

Expanded Access Guidance Document

The Food and Drug Administration's (FDA) Expanded Access Program (EAP) provides provisions for the treatment of patients with medical products (drugs, biologics, or medical devices) that are investigational (not FDA approved) outside of a clinical trial. Expanded Access may also be referred to as compassionate use or treatment use. The treatment with investigational drugs or devices is not considered a clinical investigation (research). Even so, both **FDA submission and IRB review are required**. The criteria for Expanded Access are largely determined by (1) the seriousness of a patient's condition, (2) other available FDA-approved treatment options, (3) patient population size needing treatment, and (4) drug status.

Expanded Access to Investigational Drugs for Treatment Use

Requirements for all expanded access uses (21 CFR 312.305):

1. Patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition;
2. The potential patient benefit justifies the potential risks of the treatment use and those potential risks are not unreasonable in the context of the disease or condition to be treated; and
3. Providing the investigational drug for the requested use will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use.

Types of Expanded Access

There are four categories of Expanded Access and each have different qualifying criteria (in addition to those listed above) and will follow different regulatory pathways to get started.

- 1. Single patient, emergency use (21 CFR 312.310)**
 - a. The patient must be in an immediately life-threatening situation.
 - b. The patient cannot obtain the drug under an existing IND or protocol.
 - c. There is not sufficient time to obtain IRB approval. (21 CFR 56.102(d))
- 2. Single patient, non-emergency use (21 CFR 312.310)**
 - a. The patient has a serious condition and *is not* in an immediately life-threatening situation.
 - b. The patient cannot obtain the drug under an existing IND or protocol.

- 3. Intermediate-size patient population (Expanded Access IND or Protocol) (21 CFR 312.315)**
 - a. The investigational use of a drug for the treatment of a patient population smaller than that typical of a treatment IND or treatment protocol
 - b. FDA may ask a sponsor to consolidate expanded access under this section when the agency has received a significant number of requests for individual patient expanded access to an investigational drug for the same use.

- 4. Large patient population (Treatment IND or Treatment Protocol) (21 CFR 312.320)**
 - a. Investigational drug to be used for widespread treatment use.
 - b. Trial Status:
 - i. The drug is being investigated in a controlled clinical trial under an IND designed to support a marketing application for the expanded access use, **or**
 - ii. All clinical trials have been completed.
 - c. Marketing Status:
 - i. The sponsor is actively pursuing marketing approval of the drug for the expanded access use with due diligence.
 - d. Evidence:
 - i. When the expanded access use is for a serious disease or condition, there is sufficient clinical evidence of safety and effectiveness to support the expanded access use. Such evidence would ordinarily consist of data from phase 3 trials, but could consist of compelling data from completed phase 2 trials, **or**
 - ii. When the expanded access use is for an immediately life-threatening disease or condition, the available scientific evidence, taken as a whole, provides a reasonable basis to conclude that the investigational drug may be effective for the expanded access use and would not expose patients to an unreasonable and significant risk of illness or injury. This evidence would ordinarily consist of clinical data from phase 3 or phase 2 trials, but could be based on more preliminary clinical evidence.

Types of Regulatory Submission for Expanded Access

- Expanded access protocol submitted as a protocol amendment to an existing IND (i.e., an expanded access protocol), or
- New IND submission, which is separate and distinct from any existing INDs and is intended only to make a drug available for treatment use (i.e., an expanded access IND).

Why

Why Do I Have to Request Approval from the FDA and IRB to Treat My Patient(s) with an Investigational Drug?

Investigational Drugs are not yet approved by the FDA. Approval to treat with them under the EAP is required by FDA Regulations.

*Failure to comply may result in termination of EAP, Warning Letters (posted on FDA website), Disqualifications/ Restrictions/ Debarments (posted on FDA website), criminal prosecutions, prison, and/or fines.

How

1. Determine which expanded access pathway you will be using:
 - a. Evaluate the seriousness of the patient(s)' condition using the FDA criteria outlined above
 - b. Determine the patient population size that requires treatment use and evaluate the drug status using the FDA's criteria
 - c. Determine if the Expanded Access requires a new IND or can be amended to an existing IND
2. Submit to the FDA
 - a. For assistance with Single Patient and Non-Emergency Use, contact IRB@ttuhsc.edu.
 - b. For assistance with Intermediate and Large Patient Population, contact IRB@ttuhsc.edu.
3. Submit for IRB review
 - a. Single Patient Emergency and Non-Emergency - obtain IRB chair concurrence by contacting IRB@ttuhsc.edu.
 - b. Intermediate and Large Patient Population - submit the application in eIRB for full IRB approval.
4. After initiating the treatment, ensure that all case histories and adverse events are properly recorded and reported

<https://www.fda.gov/news-events/expanded-access/expanded-access-how-submit-request-forms>

<https://www.fda.gov/medical-devices/investigational-device-exemption-ide/expanded-access-medical-devices>