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| --- | --- | --- | --- | --- | --- | --- | --- |
| Expanded Access Mechanism | Regulatory Authority | Criteria for Use | When Can It Be Used? | Number of Patients to be Treated | FDA Approval Needed? | How is FDA Approval Obtained? | Patient Protection Measures |
| **Emergency Use** | "Guidance for the Emergency Use of Unapproved Medical Devices"50 FR 4286621 CFR 812.35(a) | 1. Life-threateningcondition‡;2. No alternative;and3. No time to obtainFDA approval. | Before or after initiation of clinical trial | Limited to few patients | No; submit report to FDA following device use | Not applicable | 1. Independentassessment byuninvolved doctor;2. IRB chairperson'sconcurrence;3. Institutionalclearance; and4. Informed consent |
| **Compassionate Use** | 21 CFR 812.35(a) | 1. Serious diseaseor condition and2. No alternative. | During clinical trial | Individual patient or small groups of patients | Yes | IDE supplement with:1. Explanation ofcircumstancesconstituting need forthe device;2. Reasons alternatives notacceptable;3. Deviations fromprotocol, if any; and4. Patient protectionmeasures. | 1. Independentassessment byuninvolved doctor;2. IRB chairperson'sconcurrence;3. Institutionalclearance; and4. Informed consent. |
| Treatment IDE | 21 CFR 812.36 | 1. Life-threateningor seriousdisease;2. No alternative;3. Controlledclinical trial; and4. Sponsor pursuingmarketingapproval. | During clinical trial | Wide access; depends on patient/physician need | Yes | Trt IDE supplement with:1. Intended Use, protocol,and patient selectioncriteria;2. Rationale for trt use3. Methods used toevaluate device use andminimize risks;4. Monitoring plan;5. Summary of S&E data6. Instructions for use anddevice labeling;7. Commitment topatient protection;8. Investigator agreement; and9. Price, if will be sold. | 1. IRB approval and2. Informed consent. |
| Continued Access | "Continued Access to Investigational Devices During PMA Preparation and Review"ODE Blue Book IDE Memorandum #D96-1 | 1. Public healthneed; or2. Preliminaryevidence thatdevice will beeffective andno significantsafety concerns. | After completion of clinical trial | Same rate of enrollment as study | Yes | IDE supplement with:1. Justification forextended study;2. Summary of S & Edata and risks posed bythe device;3. Proposed enrollmentrate;4. Clinical protocol; and5. Progress towardsmarketing approval. | 1. IRB approval and2. Informed consent. |

‡As a matter of practice, FDA has expanded the criteria of "life-threatening condition" to include serious conditions such as sight-threatening and limb-threatening conditions as well as other situations involving risk of irreversible morbidity.

For questions or further information regarding the above table, contact the FDA IDE Staff at (301) 594-1190. Downloaded from the FDA website 5/20/2013: <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080202.htm>

***Chapter III*
*Expanded Access to Unapproved Devices***

According to the statute and FDA regulations, an unapproved medical device may normally only be used on human subjects when the device is under clinical investigation and when used by investigators participating in the clinical trial. FDA recognizes, however, that there may be circumstances under which a health care provider may wish to use an unapproved device to save the life of a patient, to prevent irreversible morbidity, or to help a patient suffering from a serious disease or condition for which there exists no other alternative therapy. Below is a discussion of the four main mechanisms by which FDA may make unapproved devices available to patients/physicians faced with circumstances such as those described. These mechanisms are consistent with the Expanded Access provisions of the FDA Modernization Act of 1997 (See section 561 of the Federal Food, Drug, and Cosmetic Act). FDA plans to modify existing guidance in minor ways, as needed, to track the language in the new law.

***Emergency Use of Unapproved Medical Devices***

Procedures governing the emergency use of an investigational device are covered in two separate documents: the IDE regulation (21 CFR Part 812) and FDA's "Guidance for the Emergency Use of Unapproved Medical Devices," (hereinafter referred to as the Emergency Use Guidance) which appeared in the **Federal Register** of October 22, 1985 (50 FR 42866).

The IDE regulation recognizes that emergency situations may arise in which there will be a need to use an investigational device in a manner inconsistent with the approved investigational plan or by a physician who is not part of the clinical study. Therefore, the regulation permits deviations from the investigational plan when necessary to protect the life or physical well-being of a subject in an emergency. (See 21 CFR 812.35(a)). Prior approval for shipment or emergency use of the investigational device is not required, but the use should be reported to FDA by the IDE sponsor via a supplement within 5 working days from the time the sponsor learns of the use. The supplement should contain a summary of the conditions constituting the emergency, the patient protection measures that were followed (as discussed below), and patient outcome information.

In addition to the IDE regulation, emergency use is also addressed in an FDA guidance document. The Agency issued the Emergency Use Guidance because the IDE regulation does not address emergency use comprehensively (e.g., by not defining the term "emergency use," identifying the patient protection measures that should be followed in such situations, or addressing emergency use of devices not covered by an IDE). This guidance defines an unapproved medical device as a device that is utilized for a purpose, condition, or use for which the device requires, but does not have, an approved application for premarket approval under section 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360e)(the act) or an approved IDE under section 520(g) of the act (21 U.S.C. 360j(g)). As discussed in the Guidance, an unapproved device should normally only be used in human subjects if it is approved for clinical testing under an IDE and if it is used by an investigator for the sponsor in accordance with the terms and conditions of the application. Emergency use of an unapproved device, however, may also occur when: (i) an IDE for the device does not exist, (ii) when a physician wants to use the device in a way not approved under the IDE, or (iii) when a physician is not an investigator under the IDE.

The Emergency Use Guidance document was intended to address these *emergency* situations. As stipulated in the guidance, a physician who intends to treat a patient with an unapproved medical device in an emergency situation should conclude that:

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

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 IDE sponsor, if an approved IDE exists for the device.

Although not provided for under this guidance, often times a physician, who is faced with an emergency situation as described above, will contact FDA to discuss his/her patient's condition. In this situation, ODE acts in an advisory role, rather than in an approving role. The ODE employee who receives the call should discuss the emergency use criteria with the physician, but the responsibility for making the decision as to whether the situation meets the emergency use criteria and whether the unapproved device should be used lies with the physician. If the physician decides to proceed with the emergency use of the device, the ODE employee should advise the physician of the above patient protection procedures to be followed before the emergency use occurs and fill out the Emergency Use Checklist. This checklist helps to ensure that the criteria for emergency use have been met and that the physician has been informed that he/she is expected to follow as many patient protection procedures as possible. After discussing the situation with the physician and completing the checklist, it should be filed in the Emergency Use Report File located in the Program Operations Staff.

† As a matter of preactice, FDA has expanded the criteria of "life-threatening condition" to include serious diseases or conditions such as sight-threatening and limb-threatening conditions as well as other situations involving risk of irreversible morbidity. This is consistent with the new law.

After the emergency use occurs, the treating physician is responsible for ensuring that certain follow-up procedures occur. If an IDE exists for the device, the physician should provide the IDE sponsor with sufficient patient follow-up information to allow the sponsor to comply with the reporting requirements of the IDE regulation. If no IDE exists, the physician should submit a follow-up report on the use of the device to the IDE Staff. This report should contain a summary of the conditions constituting the emergency, patient protection measures that were followed, and patient outcome information.

For more information on emergency use of investigational devices, see 50 FR 42866 and 21 CFR 812.35(a).

***[Compassionate Use] Individual Patient Access to Investigational Devices Intended for Serious Diseases***

As discussed above, the IDE regulation and the Emergency Use Guidance address those situations in which an investigational or unapproved device, respectively, is needed to save the life of a patient or to prevent irreversible morbidity. FDA recognizes, however, that there are circumstances in which an investigational device is the only option available for a patient faced with a serious, albeit not life-threatening condition (hereinafter referred to as "compassionate use"). In these circumstances, FDA uses its regulatory discretion in determining whether such use of an investigational device should occur.

Unlike emergency use of an unapproved device, prior FDA approval is needed before compassionate use occurs. In order to obtain Agency approval, the sponsor should submit an IDE supplement requesting approval for a protocol deviation under section 812.35(a) in order to treat the patient. The IDE supplement should include:

1. A description of the patient's condition and the circumstances necessitating treatment;
2. 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;
3. An identification of any deviations in the approved clinical protocol that may be needed in order to treat the patient; and
4. The patient protection measures that will be followed. (These measures were previously discussed under the Emergency Use Guidance.)

The sponsor should not treat the patient identified in the supplement until FDA approves use of the device under the proposed circumstances. (IDE boilerplate G-16A has been developed for reviewers to use when addressing this type of request.) 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. Following the compassionate use of the device, a follow-up report should be submitted to FDA as an IDE supplement in which summary information regarding patient outcome is presented. If any problems occurred as a result of device use, these should be discussed in the supplement and reported to the reviewing IRB as soon as possible.

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 serious disease or condition for which no alternative therapy adequately meets the medical need. In this case, the physician should request access to the investigational device through the IDE sponsor. The sponsor should submit an IDE supplement that includes the information identified above and indicates the number of patients to be treated. Such a supplement should include the protocol to be followed or 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 an IDE supplement after all compassionate use patients have been treated.

***Treatment Use of Investigational Devices***

**Provisions of the Regulation**

In the **Federal Register** of September 18, 1997 (62 FR 48940), FDA established procedures to allow for the treatment use of investigational devices. These procedures are intended to facilitate the availability of promising new therapeutic and diagnostic devices to desperately ill patients as early in the device development process as possible, i.e., before general marketing begins, and to obtain additional data on the device's safety and effectiveness. These procedures apply to patients with serious or immediately life-threatening diseases or conditions for which no comparable or satisfactory alternative device, drug, or other therapy exists.

Under the final rule, treatment use of an investigational device will be considered when:

1. The device is intended to treat or diagnose a serious or immediately life-threatening disease or condition;
2. There is no comparable or satisfactory alternative device available to treat or diagnose the disease or condition in the intended patient population;
3. 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
4. The sponsor of the controlled clinical trial is pursuing marketing approval/clearance of the investigational device with due diligence.

**Procedures**

If a sponsor is considering submitting a treatment IDE, the sponsor should consult with the appropriate review division in order to determine if the device/indication would meet the criteria for approval. Note that treatment IDEs are limited to those devices/indications which meet the criteria defined above. According to 21 CFR 812.36, requests for treatment use should be submitted as a supplement to the existing IDE and should include:

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 the use of the device, including either a list of the available regimens that ordinarily should be tried before using the device or an explanation of why the use of the device is preferable to the use of available marketed treatments;
4. A description of clinical procedures, laboratory tests, or other measures to be used to monitor the effects of the device and to minimize risk;
5. Written procedures for monitoring the treatment use and the name/address of the monitor;
6. Instructions for use and all labeling for the device as required under section 812.5(a) and (b);
7. Information relevant to the safety and effectiveness of the device for the intended treatment use;
8. A statement of the sponsor's commitment to meet all applicable responsibilities under Parts 812 and 56 and to ensure compliance of all participating investigators with Part 50;
9. An example of the investigator agreement to be signed by all investigators 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 that the price is based on manufacturing and handling costs only.

As with all IDEs, treatment IDEs may begin 30 days after FDA receives the application, unless FDA notifies the sponsor earlier than 30 days that the treatment use may or may not begin. The Agency may approve the treatment use as proposed, approve it with modifications/conditions, or disapprove it. FDA may withdraw approval of the treatment IDE if it is determined that the above criteria are no longer met.

In order to protect the rights, safety, and welfare of human subjects involved in the clinical trial, while at the same time facilitating the development of beneficial device therapies, FDA included certain safeguards in the Treatment IDE process. Some of these measures were already in place as part of the IDE regulation, while other safeguards were specifically designed for treatment use. Safeguards for this process include: the distribution of the device through qualified experts; maintenance of adequate manufacturing facilities; the submission of reports pursuant to 21 CFR 812.150; and compliance with the regulations governing informed consent and institutional review boards. Sponsors should review these sections of the regulation when preparing a Treatment IDE application to ensure that these issues are properly addressed.

When an IDE supplement requesting approval for treatment use is received in the reviewing division, the reviewer should immediately notify the IDE Staff. The IDE Staff will assist the division with the review of the application to ensure that all applicable safeguards have been satisfied and that all of the criteria identified in the regulation (see above) have been adequately addressed before the application can be approved. Three boilerplate letters are available for responding to requests for treatment use: G-46 for approval, G-47 for conditional approval, and G-48 for disapproval.

ODE review divisions should note that the IDE tracking sheets include a reason-for-submission code for Treatment IDE supplements. It is important that the division indicate on the tracking sheets that the application was a Treatment IDE, so that these applications can be properly tracked.

The Treatment IDE regulation is effective on January 16, 1998. For further guidance on Treatment IDEs, see the **Federal Register** of September 18, 1997 (62 FR 48940) or contact the IDE Staff at (301) 594-1190.

***Continued Access to Investigational Devices***

As discussed in ODE's Blue Book Memorandum entitled, "Continued Access to Investigational Devices During PMA Preparation and Review," (hereinafter referred to as the Continued Access Policy) the sponsor of a clinical investigation is permitted to continue to enroll subjects while a marketing application is being prepared by the sponsor and/or reviewed by the Agency if there is:

1. A public health need for the device; or
2. Preliminary evidence that the device is likely to be effective and no significant safety concerns have been identified for the proposed indication.

The continued enrollment of subjects in an investigation while a marketing application is being prepared by the sponsor and/or reviewed by ODE is known as an "extended investigation." Extended investigations permit patients and/or physicians continued access to the devices while also allowing the collection of additional safety and effectiveness data to support the marketing application or to address new questions regarding the investigational device. The Continued Access Policy may be applied to any clinical investigation that meets the criteria identified above; however, it is intended to be applied late in the device development process, i.e., after the controlled clinical trial has been completed.

A sponsor's request for an extended investigation should be submitted as an IDE supplement and include the following information:

1. A justification for the extension;
2. A summary of the preliminary safety and effectiveness data generated under the IDE;
3. A brief discussion of the risks posed by the device;
4. The proposed rate of continued enrollment (the number of sites and subjects);
5. The clinical protocol, if different from that used for the controlled clinical trial, as well as the proposed objectives for the extended study; and
6. A brief discussion of the sponsor's progress in obtaining marketing approval/clearance for the device.

The reviewer should consider all of the above factors, in addition to ODE's progress in the review of the marketing application, when determining whether to approve, approve with modifications, or disapprove the proposed request for the extended investigation. The above factors should also be considered when determining the appropriate rate of enrollment, the number of investigators, and the number of investigational sites for the extended investigation. A sponsor's past compliance with applicable FDA regulations should also be considered when making these decisions. For example, sponsors who have been negligent in their monitoring responsibilities or who have other unresolved compliance problems would not be permitted to participate in an extended investigation.

It is important to recognize that there is significant overlap between the treatment IDE regulation and the Continued Access Policy. As discussed in the preamble to the treatment IDE final rule, both the Continued Access Policy and the treatment IDE regulation are intended to provide additional access to an unapproved device, once preliminary evidence regarding safety and effectiveness is available to FDA. However, because a treatment IDE can be submitted earlier in the IDE process, i.e., once promising evidence of safety and effectiveness has been collected under the IDE but while the clinical study is ongoing, it could provide access to a wider group of patients at an earlier stage in the IDE process. 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.

For further information, see ODE Blue Book Memorandum #D96-1 entitled, "Continued Access to Investigational Devices During PMA Preparation and Review."