

Guidance and Procedures Number: 36
Title: Emergency Use of a Test Article
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I. Introduction

- A. ***The University, the OPRS HRPP and the Food and Drug Administration wish to support a physician's obligation to treat a seriously ill patient with all available treatment modalities.*** The emergency use provision in the FDA regulations [21 CFR 56.104(c)] allows physicians restricted access to experimental treatments that would otherwise be off limits. This OPRS/HRPP guidance and set of procedures is aimed to support physicians by clarifying the strict FDA emergency use requirements and by outlining the necessary procedures to help ensure physicians are in full compliance with those requirements.
- B. ***The FDA and the Department of Health and Human Services regulations differ*** in that under FDA regulations an emergency use is a "clinical investigation" while DHHS regulations do not consider an instance of emergency use "research" because neither the patient nor the data will be part of systematic investigation designed to develop or contribute to generalizable knowledge. Therefore, emergency use is not subject to DHHS regulations 45 CFR 46.
- C. Contrary to frequent usage, ***the terms "emergency use" and "compassionate use" are not synonymous*** according to federal regulations. Researchers need to be aware of and understand the specific standards for emergency use and compassionate use to avoid violating federal regulations and UCLA policy regarding the use of unapproved drugs, biologics and devices. The separate definitions and a brief outline of the rules that govern both emergency use and compassionate use are described in Section II below.
- D. ***A physician who treats a patient under emergency use provisions must strictly follow UCLA procedures.*** The physician must justify the treatment according to strict criteria, follow all procedures described in this guidance document before administering the investigational product, and fulfill specific follow-up responsibilities in a timely manner as described below in Section VI below.

II. Terms and Definitions

- A. **Emergency Use:** One-time (per institution) use of a test article (i.e., an unapproved device, drug or biologic) for a patient in a life-threatening situation where no standard acceptable treatment is available and there is not sufficient time to obtain IRB approval [21 CFR 21 56.102(d)]. Generally, emergency use of a test article requires either an IND (for unapproved drugs and biologics) or an IDE (for unapproved devices). FDA regulations provide an "emergency use" exemption from rules requiring IRB review and approval. However, reporting the use to the IRB is required by the FDA.

The following five criteria must be met in order to comply with federal regulations and University policy:

1. The test article is used one time per institution to treat a single patient, and
2. The patient has a condition that is life-threatening or severely debilitating (see definitions below in this section), and
3. No standard treatment is available, and
4. There is not sufficient time to obtain IRB review and approval, and
5. The emergency use is reported to the IRB within five working days; when possible, the treating physician should consult with the IRB prior to use.

IMPORTANT NOTE: See Sections III, IV, V, VI and VI below for additional UCLA requirements.

- B. **Life-threatening** refers to 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.
- C. **Severely debilitating** means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.
- D. **Sufficient time to obtain IRB approval:** For the purposes of this guidance, a physician is considered to have sufficient time to obtain IRB approval if the decision that the test article is needed is made 5 working days or more prior to a scheduled meeting of any of the three Medical IRBs and if the meeting will occur before use of the test article is necessary (according to the treating physician's judgment of when use of the test article is necessary).¹
- E. **Compassionate use** is often used by physicians tend to refer to the treatment of a seriously ill patient using an unapproved test article where no other available treatments are satisfactory. Such use of an investigational drug, biologic, or device actually falls into one of the following treatment mechanisms and 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 following the mechanisms of "**Expanded Access:**"
1. **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

¹ In most weeks of the year, at least one of the Medical IRBs is scheduled to meet, usually on a Wednesday or Thursday. Medical IRB meeting calendars are available at <http://www.oprs.ucla.edu/human/directory/>.

research, including both IRB approval and FDA approval in the form of an IDE (medical device) or an IND (drug/biologic).

2. Open Protocols (Parallel Track, Open Label Protocol, Open Label IND) or Continued Access IDEs: Uncontrolled studies, 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 CHR approval are required.

F. **Research in Emergency Medicine:** Planned research designed to evaluate emergency care treatments is not “emergency use.” As with all other clinical research, prospective IRB review and approval are required before a clinical study in emergency medicine can begin. The unique exception from informed consent for these studies is provided by federal regulations enforced by the Food and Drug Administration [21 CFR 50.24] and the Office for Human Research Protections [45 CFR 46.101(i)]. The emergency medical research waiver of informed consent is described elsewhere. See [HRPP Guidance and Procedure #35: IRB Approval of Research in an Emergency Setting](#).

G. **Innovative Treatment (Off-Label Use):** Emergency use provisions apply to investigational drugs, biologics, and devices. The innovative use of a marketed drug or device (sometimes called “off-label” use) for individual patient treatment rather than for research purposes does not require IRB review.

IMPORTANT NOTE: Treating a series of patients in a novel or innovative manner and analyzing the results for publication is research requiring prior IRB review.

H. **Humanitarian Device Exemption:** A Humanitarian Device Exemption (HDE) is a special approval given by the FDA that allows marketing a device that is designed to treat or diagnose a condition that affects fewer than 4,000 individuals per year. An HDE is given even though the efficacy of the device has not been tested or proven, because it is not financially feasible to do the usual clinical testing when so few individuals are affected. The FDA requires IRB approval prior to use of a Humanitarian Use Device (HUD), even though the use is not considered research. See [HRPP Guidance and Procedure #34: FDA Requirements](#) for a discussion of and the requirements for an HUD.

III. Regulatory Requirements for Drugs or Biologics

- A. ***FDA permits one emergency use of an unapproved drug or biologic per institution without prospective IRB review.*** FDA requires that any subsequent use of the investigational product at the institution have prospective IRB review and approval. **IMPORTANT NOTE:** FDA guidance acknowledges that it would be inappropriate to deny an unapproved drug or biologic to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the second use.² In cases at UCLA in which an IRB does not have sufficient time to convene, a determination regarding acceptability of the second use of an unapproved drug or biologic in an emergency situation must be made by the Department Chair or his/her designee.
- B. ***Emergency use of an unapproved drug or biologic requires an Investigational New Drug (IND) exemption.*** This may be accomplished in one of three ways:
1. The physician identifies an existing protocol for the same test article that is already approved by the UCLA IRB and for which the patient may be enrolled and is able to provide consent according to the requirements of the protocol and its IRB approval. In this case, the emergency use procedure is not needed. If an enrollment exception is needed in order to enroll the patient, the study PI should consult the sponsor.
 2. The physician should communicate with the holder of an IND for the product (such as the manufacturer) to ascertain whether the emergency use may occur under an existing IND and the IND holder is willing to provide the test article.
 3. If the use may not occur under an existing IND, but the IND holder is willing to provide the test article, the physician must obtain an IND from the FDA.³ If the situation does not allow time for submission of an IND, the FDA may issue an authorization of shipment in advance of an IND.
- C. ***The physician must obtain the consent of the patient or a legally authorized representative,*** or else determine that the emergency use meets the criteria for an exception to the requirement for consent. See Section V below. If consent is sought from the prospective recipient or the recipient's legally authorized representative, it will be obtained in accordance with FDA regulations and would be appropriately documented in accordance with FDA regulations.
- D. ***The physician must file a report with the IRB within 5 working days*** after use of the test article. This report should contain a summary of the conditions constituting the emergency, patient outcome information and the patient protection measures that were followed.
- E. ***Subsequent to the emergency use, the physician should evaluate the potential for future use of the test article at UCLA*** and, if necessary, initiate efforts to obtain IRB approval and regulatory clearance of the unapproved drug or biologic for such future uses.

² FDA IRB Information Sheets: <http://www.fda.gov/oc/ohrt/irbs/drugsbiologics.html#emergency>

³ See <http://www.fda.gov/oc/ohrt/irbs/drugsbiologicsNEW.html> for contact information. **Nights and weekends for any test article**, contact the FDA Office of Emergency Operations at (301) 443-1240.

IV. Regulatory Requirements for Devices

- A. ***FDA permits one emergency use of an unapproved device without prospective IRB review.*** The FDA requires that any subsequent use of the investigational product at the institution have prospective IRB review and approval.
- B. ***FDA requires that use of an unapproved device occur under an Investigational Device Exemption (IDE).*** The physician should communicate with the holder of an IDE for the product (such as the manufacturer) to ascertain whether the emergency use may occur under an existing IDE or if the physician must obtain an IDE from the FDA.⁴
1. If there is no IDE for the device, or if the proposed use, the treating physician or UCLA are not approved under an existing IDE, a device may be used without FDA approval ***if*** there is an immediate need to use the device and there is no time to use existing procedures to get FDA approval for use of the device. The manufacturer or physician must notify the FDA immediately after shipment of the device to UCLA and again in writing after use.
 - a. The FDA expects the physician to assess the potential for benefits from the unapproved use of the device and to have substantial reason to believe that benefits will exist.
 - b. The FDA advises that the physician may not conclude that an “emergency” exists based solely on the expectation that IDE approval procedures may require more time than is available. The FDA expects physicians to exercise reasonable foresight with respect to potential emergencies and to make appropriate procedures under IDE procedures far enough in advance to avoid creating a situation in which such arrangements are impracticable.
 2. ***Subsequent emergency use of an unapproved device may not occur unless*** the physician or another person obtains FDA approval of an Investigational Drug Exemption (IDE) for the device and its use. If the FDA disapproves an IDE application for subsequent uses, the device may not be used again even if the circumstances constituting an emergency exist.
- C. ***The FDA expects the physician to obtain as many of the following protections as possible:***
1. An independent assessment by an uninvolved physician (at UCLA, the Department Chair or designee);
 2. Informed consent from the patient or a legal representative (see Section V below);
 3. Clearance from the institution as specified by its policies;
 4. Concurrence of the IRB Chair; and
 5. Authorization from the IDE holder if an approved IDE for the device exists.

⁴ Contact the Center for Devices and Radiological Health, Program Operation Staff at (301) 594-1190. **Nights and weekends for any test article**, contact the FDA Office of Emergency Operations at (301) 443-1240.

D. *After an unapproved device is used in an emergency, the physician should:*

1. Report to the IRB within 5 working days;
2. Evaluate the likelihood of a similar need for the device occurring again, and if future use is likely, immediately initiate efforts to obtain IRB approval and an approved IDE for subsequent use; and
3. Report to the FDA within 5 working days (if there is an IDE, the physician should provide the necessary information to the IDE sponsor so that the IDE sponsor may report to the FDA). This report should contain a summary of the conditions constituting the emergency, patient outcome information and the patient protection measures that were followed.

V. Regulatory Requirements Regarding Informed Consent for Emergency Use

- A. Except as outlined in V.B and V.C below, physicians are required to obtain legally effective informed consent for the emergency use of a test article. FDA requirements for legally effective informed consent are detailed in 21 CFR 50.20, 50.25 and 50.27.
- B. FDA regulations at 21 CFR 50.23(a) provide for an exception from general requirements for informed consent if the treating physician and a physician not otherwise involved in the emergency use (at UCLA, the Department Chair or designee), certify in writing that all of the following criteria are met:
 1. The prospective recipient is confronted by a life-threatening situation necessitating the use of the test article.
 2. Informed consent cannot be obtained from the recipient because of an inability to communicate with, or obtain legally effective consent from, the recipient.
 3. Time is not sufficient to obtain consent from the recipient's legal representative.
 4. 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.
- C. If immediate use of the test article is, in the treating physician's opinion, required to preserve the life of the recipient, and time is not sufficient to obtain independent certification of the criteria listed above in advance of using the test article, the determinations of the treating physician shall, within 5 working days after the emergency use, be reviewed and evaluated in writing by a physician who is not otherwise involved in the emergency use (at UCLA, the Department Chair or designee).

VI. Physician Responsibilities

- A. Physicians are encouraged to obtain consultation from an OPRS Medical IRB Chair prior to the emergency use of a test article, whenever possible.
- B. Physicians should attempt to identify any protocols already approved by the UCLA IRB using the same test article for which either the patient might qualify or the sponsor would grant an exception to the inclusion/exclusion criteria.
- C. Physicians are responsible for confirming that there has not been a prior emergency use of the test article at UCLA.⁵ However, if the product is a drug or biologic and has been used previously, a second use may be allowed if the Department Chair (or designee) provides the determination described in Section III.A.1 above.
- D. Physicians are responsible for following the appropriate regulatory criteria above by using the OPRS emergency use checklist specific to the type of test article.⁶
- E. Physicians are responsible for obtaining an independent assessment and approval from their Department Chair or his/her designee. The Department Chair's designee should provide the assessment and approval if the Department Chair is involved in the patient's care or if the Department Chair is unavailable.
- F. Physicians are responsible for identification of and compliance with any institutional policies regarding receipt, dispensing, use and/or control of test articles (for example, use of the UCLA Drug Information Center, Investigational Drug Section for any investigational drug or biologic used in the UCLA Medical Center).
- G. Physicians are required to submit a report to the IRB within 5 working days of administering the test article. The UCLA OPRS HRPP Checklist for Emergency Use, which is posted on the OPRS Human Research website, details the information and materials required for such a report. There are two checklists: one for unapproved drugs or biologics and a separate one for unapproved devices.
- H. Subsequent to the emergency use, the physician should evaluate the potential for 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.
- I. Physicians are responsible for ensuring that the patient is not included in a systematic investigation designed to develop or contribute to generalizable knowledge.
 - 1. This above provision does not limit the provision of outcomes or safety information as required by the FDA.
 - 2. The above provision does not preclude the retrospective use of data (under appropriate IRB review and approval for such a study).

⁵ A list of test articles previously used according to emergency use guidelines is available at http://www.oprs.ucla.edu/human/forms/emergency_use..

⁶ Materials related to emergency use, including checklists specific to drugs/biologics or devices, are available on the OPRS website at http://www.oprs.ucla.edu/human/forms/emergency_use.

3. The above provision does not preclude the use of information in publication or presentation of a case history. When publishing or presenting more than one case, please contact OPRS to ascertain whether this constitutes human recipients research requiring IRB review and approval.

VII. IRB Responsibilities

- A. The OPRS/IRB will respond to physician inquiries prior to the emergency use of a test article, and will provide appropriate advice and counsel as to the acceptability of proceeding with the proposed activity.
- B. The OPRS/IRB will maintain a database of test articles used according to emergency use guidelines. A list derived from the database will be available on the OPRS Human Research web site for consultation by physicians.⁷ The database and list will be updated after each emergency use of a test article reported to OPRS IRB.
- C. The IRB Chair will determine whether the treating physician met FDA regulations and guidance.
 1. In instances where the IRB Chair has been involved in the care of the patient, or serves as the Department Chair (or designee), an alternate physician member of the IRB will review the physician's report.
 2. The IRB Chair or designee will document his/her review of the report on the emergency use checklist provided with the physician's report.
- D. The IRB Chair or designee, with assistance from the OPRS IRB staff, will communicate any questions or concerns to the physician in writing.
- E. The IRB's receipt of the notification of an Emergency Use and the Chair's review is neither an IRB approval nor an indication that the specific use was prospectively reviewed by the IRB. Formal approval of a protocol requesting the use of an investigational product may only be obtained through full IRB review.
- F. Non-compliance with emergency use requirements will be processed following OPRS/HRPP policies and procedures for noncompliance.
- G. If the IRB Chair or designee determines that the report requires notification to or review by the convened Board, HRPP senior staff will prepare the report for discussion at the next scheduled IRB meeting, and add the report to the meeting agenda.
- H. The IRB will receive, review, and file physicians' reports following administration of the test article. The OPRS/HRPP will maintain documentation of all emergency use reports submitted to the IRB.

⁷ See http://www.oprs.ucla.edu/human/forms/emergency_use.

VIII. UCLA Department Chair Responsibility

- A. The UCLA Department Chair is responsible for providing physicians with an independent assessment and approval for the emergency use of a test article and, if applicable, for the exception to the informed consent requirement. The Department Chair's designee should provide the assessment and approval if the Department Chair is involved in the patient's care.
1. The Department Chair (or designee) shall document his or her determinations on the same checklist as the treating physician and sign and date where required.
 2. If the emergency use proceeds without informed consent without the determinations of the Department Chair (or designee) (see Section V.B above), such determinations must be obtained within 5 working days after the emergency use.
- B. In cases where an unapproved drug or biologic has previously been used in an emergency at UCLA, but the IRB has not had sufficient time to convene a meeting to review the issue, the Department Chair (or a designee if the Chair is involved in the care of the patient) must make a prospective determination regarding the acceptability of a second use of the test article in an emergency situation.⁸
1. The Department Chair or designee must determine that although the test article has been used at UCLA in a previous emergency, there is insufficient time to obtain IRB review and approval for the second emergency use.
 2. The determination must also include justification for the additional use.
 3. The determination must be made prior to the emergency use.
 4. A written statement of the determinations regarding second use, signed and dated by the Department Chair or designee, must accompany the physician's post-use report to IRB/OPRS.

Regulations:

21 CFR 50.23(a)
21 CFR 56.102(d)
21 CFR 56.104(c)
21 CFR 312
21 CFR 812
21 CFR 814,803.30
45 CFR 46.103(b)
45 CFR 46.116(f)
California Health & Safety Code, Section 24178

⁸ FDA IRB Information Sheets: <http://www.fda.gov/oc/ohrt/irbs/drugsbiologics.html#emergency>

References:

FDA, *Guidance on IDE Policies and Procedures*, January 20, 1998.
www.fda.gov/cdrh/ode/idepolicy.html

FDA, *Humanitarian Device Exemption (HDE) Regulation: Questions and Answers*, July 18, 2006. <http://www.fda.gov/cdrh/ode/guidance/1381.html>

FDA, *Information Sheet Guidance: Frequently Asked Questions about Medical Devices*, January 2006. <http://www.fda.gov/oc/ohrt/irbs/irbreview.pdf>

FDA, *IRB Information Sheets: Emergency Use of an Investigational Drug or Biologic*, September 1998. <http://www.fda.gov/oc/ohrt/irbs/drugsbiologics.html>

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FDA, *IRB Information Sheets: FDA Contacts for Obtaining an Emergency IND*, 1998 (revised July 25, 2003). <http://www.fda.gov/oc/ohrt/irbs/drugsbiologicsNEW.html>

OHRP, *OPRR Reports: Emergency Medical Care*, May 15, 1991.
<http://www.hhs.gov/ohrp/humanrecipients/guidance/hcdc91-01.htm>

[HRPP Policy #53: Noncompliance and Allegations of Noncompliance Regarding the Conduct of Human Research](#)