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 that facilitates availability of investigational drugs (as early in the drug development process as possible) for patients with serious or immediately life-threatening disease or conditions for which there are no satisfactory alternative treatments.

The FDA defines an immediately life-threatening disease as a stage of a disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.

A Serious disease means a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity is not usually sufficient, but the morbidity needs not be irreversible, provided it persists or recurs.

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

General Requirements

The FDA permits investigational drug’s use under the expanded access program (EAP) after sufficient data collection shows that the drug “may be effective” or does not have unreasonable risks relative to the risk of the condition of treatment.

FDA describes three distinct categories of EAP based on the number of people who need access and the level of risk. Each type of expanded access requires an expanded access IND submission.
1. Individual patient IND, including emergency use IND (21 CFR 312.310) is commonly held by a treating physician or an investigator for treatment of an individual patient.

2. Intermediate population treatment IND (21 CFR 312.315) is 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) is commonly held by the sponsor for widespread treatment use. For a large population treatment INDs, the sponsor must pursue marketing approval.

Before submitting an Individual Patient IND to FDA, a physician or PI confirms that the manufacturer provides the drug. If a large or intermediate scale EAP is available through the manufacturer, the PI coordinates access to the drug through the manufacturer’s approved Treatment IND rather than filing a separate Individual Patient IND.

FDA regulations require prospective review by the IRB Chair or an appropriate IRB member.

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 applies for individual patients, administration takes place according to emergency use federal regulations (21 CFR 56.104) following procedures in the Emergency Use SOP.

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

- **Drug Development:** In considering EAP use, individual needs weigh against societal needs. The FDA stipulates that expanded access use does not compromise enrollment or interferes with active clinical investigations that supports approval of the drug.

- **Informed Consent:** Informed consent is crucial in expanded access use situations because the subjects are desperately ill and particularly vulnerable. Subjects in EAPs receive medications which have not been proven either safe or effective in a clinical setting. Subjects’ desperation and the setting they are in may work against their ability to make an informed assessment of the risk involved. Therefore, the PI ensures that potential subjects are fully aware of the risks involved in the 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. Economically disadvantaged persons are impedied from receiving access to test articles if they are charged for the use of the test article. The IRB balances this interest against the
possibility that unless the sponsor can charge for the drug, it will not be available for treatment use until it receives full FDA approval.

- Regulatory Responsibilities: Per FDA a licensed physician under whose immediate direction an investigational drug is administered for an expanded access use is considered an investigator assuming applicable regulatory responsibilities. An individual who submits an IND for expanded access use, is considered a sponsor-investigator, assuming 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 for review by the IRB Chair or an appropriate IRB member:
   - required IRB Expanded Access Information;
   - individual patient IND approval letter from FDA;
   - investigator’s brochure if applicable;
   - brief description of patient situation and treatment plan; and
   - copy of the informed consent form.

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

3. The IRB Chair or appropriate IRB member reviews the submission 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 summary of the results of the expanded access use, including any safety related information, to the IND sponsor or FDA and the IRB.

*Individual Patient IND with Central IRB Approval*

1. When 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 ORI policy and procedures.
Individual Patient IND in an Emergency Situation

1. When the emergency requires that the patient be treated before an IND submission can be made, the PI obtains authorization for individual use from FDA by telephone or electronic communication with subsequent submission of IND filing (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 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:
   - check that study is being conducted under FDA's Expanded Access Program (e.g., Treatment IND) in the drug section of the IRB application;
   - documentation of FDA treatment IND approval (i.e., correspondence from FDA or commercial sponsor, IND number printed on sponsor protocol); and
   - related materials including the treatment protocol, investigator’s brochure, informed consent form, and potential investigational drug costs.

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

3. The full 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 summary of the results of the expanded access use, including any safety related information, to the IND sponsor or FDA and the IRB.

REFERENCES
21 CFR 312.300
21 CFR 312.8