Guidance -
Expanded Access Program (EAP) for Drugs

The FDA allows investigational drugs to be used under the expanded access program (EAP) after sufficient data have been collected to show 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. 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 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 INDs, the sponsor must be pursuing marketing approval.

Before submitting an Individual Patient IND to FDA, a physician or PI must confirm the manufacturer will provide the drug. If a large or intermediate scale EAP is available through the manufacture, the PI may coordinate 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 full convened IRB.

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).

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**: 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 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. 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 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).

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 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 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.

	Prior Convened IRB Review and Approval		Comments
	Yes	**No**	
Individual Patient IND	X		
Individual Patient IND in an Emergency Situation		X	PI obtains authorization for individual use from FDA by telephone or electronic communication with subsequent submission of IND
Intermediate or Large Population Treatment IND	X		

REFERENCES

21 CFR 312.300
21 CFR 312.8