Centralized Institutional Review for the CDC Expanded Access Investigational New Device (EA-IND) for "Use of Tecovirimat (TPOXX®) for Treatment of Human Non-Variola Orthopoxvirus Infections in Adults and Children" (IND 116039/CDC #6402).

Request for OMB approval of an Emergency Information Collection

July 28, 2021

Supporting Statement A

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- **Goal of the study:** Centralized Institutional Review for the CDC Expanded Access Investigational New Device (EA-IND) for "Use of Tecovirimat (TPOXX®) for Treatment of Human Non-Variola Orthopoxvirus Infections in Adults and Children" (IND 116039/CDC #6402). This information is essential to CDC's Monkeypox emergency response consistent with requirements set forth by the Food and Drug Administration (FDA). CDC, in partnership with FDA, has made it easier for healthcare providers to provide tecovirimat (TPOXX) treatment to patients with monkeypox under the expanded access investigational new drug (EA-IND). CDC holds an intermediate-size patient population EA-IND (IND 116,039/Protocol 6402) to allow access to and use of TPOXX for treatment of orthopoxvirus infections, including monkeypox. The EA-IND provides an umbrella regulatory coverage so that clinicians and facilities do not need to request and obtain their own INDs.
- **Intended use of the resulting data:** CDC will use collected data to track and document the institutions relying on the CDC IRB so they can provide tecovirimat (TPOXX) treatment to their patients with monkeypox under the expanded access investigational new drug (EA-IND).
- **Methods to be used to collect:** CDC will accept electronic signed copies of the reliance agreement via email from healthcare providers to the huma@cdc.gov address.
- **The subpopulation to be studied:** Healthcare providers that ask for reliance agreement for tecovirimat expanded access IND protocol.
- **How data will be analyzed:** There are no statistical methods.

1. Circumstances Making the Collection of Information Necessary

The Centers for Disease Control and Prevention (CDC) Office of Science (OS) requests an emergency 6-month approval for an Information Collection titled Centralized Institutional Review for the CDC Expanded Access Investigational New Device (EA-IND) for "Use of Tecovirimat (TPOXX®) for Treatment of Human Non-Variola Orthopoxvirus Infections in Adults and Children" (IND 116039/CDC #6402). The information is essential to CDC's Monkeypox emergency response consistent with requirements set forth by the Food and Drug Administration (FDA). CDC, in partnership with FDA, has made it easier for healthcare providers to provide tecovirimat (TPOXX) treatment to patients with monkeypox under the expanded access investigational new drug (EA-IND). CDC holds an intermediate-size patient population EA-IND (IND 116,039/Protocol 6402) to allow access to and use of TPOXX for treatment of orthopoxvirus infections, including monkeypox. The EA-IND provides an umbrella regulatory coverage so that clinicians and facilities do not need to request and obtain their own INDs.

FDA regulations require that an Institutional Review Board (IRB) review, approve and maintain oversight of the activities under the EA-IND as set forth in 21 CFR Parts 50, 56, and 312. The CDC IRB is positioned to serve as the central IRB for review and approval of the EA-IND consistent 21 CFR

56.114. This arrangement allows facilities to use or rely on the CDC IRB for centralized review and approval for this protocol in place of review by the site-specific IRB to help reduce duplication of effort, delays, and increased expenses. Any facility that receives tecovirimat for treatment of orthopoxvirus infection under the EA-IND may elect to rely on the CDC IRB to meet FDA's regulatory requirements.

However, FDA also requires that IRBs and institutions prepare and maintain adequate documentation of IRB activities (21 CFR 56.115(a)). IRBs are also required to follow written procedures for the conduct of initial and continuing review of clinical research and for reporting their findings and actions to the investigator and the institution (21 CFR section 56.108(a), 56.115(a)(6)).

FDA recommends ways to fulfill the recordkeeping requirements in their 2006 guidance "Using a Centralized IRB Review Process in Multicenter Clinical Trials." FDA indicates that if an institution, its IRB, and a central IRB agree (under 21 CFR 56.114) to participate in a centralized IRB review process, they should document that action in an agreement signed by the parties. This requires CDC to collect a minimal amount of information from facilities that elect to rely on the CDC IRB to establish such an agreement.

Similar arrangements exist within the federal government. For example, the National Institutes of Health, National Cancer Institute (NCI) has created a freestanding central IRB (CIRB) to provide the option for centralized IRB review for the many multicenter cancer trials conducted by NCI. This NCI central IRB is a standing body with subject matter expertise that reviews all NCI-sponsored phase 3 trials in adults with cancer. The IRBs affiliated with the study sites have the option of accepting the review of the NCI central IRB or doing their own complete review of the protocol and informed consent. For those sites electing to rely on the CIRB for review, NCI collects standard information to establish and execute such agreements consistent with regulatory requirements (OMB#:0925-0753).

Additionally, because IRB review is required by FDA under the CDC's approved EA-IND, CDC must maintain records of which facilities have elected to rely on the CDC IRB for centralized review and which facilities elect to obtain IRB review on their own.

2. Purpose and Use of Information Collection

The IRB review is required by FDA under the CDC's approved EA-IND. Therefore, CDC must maintain records of which facilities have elected to rely on the CDC IRB for centralized review and which facilities elect to obtain IRB review on their own.

FDA Approved CDC's Application for an EA-IND for TPOXX to expand access to treatment for monkeypox. Under the EA-IND, FDA requires that any treating physician/facility accessing TPOXX through CDC's EA-IND have/obtain IRB approval for its use at that facility/institution. CDC's EA-IND is intended to provide access to use TPOXX in a facility/institution that is not currently licensed for this indication to treat monkeypox and this is not designed to be a clinical trial or will not be used in support of any application that manufacturer may or may not submitted to FDA. FDA allows for facilities/institutions/providers to use a central IRB/reliance to fulfill the requirements for IRB approval as option to obtaining IRB approval at their own institution or elsewhere. Central IRB/reliance arrangement is intended to streamline the process and reduce burden for providers/facilities/institutions

to meet the FDA requirement for IRB approval. This is especially helpful for smaller facilities or individual providers because it provides access to an IRB to fulfill the FDA requirement when access TPOXX for treatment purposes. If the facility/provider elects to use CDC IRB for centralized IRB review/reliance, then FDA requires a written agreement to document the responsibilities of each institution related to the IRB review requirements for the EA IND. The reliance agreement specifies the reporting requirements of the CDC IRB and the relying institution/facility as required by FDA. These reporting requirements are limited to specific events that meet the criteria for reporting to FDA as described at 21 CFR 56.108. Without a reliance agreement, the provider/facility will have to meet the FDA requirements for IRB review through some other mechanism other than the existing CDC IRB approval.

3. Use of Improved Information Technology and Burden Reduction

CDC will accept electronic signed copies of the reliance agreement via email from healthcare providers to the huma@cdc.gov address.

4. Efforts to Identify Duplication and Use of Similar Information

CDC is not aware of any duplication of information collection by other federal governmental authorities.

5. Impact on Small Businesses or Other Small Entities

This data collection effort does not involve any small businesses or other small entities.

6. **Consequences of Collecting the Information Less Frequently**

First, many persons with monkeypox will not receive treatment or will experience delays in receipt of treatment. CDC could also be put in a situation of noncompliance with FDA recommendations. FDA recommends ways to fulfill the recordkeeping requirements in their 2006 guidance "Using a Centralized IRB Review Process in Multicenter Clinical Trials." FDA indicates that if an institution, its IRB, and a central IRB agree (under 21 CFR 56.114) to participate in a centralized IRB review process, they should document that action in an agreement signed by the parties. This requires CDC to collect a minimal amount of information from facilities that elect to rely on the CDC IRB to establish such an agreement.

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 60-day Federal Register Notice has not been published in the Federal Register.

9. Explanation of Any Payment or Gift to Respondents

There will be no payments or gifts to respondents.

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

The information collection will not involve collection of any private or confidential information from respondents. The information requested is information that is publicly available. The information will be sent to CDC by email to a CDC functional mailbox (huma@cdc.gov). Once the information is received by email, the information collection form will be stored in a restricted SharePoint file. Access to the data collected will be further restricted to users with permission to include the CDC Institutional Official for Human Research Subjects, the Director and Deputy Director of the Office of Scientific Integrity and the Human Research Protection Office, the reliance administrators in the Human Research Protection Office, Monkeypox Response Leadership, and an informatics specialist. Per regulation, these data must also be made available to the Food and Drug Administration upon request.

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

CDC Office of Science Human Research Protection Office has determined that this information collection is not research involving human subjects. IRB approval is not required for this collection form.

12. Estimates of Annual Burden Hours and Costs

CDC requests OMB approval for an estimated 533 annualized burden hours as Hospital/IRB Administrators will be required to review and complete the CDC IRB Authorization Agreement.

A. Estimated Annual Burden Hours

Type of Respondent	Form Name	No. of Respondents	No. Responses per Respondent	Avg. Burden per response (in hrs.)	Total Burden (in hrs.)
Hospital/IRB Administrators	CDC IRB Authorization Agreement (for review)	5000*	1	1	5,000
Hospital/IRB Administrators	CDC IRB Authorization Agreement (for completion and submission to CDC	5000*	10	10/60	8,333
Total					13,333

B. Estimated Annual Burden Costs

Type of	Total Burden	Hourly Wage	Total Respondent Cost

Respondent	Hours	Rate	
Hospital/IRB Administrators	13,333 hours	$43.80/hour	$583,985.40

***Note:** *To date, 90 institutions have indicated interest in establishing an agreement to rely on the CDC IRB. The ultimate number of institutions/respondents will depend on the spread of Monkeypox and may not reach 5000.*

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

Estimates for the average hourly wage for respondents are based on the Bureau of Labor Statistics mean hourly wage for Healthcare Practitioners and Technical Occupations. The hourly wage rate is $43.80. The total estimated annual cost burden, should the number of institutions reach 5000, is $365,000.

14. Annual Cost to the Government

The total estimated costs to CDC to create this form and to place it on the website are $92,500.

Total Costs to the Federal Government	Personnel- Software development, support, and management	$92,500	

15. Explanation for Program Changes or Adjustments

This is an emergency 6-month clearance request for an Information Collection Request. This emergency extension is necessary because the information is essential to CDC's Monkeypox emergency response consistent with requirements set forth by the Food and Drug Administration (FDA). CDC, in partnership with FDA, has made it easier for healthcare providers to provide tecovirimat (TPOXX) treatment to patients with monkeypox under the expanded access investigational new drug (EA-IND).

16. Plans for Tabulation and Publication and Project Time Schedule

To expedite treatment availability for patients, data collection will begin immediately upon receipt of OMB approval. CDC has no current plans to publish data associated with this specific data collection, but may share information about approved sites to enhance public access to treatment.

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.