Expanded Access for Medical Devices

Introduction

When a patient has a serious or life-threatening condition that is not addressed by current approved treatments, options may exist to use an investigational medical device (i.e., one that has not been approved or cleared by FDA) to treat the patient. Normally, such investigational devices with significant risks may only be used on human subjects through an FDA-approved clinical trial for which an investigational device exemption (IDE) allows the investigational device to be used in a clinical study. However, there are circumstances under which a health care provider may use an investigational device outside of a clinical study to save the life of a patient or to help a patient suffering from a serious disease or condition for which no other alternative therapy exists. The use of an investigational device outside of a clinical trial for treatment of a patient is called “expanded access.” If enrollment in an existing clinical trial protocol is not possible (e.g., a patient is not eligible for any ongoing clinical trials, or there are no ongoing clinical trials to address the patient’s condition), patients/physicians have the potential to receive expanded access to investigational devices under one of three alternative mechanisms.

- Emergency Use
- Compassionate Use (or Individual Patient/Small Group Access)
- Treatment Use

FDA approval is required except in the case of emergency use. The mechanisms are summarized below, followed by an in-depth discussion of criteria.

Emergency Use

What is Emergency Use?

Emergency use is the use of an investigational device in an emergency situation. It is intended to provide patients and physicians with access to devices intended to treat life-threatening or serious diseases or conditions when there is no available

alternative and no time to obtain FDA approval. Emergency use may apply even if the investigational device is being studied in a clinical trial under an IDE: if a physician needs to use the device in a manner inconsistent with the approved investigational plan; or a physician who is not part of the clinical study, wishes to use the device to treat a patient with a life-threatening or serious disease or condition. Emergency use of an investigational device may occur before an IDE is approved and when a device is not being studied under an IDE.

Criteria:

- The patient has a life-threatening or serious disease or condition that needs immediate treatment;
- No generally acceptable alternative treatment for the condition exists; and
- Because of the immediate need to use the device, there is no time to use existing procedures to obtain FDA approval for the use.

Is FDA approval required prior to Emergency Use?

No. If all of the above criteria are met, an unapproved device may be used in an emergency situation without prior approval by FDA.

FDA expects the physician to make the determination that the patient's circumstances meet the above criteria, to assess the potential for benefit from the use of the unapproved device, and to have substantial reason to believe that benefits will exist. In the event that a device is used in circumstances meeting the criteria listed above, the physician should follow as many patient protection procedures as possible. Such patient protection procedures include obtaining:

1. Informed consent from the patient or a legal representative;
2. Clearance from the institution as specified by their policies;
3. Concurrence of the IRB chairperson;
4. An independent assessment from an uninvolved physician; and
5. Authorization from the device manufacturer.

Do I need to report Emergency Use to the FDA?

Yes. If there is an IDE for the device, the IDE sponsor must notify the FDA of the emergency use within 5 days through submission of an IDE Report (§812.35(a)(2)).This follow-up report should include a summary of the conditions constituting the emergency, the patient protection measures that were followed, and patient outcome information.

If no IDE exists, the physician should submit a follow-up report on the use of the device (description of device used, details of the case, and the patient protection

measures that were followed) to:

Food and Drug Administration
Center for Devices and Radiological Health
10903 New Hampshire Ave
Document Control Center
WO66 Rm G-609
Silver Spring, MD 20993

Top

Compassionate Use (or Individual Patient/Small Group Access)

What is Compassionate Use?

FDA recognizes that there are circumstances in which an investigational device is the only option available for a patient faced with a serious or life-threatening disease or condition.

The compassionate use provision provides a path to accessing investigational devices that have not received FDA approval or clearance for patients for whom the treating physician believes the device may provide a benefit in treating and/or diagnosing their disease or condition. Compassionate use can be for devices that are being studied in a clinical trial under an IDE for patients who do not meet the requirements for inclusion in the clinical investigation but for whom the treating physician believes the device may provide a benefit in treating and/or diagnosing their disease or condition. It can also be used for devices that are not being studied in a clinical investigation (i.e., 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.

Criteria:

- The patient has a life-threatening or serious disease or condition; and
- No generally acceptable alternative treatment for the condition exists.

Is FDA approval required prior to Compassionate Use?

Yes. Prior FDA approval is needed before compassionate use occurs.

How do I request approval for Compassionate Use of a device?

If a licensed physician would like to obtain an investigational device for an individual patient, the medical device company must first agree to provide the investigational device for compassionate use. FDA cannot require a company to provide an

investigational device for compassionate use to proceed. If the device manufacturer agrees to provide the device under compassionate use, there are two different processes to follow to obtain FDA approval, depending on whether or not there is an IDE for a clinical trial for that device.

If there is an IDE for the device, the IDE sponsor (who may be the device manufacturer or a physician who has submitted the IDE to conduct the clinical study for the device) should submit an IDE supplement requesting approval for a compassionate use under section §812.35(a) in order to treat the patient. The IDE supplement should include:

- A description of the patient's condition and the circumstances necessitating treatment;
- A discussion of why alternatives therapies are unsatisfactory and why the probable risk of using the investigational device is no greater than the probable risk from the disease or condition;
- An identification of any deviations in the approved clinical protocol that may be needed in order to treat the patient;
- The patient protection measures that will be followed:
  - A draft of the informed consent document that will be used;
  - Clearance from the institution as specified by their policies;
  - Concurrence of the IRB chairperson;
  - An independent assessment from an uninvolved physician; and
  - Authorization from the device manufacturer on the use of the device.

In some cases, the IRB will not approve the request until they have approval from FDA. In such cases, the original request should indicate that IRB approval will be obtained prior to use of the device. Proof of the approval by the IRB Chairperson will need to be submitted with the follow-up report after the patient is treated. The physician should ask the IRB or risk management staff if institutional clearance is needed in addition to the IRB Chair concurrence.

If there is no IDE for the device, the physician or manufacturer submits the above information to FDA, along with a description of the device provided by the manufacturer. Physicians and manufacturers can contact CDRHExpandedAccess@fda.hhs.gov for assistance.

The physician should not treat the patient identified in the request until FDA approves use of the device under the proposed circumstances. In reviewing this type of request, FDA will consider the above information as well as whether the preliminary evidence of safety and effectiveness justifies such use and whether such use would interfere with the conduct of a clinical trial to support marketing approval.

If the request is approved, the attending physician should devise an appropriate schedule for monitoring the patient, taking into consideration the investigational nature of the device and the specific needs of the patient. The patient should be monitored to detect any possible problems arising from the use of the device.

The above 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. In this case, that the request should include the information identified above and indicate the number of patients to be treated. If there is an IDE for the device, the supplement should include the protocol to be followed or should identify deviations from the approved clinical protocol. As with single patient compassionate use, a monitoring schedule should be designed to meet the needs of the patients while recognizing the investigational nature of the device. Follow-up information on the use of the device should be submitted in a report after all compassionate use patients have been treated.

What actions does FDA take on Compassionate Use requests?

After a compassionate use request is received, FDA will approve, approve with conditions, or disapprove the request. When there is an IDE for the device, compassionate use request IDE supplements have the same statutory 30-day review cycle as other IDE submissions. However, the patient need is considered when reviewing these requests and they are often expedited if necessary. For example, in 2015, compassionate use requests received under an IDE were reviewed in as little as 1 day, and on average in 18 days. Compassionate use requests received without an IDE were reviewed in as little as the same day as receipt, and on average in 10 days.

Do I need to report anything to FDA after the Compassionate Use occurs?

Yes. Following the compassionate use of the device, a follow-up report should be submitted by whoever submitted the original compassionate use request to FDA. This report should present summary information regarding patient outcome. If any problems occurred as a result of device use, these should be discussed in the follow-up report and reported to the reviewing IRB as soon as possible.

How many Compassionate Use requests does FDA/CDRH receive each year?

COMPASSIONATE USE IDE SUPPLEMENTS

Year	Total Submissions	Evaluable Submissions*	Percent Approved**
2012	135	123	99.19%
2013	181	175	98.86%

2014	228	216	99.54%
2015	215	208	99.04%

*Excludes those withdrawn or converted to Emergency Use while under review

**Based on Evaluable Submissions

COMPASSIONATE USE REQUESTS WITHOUT AN IDE

Year	Total Submissions	Evaluable Submissions*	Percent Approved**
2012	53	53	98.11%
2013	138	134	91.79%
2014	112	101	99.01%
2015	170	167	98.80%

*Excludes those withdrawn or converted to Emergency Use while under review

**Based on Evaluable Submissions

Top

Treatment Use

What is Treatment Use?

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

Criteria:

- The device is intended to treat or diagnose a serious or immediately life-threatening disease or condition;
- There is no comparable or satisfactory alternative device available to treat or diagnose the disease or condition in the intended patient population;
- The device is under investigation in a controlled clinical trial for the same use under an approved IDE, or all clinical trials have been completed; and
- The sponsor of the controlled clinical trial is pursuing marketing approval/clearance of the investigational device with due diligence.

A device that is not approved for marketing may be under clinical investigation for a

serious or immediately life-threatening disease or condition in patients for whom no comparable or satisfactory alternative device or other therapy is available. During the clinical trial or prior to final action on the marketing application, it may be appropriate to use the device in the treatment of patients not in the trial under the provisions of the treatment investigational device exemption (IDE) regulations. (§812.36)

The treatment use provision of the IDE facilitates the availability of promising new devices to desperately ill patients as early in the device development process as possible, before general marketing begins, and to obtain additional data on the device's safety and effectiveness. 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 "immediately life-threatening" disease means 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. "Treatment use" of a device includes the use of a device for diagnostic purposes.

How does a sponsor apply for a Treatment Use IDE?

A treatment IDE application must include, in the following order:

1. The name, address, and telephone number of the sponsor of the treatment IDE;
2. The intended use of the device, the criteria for patient selection, and a written protocol describing the treatment use;
3. An explanation of the rationale for use of the device, including, as appropriate, either a list of the available regimens that ordinarily should be tried before using the investigational device or an explanation of why the use of the investigational device is preferable to the use of available marketed treatments;
4. A description of clinical procedures, laboratory tests, or other measures that will be used to evaluate the effects of the device and to minimize risk;
5. Written procedures for monitoring the treatment use and the name and address of the monitor;
6. Instructions for use for the device and all other labeling as required under section §812.5(a) and (b);
7. Information that is relevant to the safety and effectiveness of the device for the intended treatment use. Information from other IDEs may be incorporated by reference to support the treatment use;
8. A statement of the sponsor's commitment to meet all applicable responsibilities under the IDE regulations (21 CFR 812) and Institutional Review Boards regulations (21 CFR 56) and to ensure compliance of all participating

investigators with the informed consent requirements of 21 CFR 50;

9. An example of the agreement to be signed by all investigators participating in the treatment IDE and certification that no investigator will be added to the treatment IDE before the agreement is signed; and
10. If the device is to be sold, the price to be charged and a statement indicating that the price is based on manufacturing and handling costs only.

A licensed practitioner who receives an investigational device for treatment use under a treatment IDE is an "investigator" under the IDE and is responsible for meeting all applicable investigator responsibilities under 21 CFR 812, 21 CFR 50, and 21 CFR 56.

Applications should be identified on the outside envelope as a treatment IDE application and reference the IDE number. The original and two copies should be mailed to the following address:

Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

What are FDA actions on Treatment IDE applications?

Approval of treatment IDEs

Treatment use may begin 30 days after FDA receives the treatment IDE submission. FDA may notify the sponsor in writing earlier than the 30 days that the treatment use may or may not begin. FDA may approve the treatment use as proposed or approve it with modifications.

Disapproval or withdrawal of approval of treatment IDEs

FDA may disapprove or withdraw approval of a treatment IDE if:

- The required criteria [§812.36(b)] are not met or the treatment IDE application does not contain the required information [§812.36(c)];
- FDA determines that any of the grounds for disapproval or withdrawal of approval apply [§812.30(b)(1) through (b)(5)]. See Approval Process, FDA Actions, for additional information;
- The device is intended for a serious disease or condition and there is insufficient evidence of safety and effectiveness to support such use;
- The device is intended for an immediately life-threatening disease or condition and the available scientific evidence, taken as a whole, fails to provide a reasonable basis for concluding that the device:

  - may be effective for its intended use in its intended population; or
  - would not expose the patients to whom the device is to be administered to an unreasonable and significant additional risk of illness or injury;
- There is reasonable evidence that the treatment use is impeding enrollment in, or otherwise interfering with the conduct or completion of, a controlled investigation of the same or another investigational device;
- The device has received marketing approval/clearance or a comparable device or therapy becomes available to treat or diagnose the same indication in the same patient population for which the investigational device is being used;
- The sponsor of the controlled clinical trial is not pursuing marketing approval/clearance with due diligence;
- Approval of the IDE for the controlled clinical investigation of the device has been withdrawn; or
- The clinical investigator(s) named in the treatment IDE are not qualified by reason of their scientific training and/or experience to use the investigational device for the intended treatment use.

Safeguards

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 (21 CFR 50) and institutional review boards (21 CFR 56).

What are the reporting requirements for a Treatment Use IDE?

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 dates of these reports are based on the period of time since initial approval of the treatment IDE. *After* filing of a marketing application, progress reports must be submitted annually in accordance with the IDE regulations.

See "Suggested Format For IDE Progress Report" under Reports for guidance on the content of a progress report. 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 §812.150 (Reports), such as unanticipated adverse device effects and final reports. The reports are submitted as reports to the original IDE application. See Reports for additional guidance.

Top

References:

- 21 CFR 812.36
- Guidance on IDE Policies and Procedures

More in Investigational Device Exemption (IDE)

IDE Tracking Improvements

IDE Approval Process

IDE Definitions and Acronyms

IDE Responsibilities

IDE Application

IDE Reports

IDE Records

IDE Institutional Review Boards (IRB)

IDE Informed Consent

IDE Financial Disclosure

Expanded Access for Medical Devices

IDE Enforcement of Good Clinical Practices (GCP) Regulations

Import and Export of Investigational Devices

FAQs about IDE

IDE Related Topics

IDE Guidance

IDE Regulations

IDE Links

Page Last Updated: 06/02/2016
Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewers and Players.

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Contact FDA