

UNIVERSITY OF KENTUCKY (UK) OFFICE OF RESEARCH INTEGRITY (ORI) GUIDANCE FDA EMERGENCY AND EARLY/EXPANDED ACCESS PROGRAM FOR DRUGS AND DEVICES

I. FDA Emergency Use of FDA Regulated Test Articles (Drug/Device/Biologic)



Emergency

Under the Food and Drug Administration (FDA) [regulations](#), "emergency use" is defined as the use of a test article (e.g. investigational drug, biologic, or device) on a human subject in a life-threatening or severely debilitating situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain Institutional Review Board (IRB) approval.

Although the FDA may exempt the requirement for prospective review by the full IRB in emergency use cases, it is the policy of the University of Kentucky Medical IRB that in these situations prior review by the IRB Chair or designee is required.

Unless the healthcare provider determines that immediate use of the test article is required to preserve a patient's life, the UK IRB requires confirmation that the article meets the FDA emergency use criteria by the IRB Chair or designee. The provider or Principal Investigator (PI) provides the following information directly to the IRB Chair:

1. Required Emergency Use information with an explanation which justifies administration of the test article.
2. A copy of the informed consent form.

The IRB Chair forwards the request and his/her response to the Office of Research Integrity (ORI). The ORI adds the use request as committee business to the next applicable agenda for full review by the convened IRB. This notification also initiates tracking to ensure the PI submits a report of the use within the five working day time frame required by FDA regulation [\[21 CFR 56.104\(c\)\]](#).

Informed consent from the individual or the legally authorized representative is required. The only exception to this policy requires a corroborative evaluation by an independent physician as described in the Emergency Use Standard Operating Procedure (SOP) and FDA regulations [\[21 CFR 50.23\(a\)\]](#). See the Emergency Use SOP for required elements.

In accord with federal regulations, any subsequent use of the test article in another subject should first receive full IRB review.



See the [Emergency Use SOP](#) for detailed IRB submission and review procedures.

II. EARLY/EXPANDED ACCESS PROGRAM FOR DRUGS



Compassionate and Treatment Use

The [FDA Expanded Access Program \(EAP\)](#) allows for compassionate use for treatment purposes in patients with serious diseases or conditions when there are no comparable or satisfactory alternative therapies to diagnose, monitor or treat the patient's disease or condition and the sponsor or manufacturer agrees to provide the drug for treatment purposes. Expanded Access may not be used in any way that might threaten the integrity or validity of the research that is being conducted at the same time on the drug in question.

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. The submission may be a new IND or a protocol amendment to an existing IND.

Under the 2017 final EAP rule, expanded access to investigational drugs for treatment use will be available to:

- **Individual Patient IND**, including **Emergency Use IND** [21 CFR 312.310] - commonly held by treating physician or investigator for treatment of an individual patient. See [FDA Individual Patient Expanded Access Application Instructions](#). FDA developed [Form FDA 3926](#) specifically for Individual Patient IND request. The two-page form is streamlined with specific information to facilitate the access. Check item **10B, Request for Authorization to Use Alternative IRB Review** to request concurrence by the IRB chairperson or by a designated IRB member, before the treatment use begins. Instructions for completing FDA 3926 are available on Part 3 of the [FDA Expanded Access Video series](#).
- **Intermediate Population Treatment IND** [21 CFR 312.315] – commonly held by the sponsor (manufacturer) for use in population smaller than typical of treatment IND or treatment protocol. See [FDA Intermediate Population Expanded Access Application Instructions](#). 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.
- **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.

General Criteria for all three EAP types:

- The patient or patients to be treated 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;
- 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
- 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.

Additional Criteria for Individual Patient Access:

- The probable risk to the person from the investigational drug is not greater than the probable risk from the disease or condition; and
- There is no opportunity for patient to gain access to drug through a clinical trial or large or intermediate scale EAPs offered through the sponsor/manufacturer.

IRB Review Requirements

After FDA approval of the IND, a sponsor may ship drug to the treating physician or investigator, however IRB approval must be obtained prior to administration of the drug.

IRB approval for EAP for an individual patient requires IRB approval from the IRB Chair or an appropriate IRB member. Contact ORI for assistance. In cases where a drug is made available for an individual patient through a manufacturer's expanded access program which has approval from a central IRB, UK may, on a case-by-case basis, coordinate with or defer IRB review consistent with the off-site SOP.

If the PI is seeking approval for an expanded access protocol involving an intermediate or large treatment population, then the protocol must receive full review (i.e., be reviewed at a convened meeting with a quorum present). The PI submits a standard IRB application and indicates on the drug section that the study is being conducted under FDA's Expanded Access Program.

The investigator submits a full review application to the IRB. The IRB review information about the treatment plan, IND approval letter from FDA, the informed consent/HIPAA authorization form, subject/patient costs, and investigator's brochure.

While most EAP's involve planned use, the FDA regulations allow (via electronic communication) authorization of an Emergency Use IND as described in 312.310(d). Emergency use IND may apply when need is clinically assessed as urgent and patient may suffer irreversible morbidity or mortality if not treated immediately. In rare cases in which emergency use does apply for individual patients, administration takes place according to emergency use as described above.

⇒ FDA's instructions for [Physician Request for an Individual Patient IND under Expanded Access for Non-emergency or Emergency Use](#).

⇒ See the [Expanded Access Program/Treatment IND SOP](#) IRB submission and detailed review procedures.

Additional summary points from the 2017 final EAP rule:

1. Before submitting an Individual Patient IND to FDA, a physician investigator should confirm the manufacturer will provide the drug. If a large or intermediate scale EAP is available through the manufacture, the physician may coordinate access to the drug through the manufacturer's approved Treatment IND rather than filing a separate Individual Patient IND. If FDA receives a significant number of requests for individual patient INDs for the same use, the agency may request the sponsor consolidate into a large or intermediate scale EAP.
2. An expanded access IND goes into effect 30 days after FDA receives the IND or on earlier notification by FDA that the expanded access use may begin.
3. 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 \(c\)\]](#).
4. EAP training is available to investigators and physicians with limited or no experience with investigational drugs to ensure regulatory compliance and patient safety.
 - [FDA Expanded Access Programs Presentation](#)
5. With prior approval from the FDA, manufacturers may charge for all three types of expanded access INDs. Only the direct costs of the drug plus the cost of administering the expanded access program can be recovered. Specific criteria are detailed in the FDA final charging rule, [Charging for Investigational Drugs](#).



III. EARLY/EXPANDED ACCESS PROGRAM FOR MEDICAL DEVICES

The [FDA Early/Expanded Access website](#) describes circumstances under which a healthcare provider may wish to use an unapproved device to save a life or help a patient suffering from a serious disease or condition.

A. Compassionate Use (single patient /small group)

Compassionate use provision allows access for patients who do not meet the requirements for inclusion in a clinical investigation but for whom the treating physician believes the device may provide a benefit in treating and/or diagnosing their disease or condition. This provision is typically approved for individual patients but may be approved to treat a small group.

Criteria:

- Serious disease or condition
- No alternative

Prior FDA approval is needed before compassionate use occurs. In order to obtain FDA approval, the sponsor submits an IDE supplement requesting approval for a protocol deviation under section [\[21 CFR 812.36\]](#) in order to treat the patient.

Compassionate use criteria and procedures can also be applied when a physician wishes to treat a few patients rather than an individual patient suffering from a serious disease or condition for which no alternative therapy adequately meets their medical need.

The physician should not treat the patient identified in the supplement until FDA approves use of the device under the proposed circumstances. An FDA approved compassionate use of a device may proceed with concurrence from the IRB chair or his/her designee.

Treating physicians must monitor patient(s) receiving compassionate use devices and submit a detailed summary of the results of the use, including any safety related information, to the IDE sponsor or FDA and the IRB.

B. Treatment Use IDE

Treatment Use IDE may occur during the clinical trial or prior to final action on the marketing application in cases where it is appropriate to use the device in the treatment of patients not in the trial under the provisions of the treatment investigational device exemptions (IDE) regulation.

Criteria:

- Life-threatening or serious disease
- No alternative
- Controlled clinical trial
- Sponsor pursuing marketing approval

In the case of a serious disease, a device ordinarily may be made available for treatment use under this section after all clinical trials have been completed. In the case of an immediately life-threatening disease, a device may be made available for treatment use under this section prior to the completion of all clinical trials.

An approved IDE specifies the maximum number of clinical sites and the maximum number of human subjects that may be enrolled in the study. During the course of the clinical trial, if the data suggests

that the device is effective, then the trial may be expanded to include additional patients with life-threatening or serious diseases.

Treatment use of an investigational device is conditioned upon the sponsor and investigators complying with the safeguards of the IDE process and the regulations governing informed consent/HIPAA authorization (21 CFR 50) and IRB review (21 CFR 56). The full IRB reviews the protocol using the same procedures as regular, full IDE protocols.

The sponsor of a treatment IDE must submit progress reports on a semi-annual basis to all reviewing IRB's and FDA until the filing of a marketing application. The progress report must also include the number of patients treated with the device under the treatment IDE, the names of the investigators participating in the treatment IDE, and a brief description of the sponsor's efforts to pursue marketing approval/ clearance of the device.

The sponsor of a treatment IDE is responsible for submitting all other reports required under 21 CFR 812.150, such as unanticipated adverse device effects and final reports. The reports are submitted as supplements to the original IDE application.



See the [Medical Device SOP](#) for detailed IRB submission and review procedures.

C. Continued Access

FDA may allow continued enrollment of subjects after the controlled clinical trial under an IDE has been completed in order to allow access to the investigational medical device while the marketing application is being prepared by the sponsor or reviewed by FDA.

Criteria:

- Public health need or
- Preliminary evidence that the device will be effective and there are no significant safety concerns have been identified for the proposed indication.

The treatment IDE regulation also has a more narrow application than the Continued Access Policy in that treatment use is intended to address only those patients who have an immediately life-threatening or serious disease or condition whereas the Continued Access Policy, which is applied after completion of the clinical trial, may be considered for any clinical investigation.

6/3/21

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