VA Facility Participation in the Expanded Access Program: "Protocol #6402 "Use of Tecovirimat (TPOXX®) for Treatment of Human Non-Variola Orthopoxvirus Infections in Adults and Children" (IND 116039)

Document Initially Issued by ORD: July 26, 2022

Prior revisions – 07/28/2022; 08/05/2022; 08/23/2022; 09/06/2022; November 9, 2022, July 12, 2023
Current Revision: July 23, 2024

Current Status: The current CDC IRB-approved protocol version is Version 6.4, Dated June 5, 2024; .the current CDC IRB-approved informed consent document is Version 6.4, Dated June 5, 2024. The CDC IRB approved continuing review of this Expanded Access Program on 6/20/2024; CDC IRB approval will expire on 7/23/2025. These documents can be accessed at Tecovirimat (TPOXX) IND Information (cdc.gov).

Background: The Centers for Disease Control and Prevention (CDC) has worked with the VHA Offices of Research and Development (ORD) and the Office of Research Oversight (ORO) on establishing a mechanism for VHA Facilities to rely upon the CDC Institutional Review Board (IRB) to participate in the expanded access program: "Protocol #6402 "Use of Tecovirimat (TPOXX®) for Treatment of Human Non-Variola Orthopoxvirus Infections in Adults and Children" (IND 116039)"

In order for your VA Facility to participate in the program, the following must occur:

1. **Submit IRB Reliance Concurrence Form**: The CRADO has signed a National IRB Authorization Agreement Between the CDC and ORD. A copy of the Agreement is included in this communication. Your VA Facility Medical Center Director should review the terms of the Agreement with CDC prior to signing and dating the form titled:

   "Concurrence with the Office of Research and Development (ORD) Agreement with Centers for Disease Control and Prevention (CDC) Institutional Review Board (IRB) For CDC IRB Oversight For Participation in the Expanded Access Program: "Protocol #6402 "Use of Tecovirimat (TPOXX®) for Treatment of Human Non-Variola Orthopoxvirus Infections in Adults and Children" (IND 116039)" ".

   i. Page 1: Type in the name of your VHA Facility in the fillable box at the top of page 1.

ii. Page 2: On page 2, type in the name of your Medical Center Director and give the form to the Medical Center Director to sign and date the form; the form can be signed electronically.

iii. Retain a copy for your files and send a copy of the signed and dated agreement by email to ORD and ORO. Please also include in your email:

(a) the name and position of the primary point of contact for the CDC IRB for administrative issues, and

(b) email and phone number of the VA Facility's point of contact. This information will be provided by ORD to the CDC IRB conveying your VA Facility's reliance on the CDC IRB.

NOTE: You can choose to include two VA Facility points of contacts. If you choose two, please indicate which one is the primary.

Please send the signed concurrence form and requested information to the following parties at ORD and ORO:

ORO: Priscilla Craig: priscilla.craig@va.gov and

Elizabeth Clark: Elizabeth.clark3@va.gov

ORD: Don Workman: don.workman@va.gov and

irbrelianceandsirbexceptions@va.gov

iv. Your VA Facility's reliance upon the CDC IRB for this program is in effect once the concurrence form signed and dated by the VA Facility Director has been received by ORD. Your VA Facility does not have to wait upon ORD sending a written confirmation by email. However, ORD will send the Institutional Official and point of contacts an email confirming receipt of the concurrence document within one to three business days.

v. Your VA Facility is not required to submit the concurrence document to CDC IRB. ORD will send the document to CDC IRB with the points of contact and Institutional Official information for your VA Facility.

2. **Updating Federalwide Assurances Not Required**: Your facility does not need to update your FWA to add the CDC IRB.

3. **Facility policies to use the CDC IRB**: A standard operating policy and procedure template (SOP) will be sent to VA sites when ORD receives your

signed concurrence form. The SOP must be customized and provided to ORO to the ORO contacts (Ms. Craig and Ms. Clark). However, please note that patient treatment under the program can begin prior to the SOP being reviewed by ORO. ORD will be also reviewing the SOPs in consultation with ORO.

Note: If the CDC IRB SOP is updated during the protocol, a revised version will be sent by ORD to the individuals designated at the VA Facility point of contact.

4. **IRB Review and Approval**: CDC IRB serves as the central IRB for review and approval of the TPOXX EA-IND protocol. However, the CDC has permitted IRB review and approval by other IRBs when the CDC IRB cannot be used by institutions for IRB reliance.

   If your VA Facility had previously obtained IRB review and approval for the CDC's expanded access program from your internal VA, another VA Facility, or your University IRB, and you wish to rely on the CDC IRB for this protocol, your VA Facility cannot rely upon the CDC IRB until the current IRB of Record approving the study agrees to transfer its IRB oversight, That transfer can only be effective if your VA Facility Medical Center Director signs and dates the concurrence form for reliance on the CDC IRB and submits the form as described in these instructions. Your facility does not have to rely on the CDC IRB for review of the CDC's expanded access program if you have already obtained IRB review and approval from another IRB.

5. **VA Research and Development Committee Approval**: R&D Committee review and approval must be done by designated review (VHA Directive 1200.01(1), Paragraph 9.e.(5)) or by a convened R&D Committee (ad hoc meeting may be convened). Approval is not patient-specific; subsequent uses for different multiple patients do not require separate CDC IRB and/or R&D Committee approvals.

6. **Privacy and Information Security Reviews**: A central privacy review and information security review were not required for CDC protocol version 6.3 (May 5, 2023) as no revisions impacted privacy or information security. The prior privacy and information security reviews for the earlier amendment to this CDC Program are available for access on the ORD webpage for this CDC expanded access IND program. Any amendments to this expanded access program will have central privacy and information security reviews.

   If your VA Facility has any technical issues with accessing the documents, please email the ORD Regulatory box at **vhacoordregulatory@va.gov**.

7. **Informed Consent for VA Subjects**: The CDC IRB has approved the Informed Consent Form for this program. The informed consent document is located at Tecovirimat (TPOXX) IND Information (cdc.gov).

    i. Ensure that informed consent is obtained as described in the CDC IRB-approved protocol. A waiver of documentation of informed consent (I.e., telephone consent with a written informed consent document approved by the CDC IRB that is signed and dated by the patient or patient's legally authorized representative) is not acceptable or approved by the CDC IRB. You are not required, nor does CDC request a copy of the signed and dated patient's CDC-IRB approved informed consent be sent to them or another party, such as the state health department, at the time of consent or when drug is initiated. You are also not required to inform the CDC IRB each time a patient is enrolled. The only time the patient informed consents must be sent to the CDC is if the institution using the CDC IND protocol could not maintain the signed and executed consent documents – that will not occur for any VA Facility.

    ii. No alterations in the IRB-approved informed consent document are permitted.

    iii. For VA subjects, a VA Informed Consent Addendum approved by the CDC IRB is being deferred at the present time. Please convey the following information to the patient or patient's legally authorized representative during the consent process:

    #1: The patient and/or his or her insurance will not be charged for any treatments or procedures that are part of this Expanded Access IND. If the patient has co-payments for VA care and medications, these co-payment requirements will continue to apply to medical care and services provided by VA that are not part of this treatment program.

    #2. The VA will provide necessary medical treatment should the patient be injured by being in this program. The patient will be treated for the injury at no cost. This care may be provided by the local VAMC, or arrangements may be made for contracted care at another facility. The patient has not released the VA Facility from liability for negligence. In case of injury resulting from being in this program, the patient should contact their treating clinician.

8. **Written HIPAA authorization for research and authorization for a waiver of HIPAA authorization**: This expanded access program does not meet the definition of research under the HIPAA Privacy Rule; it is treatment. If the program evolves to where it involves a research component requiring a waiver of HIPAA authorization for research to be approved, the CDC IRB will be the IRB reviewing and approving the waiver of HIPAA authorization for research.

   The CDC IRB-approved informed consent form does not contain HIPAA authorization language. Therefore, the patients are to sign a VA Form 0-5345: "Request for and Authorization to Release Health Information. The VA Form 10-5345 is already present in iMED. A sample VA Form 10-5345 completed for this CDC expanded access program is available on ORD website for the CDC Expanded Access Tecorivimat Program for Monkeypox located at https://www.research.va.gov/programs/orppe/CDC-IRB-TPOXX-EAIND-Program.cfm.

9. **Changing Lead Clinician Provider/Principal Investigator**

   Anytime the lead clinician (i.e., site investigator) changes (Box 1 of Form FDA 1572), regaffairs@cdc.gov should be alerted of who the new site investigator is and who they are replacing. The new site investigator should register via the TPOXX IND Online Registry, which includes completing and signing Form FDA 1572.

   Please remember the following for all lead clinicians participating in the CDC's Tecovirimat EAP for MPOX:

   - Lead clinicians (i.e., site investigators) need to register under the CDC TPOXX IND EAP by completing the TPOXX IND Online Registry prior to or no later than 7 calendar days of first prescribing or administering Tecovirimat, including:

     - Completing and signing Form FDA 1572, which serves as an agreement to abide by the IND regulations for use of Tecovirimat under the CDC-held EA-IND protocol.

     - A licensed clinician who is trained and qualified to manage and care for patients with orthopoxvirus or Mpox virus infection can serve as the lead site investigator on the Form FDA 1572 (Box 1).

     - Other healthcare providers involved in patient care can be listed as sub-investigators in Box 6 of Form FDA 1572.

- One signed Form FDA 1572, with all other healthcare providers providing care listed in Box 6 as sub-investigators, suffices for all Tecovirimat treatments administered under the EA-IND at the same facility.

10. **Voluntary Closure Procedures:**

If a VA Facility wishes to voluntarily close its participation in the CDC Tecovirimat with the CDC IRB, please email the CDC Regulatory Affairs Office at regaffairs@cdc.gov and include the answers to these questions:

- How many patients have been treated with Tecovirimat at the VA Facility?
- Does the VA Facility pharmacy have any Tecovirimat at the VA Facility?

Please copy the following on the VA Facility's email to the CDC Regulatory Affairs Office:

- **Irbrelianceandsirbexceptions@va.gov**
- **Priscilla.Craig@va.gov**
- **Elizabeth.Clark3@va.gov**

The clinician listed as the lead provider and the individual(s) submitted by ORD as the CDC IRB liaisons will receive an email which includes a letter as an attachment from CDC Regulatory Affairs acknowledging receipt of the VA Facility's request to close the program and closing the program at the VA Facility by stating that the VA Facility is unregistered with the CDC-sponsored EA-IND for tecovirimat (IND 116,039/CDC IRB #6402). Please upload the letter into the VAIRRS study file for the program. The program can then be closed by the VA Facility's Research and Development Committee. CDC or the Food and Drug Administration (FDA) can request access to your VA Facility's records for your site's participation in the program as part of the agreement when your VA Facility registered to be part of this CDC program.

11. **Miscellaneous**:

i. ORD Dedicated Website for the CDC Expanded Access Tecovirimat IND Program: ORD has established a dedicated webpage supporting the CDC IRB reliance by VA Facilities. It can be accessed at https://www.research.va.gov/programs/orppe/CDC-IRB-TPOXX-EAIND-Program.cfm.

ii. VAIRRS: This program must still be entered into VAIRRS, including all program staff changes. Both a cover sheet and IRB information sheet must be included as part of the VAIRRS

submission. A sample completed cover sheet and IRB information sheet from a VA Facility can be requested by emailing VHACOORDRegulatory@va.gov.

iii. Drug Procurement/VA Form 10-9012: ORD does not establish procurement of this drug. However, Pharmacy Benefits Management (PBM) has issued guidance to the pharmacists. Please note that a VA Form 10-9012 is not required.

iv. Research Compliance Audits: Research Compliance officers are not required and do not audit expanded access programs, which includes this CDC expanded access program for Tecovirimat.

v. Consent mechanisms – iMED and DocuSign:

The CDC IRB has approved both VA DocuSign and iMED for use in this expanded program. ORD is announcing the release and availability of the CDC IRB-approved consent template for IMED in late November; the November Bi-Monthly ORD HRPP webinar will discuss how to access the form. A VA Form 10-5345 is also available in iMED templates.

ORD and the Office of Identity and Access Management (IAM) have developed a streamlined process for sites to implement use of VA DocuSign for this program. The following tools are available on the ORD CDC website for this program to assist VA Facilities with use of VA DocuSign for this program:

a. ORD Guidance: Instructions for Use of VA DocuSign for VA Facilities Conducting the CDC Expanded Access Program: "Protocol #6402 "Use of Tecovirimat (TPOXX®) for Treatment of Human Non-Variola Orthopoxvirus Infections in Adults and Children" (IND 116039)"

b. Example Table for Submission to IAM to Request Use of the VA Facility's ORD-Approved DocuSign Envelopes (September 6, 2022)

c. A Tool called the "DocuSign – ORD TPOXX Study Job Aid" that will guide users on how to access the CDC IRB-approved informed consent and VA Form 10-5345 for this program, including how to obtain signatures and retrieve the document.

Please also note that the CDC IRB has approved an exception from informed consent that may be used In the event that obtaining informed consent is not feasible because the patient is unable to respond and make wishes known about tecovirimat treatment and

no legal guardian or next-of-kin is present the following provides for the treating physician to make a clinical determination to treat with tecovirimat provided that the treating physician and an independent physician certifies to the following within 3 working days of initiating treatment with tecovirimat:

1. Patient is confronted by a life-threatening situation necessitating the use of tecovirimat.

2. Informed consent cannot be obtained from the patient because of an inability to communicate with, or obtain legally effective consent from, the patient.

3. Time is not sufficient to obtain consent from the patient's legal representative.

4. There is no available alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the patient.

The CDC IRB-informed consent document includes check boxes to be completed when an exception from informed consent occurs. CDC must be notified by email at:

(regaffairs@cdc.gov)

within 3 working days of tecovirimat initiation when the treatment determination was made based on the above-mentioned certification by the treating physician and an independent physician.

vi. Consent: Obtaining a digital image (photograph/image) of each page of the patient's executed CDC IRB-approved informed consent document and VA Form 10-5345.

The CDC IRB has approved obtaining visual images of the CDC IRB-approved informed consent document with the executed signatures is permitted in lieu of the original signed and dated document. The VA Form 10-5345 may also be sent in this manner for this program.

a. The VA patient signs and dates the CDC IRB-approved informed consent form and VA Form 10-5345 at home and takes a digital image of each page to send via MyHealtheVet secure messaging.

b. The images could also be taken by the VA treating clinician or delegate by using a VA-approved videoconferencing platform; the treating clinician or delegate takes a screen shot of each page as

the patient holds up the page on the screen. The VA treating clinician or delegate may also use a Government Furnished Equipment (GFE) iPhone, if available to take the images. NOTE: VA Employees' personal cell phones may NOT be used.

c. The executed patient documents contain sensitive information. While some Veterans may not have MyHealth*e*Vet accounts and want to send images of the executed documents using personal computers or personal cell phones, VHA cannot require or demand that a VA patient or their legally authorization representative send sensitive information, including personally identifiable information (PII) or protected health information (PHI) by a non-secure method in order to receive treatment or participate in a VA study. If the VA patient wishes to use his or her personal computer or phone to send the images to VHA, the patient must be told prior to sending the images that there is a risk when sending sensitive information in an insecure manner. The risk includes loss of control of the documents. For example, the documents could be intercepted and received by a non-VA system. If the VA patient wishes to use his or her personal computer or personal cell phone to send the images after being informed of the risks of using non-secure methods, it becomes the patient's choice on how to return the forms. VHA will accept the images from the patient.

d. The CDC-IRB-approved informed consent document contains signature lines with dates for the person obtaining consent; this is required as per the CDC IRB. When images are used, the person obtaining consent must still sign and date page 5 of the informed consent document and include the entire 6-page document and the VA Form 10-5345 with the patient's program file materials. Both are to be placed in the patient's VHA medical record. Please print the name of the patient on page 5 of the informed consent document in the designated line stating: "Print Patient's Name".

vii. Location of CDC protocol and CDC IRB-approved informed consent document: The CDC website for the CDC Expanded Access Tecovirmat Program for Monkeypox contains information and documents related to the program: Tecovirimat (TPOXX) IND Information (cdc.gov).

viii. Reduced Training Requirements for Clinicians and Supporting Program Staff: ORD has established a training slide set for healthcare providers participating in this expanded access program who have not previously completed human subjects training in human subjects protections. A certificate of completion is issued

that can be retained by the VA health provider and/or VA Facility's research office. This slide set is located on the ORD website for the CDC Expanded Access Tecorivimat Program for Monkeypox located at https://www.research.va.gov/programs/orppe/CDC-IRB-TPOXX-EAIND-Program.cfm.

ix. Investigator Conflict of Interest Forms: Treating clinicians/all individuals listed on the Form 1572 for this expanded access program **are not required to complete** the OGE 450-alt VA Research Financial Conflict of Interest Statement.

Summary of Revisions:

Topic	Summary of Revision	Date
2.0 Program Objective	Amended to better clarify patients with mpox who are eligible for tecovirimat treatment under the EA-IND protocol – those with severe immunocompromise, with active skin conditions, who are pregnant and/or lactating or children (< 18 years), and those with or are at high risk for protracted or life-threatening manifestations as defined in the protocol.	7-5-2024
	Text revision on early intervention in patients with mpox who are at high risk for protracted or life-threatening manifestations of mpox due to severe immunocompromising conditions through initiation of effective HIV antiretrovirals or delaying immunosuppressant treatments to optimize immune function and consideration for tecovirimat treatment in combination with additional therapeutics for mpox (e.g., IV cidofovir or oral brincidofovir (prodrug of cidofovir) and/or vaccinia immune globulin).	7-5-2024
1.0 Background and 10.2 Clinical Use of Tecovirimat	Text revisions to reflect updated information.	7-5-2024
Informed Consent Version 6.4	Informed Consent Form was revised to clarify oral tecovirimat availability for treatment of mpox through STOMP or EA-IND protocol, and tecovirimat use experience to da	7-5-2024
Attachment 2	Patient Intake Form and Clinical Outcome Form were revised to reflect the eligibility-related changes in the protocol.	7-5-2024
Created New Section 9: Changing Lead Clinician Provider/Principal Investigator	Included instructions from CDC Regulatory Affairs on procedures for changing Lead Clinician/Principal Investigator	7-12-2023

Topic	Summary of Revision	Date
Created New Section 10: Voluntary Closure Procedures:	Included instructions from CDC Regulatory Affairs on procedures for voluntary closure of the EAP by a VA Facility, including required notifications to the CDC Regulatory Affairs office.	7-12-2023
6. Privacy and Information Security Reviews	Updated to provide access instructions for central privacy and information security reviews for revised CDC protocol version 6.2.	11-9-2022
7. Informed Consent for VA Subjects	Updated to indicate that the VA ICF addendum is being deferred, but the information must still be provided to the patient or patient's legally authorized representative.	11-9-2022
9.v. Miscellaneous	Updated to provide updated instructions on how to access tools to use VA DocuSign, upcoming release of the VA iMED consents.	11-9-2022
9. Miscellaneous	Updated to provide information as to how VA participating facilities can access instructions on how to use VA DocuSign for this expanded access program on the ORD dedicated webpage for this program.	9-6-2022
7.Informed Consent for VA Subjects	As of 09-06-2022, the VA ICF addendum is not approved.	9-6-2022
3. Facility policies to use the CDC IRB	Note added to indicate that a copy of revisions in the CDC IRB SOP developed for VA Facilities will be sent by ORD to the individuals listed as contacts.	8-23-2022
6. Privacy and Information Security Reviews	Deleted section regarding obtaining central privacy officer and information security reviews prior to 07-22-2022 as it is no longer applicable.	8-23-2022
7.Informed Consent for VA Subjects	As of 08-23-2022, the VA ICF addendum is not approved.	8-23-2022
9. iii. Drug Procurement/VA Form 10-9012	No changes in drug procurement have occurred; no VA Form 10-9012 is required.	8-23-2022
9. iv. Consent mechanisms	As of 08-23-2022, DocuSign approval is pending.	8-23-2022
9. viii. Investigator Conflict of Interest Forms	Treating clinicians/all individuals listed on the Form FDA 1572 are not required to complete the OGE 450-alt VA form.	8-23-2022
3. Facility policies to use the CDC IRB	Revised prior statement to clarify that SOP for the VA Facility's use of the CDC IRB will be sent upon receipt of the signed concurrence form by ORD. Prior revision stated SOP would be sent when it is available.	8-5-2022
5. VA Research and Development Committee Approval	Clarified that R&D Committee must (not can) be done by either designated review or convened R&D review.	8-5-2022

Topic	Summary of Revision	Date
7. Informed Consent for VA Subjects	A waiver of documentation of informed consent (I.e., telephone consent with a written informed consent document approved by the CDC IRB that is signed and dated by the patient or patient's legally authorized representative) is not acceptable or approved by the CDC IRB.	8-5-2022
7. Informed Consent for VA Subjects	There is no requirement for a copy of the signed and dated patient's CDC-IRB approved informed consent to be sent to the CDC at the time of enrollment or to inform the CDC IRB.	8-5-2022
9. Miscellaneous	Added a VAIRRS section to include that both a cover sheet and IRB information sheet must be included and how to obtain a sample completed cover sheet and IRB information sheet from a VA Facility by emailing VHACOORDRegulatory@va.gov.	8-5-2022
9. Miscellaneous	Added a Drug Procurement section.	8-5-2022