Expanded Access of a Test Article – (Includes Emergent Use)

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Background:

Expanded access, sometimes called "compassionate use," is the use of an investigational medical product (e.g. one that has not been approved by FDA) outside of a clinical trial. Wherever possible, use of an investigational medical product by a patient as part of a clinical trial is preferable because clinical trials can generate data that may lead to the approval of products and, consequently, to wider availability. However, when patient enrollment in a clinical trial is not possible (e.g., a patient is not eligible for any ongoing clinical trials, or there are no ongoing clinical trials), patients may be able to receive the product, when appropriate, through expanded access.

http://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm

Q: What is the purpose of the Expanded Access program?

The Expanded Access program (EAP) is for the use of an investigational drug, device or biologic to treat a patient with a serious disease or condition who does not have comparable or satisfactory alternative therapies to treat the disease or condition. Contrast with investigational drug in a clinical trial where the primary intent is research (systematic collection of data with the intent to analyze it to learn about the drug). EAP’s:

- Can provide access to patients with serious/life-threatening diseases who have no other alternatives, and may accept greater risks
- Can provide patients a measure of autonomy over their own health care decision
- Can help bridge the gap between the latter stages of product development and approval by making a drug widely available during that period
- Can help foster development of additional uses of a drug (e.g., from anecdotal evidence of benefit in a disease other than that being studied)
- May offer hope for patients with no other available options

Note, however, DHHS regulations do not permit data obtained from patients to be classified as human subjects research, nor permit the outcome of such care to be included in any report of a research activity subject to DHHS regulations.

Q: What types of Expanded Access use are available?

The categories are based on the proposed number of patients to be treated and the nature of the urgency to treat. These categories are:

- Emergent Use
- Single Patient IND
- Intermediate-size patient populations (n>1)
- Larger populations for use of the drug under a treatment protocol or treatment IND application
Q: How is the need for an Emergent Use determined?

The UF IRB may allow for “emergency treatment use” of a test article with an IND or IDE in accordance with FDA regulations. See FDA Information Sheet updated 2011 - "Emergency Use of an Investigational Drug or Biologic"

- For drugs, the situation must meet the definition of Life-threatening, for the purposes of section 56.102(d), which includes the scope of both life-threatening and severely debilitating, as defined below:
  - **Life-threatening** means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.
  - **Severely debilitating** means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

- For devices, in the case of serious disease, a device may ordinarily be made available for treatment use after all clinical trials are completed; in the case of an immediately life-threatening condition, the device may be made available before completion of clinical trials (21 CFR 812.36).

Q: Is prior approval for the emergent use of a test article needed from the IRB?

**Maybe.** Although a clinician may use an unapproved treatment/article (drug, device or other) prior to obtaining IRB approval, sometimes the manufacturer of the test article requires something in writing that the local IRB is aware of the emergent use prior to the manufacture providing the test article. If this is the case, the physician involved in using the emergent test article must submit, in writing or email, to the IRB chair, a de-identified description of the patient’s situation and how that situation meets the definitions above. Assuming the Chair agrees, a signed template letter will be provided to the physician involved that confirms the Chair acknowledges that the criteria for an emergent use has been met.

Q: What does the physician involved have to do in order to obtain the test article for Emergent Use?

- Check with manufacturer to see if patient can be treated under company’s IND
- Call the FDA 24/7 hotline, an Emergency IND can be obtained over the phone.

Q: Is patient or legally authorized representative (LAR) consent required when administering a test article under an Emergent Use?

Yes.

- Consent will be obtained in accordance with FDA regulations, or the circumstances meet the exception to the requirement for consent in FDA regulations.
- If the research involves an investigational drug, the FDA has issued an IND. (see comment on left column)
• Informed consent is not required because all of the following are true:
  • Before the use of the test article both the investigator and a physician who is not otherwise participating in the clinical investigation certified in writing.
  • Informed consent is not required because all of the following are true:
    o Immediate use of the test article is, in the investigator's opinion, required to preserve the life of the subject.
    o Time is not sufficient to obtain the independent determination a physician who is not otherwise participating in the clinical investigation.
    o Before the use of the test article the investigator will certify in writing.

A consent provided by the manufacture can be used. If one does not exist, then the IRB has a template consent for Emergent Use that can be completed by the physician involved, and provided to the patient or LAR for signature.

If the patient is unable to consent, and there is no appropriate LAR available, then the treating physician must consult a suitable physician, not involved with this patient, and document in writing that they agree the patient’s condition is consistent with the definitions for Emergent Use.

Q: Once the test article is administered under an Emergent Use, is there anything else the physician involved must provide to the IRB?

Yes. The clinician must submit the IRB’s Emergency Use paperwork within 5 days of using the unapproved article.

Q: How many times can the same test article be used in an institution under the Emergent Use exclusion?

The regulations indicate that each institution may only use an article emergently once. Regulations indicate that researchers at the institution must obtain IRB approval prior to any subsequent uses of the article.

Q: What are the requirements for “compassionate use” of FDA test articles in clinical care situations?

“Compassionate use” is not an official FDA term. Compassionate use generally implies the use of non-FDA approved test articles for a single patient or a small group of seriously ill patients, where no other available treatments are satisfactory.


This is sometimes called an “Expanded Access IND.” It is typically used for treatment only, in a small population of patients that may meet one or more of these criteria:

• The investigational drug (ID) is not being developed
• Patient doesn’t meet the criteria for clinical trial with ID
• The drug is no longer marketed
• Same drug as one that is approved, but unavailable (drug shortage)
Q: What is the IRB approval process for an “Intermediate-size patient population” expanded access?

Such a protocol must be submitted to the IRB in the usual fashion, there is nothing different.

Q: What constitutes “Larger patient population” Expanded Access?

This is sometimes called a “Treatment IND.” It is typically used for treatment only, in a larger population of patients that may meet one or more of these criteria:

- The drug is intended to treat or diagnose serious or life-threatening condition
- No satisfactory alternative is available
- Controlled clinical trials are not in progress under an IND
- When trials are completed & FDA review of request to market is pending
- Sponsor is actively pursuing device marketing approval with FDA

Q: What is the IRB approval process for an “Intermediate-size patient population” Expanded Access?

Such a protocol must be submitted to the IRB in the usual fashion, there is nothing different.