6.5 Expanded Access to Investigational Drugs and Devices for Treatment Use

1.0 Purpose

- 1.1. The purpose of this policy and procedure is to describe the requirements for utilization of an investigational drug or device (test article) for treatment use. This applies to expanded access for individuals or groups of patients with serious or immediately life-threatening diseases or conditions who lack therapeutic alternatives (compassionate use).
- 1.2. Emergency use of a test article on a human patient in a life-threatening or severely debilitating circumstance where no standard medically acceptable treatment is available and where there is not sufficient time to obtain IRB approval at a convened meeting is addressed in HRPP Policy 6.4 (Emergency Use of a Test Article).

2.0 Policy

- 2.1. It is the policy of the Organization that expanded access to investigational drugs and devices for individuals or groups of patients with serious or immediately life- threatening diseases or conditions who lack therapeutic alternatives (compassionate use) must be conducted in full compliance with the requirements of FDA regulations at 21 CFR 312 subpart I.

3.0 Definitions

- 3.1. Expanded Access: Expanded access refers to the treatment use of an investigational drug or device for patients with serious or immediately life-threatening diseases who lack therapeutic alternatives
  - 3.1.1. Expanded access may also refer to (1) use in situations when a drug has been withdrawn for safety reasons, but there exists a patient population for whom the benefits of the withdrawn drug continue to outweigh the risks; (2) use of a similar, but unapproved drug (e.g., foreign-approved drug product) to provide treatment during a drug shortage of the approved drug; (3) use of an approved drug where availability is limited by a risk evaluation and mitigation strategy (REMS) for diagnostic, monitoring, or treatment purposes, by patients who cannot obtain the drug under the REMS.
  - 3.1.2. The primary purpose of the expanded access use is to diagnose, monitor, or treat a patient’s disease or condition rather than to obtain the kind of information about the drug that is generally derived from clinical trials. The terms expanded access, treatment use, and compassionate use may be used interchangeably.
- 3.2. Immediately life-threatening disease or condition: a stage of disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.
- 3.3. Serious disease or condition: a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one (21 CFR 312.300(b)).
- 3.4. Intermediate size population: refers to a group of patients generally fewer than are treated under a typical treatment IND or protocol. FDA regulations do not impose specific numerical limitations for when an intermediate size patient population expanded access IND or protocol (as opposed to a treatment IND or protocol) may be appropriate.
- 3.5. Treatment IND/IDE: refers to a mechanism for providing eligible subjects with investigational drugs or devices for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. A treatment IND/IDE may be granted by FDA after sufficient data have been collected to show that the investigational drug or device may be effective and does not have unreasonable risks. Because data related to safety and side effects are collected, treatment IND/IDEs also serve to expand the body of knowledge about the article [21 CFR 312.34 and 21 CFR 812.36].

4.0 General Considerations

- 4.1. Except as described below, use of an investigational drug or device (test article) for treatment under expanded access requires review and approval by the convened IRB before treatment with the test article may begin (21 CFR 312.305(c)(4)).
- 4.2. Individual patient expanded access may proceed without IRB approval provided:
  - 4.2.1. The physician submitting an individual patient expanded access requests waiver of convened IRB review under 21 CFR 56.105 by checking box 10b on FDA form 3926; and
  - 4.2.2. The physician submitting an individual patient expanded access requests and obtains concurrence by the IRB chairperson or another designated IRB member before treatment use begins.
- 4.3. Expanded access to an investigational drug or device for treatment use requires informed consent as described in 21 CFR Part 50, unless one of the exceptions found in Part 50 applies.
- 4.4. Individual patient expanded access is generally limited to a single course of therapy for a specified duration (21 CFR 312.310(c)(1)). However, the FDA may authorize multiple courses of therapy or chronic therapy for individual patient expanded access, including authorizing individual patient expanded access to treat a chronic disease or condition that requires extended treatment (as reflected in 21 CFR 312.310(c)(1))
- 4.5. Emergency use of a test article as described in HRPP Policy 6.4 may proceed without IRB approval provided conditions described in that policy are satisfied.

5.0 Investigator procedures

- 5.1. Physicians intending to use an investigational drug or device for treatment of a single patient must:
  - 5.1.1. Determine that the probable risk to the patient from the investigational drug is not greater than the probable risk from the disease or condition (21 CFR 312.310(a)(1))
  - 5.1.2. Complete and submit to the IRB the Application for Single Patient Expanded Access thru RSS.
  - 5.1.3. Submit to the IRB a copy of the completed FDA Form 3926.
  - 5.1.4. Submit written permission from the holder of the IND or IDE to use the investigational drug or device.

    - 5.1.5. Submit consent form (and information sheet as appropriate) for use by single patient.
- 5.2. Protocols for expanded access for intermediate-size patient populations (21 CFR 312.315) and expanded access for widespread treatment use through a treatment IND or treatment protocol (21 CFR 312.320) must be submitted on the Biomedical Application thru RSS.
- 5.3. If the physician intending to use the test article submits the expanded access IND or protocol to the FDA he/she is considered a sponsor, and must comply with the responsibilities for sponsors set forth in 21 CFR 312.305(c)(5).

6.0. IRB / ORA procedures

- 6.1. When the ORA is contacted by a physician intending to use the test article for single patient expanded access, the IRB Analyst will instruct the treating physician to complete and submit the Single Patient Expanded Access application thru RSS and to contact the IRB Executive Chair/designee if additional information is required.
- 6.2. The IRB application for Single Patient Expanded Access must be reviewed and approved by the convened IRB except when the physician submitting an individual patient expanded access IND requests waiver of convened IRB review under 21 CFR 56.105 (by checking box 10b on FDA form 3926).
- 6.3. The Biomedical application for expanded access for an intermediate size population or for Treatment IND/IDE must be reviewed and approved by the convened IRB.
- 6.4. The convened IRB must review the application and request using the criteria described in 21 CFR 56.111. Recognizing that the purpose is treatment, the IRB should interpret the criteria appropriately. The board should:
    - 6.4.1. Consider whether the safety information is reasonable in relationship to the anticipated benefit from the treatment plan;
    - 6.4.2. Ensure risks are minimized to the extent possible in the proposed treatment plan;
    - 6.4.3. Determine that there are adequate provisions for ensuring the safety of the patient, including adequate monitoring and appropriate plans for collecting and reporting the data;
    - 6.4.4. Confirm that HIPAA requirements will be followed to ensure confidentiality of the medical record;
    - 6.4.5. Confirm that the treating physician will follow standard medical practice to protect the privacy interests of the patient;
    - 6.4.6. When the patient is likely to be vulnerable to coercion or undue influence additional safeguards are included in the treatment plan to protect the rights and welfare of the patient;
    - 6.4.7. When the patient is a child, confirm the provisions of 21 CFR 50.52 are met; and
    - 6.4.8. Review and approve an informed consent document and process that is appropriate to the treatment use (see section 7.2).

- 6.5. If a physician submitting an individual patient expanded access IND requests waiver of convened IRB review under 21 CFR 56.105 by checking box 10b on FDA form 3926, the IRB application for Single Patient Expanded Access Program application must be reviewed by the IRB Executive Chair or IRB Chair/VC or designee.
  - 6.5.1. The IRB Executive Chair or IRB Chair/VC or designee may determine concurrence utilizing the criteria described in section 6.4.
- 6.6. Expanded access protocols will undergo continuing review at intervals appropriate to the degree of risk, but not less than once per year.
  - 6.6.1. Individual Patient Expanded Access protocols which have undergone chair concurrence (in lieu of IRB review) may undergo continuing review by chair concurrence.
  - 6.6.2. Individual Patient Expanded Access protocols which were reviewed and approved by the convened IRB will undergo continuing review by the convened IRB, unless the protocol now satisfies criteria for expedited review (Category 8), in which case continuing review may be expedited.
  - 6.6.3. Intermediate Size Population Expanded Access or Treatment IND/IDE will undergo continuing review by the convened IRB, unless the protocol now satisfies criteria for expedited review (Category 8), in which case continuing review may be expedited.

7.0 Informed Consent

- 7.1. Written informed consent must be obtained from the patient or patient's legally authorized representative (LAR) in accordance with provisions of 21 CFR 50.25 and HRPP Policy 5.1 (Obtaining Informed Consent from Research Subjects).
- 7.2. Given the treatment nature of the use, consent documents should meet the requirements listed in 21 CFR 50.25, using plain language that is specifically aimed at "patients" who expect direct benefit, as opposed to "subjects" who may not expect direct benefit.
- 7.3. The ICF must include HIPAA required information and a clear disclosure of the financial obligations of the patient.

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