

INSTITUTIONAL REVIEW BOARD (IRB)	
COMPASSTIONATE/TREATMENT USE POLICY	
Version:006	Effective Date: 02-Feb-2024

COMPASSTIONATE/TREATMENT USE

SECTION 1. Purpose

To specify the procedures for securing IRB approval for compassionate use/treatment use of investigational drugs, biologics and devices.

SECTION 2. Background

FDA regulations permit treatment use of unapproved drugs, biologics and devices outside the context of clinical trials for single or multiple patients under the provisions of its expanded access program. Expanded access is available when patients have a serious or life-threatening condition, an investigational agent or article may offer potential benefit that outweighs its risk, there is no satisfactory alternative to diagnose, monitor, or treat the condition, and enrollment in a clinical trial of the investigational agent or article is not possible. The FDA permits expanded access only if it will not impede the active pursuit of marketing approval by the sponsor.

The **treatment use provisions of the drug and biologic regulations** allow access to a drug or biologic when (1) it is undergoing clinical development, (2) it is withdrawn from marketing for safety reasons, but continues to have a favorable risk-benefit ratio for a specific patient population, (3) it is unapproved, but similar to an approved agent that is in short supply, or (4) it is approved for marketing but in short supply due to a risk evaluation and mitigation program. Under the expanded access provisions, investigational drugs and biologics can be made available for treatment purposes in individual patients, intermediate-sized patient groups, or widespread patient populations, depending on the current phase of clinical trials and/or accumulated evidence for their safety and efficacy.

There are two routes that physicians may use to access an investigational drug or biologic for treatment use. One is to secure the investigational agent under an expanded access protocol submitted to the FDA by the sponsor as a protocol amendment to its existing IND (treatment protocol). Alternatively, an individual physician may submit a new IND submission, which is separate from any existing IND and is intended only to make an investigational agent available for treatment use (treatment IND). For a treatment IND submitted by a physician for use of an investigational agent in a single patient, the FDA has created the short Form 3926, which can be used in lieu of the regular IND application Form 1571. While treatment use of an investigational drug or biologic normally requires

approval of the convened IRB, it may proceed with only the concurrence of the IRB chair when the physician checks the box on FDA Form 3926 that requests a waiver of full IRB review OR the physician includes a separate waiver request with FDA Form 1571.

The **treatment use provisions of the medical device regulations** allow access to an unapproved medical device during its clinical investigation or prior to final action on the marketing application for patients who would meet the inclusion criteria for a clinical trial, but are not otherwise able to participate in the study. The patient(s) must have a serious or life-threatening condition for which there is no satisfactory alternative treatment. In the case of a serious disease, an unapproved medical device can ordinarily be made available for treatment use after all clinical trials have been completed. In the case of an immediately life-threatening disease, an unapproved medical device can be made available prior to the completion of all clinical trials. The sponsor must be actively pursuing marketing approval. The treatment use may only occur after the FDA has approved a treatment IDE application from the sponsor of the investigational device. Treatment use of an unapproved medical device requires approval of the full Board and the informed consent of patients, as well as clearance from the institution in which the use will occur.

The **compassionate use provisions of the medical device regulations** allow access to an unapproved medical device being evaluated in a clinical trial under an investigational device exemption (IDE) when patients do NOT meet the inclusion criteria for the study. Access to an unapproved device may also be permitted even if an IDE does not exist. The device may be used in a single patient or in a small group of patients. The patient(s) must have a serious or life-threatening disease or condition for which there is no satisfactory alternative treatment. Prior FDA approval is needed before compassionate use occurs. If there is a currently approved IDE, the sponsor must submit an IDE supplement requesting FDA approval in order to treat the patient(s). This supplement must describe the patient's condition, the absence of satisfactory alternatives, and the patient protection measures that will be followed. When an IDE does not exist, similar information must be submitted by the physician or manufacturer of the device, along with a detailed description of the device. Compassionate use of an unapproved medical device requires the concurrence of the IRB chairperson and the informed consent of patients, as well as clearance from the institution in which the use will occur.

SECTION 3. Scope

This SOP applies to all investigators performing research under the auspices of the University of Tennessee Health Science Center IRB and its affiliated institutions.

Personnel responsible:

IRB administrative staff, IRB members, and investigators.

SECTION 4. Procedures

1. Treatment Use of an Unapproved Drug or Biologic

- a. The applicant must submit a *UTHSC IRB Form 1: Study/Project Application*, request treatment use of an unapproved drug or biologic in Section (418) and complete Section (1446).
- b. Identify the sponsor who holds the investigational new drug exemption (IND) for the drug or biologic and provide the IND number;
- c. For **multiple patient treatment use**, in Section (1446) of the *UTHSC IRB Form 1: Study/Project Application*, the applicant should include the following information:
 - i. The criteria for patient selection;
 - ii. The respects in which the patients have a serious or life threatening condition necessitating treatment with the drug or biologic;
 - iii. Why alternative therapies are unsatisfactory and why it is probable that the risk-benefit ratio of using the unapproved drug or biologic is better than available alternatives;
 - iv. The proposed daily dose, route, and frequency of administration of planned treatment; duration of planned treatment; criteria for discontinuation of treatment; and planned dose modifications for adverse events;
 - v. The planned monitoring for adverse events, response to treatment, and changes in clinical status, as well as proposed modification to treatment plan to mitigate risks to the patients, if appropriate; and
 - vi. A summary of the known risks of the drug or biologic.
- d. For **single patient treatment use**, in Section (1446) of the *UTHSC IRB Form 1: Study/Project Application*, the applicant should provide a thorough patient history and treatment plan, including the following information:
 - i. The key details of the patient's history, including diagnosis and summary of prior therapy (including response to such therapy) and information regarding a patient's relevant clinical characteristics (such as comorbid conditions and concomitant medications) that is necessary to assess the potential for increased risks of the drug;
 - ii. The respects in which the patient has a serious or life threatening condition necessitating treatment with the drug or biologic;
 - iii. Why alternative therapies are unsatisfactory and why it is probable that the risk-benefit ratio of using the unapproved drug or biologic is better than available alternatives;
 - iv. The proposed daily dose, route, and frequency of administration of planned treatment; duration of planned treatment; criteria for discontinuation of treatment; and planned dose modifications for adverse events, if appropriate;
 - v. The planned monitoring for adverse events, response to treatment, and changes in clinical status, as well as proposed modification to treatment plan to mitigate risks to the patient, if appropriate; and
 - vi. A summary of the known risks of the drug or biologic.
- e. The following documents must be attached to the application:
 - i. The formal protocol associated with the treatment use, if one is being used;

- ii. The treatment IND application submitted to the FDA if the treatment use is being sponsored by an individual physician;
 - iii. The notice from the FDA approving the treatment use;
 - iv. A statement of approval from the institutional site(s) where the drug or biologic will be administered;
 - v. The notice from the manufacturer agreeing to provide the drug or biologic; and
 - vi. An informed consent document prepared according to the UTHSC IRB consent form template for treatment use/compassionate use.
- f. The application will be reviewed by the full Board in accord with standard operating procedures (see SOP: UTHSC IRB Procedures for Full Board Review, and SOP: UTHSC IRB Criteria for IRB Approval of New Research Applications). However, if the physician selected the box on FDA Form 3926 (submitted for an individual patient expanded access IND in lieu of FDA Form 1571) that requests a waiver of full IRB review OR the physician included a separate waiver request with FDA Form 1571, then the treatment use of an unapproved drug or biologic may proceed with the concurrence of the IRB chairman (rather than approval of the full Board) once documentation of FDA approval of the waiver has been provided.

2. Treatment Use of an Unapproved Medical Device

- a. The applicant must submit a *UTHSC IRB Form 1: Study/Project Application*, request treatment use of an unapproved medical device in Section (418) and complete Section (1444).
- b. In Section (1444) of the *UTHSC IRB Form 1: Study/Project Application*, the applicant should:
 - i. Identify the sponsor who holds the investigational device exemption (IDE) for the device and provide the IDE number;
 - ii. Explain in what respects the patient(s) has (have) a serious or life-threatening condition necessitating treatment with the device;
 - iii. Explain why alternative therapies are unsatisfactory and why it is probable that the risk-benefit ratio of using the unapproved device is better than available alternatives; and
 - iv. Identify any significant ways in which the use of the device to treat the patient will differ from the manner in which it has been used in the approved protocol conducted under the primary IDE.
- c. The following documents must be attached to the application:
 - i. A written protocol describing the treatment use;;
 - ii. The treatment IDE application submitted to the FDA;
 - iii. The letter from the FDA approving the treatment IDE;
 - iv. A statement of approval from the institutional site(s) where the device will be administered; and
 - v. An informed consent document prepared according to the UTHSC IRB main consent form template.
- d. The application will be reviewed by the full Board in accord with standard operating procedures (see SOP: UTHSC IRB Procedures for Full Board Review, and SOP: UTHSC IRB Criteria for IRB Approval of New Research Applications).

3. **Compassionate Use of an Unapproved Medical Device**

- a. The applicant must submit a *UTHSC IRB Form 1: Study/Project Application*, request compassionate use of an unapproved device in Section (418) and complete Section (1442).
 - b. In Section (1442) of the *UTHSC IRB Form 1: Study/Project Application*, the applicant should:
 - i. Identify the sponsor of the device and, if the sponsor holds an investigational device exemption (IDE), provide the IDE number OR if there is no current IDE, this should be stated;
 - ii. Explain in what respects the patient(s) has (have) a serious or life-threatening condition necessitating treatment with the device;
 - iii. Explain why alternative therapies are unsatisfactory and why it is probable that the risk-benefit ratio of using the unapproved device is better than available alternatives;
 - iv. If the device has been used in an approved clinical protocol under an IDE, identify any significant ways in which the use of the device to treat the patient(s) will differ from the manner in which it is used in the clinical trial; and
 - v. Identify the uninvolved physician who will provide an assessment in writing that the use of the device in this (these) patient(s) involves the treatment of a serious or life-threatening disease or condition, that there is no satisfactory alternative treatment, and that the risk-benefit ratio of administering the device is better than available alternatives.
 - c. The following documents must be attached to the application:
 - i. The letter from the sponsor authorizing use of the device in the present case(s);
 - ii. A statement of approval from the institutional site where the device will be administered;
 - iii. The protocol for the clinical research study in which the device is currently being evaluated, if there is an existing IDE;
 - iv. An assessment from an uninvolved physician that use of the device in this (these) patient(s) involves treatment of a serious or life-threatening disease or condition, that there is no satisfactory alternative treatment, and that the risk-benefit ratio of administering the device is better than available alternatives;
 - v. The application that was submitted to the FDA seeking approval for compassionate use of the device in the present case(s);
 - vi. The letter from the FDA approving the compassionate use; and
 - vii. An informed consent document prepared according to the UTHSC IRB main consent form template.
 - d. The compassionate use of an unapproved medical device may proceed with the concurrence of the IRB chairman.
4. The IRB will review treatment use/compassionate use applications according to the criteria for IRB approval at 21 CFR 56.111.
 5. Any revisions in the approved treatment use or compassionate use must be reviewed and approved as required by IRB policy (see IRB SOP: UTHSC IRB Procedures for Full Board Review).

6. Any unanticipated problems, including serious adverse events or other problems involving risks to the patient or others, must be reported in the manner required by IRB policy (see IRB SOP: UTHSC IRB Reporting Unanticipated Problems, Including Adverse Events).
7. IRB approval for treatment use/compassionate use applies only to the patient(s) described in the application.

SECTION 5. Penalties/Disciplinary Action for Non-Compliance

See the UTHSC IRB policies regarding regulatory compliance

SECTION 6. Responsible Official & Additional Contacts

Subject Matter	Office Name	Telephone Number	Email/Web Address
Policy Clarification and Interpretation	UTHSC IRB	901.448.4824	irb@uthsc.edu
Policy Training	UTHSC IRB	901.448.4824	irb@uthsc.edu

SECTION 7. Policy History

Revision 4: 29-Mar-2022
Revision 3: 21-Jan-2019
Revision 2: 14-Sep-2018
Revision 1: 08-May-2015
Effective Date: 01-Aug-2010

SECTION 8. Related Policies/Guidance Documents

In accordance with:

21 CFR 312.300-320; 21 CFR 812.35(a) and 21 CFR 812.36

FDA Guidance on Expanded Access to Investigational Drugs for Treatment Use—Questions and Answers

<https://www.fda.gov/downloads/drugs/guidances/ucm351261.pdf>

Institutional Review Board (IRB) Review of Individual Patient Expanded Access Submissions for Investigational Drugs and Biological Products: Guidance for IRBs and Clinical Investigators

<https://www.fda.gov/media/171902/download>

FDA Guidance on Patient Expanded Access Applications: Form FDA 3926

<https://www.fda.gov/regulatory-information/search-fda-guidance-documents/individual-patient-expanded-access-applications-form-fda-3926>

FDA Form 3926

<https://www.fda.gov/downloads/aboutfda/reportsmanualsforms/forms/ucm504572.pdf>

FDA Guidance on Expanded Access for Medical Devices

<https://www.fda.gov/medical-devices/investigational-device-exemption-ide/expanded-access-medical-devices>

Compliance with this policy also requires compliance with state or local laws or regulations that provide additional protections for human subjects.

IRB SOP: UTHSC IRB Procedures for Full Board Review

IRB SOP: Criteria for IRB Approval of New Research Applications

IRB SOP: Informed Consent

IRB SOP: UTHSC IRB Reporting Unanticipated Problems, Including Adverse Events
