Compassionate Use (Expanded Access)

Contrary to common usage, the terms "emergency use" and "compassionate use" are not synonymous**.** For information about emergency use of a test article, refer to that policy.

Definition

Compassionate use (expanded access) - the use of a new, unapproved drug or device to treat a seriously ill patient when no other treatments are available.

According to FDA regulations, an unapproved drug or medical device may normally only be used on human subjects when the drug/device is under clinical investigation and when used by investigators participating in the clinical trial. There may be circumstances, however, in which an investigational drug or device is the only option available for a patient faced with a serious, but not life-threatening condition (called "compassionate use").

Compassionate use can be for drugs/devices that are being studied in a clinical trial under an IND/IDE for patients who do not meet the requirements for inclusion in the clinical investigation but for whom the treating physician believes the drug/device may provide a benefit in treating or diagnosing their disease or condition.

Criteria for Compassionate Use

- The patient has a life-threatening or serious disease or condition;
- There is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; and
- Potential patient benefit justifies the potential risks of the investigational drug/device

IRB Review and FDA Requirements

Prior IRB review and approval is required**,** even if only one patient is to be treated under the following mechanisms. In most circumstances, prior approval by the FDA is also required. To request single patient compassionate use, the physician should complete and submit FDA form 3926.

A physician submitting an individual patient expanded access IND using Form FDA 3926 may select the appropriate box on that form to request authorization to obtain concurrence by the IRB chairperson or by a designated IRB member before the treatment use begins, in lieu of complying with the requirements in § 56.108(c), which relate to full IRB review.

The physician is responsible for obtaining FDA approval before the unapproved investigational drug/device is administered to or implanted in a patient. No emergency use is allowed.

A single IRB member may review the compassionate use request if the physician has requested a waiver of full board review on FDA Form 3926. The IRB member reviewing the compassionate use should:

- Document their decision to concur or not concur with the administration of the investigational drug

- Review adequate information submitted by the investigator and/or sponsor about the investigational drug to assess:
    1. the risks/benefits of the drug
    2. the patient's medical history and treatment plan
    3. the dose, route, frequency of administration, duration of treatment, criteria for discontinuation of treatment, and planned dose modification to mitigate adverse events
    4. planned monitoring for adverse events, response to treatment, changes in clinical status, modifications to the treatment plan to mitigate risks to the patient
    5. details of the patient's history, diagnosis, summary/response to prior therapy, co-morbidities, and concomitant medications
    6. assessment of known risks of the drug

- Assess the qualifications of the physician to administer the investigational drug

- If the patient is a minor, the process to obtain age-appropriate assent and parental permission

- Assess that the informed consent form has the required information under 21 CFR 50.25 The consent form explains that the primary purpose is to diagnose and/or treat the patient's disease/condition rather than generate scientific information for the safety and effectiveness of the drug. Although the primary purpose is for treatment, the drug is investigational and the FDA has not determined that the drug is safe and effective to treat the patient's condition.

Expanded Access Treatment Mechanisms

Treatment INDs or Individual Patient Access to Investigational Drugs/Devices for Serious Diseases:

These mechanisms are primarily intended to give seriously ill patients access to experimental drugs or devices where no comparable or satisfactory alternative treatment is available. Although the test article sponsor is expected to continue conventional clinical trials and pursue marketing approvals with due diligence, expanded access studies involve systematic use of experimental treatments, and, with very rare exceptions, require the same review and approval as research, including both IRB approval and FDA approval in the form of an IDE (medical device) or an IND (drug/biologic).

Open Protocols (Parallel Track, Open Label Protocol, Open Label IND) or Continued Access IDEs:

These uncontrolled studies are typically used when controlled trials have ended and treatment is continued so the subjects may continue to receive the benefits of the test article until marketing approval is obtained. Informed consent and prior IRB approval are required.

Compassionate Use of Devices

Compassionate use of devices can also be used for devices that are not being studied in a clinical investigation (such as when an IDE for the device does not exist). This provision is typically approved for individual patients but may be approved to treat a small group, if the small group request is under an IDE.

A physician who wishes to use a device for compassionate use should provide the HDE or IDE holder with:

- a description of the patient's condition,
- the circumstances necessitating treatment with the device,
- a discussion of why alternative therapies are unsatisfactory,
- why the probable risk of using the investigational device is no greater than the probable risk from the disease or condition
- identification of any deviations in the approved clinical protocol that may be needed in order to treat the patient and information to address the patient protection measures.

Patient protection measures should include:

- informed consent from the patient or a legal representative
- concurrence with the IRB Chair
- an independent assessment from an uninvolved physician
- authorization from the sponsor
- notification of R&D Chair

The HDE holder is required to submit an HDE amendment to the FDA for approval before the use occurs. If the FDA approves the request for compassionate use, the physician should devise an appropriate schedule for monitoring the patient taking into consideration the limited information available regarding the potential risks and benefits of the device and the specific needs of the patient. Further post-approval procedures for compassionate use cases, including the submission of a follow-up report to the FDA, are required and are the responsibility of the physician.

For guidance on Compassionate Use:

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

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/expanded-access-investigational-drugs-treatment-use-questions-and-answers

https://www.fda.gov/news-events/expanded-access/expanded-access-information-physicians