

**Policy Number: 36**

**Title: Emergency Use of a Test Article**

**Date of Last Revision: February 11, 2008**

## **I. Introduction**

FDA regulations permit the emergency use of an investigational drug, agent, biologic or device without prospective IRB approval when a patient is in an immediately life-threatening situation for which no standard acceptable treatment is available, and there is not sufficient time to obtain IRB approval.<sup>1</sup>

The emergency use exemption should not be confused with research designed to evaluate an intervention to be used in emergency situations (see [OPRS/IRB Policy 35: IRB-Approved Research in an Emergency Setting](#) for details). Nor should the exemption be confused with compassionate use protocols, open protocols, or Humanitarian Device Exemptions (see [OPRS/IRB Policy 34: FDA Requirements](#)).

This policy does not apply to “off-label” use of a marketed product for individual patient treatment.

Because research is planned in advance, and medical emergencies are not, UCLA IRBs do not recognize the term “emergency research.” Emergencies that involve patient care are “medical emergencies” and are to be resolved by the physician(s)-in-charge rendering “best patient care” and “best medical practice.”

While an emergency use is a “clinical investigation” under FDA regulations, it is not “research” under DHHS regulations insofar as the patient or the data will not be part of a systematic investigation designed to develop or contribute to generalizable knowledge.

Because DHHS regulations do not allow for emergency uses of test articles, the exemption would not apply if the patient were to be part of a systematic investigation designed to develop or contribute to generalizable knowledge. Prospective IRB review would be required.

UCLA physicians must follow all procedures set forth in this policy before administering an investigational product to a patient in an emergency.

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<sup>1</sup> 21 CFR 56.104(c), with applicable terms defined in 21 CFR 56.102(d)

## II. Definitions

- A. **Emergency use** means the 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)]. Life-threatening, for the purposes of section 56.102(d), includes the scope of both life-threatening and severely debilitating.
- B. **Life-threatening** means 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 subjects 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. For the purposes of this policy, 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).<sup>2</sup>

## III. Regulatory Requirements for Drugs or Biologics

- A. FDA permits one emergency use of an unapproved drug or biologic without prospective IRB review. FDA requires that any subsequent use of the investigational product at the institution have prospective IRB review and approval.
1. 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 issue.<sup>3</sup> 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:

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<sup>2</sup> 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/>.

<sup>3</sup> FDA IRB Information Sheets: <http://www.fda.gov/oc/ohrt/irbs/drugsbiologics.html#emergency>

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 and [OPRS/IRB Policy 11: IRB Review of Modifications to Previously Approved Research](#).
  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.<sup>4</sup>
    - a. 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.
- D. The physician must file a report with the IRB within 5 working days after use of the test article.

#### **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.<sup>5</sup>
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

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<sup>4</sup> 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.

<sup>5</sup> 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.

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 that the physician will 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.
- 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 (B) and (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. Please refer to [OPRS/IRB Policy 29- Informed Consent Process and Documentation](#) for more details.
- 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 human subject is confronted by a life-threatening situation necessitating the use of the test article.
  2. Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject.
  3. Time is not sufficient to obtain consent from the subject'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 subject.
- C. If immediate use of the test article is, in the treating physician's opinion, required to preserve the life of the subject, 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 Responsibility**

- A. Physicians are encouraged to obtain consultation from the MIRB Chair/OPRS 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 following the appropriate regulatory criteria above by using the OPRS emergency use checklist specific to the type of test article.<sup>6</sup>
- D. 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.
- E. Physicians are responsible for confirming that there has not been a prior emergency use of the test article at UCLA.<sup>7</sup>
  - 1. 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.
- 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 emergency use checklist details the information and materials required for such a report.
- 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.
  - a. This above provision does not limit the provision of outcomes or safety information as required by the FDA.
  - b. The above provision does not preclude the retrospective use of data (under appropriate IRB review and approval for such a study).
  - c. 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 subjects research requiring IRB review and approval.

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<sup>6</sup> 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](http://www.oprs.ucla.edu/human/forms/emergency_use).

<sup>7</sup> A list of test articles previously used according to emergency use guidelines is available at [http://www.oprs.ucla.edu/human/forms/emergency\\_use](http://www.oprs.ucla.edu/human/forms/emergency_use).

## **VII. IRB/OPRS Responsibility**

- A. The IRB/OPRS 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 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 web site for consultation by physicians.<sup>8</sup> The database and list will be updated after each emergency use of a test article reported to OPRS.
- 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 shall 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 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 IRB/OPRS policies and procedures for non-compliance. Please see [OPRS/IRB Policy 53: Non-Compliance](#) for details.
- G. If the IRB Chair or designee determines that the report requires notification to or review by the convened Board, IRB staff will prepare the report for discussion at the next scheduled IRB meeting, and add the report to the meeting agenda.
- H. The IRB/OPRS will receive, review, and archive physicians' reports following administration of the test article. The OPRS will maintain documentation of all emergency use reports submitted to the IRB.

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<sup>8</sup> See [http://www.oprs.ucla.edu/human/forms/emergency\\_use](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 .<sup>9</sup>
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.

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<sup>9</sup> FDA IRB Information Sheets: <http://www.fda.gov/oc/ohrt/irbs/drugsbiologics.html#emergency>

**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

**References:**

FDA, *Guidance on IDE Policies and Procedures*, January 20, 1998.  
[www.fda.gov/cdrh/ode/idepolicy.html](http://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>

FDA, *IRB Information Sheets: Emergency Use of Unapproved Medical Devices*, September 1998. <http://www.fda.gov/oc/ohrt/irbs/devices.html>

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/humansubjects/guidance/hsdc91-01.htm>

**Attachments:**

OPRS-36      Emergency Use of a Test Article Checklists