UNIVERSITY OF TENNESSEE HEALTH SCIENCE CENTER INSTITUTIONAL REVIEW BOARD COMPASSIONATE/TREATMENT USE OF DRUGS, BIOLOGICS AND DEVICES UNDER THE FDA EXPANDED ACCESS PROGRAM

I. PURPOSE

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

II. 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.

III. 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 an unapproved drug or biologic during its clinical investigation or prior to final action on the marketing application. The treatment use of an investigational drug or biologic may only occur if FDA has approved an investigational new drug exemption (IND). 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. Alternatively, an individual physician may submit a new IND submission, which is separate and distinct from any existing IND and is intended only to make an investigational agent available for treatment use.

For new IND applications submitted by physicians for treatment use of an investigational agent in single patients, 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 an IRB chair or designee 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 provision 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 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 an IRB chairperson or designee and the informed consent of patients, as well as clearance from the institution in which the use will occur.

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

FDA Guidance on Patient Expanded Access Applications: Form FDA 3926
https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm432717.pdf

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/medicaldevices/deviceregulationandguidance/howtomarketyourdevice/investigationaldeviceexemptionide/ucm051345.htm

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

IV. PROCEDURES

1. Treatment Use of an Unapproved Drug or Biologic

    a. The applicant must submit a Form 1 application and complete section 1446 requesting treatment use of an unapproved drug or biologic.
    b. In section 1446 of the Form 1 application, the applicant should:
        i. Identify the sponsor who holds the investigational new drug exemption (IND) for the drug or biologic and provide the IND number;
        ii. Explain in what respects the patient(s) have a serious or life threatening condition necessitating treatment with the drug or biologic;
        iii. Explain 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; and
        iv. Identify any significant ways in which the use of the drug or biologic to treat the patient will differ from the manner in which it is used in the approved protocol implemented under the primary IND.
    c. The following documents must be attached to the application:

i. The protocol for the clinical research study in which the drug or biologic is currently being or has been evaluated under the IND;
ii. The treatment IND application submitted to the FDA by the individual physician, or the protocol amendment to the existing IND submitted to the FDA by the sponsor;
iii. The letter from the FDA approving the treatment use;
iv. A statement of approval from the institutional site(s) where the drug 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). 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 an IRB chairman or designee (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 Form 1 application and complete section 1444 requesting treatment use of an unapproved medical device.
   b. In section 1444 of the Form 1 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) 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 is used in the approved protocol conducted under the primary IDE.
   c. The following documents must be attached to the application:
      i. The protocol for the clinical research study in which the device is currently being evaluated under the IDE;
      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 Form 1 application and complete section 1442 requesting compassionate use of an unapproved device.
   b. In section 1442 of the Form 1 application, the applicant should:
      i. Identify the sponsor who holds the investigational device exemption (IDE) for the device and provide the IDE number, if applicable;
      ii. Explain in what respects the patient(s) 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. 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 approved clinical protocol, if any; 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 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 any;
      iv. An assessment from an uninvolved physician that use of the device in this patient involves treatment of a serious disease or condition, that there is no satisfactory alternative treatment, and that the risk-benefit ratio of administering the device is better than available alternative;
      v. The letter that applicant will submit 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 an IRB chairman or designee.

4. 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).

5. Any unanticipated problems, including serious adverse events or other problems involving risks to patient or others, must be reported in the manner required by IRB policy (see IRB SOP: UTHSC IRB Reporting Unanticipated Problems, Including Adverse Events).

6. IRB approval for treatment use/compassionate use applies only to the patient(s) described in the application.