



**August 3, 2022**

Dominic Mancini  
Deputy Director  
Office of Information and Regulatory Affairs  
Office of Management and Budget  
Washington, DC

Subject: Request for Emergency Review and Clearance

Dear Dr. Mancini:

Pursuant to Office of Management and Budget (OMB) procedures established at 5 CFR Part 1320, *Controlling Paperwork Burdens on the Public*, CDC requests that the proposed information collection project, 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) be processed in accordance with section 1320.13, Emergency Processing.

We have determined that this information must be collected, it is essential to CDC's Monkeypox emergency response, and it is 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)). 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.

As illustrated in our attached submitted package on the CDC IRB Authorization Agreement form, the specific data elements that CDC would collect from institutions that are relying on CDC's IRB so they can provide tecovirimat treatment to patients with monkeypox are:

- Name of the requesting institution
- Name, phone and email of the site investigator, IRB Contact, and agreement signatory

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.

Given the urgent need to provide treatment to the increasing number of persons infected with monkeypox and the exponential increase in demand for access to tecovirimat under CDC's EA-IND, CDC is not able to reasonably comply with the standard PRA approval process and timeline which normally takes six months or longer. In the United States, as of July 27, 2022, there were over 4,600 cases in 47 states and Puerto Rico, and to date more than 90 facilities have already requested to rely on the CDC IRB.

In order to facilitate access to tecovirimat, ease the suffering of persons with monkeypox, and ensure CDC's ability to adhere to human subject protection requirements, CDC requests an approval of this request to collect information under an emergency clearance as soon as possible.



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Respectfully,

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Rebecca Bunnell, PhD, MEd  
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CDC Institutional Official for Human Research Subjects  
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