

Guidance and Procedure: Emergency Use of a Test Article

(last updated May 1, 2013)

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Overview

The emergency use provision in the Food and Drug Administration (FDA) regulations [[21 CFR 56.104\(c\)](#)] allows physicians a onetime use of an unapproved investigational drug, biologic, or device (referenced hereafter as “test article”). ***This OHRPP guidance and procedure document is intended to assist physicians by outlining the FDA emergency use requirements*** and the necessary procedures to ensure both the treatment of seriously ill patients in a life threatening situation and compliance with FDA regulatory requirements.

The FDA expects the physician to assess the potential benefits from the use of an unapproved device and to have substantial reason to believe that the benefits will exist *in addition to* determining whether the patient meets the qualifying criteria for emergency use.

IMPORTANT NOTES:

1. FDA and Department of Health and Human Services (DHHS) regulations differ:

- **Under FDA regulations** although an emergency use is considered a “clinical investigation, it allows an exemption from IRB review. However, patients who receive a test article in an emergency use may not be considered a research participant.
 - **DHHS regulations** do not permit data obtained from patients who receive a test article in an emergency use to be classified as human participants research, nor do they permit the outcome of such care to be included in any report of a research activity subject to DHHS regulations.
2. **Do not confuse “Emergency Use” with “Compassionate Use,”** also known as “expanded access”. See links in definition below of “Expanded Access Programs”.

Definitions and Terms

Emergency Use: The use of a test article (unapproved drug, biologic, or device) in a life-threatening situation where no standard acceptable treatment is available and there is not sufficient time to obtain IRB approval ([21 CFR 56.102\(d\)](#)). The FDA allows one emergency use of a test article without prospective IRB review, and requires reporting of the emergency use to the IRB within 5 working days ([21 CFR 56.104\(c\)](#)). Generally, the emergency use of a test article requires either an IND (for unapproved drugs and biologics) or an IDE (for unapproved devices).

Enrollment Exception to the Inclusion/Exclusion Criteria of an IRB Approved Protocol: In order to allow the treatment of a single patient (one time only) who does not meet the entry criteria of an IRB-approved protocol, the Principal Investigator should submit a request for a “Single-Subject Exception”. Such a request, which should be rare, must be justified in terms of serving the best interests of the patient. If there is a study sponsor, an enrollment exception usually requires sponsor approval as well. Data collected will become part of the scientific evaluation of the test article. See the section “Anticipated Deviation from the Approved Protocol” in [OHRPP Guidance and Procedures: IRB Review Type – Amendments to Previously Approved Research](#).

Expanded Access Programs is allowed only after prior review and approval by the IRB and, in most circumstances, prior approval by the FDA as well. Prior IRB approval is needed even if only one patient is to be treated under the any of the mechanisms of the expanded access to unapproved devices or drugs or biologics. See the section “Situations and Methods that Allow for Expanded Access to Unapproved Drugs for Treatment” in the [OHRPP Guidance and Procedures: Use of Drugs and Biologics in Clinical Research and Treatment](#) and [OHRPP Guidance and Procedures: Use of Devices in Clinical Research and Treatment](#).

Life-threatening: Diseases or conditions where the 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 recipients must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

Severely debilitating diseases or conditions cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

Sufficient time to obtain IRB approval: In most cases, **a minimum** of two working days before a meeting is required for the Full Board to be able to review an emergency use application. For the purposes of this guidance, there **is** sufficient time to obtain IRB approval **if** the physician decides that the test article is **not** needed prior to the next scheduled Medical IRB meeting and the application for the use of the test article can be submitted at least two days prior to that meeting.

On the other hand, if there is insufficient time to prepare the application and to get it reviewed at Full Board before its use is needed to treat the life-threatening or potentially debilitating condition,

then the emergency use without IRB approval criteria may be met. The clinician should not delay treatment if waiting for Full Board review would jeopardize the patient's health or safety.

With the exception of holidays, there are usually six UCLA Medical IRB meetings per month. See the [UCLA IRB Meeting Calendar](#).

Emergency Use Requirements (Step-by-Step Procedures)

The following is an overall summary the requirements (FDA regulations and UCLA policy) for emergency use of a test article. The [Emergency Use Checklist-Drugs/Biologics](#), the [Emergency Use Checklist-Devices](#) and the [Post Emergency Use Report Form](#) are provided to help facilitate the process and can be found on the OHRPP website.

PRIOR USE REQUIREMENTS

1. **Qualifying Criteria for Emergency Use:** *All* of the following five criteria must be met in order to comply with federal regulations and University policy:
 - a. The patient has a condition that is ***life-threatening or severely debilitating***,
 - b. ***No standard treatment*** is available,
 - c. There is ***not sufficient time to obtain IRB review*** and approval for an unapproved investigational drug, biologic, or device.
 - d. This is the first emergency use of the test article (***one time per institution to treat a single patient***), and
 - e. There is ***no known available IRB approved study protocol*** using the same test article or the patient cannot be enrolled into an existing protocol.

2. **For Drugs/Biologics:**
 - a. **Contact the Sponsor/Manufacturer.** Determine whether the test article can be made available for the emergency use under the sponsor/manufacturer's IND.

NOTE: If the sponsor/manufacturer of the test article requires a letter from the IRB before shipping the test article, an acknowledgement letter of the emergency use can be provided (which should not be construed as IRB approval).
 - b. **Contact the FDA:** If the manufacturer of a drug or biologic declines permission to use its IND, the physician may contact the FDA to obtain an IND at the numbers below (for drug or biologic). The physician may also contact the FDA for additional information and guidance, and for notification about the emergency use.
 - c. **Contact the UCLA Investigational Drug Pharmacy.** If the emergency use involves a drug or biologic, you must comply with institutional policies regarding the receipt, storage, and dispensation of the drug/biologic. Please contact the UCLA Department of Pharmaceutical Services – Investigational Drug Section at (310) 267-8522 and ask to speak with an Investigational Drug Pharmacist.

3. **For Devices:**
 - a. **The emergency use of any unapproved device may occur:**
 - When a physician wants to use the device in a way not approved under the IDE,
 - When a physician is not an investigator under the IDE, **or**
 - When an IDE for the device does not exist.
 - b. **Contact the Sponsor/Manufacturer.** Obtain authorization from the IDE sponsor, if an IDE exists (if possible).

IMPORTANT NOTE: *Contacting the FDA* for prior use notification or approval is *not* required for shipment or emergency use of the unapproved device. The FDA does not need to be notified prior to the emergency use of a device when a patient meets the criteria for emergency use.

- c. ***If possible, seek an independent assessment*** (written) of an uninvolved physician regarding the emergency use of the unapproved device.

4. Contact the OHRPP/IRB

- a. **Check the [List of Test Articles Used at UCLA in Previous Emergencies](#)** to see if the test article has previously been used at UCLA
- b. **Contact any of the following OHRPP staff members:** The Medical Institutional Review Board (MIRB) Administrators - Dannie Hoffman MIRB-1 (310) 825-2235, Greg Ellis MIRB-2 (310) 825-5406, and Mark Mimnaugh MIRB-3 (310) 825-4804. Calls regarding emergency use are handled as expeditiously as possible. The staff member will ask a few questions and direct the treating physician to the appropriate IRB Chair.
- c. **Discuss with a Medical IRB Chair or Vice Chair.** The treating physician should discuss the case to determine if it meets the FDA criteria for emergency use and, if relevant, whether the use meets FDA criteria for waiving consent. If contact with the MIRB Chair or Vice Chair is not possible, the physician should proceed with the emergency use if the patient meets the qualifying criteria.

IMPORTANT NOTE: Contacting the OHRPP or concurrence by an MIRB Chair or Vice Chair should not be construed as IRB approval.

5. **Obtain Informed consent:** Written informed consent is required, and must be obtained from the patient or the patient's legally authorized representative unless the criteria for an exception from the informed consent requirement is met, as described below in [Obtaining Informed Consent for Emergency Use](#).

POST-USE REQUIREMENTS

1. **Submit to the IRB within 5 working days** after the test article use :
 - Copy of the completed [UCLA Post Emergency Use Reporting Form](#)
 - Copy of the signed informed consent form or certification of informed consent waiver
 - Copy of the completed Emergency Use Checklist for either
 - [Drug/Biologic](#) or
 - [Device](#)
2. **Notify the FDA and Sponsor/Manufacturer**
 - a. **The physician must provide outcomes or safety information** as required by the FDA.
 - b. **For Drugs/Biologics:** If the treating physician is the IND holder, any follow-up information should be reported to the FDA.
 - c. **For Devices:** The FDA requires the following post-use reporting:
 - If an IDE exists, the physician must provide the IDE sponsor a report. The sponsor is required to submit a report to the FDA within 5 working days the sponsor is aware of the emergency use.
 - If an IDE does not exist, the physician must submit a report to the FDA within 5 working days of device use.
 - The report should include a summary of the conditions constituting the emergency, the patient protections measures taken, and patient outcome information

3. The physician should consider possible future use of the test article at UCLA and, if necessary, initiate efforts to obtain IRB approval and regulatory clearance (IND or IDE) for such future uses.

FDA Contact Information

Test Article	Office/Division	Phone	email
Drug (CDER)	Division of Drug Information	(301) 796-3400	druginfo@fda.hhs.gov
Biologic (CBER)	Office of Communication, Outreach and Development	(301) 827-4081	ocod@fda.hhs.gov
Device	Office of Device Evaluation	(301) 796-5640 (301) 796-6563	None available
After Normal Working Hours	Office of Emergency Operations	(301) 796-8240 (866) 300-4374	emergency.operations@fda.hhs.gov

Obtaining Informed Consent for Emergency Use

- **Written informed consent for emergency use of a test article must be obtained** from the patient or legally authorized representative. See [OHRPP Guidance and Procedure: Obtaining and Documenting Informed Consent](#).
- **Exception from the informed consent requirement** may occur if both the treating physician **and** a physician not otherwise involved in the emergency use, certify in writing that **all of the following criteria are met** ([21 CFR 50.23\(a\)](#)):
 - The prospective recipient is confronted by a life-threatening situation necessitating the use of the test article.
 - Informed consent cannot be obtained from the recipient because of an inability to communicate with, or obtain legally effective consent from, the recipient.
 - Time is not sufficient to obtain consent from the recipient's legal representative.
 - There is no available alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the recipient.
- If there is not sufficient time to obtain an independent written certification of the criteria for an exception from informed consent prior to the use of the test article, the determinations of the treating physician must be made, reviewed and evaluated in writing by a physician who is not involved in the emergency use, and submitted to the IRB within 5 working days after the emergency use of the test article ([21 CFR 50.23\(b\)](#) and [21 CFR 50.23\(c\)](#)).

IRB Procedures

The OHRPP/IRB maintains a current [List of Previous Emergency Uses of Test Articles](#) on the OHRPP web site for reference. The database and list are updated after each emergency use of a test article reported to OHRPP/IRB.

Prior Use Procedures

- Whenever possible, the OHRPP/IRB will respond to physician inquiries prior to the emergency use of a test article, and will provide contact information for the appropriate MIRB chair. In addition, if needed, an acknowledgment letter of the emergency use can be provided after concurrence with the MIRB Chair (which should not be construed as IRB approval).

- An MIRB Chair will be contacted by the treating physician (if possible) to discuss the emergency use.
- The MIRB Chair's concurrence with the treating physician (if obtained) will be communicated by the MIRB Chair to the OHRPP staff identified in [Emergency Use Requirements](#).

Post Use Procedures

- The IRB Chair/Vice Chair will review the Post Emergency Use Report Form and determine whether the treating physician met FDA regulations and guidance.
- In instances where the IRB Chair/Vice Chair has been involved in the care of the patient, an alternate physician IRB member will review the report.
 - If there are any questions or concerns regarding the report from the IRB Chair/Vice Chair or designee, questions or concerns to the treating physician will be communicated, with the assistance from the OHRPP IRB staff.
 - Upon completion of the review and acceptance of the report, the IRB Chair/Vice Chair or designee will sign the report.
 - If the IRB Chair or designee determines that the report requires notification to or review by the convened Board, OHRPP senior staff will prepare and schedule the report for discussion at a convened IRB meeting.
- The OHRPP will maintain documentation of all emergency use reports submitted to the IRB.

Non-compliance with emergency use requirements will be processed as described in [OHRPP Policy: Noncompliance and Allegations of Noncompliance Regarding the Conduct of Human Subjects Research](#).

Regulations and References

FDA References

- [FDA Guidance for Institutional Review Boards and Clinical Investigators: Emergency Use of an Investigational Drug or Biologic – Information Sheet](#), September 1998.
- [FDA Guidance on IDE Policies and Procedures: Chapter III Expanded Access to Unapproved Devices – Emergency Use of Unapproved Medical Devices](#), January 20, 1998
- [FDA Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors: Frequently Asked Questions about Medical Devices](#), January 2006.
- [FDA IDE Early/Expanded Access – Emergency Use](#)
- [FDA Physician Request for an Individual Patient IND under Expanded Access for Non-emergency or Emergency Use](#)
- FDA Center for Devices and Radiological Health [Training Presentation: Institutional Review Board – Compassionate and Emergency Use](#)

FDA Regulations

- Exception from general requirements of informed consent [21 CFR 50.23\(a\) – \(c\)](#)
- Exception from informed consent requirements [21 CFR 50.24](#)
- Definition of Emergency Use [21 CFR 56.102\(d\)](#)
- Exemption from IRB review [21 CFR 56.104\(c\)](#)
- Expanded access to individual patients for emergency use [21 CFR 312.310](#)
- Emergency use of a device and reporting to FDA [21 CFR 812.35\(a\)\(2\)](#)
- Treatment use of an investigational device [21 CFR 812.36](#)