University of Kentucky Office of Research Integrity and Institutional Review Board Standard Operating Procedures			
Revision #4	**TITLE: Expanded Access Program (EAP)/ for Drugs**		**Page 1 of 5**
Approved By: ORI Director	Signature	Date	Date First Effective: 07-24-06
Approved By: Nonmedical IRB Chair	Signature	Date	
Approved By: Medical IRB Chair	Signature	Date	Revision Date: 08-05-20

OBJECTIVE

To describe the procedures for utilizing the Food and Drug Administration (FDA) Expanded Access Program (EAP) including individual patient and intermediate or large population treatment investigational new drug (IND) applications

GENERAL DESCRIPTION

Definitions

Expanded Access (sometimes called Compassionate Use) is a mechanism to facilitate availability of investigational drugs (as early in the drug development process as possible) for patients with serious or immediately life-threatening diseases or conditions for which there are no satisfactory alternative treatments.

For the purpose of expanded access to investigational drugs for treatment use, *immediately life-threatening disease or condition* means 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. A *serious disease* or condition means 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.

A *treatment IND* is a large scale expanded access program typically following resolution of phase III or during phase II where sufficient safety data is available.

Emergency Use is defined as the use of a test article (e.g., investigational drug, biologic, or device) in a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval. See the Emergency Use: Single Subject SOP.

General Requirements

The FDA will permit an investigational drug to be used under the EAP for the treatment of a serious or life-threatening disease or condition When all of the following apply:

- There is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition;
- Patient enrollment in a clinical trial is not possible;
- Potential patient benefit justifies the potential risks of treatment; and
- Providing the investigational medical product will not interfere with investigational trials that could support a medical product's development or marketing approval for the treatment indication.

Expanded access requires prospective review by the IRB and informed consent/authorization from the patient or Legally Authorized Representative (LAR).

The FDA describes three distinct categories of EAP based on the number of people who need access and the level of risk. An expanded access IND submission is required for each type of expanded access.

1. Individual patient IND, including emergency use IND (21 CFR 312.310) commonly held by the treating physician or investigator for treatment of an individual patient.

2. Intermediate population treatment IND (21 CFR 312.315) commonly held by the sponsor (manufacturer) for use in a population smaller than a typical treatment IND or treatment protocol. The investigational drug for intermediate population treatment INDs may be in active development or may be an FDA approved drug that is unavailable or in limited supply.

3. Large population treatment IND or treatment protocol (21 CFR 312.320) commonly held by the sponsor for widespread treatment use. For a large population treatment IND, the sponsor must be pursuing marketing approval.

Before submitting an individual patient IND to the FDA, a physician or PI must confirm that the manufacturer will provide the drug. If a manufacturer has an existing EAP IND available, the PI may coordinate access to the drug through the manufacturer's approved IND rather than filing a separate individual patient IND.

FDA developed Form 3926 specifically for physicians requesting an expanded access IND for an individual patient. The form includes an option to request FDA waive the requirement review by the convened IRB, permitting expedited review.

FDA policy specifies that "the provision for emergency use would rarely apply to a treatment protocol or treatment IND because these are planned uses of the test article and sufficient time is available to obtain IRB review and approval." In rare cases in which emergency use does apply for individual patients, administration takes place according to emergency use federal regulations (21 CFR 56.104) following procedures in the Emergency Use: Single Subject SOP.

The FDA identifies special considerations when a patient is to be treated under an EAP:

- Drug Development: In considering EAP use, individual needs must be balanced against societal needs. The FDA stipulates that expanded access use should not compromise enrollment or interfere with active clinical investigations that could support approval of the drug.

- Informed Consent/HIPAA Authorization: Informed consent is especially important in expanded access use situations because the subjects are desperately ill and particularly vulnerable. They will receive medications which have not been proven either safe or effective in a clinical setting. Both the setting and their desperation may work against their ability to make an informed assessment of the risk involved. Therefore, the PI must ensure that potential subjects are fully aware of the risks involved in participation.

- Charging for Treatment INDs: The FDA permits charging for the drug, agent, or biologic when used in an EAP when regulatory criteria are met. Therefore, the IRB must pay particular attention to EAPs in which the subjects will be charged for the cost of the drugs. If subjects will be charged for use of the test article, economically disadvantaged persons may inadvertently be excluded from participation. Charging for participation may preclude economically disadvantaged persons as a class from receiving access to test articles. The IRB must balance this interest against the possibility that it will not be available for treatment use until it receives full FDA approval unless the sponsor can charge for the drug.

- Regulatory Responsibilities: Per the FDA, a licensed physician under whose immediate direction an investigational drug is administered for expanded access use is considered an investigator assuming all applicable regulatory responsibilities. An individual who submits an IND for expanded access use is considered a *sponsor-investigator*, and assume applicable responsibilities for sponsors and investigators (21 CFR 312.305 (c)).

RESPONSIBILITY

Execution of SOP: IRB Chair, IRB Vice Chair, IRB Members, Office of Research Integrity (ORI) Staff, Principal Investigator (PI)/Study Personnel, Physician

PROCEDURES

Individual Patient IND

1. The physician or PI submits the following individual patient expanded access:
   - a completed IRB application with the phrase "INDIVIDUAL PATIENT IND" in the title;
   - a copy of the FDA Form 3936 (for individual patient requests);
   - an individual patient IND approval letter from the FDA;
   - an investigator's brochure, if applicable;
   - a description of patient situation and treatment plan adequate to assess whether risks have been minimized and are reasonable in relation to anticipated benefits; and
   - a copy of the informed consent/authorization form which includes the statement indicating that although the primary use of the drug is for treatment, the drug is investigational, and FDA has not determined it is safe or effective for the condition of treatment.

2. ORI staff screen the IRB submission and verify the IND number according to procedures described in the Initial Full Review SOP.

3. If the IND was requested using the Form 1571 or the waiver option on Form 3936 was not checked, the ORI schedule the submission for convened review as outlined in the Initial Full Review SOP.

4. If the IND was requested using Form 3936 and the waiver option was checked, the ORI send for review by the IRB Chair or designee as outlined in the Initial Expedited Review SOP.

5. At the conclusion of treatment, the physician or PI reports a written summary of the results of the expanded access use to the IND sponsor or the FDA and any safety related information or problems encountered to the IRB and IND sponsor or FDA (as applicable).

Central IRB Approval

1. In cases where the expanded access protocol has received central IRB approval, UK may defer responsibility for IRB review of the individual patient use to the central IRB where appropriate agreements and required approvals are obtained consistent with the IRB Reliance SOP.

Individual Patient IND in an Emergency Situation

1. In rare cases in which an emergency requires that the patient be treated before a written IND submission can be made, the PI obtains authorization for individual use from the FDA by telephone or electronic communication with subsequent submission of IND paperwork (21 CFR 312.310).

2. The PI follows procedures described in the Emergency Use SOP, submitting emergency use information directly to the IRB Chair.

3. The IRB Chair, ORI staff, and the convened IRB follow review procedures as described in the Emergency Use SOP.

Intermediate or Large Population Treatment IND

1. The PI follows procedures described in the Initial Full Review SOP with the following additions and provisions:
    - inclusion of the phrase "TREATMENT IND" in the title;
    - documentation of FDA treatment IND approval (i.e., correspondence from the FDA or commercial sponsor, IND number printed on sponsor protocol); and
    - related materials including the treatment protocol, investigator's brochure, informed consent/authorization form, and potential investigational drug costs.

2. ORI staff screen the IRB submission following procedures described in the Initial Full Review SOP.

3. The convened IRB reviews the protocol as outlined in the Initial Full Review SOP and according to federal regulations.

4. At the conclusion of treatment, the physician or PI reports a written summary of the results of the expanded access use (including any safety related information) to the IND sponsor or the FDA and submits a copy to the IRB.

REFERENCES

21 CFR 312.300
Form FDA 3926 Instructions