

Policy Number: 45

Title: Emergency Use of a Test Article in a Life-Threatening Situation

Date of Last Revision: 06/06/08; 07/22/10; 03/29/16; 05/01/16; 06/29/17, 09/14/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to recognize the provisions found in the Food and Drug Administration (FDA) regulations for the emergency use of a test article in a life-threatening situation.

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.

- I. FDA regulations exempt research from prior IRB review for the use of a test article in a life-threatening situation in which no standard treatment is available. Physicians must report emergency use to the IRB within 5 working days of use. Any subsequent use of the test article at the institution is subject to IRB review as this would constitute research. Terms such as “interim,” “compassionate,” “temporary,” or other terms for an expedited approval process will not be utilized for requests for emergency use of a test article in a life-threatening¹ situation.

- II. **Criteria for Emergency Use of a Test Article:**
 - A. The patient is in an immediate serious or life-threatening condition that needs immediate treatment;
 - B. No generally acceptable alternative for treating the subject is available; and
 - C. Because of the immediate need to use the drug, agent, or biologic, there is no time to obtain full IRB approval for the use.
 - D. The physician is required to notify the IRB of all emergency uses within five days of the use and to notify the IRB in writing of all exceptions to the requirement for consent within five days of the exception.

Note: The emergency use of an unapproved drug or biologic requires an Emergency IND. The physician must contact the manufacturer of the agent or device to determine if the drug or biologic can be made available for emergency use under the manufacturer’s IND. If the manufacturer does not have an Emergency IND, the physician can contact the FDA directly.

¹ **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.

- III. Although the emergency use of a test article is exempt from IRB review, it is not exempt from the FDA regulatory requirements to obtain and document consent from the participant or the participant's legally authorized representative. There are situations in which an exception can be made to the requirement to obtain consent. Whenever physicians use a test article on an emergency basis, they need to follow the regulatory requirements for an emergency use of a test article, and either obtain consent in accordance with FDA regulations at 21 CFR 50 or follow the requirements for an exception to the requirement for consent at 21 CFR §50.23(a)-(c).

The use of informed consent is required unless the physician imposing an emergency use situation and another physician not otherwise participating in the clinical investigation certify in writing that all of 21 CFR 50.23(a) have been met:

- A. The human subject is confronted by a life-threatening situation necessitating the use of the test article.
 - B. Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject.
 - C. Time is not sufficient to obtain consent from the subject's legal representative.
 - D. There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.
- IV. FDA regulations require IRBs to be notified of all emergency uses within five days of the use and to be notified in writing of all exceptions to the requirement for consent within five days of the exception. The IRB will review these reports at a convened meeting to determine whether the circumstances follow regulatory requirements for the emergency use of a test article, consent was obtained in accordance with FDA regulations at 21 CFR §50, or the circumstances met the exception to the requirement for consent in 21 CFR §50.23(a)-(c).
- V. When following Department of Health and Human Services (DHHS) regulations and guidance, patients receiving a test article that meet the criteria for emergency use as defined by FDA regulations are not considered a research subject. DHHS regulations do not permit data obtained from patients to be classified as human subject research, nor may the outcome of such care be included in any report of research activity subject to DHHS regulations.
- VI. Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care for patients who need such care.
- VII. **Investigational Drugs, Agents, or Biologics (FDA Regulations)**
- A. The emergency use of investigational drugs, agents, or biologics will be handled in accordance with FDA regulations and institutional policies and procedures. Although 21 CFR 56.102(d) allows for an exemption from prior review and approval by the IRB for emergency use, the UCI IRB requests **prior notification** of emergency use of investigational drugs, agents, or biologics. The IRB Chair will review the notification to determine whether the circumstances met the regulatory or legal requirement for the emergency use of a test article.
 - B. FDA regulations at 21 CFR 56.104(c), allows for **one** emergency use of an investigational drug, agent, or biologic without prospective IRB review.

FDA regulations require that any subsequent use of the investigational product at the institution have prospective IRB review and approval as the subsequent use would constitute research. The only exception to this provision is if the IRB has not had sufficient time to convene a meeting to review the research protocol.

VIII. Manufacturers or sponsors that agree to allow the use of the investigational drug, agent, biologic or device, but will not ship without “an IRB approval letter”, may be provided a written statement that the IRB is aware of the proposed use and based on the information provided by the physician the proposed use meets the requirements of 21 CFR 56.102(d).

IX. **Investigational Devices (FDA Regulations)**

- A. The emergency use of investigational medical devices will be handled in accordance with FDA regulations and institutional policies and procedures. Although 21 CFR 56.102(d) allows for an exemption from prior review and approval by the IRB for emergency use, the UCI IRB requests **prior notification** of emergency use of investigational drugs, agents, or biologics. The IRB Chair will review the notification to determine whether the circumstances meet the regulatory or legal requirements for the emergency use of a test article.
- B. Subsequent emergency use of an investigational medical device may not occur unless the physician or another person obtains approval of an IDE for the device and its use. If an IDE application for subsequent use has been filed with the FDA and the FDA disapproves the IDE application, the device may not be used even if the circumstances constitute an emergency use situation.

References:

FDA 21 CFR 50.23(a)-(c)

FDA 21 CFR 50.24

FDA 21 CFR 50.25(d)

FDA 21 CFR 56.102(d)

FDA 21 CFR 56.104(c)

FDA 21 CFR 812.35(a)

U.S. Food and Drug Administration Device Exemptions Regulation: Frequently Asked Questions about IRB Review of Medical Devices, January 2006.

U.S. Food and Drug Administration IRB Information Sheets: Emergency Use of Unapproved Medical Devices, 1998 Update

U.S. Food and Drug Administration IRB Information Sheets: Emergency Use of an Investigational Drug or Biologic, 1998 Update

Procedure Number 45.A**Title: Procedure for Emergency of a Test Article in a Life-Threatening Situation****Procedure:**

This procedure outlines the process for the emergency use of investigational drugs, agents, biologics, or devices.

I. Physician Responsibilities

- A. Requirements of the emergency use of investigational drugs, agents, or biologics
 1. Review the HRP webpage to see whether the investigational drug, agent or biologic has been previously used at UCI. If the test article has previously been used at UCI in a life-threatening situation for emergency use, the physician must obtain IRB approval.
 2. The emergency use of an investigational drug, agent, or biologic in a life-threatening situation requires an IND. Therefore, the physician must:
 - a) Contact the manufacturer of the drug, agent, or biologic first to determine if the test article can be made available for the emergency use under the manufacturer's IND; or
 - b) Contact the FDA for an Emergency IND. The FDA may authorize shipment of the test article in advance of the IND submission. Requests for such authorization must be made by the physician to the appropriate department at the FDA.
 3. The physician should submit the following information via the electronic IRB submission and management system via a New Application for Expanded Access Single Patient Emergency Use :
 - a) An authorization from the sponsor or manufacturer to allow the emergency use by the Physician of the test article;
 - b) An adequate description of the situation regarding the use of the test article;
 - c) An approved Emergency Use IND or a letter explaining exemption from the FDA;
 - d) The unsigned informed consent document or the certification for the exception from obtaining informed consent; and
 - e) Any other materials that may aid in the understanding the emergency use situation.
 4. The IRB Chair, IRB Vice-Chair or medical physician designee will review the electronic IRB submission to determine whether the circumstances met the regulatory requirement for the emergency use of a test article. The criteria are:
 - a) The subject is in an immediate serious or life-threatening condition that needs immediate treatment;
 - b) No generally acceptable alternative for treating the subject is available; and
 - c) Because of the immediate need to use the drug, agent, or biologic, there is no time to obtain full IRB approval for the use.
 - d) The physician is required to notify the IRB of all emergency uses within five days of the use and to notify the IRB in writing of all exceptions to the requirement for consent within five days of the exception.

5. The physician is required to obtain informed consent of the participant or the participant's legally authorized representative unless see #6 below. An Emergency Use informed consent template is available on the HRP website. The informed consent template is to be completed for the specific emergency use situation.
 6. The physician is required to obtain informed consent of the participant or the participant's legally authorized representative unless both the physician imposing the emergency use situation and a physician who is not otherwise participating in the clinical investigation certify in writing (may use an independent physician attestation form available on HRPP website) the following:
 - a) The participant is confronted by a life-threatening situation necessitating the use of the investigational drug, agent, or biologic;
 - b) Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject;
 - c) Time is not sufficient to obtain consent from the participant's legally authorized representative; and
 - d) No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the participant's life.
 7. If, in the Physician's opinion, immediate use of the test article is required to preserve the subject's life, and if time is not sufficient to obtain an independent physician's determination that the four conditions listed above apply, the physician should make the determination and, within 5 working days after the use, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.
- B. After emergency use procedures for investigational drugs, agents, or biologics
1. The IRB must be notified of all emergency uses within five days of the use and to be notified in writing of all exceptions to the requirement for consent within five days of the exception. The physician is required to complete an amendment to the original application via the electronic IRB submission and management system which should include:
 - a) Name of the investigational drug, agent or biologic;
 - b) Conditions under which the investigational drug, agent or biologic was utilized;
 - c) Date utilized;
 - d) Any unanticipated problems to recipient or others;
 - e) Outcomes, if known; and
 - f) An evaluation of the likelihood of a similar need for the drug, agent, or biologic occurring again. If future use is likely, the physician must immediately initiate efforts to obtain IRB approval and an approved IND for the drug, agent, or biologic's subsequent use.
 2. A copy of the unsigned informed consent document or both the physician imposing the emergency use situation and a physician who is not otherwise participating in the clinical investigation signature certifying in writing that the emergency use situation met the exception to the requirement for consent.

3. Written verification of approval from the IND holder authorizing release of the test article in this emergency use situation. This may have been authorized verbally, but written confirmation should be provided or a letter from the FDA authorizing emergency use of the test article.

C. Requirements for emergency use of investigational medical devices

1. For investigational devices under an IDE, the IDE regulation permits deviations from the investigational plan without prior approval when necessary to protect the life or physical well-being of a subject in an emergency. An physician may treat a patient with an unapproved medical device in an emergency situation if the following criteria must be met:
 - a) The subject is in a life-threatening condition that needs immediate treatment;
 - b) No generally acceptable alternative for treating the subject is available; and
 - c) Due to the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use.
2. The FDA expects the physician to determine the following:
 - a) Whether the criteria for emergency use have been met;
 - b) To assess the potential for benefits from the unapproved use of the device, and to have substantial reason to believe that benefits will exist; and
 - c) Assure that the decision of the Physician that an “emergency” exists is not based solely on the expectation that IDE approval procedures may require more time than is available.
3. The physician must assure that the device developer notifies the FDA immediately after an unapproved device is shipped for an emergency use. An unapproved device may not be shipped in anticipation of an emergency.
4. The physician is expected to follow as many subject protection procedures as possible. These include:
 - a) Concurrence of the IRB Chair, IRB Vice-Chair or medical physician designee;
 - b) Obtaining informed consent from the participant or the participant’s legally authorized representative; or an assessment from a physician who is not participating in the study
 - c) Obtaining a written independent assessment by an uninvolved physician;
 - d) Obtaining authorization from the IDE holder, if an approved IDE for the device exists.
5. Although the FDA regulations allows for an exemption from prior review and approval by the IRB for emergency use, the UCI IRB requests prior notification of emergency use of investigational device. The physician should submit the following information:
 - a) a New Application for Expanded Access Single Patient Emergency Use via electronic IRB submission and management system
 - b) An authorization from the sponsor or manufacturer to allow the emergency use by the Physician of the test article;
 - c) An adequate description of the situation regarding the use of the test article;

- d) The unsigned informed consent document or the certification for the exception from obtaining informed consent; and
 - e) Any other materials that may aid in the understanding the emergency use situation.
6. The IRB Chair, IRB Vice-Chair or medical physician designee will review the Expanded Access Single Patient Emergency Use application to determine whether the circumstances met the regulatory requirement for the emergency use of a test article. The criteria are:
 - a) The subject is in an immediate serious or life-threatening condition that needs immediate treatment;
 - b) No generally acceptable alternative for treating the subject is available; and
 - c) Because of the immediate need to use the device, there is no time to obtain full IRB approval for the use.
 - d) The physician is required to notify the IRB of all emergency uses within five days of the use and to notify the IRB in writing of all exceptions to the requirement for consent within five days of the exception.
 7. The physician required to obtain informed consent of the participant or the participant's legally authorized representative unless see #8 below. An Emergency Use informed consent template is available on the HRPP website. The informed consent template is to be completed for the specific emergency use situation.
 8. The physician is required to obtain informed consent of the participant or the participant's legally authorized representative unless both the physician imposing the emergency use situation and a physician who is not otherwise participating in the clinical investigation certify in writing the following:
 - a) The participant is confronted by a life-threatening situation necessitating the use of the investigational (unapproved) medical device.
 - b) Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject;
 - c) Time is not sufficient to obtain consent from the participant's legal representative; and
 - d) No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the participant's life.
 9. If, in the physician's opinion, immediate use of the test article is required to preserve the subject's life, and if time is not sufficient to obtain an independent physician's determination that the four conditions listed above apply, the physician should make the determination and, within 5 working days after the use, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.
- D. After emergency use procedures for investigational medical devices
1. The IRB must be notified of all emergency uses within five days of the use and to be notified in writing of all exceptions to the requirement for consent within five days of the exception. The physician is required to complete an amendment to the original application via the electronic IRB submission and management system which should include:

- a) Name of the investigational device;
 - b) Conditions under which the investigational device was utilized;
 - c) Date utilized;
 - d) Any adverse device effects, unanticipated problems to recipient or others;
 - e) Outcomes, if known; and
 - f) An evaluation of the likelihood of a similar need for the device occurring again. If future use is likely, the physician must immediately initiate efforts to obtain IRB approval and an approved IDE for the device's subsequent use.
2. A copy of the unsigned informed consent document or both the physician imposing the emergency use situation and a physician who is not otherwise participating in the clinical investigation signature certifying in writing that the emergency use situation met the exception to the requirement for consent.
 3. Written verification of approval from the IDE holder authorizing release of the test article. This may have been authorized verbally, but written confirmation should be provided.
 4. If an IDE does not exist, the Physician is to notify the FDA of the emergency use and provide the FDA with a written summary of conditions constituting the emergency, subject protection measures, and results.
- E. All submissions are to be made via the online IRB submission and management system.

II. IRB Committee Responsibilities

- A. The emergency use of FDA regulated products requires the involvement of an IRB Chair, IRB Vice-Chair or medical physician designee
- B. The IRB Chair, IRB Vice-Chair or medical physician designee will be promptly notified of the Physician's intent for emergency use of an investigational drug, agent, biologic, or device in a life-threatening situation.
- C. The IRB Chair, IRB Vice-Chair or medical physician designee will evaluate the Physician's submission of the Expanded Access Single Patient Emergency Use application and guide the physician in adherence to the FDA regulations and institutional policies and procedures. The IRB Chair, IRB Vice-Chair or medical physician designee will review:
 1. An authorization from the sponsor or manufacturer to allow the emergency use by the Physician of the test article;
 2. An approved IDE;
 3. An adequate description of the situation regarding the use of the test article with an independent physician's certification, if applicable;
 4. The unsigned informed consent document or the certification for the exception from obtaining informed consent; and
 5. Any other materials that may aid in the understanding the emergency use situation.
- D. The IRB Chair, IRB Vice-Chair or medical physician designee may make any of the following decisions:
 1. **Emergency Use Confirmed-CRITERIA MET:** The proposed use meets the emergency use criteria.
 2. **Emergency Use Not Confirmed- CRITERIA NOT MET:** The proposed use does not meet the emergency use criteria. The physician may choose to submit an IRB Application for approval to

conduct human subjects research. Refer to HRP Policy and Procedure # 41.

3. **Emergency Use Not Confirmed – CRITERIA NOT MET: PRIOR INSITUATIONAL USE:** If all the criteria are not met, but the use appears appropriate and there is time for the request to be added to the next IRB agenda and approved prospectively, the physician is referred back to the HRP staff for guidance in submitting the IRB application. In such circumstances, the emergency use would be allowable only if the patient's condition became more urgent while awaiting IRB action.
- E. The IRB will review the completed online Expanded Access Single Patient Emergency Use application and amendment as well as any supporting documentation including the IRB Emergency Use of as Test Article Checklist at a convened meeting to determine whether the circumstances follow regulatory requirements for the emergency use of a test article, consent was obtained in accordance with FDA regulations, or the circumstances met the exception to the requirement for consent. A checklist will be completed by the IRB Chair and a confirmation is sent to the physician for their records.

III. **IRB Administrator Responsibilities**

- A. It is the responsibility of the Administrator to facilitate any inquiries from physicians regarding the emergency use of the FDA regulated product.
- B. The Administrator will contact an IRB Chair, IRB Vice-Chair or medical physician designee to inform him/her of the Physician's notification of emergency use.
- C. The Administrator will promptly notify the Director of Human Research Protections or designee of a physician's notification of an emergency use of a test article in a life-threatening situation.
- D. The Administrator will assist the physician in providing the appropriate documentation prior to the emergency use, if possible, and follow-up with the physician if an adequate written documentation is not received within 5 days following the emergency use of a test article in a life-threatening situation.
- E. The Administrator will update the "Emergency Use" electronic folder and web page accordingly.
- F. The Administrator will add the emergency use of a test article in a life-threatening situation to the upcoming Biomedical IRB Committee Agenda.
- G. The Administrator will provide all IRB members the completed Expanded Access Single Patient Emergency Use application and amendment and any supporting documentation including the IRB Emergency Use of as Test Article Checklist.

Attachments:

FDA Contacts for Obtaining Emergency IND and Guidance on Emergency Use of a Device

Product	Contact
Drug Products	Drug Information Branch (HFD-240) (301) 827-4570
Biological Blood Products	Office of Blood Research and Review (HFM-300) (301) 827-3518
Biological Vaccine Products	Office of Vaccines Research and Review (HFM-400) (301) 827-3070
Biological Therapeutic Products	Office of Therapeutics Research and Review (HFM-500) (301) 594-2860
Nights and Weekends	Division of Emergency and Epidemiological Operations (HFC-160) (301) 443-1240
Devices	Center for Devices and Radiological Health (301) 594-1190