Guidance -
Emergency Use of a Test Article

Emergency Use of a test article is exempt from prior IRB review and approval, provided that such emergency use is reported to the IRB within 5 working days ***after the use***. Expedited IRB approval is not permitted in emergency use. Investigators should contact the IRB about their intent to use a test article in an emergency or to invoke the exception to the requirement to obtain consent. A senior staff member in the IRB Office will advise whether the circumstances follow FDA regulations.

Definitions:

Emergency Use: Use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval [21 CFR 56.102(d)].

Test Article: Any drug, biological product, or medical device for human use [21 CFR 56.102(1)].

Life-threatening includes both life-threatening and severely debilitating:

- ***Life-threatening:*** Diseases or conditions where 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 IRB meeting is feasible.
- ***Severely debilitating:*** Diseases or conditions that cause major irreversible morbidity e.g., blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

Criteria for Emergency Use – Drugs

Emergency use must meet the definition above and the FDA must determine: [21 CFR 312.305(a)]

1) The patient or patients to be treated has 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;
2) 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;
3) 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.
4) Also, the following must be determined: [21 CFR 312.310(a)]

a. The physician must determine that the probable risk to the person from the investigational drug is not greater than the probable risk from the disease or condition;
b. FDA must determine that the patient cannot obtain the drug under another IND or protocol.

Contact sponsor

Most sponsors agree to ship the test article by referencing the relevant IND/IDE. Some sponsors may require an acknowledgement from the IRB "that the proposed use meets the requirements of 21 CFR 56.104(c)".

Contact FDA

1) Emergency use may be requested by telephone, facsimile, or other means of electronic communications. See FDA guidance.
2) The licensed physician or sponsor must explain how the expanded access use will meet the requirements (of 312.305 and 312.310) and must agree to submit an expanded access submission within 15 working days of FDA's authorization of the use. See Form FDA 1571 and Instructions.

Criteria for Emergency Use – Devices

Must meet all of the following:

- Life-threatening or serious disease or condition
- No alternative
- No time to obtain FDA approval

One Emergency Use per Test Article

The FDA regulations [21 CFR 56.104(c)] allows for ***one*** emergency use of a test article at an institution. ***Any subsequent use*** of the investigational product at the institution is subject to ***prospective IRB review and approval***. ***However***, the FDA acknowledges that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue. (FDA Information Sheet, 2003 Update)

Note: For devices, if an IDE application for subsequent use has been filed with FDA and FDA disapproves the IDE application, ***the device may not be used even if the circumstances constituting an emergency exist***.

Informed Consent

Informed consent (and HIPAA Authorization) must be obtained from the subject (or the legally authorized representative), unless the requirements of an exception from the informed consent requirement [21 CFR 50.23(a)] are satisfied. The investigator may use the consent form and HIPAA Authorization template, or adapt a consent form from a previously approved research study involving the use of the same investigational drug or

biologic. Alternatively, the investigator may develop a new consent form that includes all required elements.

Exception from Informed Consent Requirement

FDA regulations [21 CFR 50.23] permit emergency use of a test article without informed consent where the investigator and an independent physician, who is not otherwise participating in the clinical investigation, certify in writing:

1) The patient is confronted by a life-threatening or severely debilitating situation, necessitating the use of the test article
2) Informed consent cannot be obtained from the patient (because the patient cannot communicate or is incompetent to give consent)
3) Time is not sufficient to obtain consent from the patient's legally authorized representative
4) No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the patient's life.

If, in the investigator's opinion, immediate use of the test article is required and if time is not sufficient to obtain the independent physician determination, the investigator should make the determination and, within 5 working days after the use of the article, have the determination reviewed and evaluated in writing by an independent physician.

Submission and Reporting to IRB and FDA

The following documentation of the emergency use must be submitted to the IRB ***within 5 working days*** after the use of the test article:

1. New study Emergency Use Study Submission in iRIS.
2. PDF of confirmation of permission from the manufacturer/sponsor for the Emergency Use of the test article attached to the iRIS submission.
3. PDF of the confirmation of the FDA authorization for Emergency Use IND attached to the iRIS submission.
4. PDF of the signed consent form and HIPAA authorization unless meets *Exception from Informed Consent Requirement* attached to the iRIS submission.

Drugs: Physician or sponsor must agree to submit an expanded access submission to FDA **within 15 working days** of FDA's authorization of the use. [21 CFR 312.310]

Devices with no IDE: Physician must report the use to FDA (CDRH or CBER) ***within 5 working day***s after the use.

Devices with an IDE: IDE sponsor must report the use to FDA ***within 5 working days*** from the time the sponsor learns of the use.

IRB Review (Retrospective)

An IRB Chair or designated IRB member reviewer will review the iRIS documentation submitted. IRB review includes an assessment of whether or not the conditions for the emergency use were satisfied. The reviewer completes an iRIS reviewer sheet and an official

letter of outcome is sent to the PI and study contact. If the emergency use did not meet the criteria allowing an exemption from prior IRB review and approval, the action will be handled according to HRPP non-compliance process.

All relevant documentation on emergency uses of test articles must be maintained by the PI as well as in the IRB records within the iRIS database.

Emergency Use is not "Research" under DHHS Regulations

The FDA regards emergency use of a test article, other than a medical device, as a "clinical investigation" and may require data from an emergency use to be reported in a marketing application. However, DHHS states, "***emergency care may not be claimed as research, nor may the outcome of such care be included in any report of a research activity***." Thus, a patient receiving an emergency use of a test article is not considered a research participant by DHHS regulation, and such emergency use is not "research" as covered under 45 CFR 46.

Resources: Regulations and Guidance

FDA

- 21 CFR 50.23 – Exception to informed consent
- 21 CFR 56.102(d) – Emergency Use definition
- 21 CFR 56.104 – Exception to IRB review
- 21 CFR 312.300 (Subpart I) - Expanded Access to Investigational Drugs for Treatment Use
- 21 CFR 812.35 – Exception to IDE requirement
- Emergency Use of an Investigational Drug or Biologic [FDA]
- Form FDA 1571 and Instructions - Investigational New Drug Application
- Information Sheet Guidance For IRBs, Clinical Investigators, and Sponsors - Frequently Asked Questions About Medical Devices
- Physician Request for an Individual Patient IND under Expanded Access for Non-emergency or Emergency Use
- IDE Early/Expanded Access [FDA] - Emergency Use of Unapproved Medical Devices
- Medical Devices- Guidance on IDE Policies and Procedures [FDA] - Guidance on IDE Policies and Procedures

Product FDA Office/Division to Contact Phone

- **Drug Division of Drug Information 301-827-4570; 310-827-1501**
- **Biological Blood Office of Blood Research and Review 301-827-3518**
- **Biological Vaccine Office of Vaccines Research 301-827-3070**
- **Device Center for Devices and Radiological Health (CDRH)**
  http://www.fda.gov
  301-594-1190; 800-638-2041
  All products:
  Nights & weekends

- **Office of Emergency Operations**
  mailto:emergency.operations@fda.hhs.gov
  866-300-4374; 301-796-8240; 301-443-1240