needed. This activity further provides information on functional limitations the patient has experienced between the time of their RMSF episode and the present time (when we are performing the neurological assessments). We also ask about any unrelated neurological impairment (traumatic brain injury, stroke etc.) which may have occurred since their RMSF episode, but unrelated to their RMSF recovery. This activity is vital for understanding if there are other potential causes of neurological impairment.

The final data collection is the neurological exam for patients with potential persistent sequela. This exam will be done by a healthcare provider on the study team and will take roughly 40 minutes to complete. The healthcare provider will make notation of standard neurological findings on a data collection form.

3. Use of Improved Information Technology and Burden Reduction

All (100%) of data collection will be performed using paper forms. Data will be transported by study staff back to CDC offices in Atlanta where they will be entered and stored electronically to preserve data quality and assure the security of PII.

Data entry will be performed by CDC staff on CDC secure equipment. Data will be entered into Microsoft Access data tools with data maintained on an encrypted CDC SQL Server database. PII will not be included in the database. Access data entry tools will utilize restricted fields and code checks to minimize data entry issues. Data collection tools have been designed to capture only necessary information.

To reduce burden, questions have been held to the absolute minimum required for the intended use of the information

4. Efforts to Identify Duplication and Use of Similar Information

Medical charts have already been summarized for cases between 2002-2011 using an IRB approved protocol. Where appropriate, those data will be utilized as is possible for background understanding of the clinical characteristics of RMSF patients in Arizona. However, medical charts of the patients involved in our study will need to be accessed in order to connect individual patient experiences during acute illness with the results of the neurological assessment. Besides reference to the previous medical chart review (also performed by CDC and IHS under an IRB approved protocol) for cases from 2002-2011, data collected under this data collection request is not expected to be duplicative or already in the possession of the federal government as similar projects in this cohort have not yet been attempted.

The primary target audience of the results of this study are healthcare providers who treat and manage cases of RMSF. Results can be used to set timelines and realistic treatment plans following acute disease recovery. Results can further be used by tribal policy makers to describe the acute and long-term disease costs.

5. Impact on Small Businesses or Other Small Entities

This data collection will not involve small businesses.

6. Consequences of Collecting the Information Less Frequently

Data collections have been kept to a minimum, requesting up to two in person encounters with patients. Patient interviews will be done in person at the patient's home or via telephone. Data from this screening assessment will need to be compiled and analyzed prior to neurological exam. Less information or fewer

collections would limit our understanding of the disease process, the recovery period, or current neurological function. Each collection will only be undertaken at one time for each participant.

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

This request fully complies with the regulation 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 February 7, 2019, vol. 84, No. 26, pp. 2517 (Attachment 2). CDC did not receive public comments related to this notice.

B. Data collection types and methods required for this OMB clearance have been developed in collaboration with partners in the Indian Health Service, state and county health departments, experts in neuro-epidemiology, healthcare providers from local facilities as well as social and behavioral experts at the CDC and in local facilities. This study has been approved and supported by the tribal councils where the majority of RMSF patients in this study reside.

9. Explanation of Any Payment or Gift to Respondents

As a token of appreciation, a \$10 gift card will be given to those who participate in the neurological exam. There will be no other compensation or gifts provided as part of this study. Individuals who are participating in the neurological exam will have already participated in the 10 minute questionnaire and will spend roughly 40 minutes for the neurological exam. The value of the gift card is reasonable considering the time spent and does not overly incentivize participation.

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

NCEZID's Office of the Chief Information Security Officer (OCISO) reviewed this submission and determined that the Privacy Act does not apply.

Informed consent will not be requested for the medical chart abstraction portion of this case review. Individuals will be consented in person whenever possible, or via telephone if not possible, for participation in the questionnaire. All individuals participating in the neurological exam will be consented in person prior to exam. Children 8 years of age will be asked to provide assent in addition to parent permission. (Consent forms can be found in attachment 7).

Medical charts will be abstracted on site and coded files will be sent to the CDC through certified mail, secured fax, or personal transportation. Printed copies of medical information and coded chart abstraction forms and all original data collections will be secured in a locked room at the CDC Rickettsial Zoonoses Branch office and all efforts will be made to maintain the security of the case reports and medical charts.

A coversheet, documenting patient name, date of birth, community, and patient ID, will be recorded on each data collection form at the time of abstraction or exam. The top sheet will then be separated from

responses by the PIs and all patient data, exam results, and responses will be connected only by patient ID. PIs will maintain coversheets in a locked room at the CDC Rickettsial Zoonoses Branch office, separate from the original documents, until the completion of the study. A key linking unique identifiers with personal information will be kept with study investigators in a password protected file.

Records will be maintained by CDC PI's in double locked facility for ten years as per CDC records management guidelines.

A Privacy Impact Assessment is included with this submission (Attachment 8).

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

Institutional Review Board (IRB)

CDC's IRB has reviewed this protocol in its entirety and approved this protocol for use citing that the study involves no greater than minimal risk to subjects (attachment 6). Continuation of human subject's approval was approved from the CDC IRB on April 1, 2019. No changes to the protocol were requested, no adverse events were reported in the first year of activities, and approval is expected prior to the expiration of the previous human subject's determination.

Justification for Sensitive Questions

There are no sensitive questions asked in this data collection.

12. Estimates of Annualized Burden Hours and Costs

A. Estimated Annualized Burden Hours

The patient screening questionnaire is designed to take no more than 10 minutes and will be given by a member of the study team. The interviewer will travel to the patient home to minimize burden on the interviewee. Anywhere from 0 to 250 living respondents are expected based on the findings of the medical chart abstraction and the number of individuals who can be contacted and agree to participate. Patient questionnaire will be facilitated by tribal health department staff working with the study as part of normal duties and no additional cost will be incurred.

The neurological exam was estimated to take 40 minutes by the neuroepidemiologist who helped design the study. The paperwork will be done during the course of the exam. Anywhere from 0 to 250 members may participate in the neurological exam portion of the study based on findings of the medical chart abstraction and the number of individuals who can be contacted and agree to participate. We estimate half (125) of the 250 screened individuals will warrant the neurological assessment. The physician performing the exam will do so as part of his/her regular duties and no additional cost will be incurred.

As of March 19, 2019, data have been collected from 22 patients (Attachment 3 Patient Screening Questionnaire) and 9 neurological exams have been administered.

Total estimated burden is 126 hours.

Type of Respondents	Form Name	Number of Respondents	Number of Responses per Respondent	Average Burden per Response (in hours)	Total Burden (in hours)
General public	Patient screening questionnaire	250	1	10/60	42
	Neurological exam form	125	1	40/60	84
Total					126

B. Estimated Annualized Burden Costs

Cost burden is estimated using the May, 2017 Bureau of Labor Statistics National Occupational Employment and Wage Estimates (https://www.bls.gov/oes/2017/may/oes_nat.htm) median hourly wage rate for all occupations: \$18.12.

The total estimated cost burden is \$2,283.12.

Type of Respondent	Form Name	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
General public	Patient screening questionnaire	42	\$18.12	\$761.04
	Neurological exam form	84	\$18.12	\$1,522.08
Total				\$2,283.12

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.

Records will be maintained by study staff and do not require additional burden.

14. Annualized Cost to the Government

The estimated average annual cost to the federal government for the proposed information collection activities is \$137,446.50. This figure encompasses 100% FTE of one GS-13 employees, 50% FTE of a second GS-13 employee, and ancillary information collection costs. The average hourly rate was obtained from the Office of Personnel Management’s website (<https://www.opm.gov/policy-data-oversight/pay-leave/salaries-wages/salary-tables/pdf/2018/ATL.pdf>). The hourly rate for a GS-13 in metro Atlanta is \$43.91 per hour, which is about \$91,631 per year.

Table 14-A: Estimated Annualized Cost to the Government

Estimated Annualized Cost to the Government per Activity and Total	
Cost Category	Total Estimated Annualized Cost

Federal employee costs, per information collection (100% FTE of one GS-13 and 50% of a second GS-13 at \$91,631/year)	\$137,446.50
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15. Explanation for Program Changes or Adjustments

Data collection for this investigation was initiated in July 2018 following OMB approval on 7/22/2018 under the Emergency Epidemic Investigations (EEI) Generic ICR (OMB # 0920-1011, exp 1/31/2020). Per the terms of the EEI Generic ICR, data collection was approved for 90 days and expired on 10/22/2018. Between 7/23/2018 and 10/19/2018, data were collected from 22 patients and 9 neurological exams were completed.

A second GenIC was approved 11/15/2018 to allow for time to complete the remaining data collections, however, subsequent collections were unable to be completed in this time due to delays in local IRB approval. A new OMB determination is being sought to complete the work outlined in both GenIC proposals.

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

A final report of the results will be developed by collaborating investigators; any scientific presentations or publications resulting from this chart review will include the input and acknowledgment of all key contributors and will undergo CDC publication clearance. It is the intention of the investigators to submit the final report for publication in a peer-reviewed journal. Manuscript approval will be sought from participating tribal governments, CDC, and IHS prior to submission for publication.

Month	Activities
January-March 2018	Protocol Development
March-April 2018	CDC IRB approval
April-June 2018	Tribe 1 approval
July 2018	OMB approval
July-October 2018	<ul style="list-style-type: none"> • Data collection tribe 1 • Chart abstractions tribes 1, 2, 3
August-September 2018	Tribe 2 approval
October 2018-March 2019	IHS regional IRB approval (required by tribe 2)
March-April 2019	CDC IRB renewal
February-June 2019	OMB approval
June-August 2019	<ul style="list-style-type: none"> • Data collection tribe 2

	<ul style="list-style-type: none"> • Tribe 3 approval
September-November 2019	Tribe 3 data collection
November 2019-March 2020	Data entry and analysis
March-August 2020	<ul style="list-style-type: none"> • Preparation of manuscripts/reports • Manuscript approval

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

The display of the OMB Expiration date is not inappropriate.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.

Attachments

1. Authorizing Legislation
2. 60-Day FRN
3. Patient screening questionnaire
4. Neurological exam form
5. Medical chart abstraction form
6. IRB determination
7. Consent forms
8. Privacy Impact Assessment
9. IRB continuation memo