



## EMERGENCY USE OF INVESTIGATIONAL DRUGS, BIOLOGICS, OR DEVICES

### 1. Overview

The emergency use provision in FDA regulations is an exemption from the requirements for prior review and approval of research by the IRB. The exemption, which must meet the specific conditions described in the regulations, allows for one emergency use of an investigational drug or biologic or unapproved medical device in a life-threatening situation for which no standard acceptable treatment is available and when there is not sufficient time to obtain IRB approval.

This policy outlines the requirements for emergency uses of investigational drugs or biologics, emergency uses of unapproved medical devices, and exceptions to the requirements for informed consent in emergency situations.

### 2. Definitions

**Emergency Use:** Use of an investigational drug or biologic or unapproved medical device for a human subject in a life-threatening situation for which no standard acceptable treatment is available and when there is not sufficient time to obtain IRB approval. *Note: Under FDA regulations, emergency use is a category of research (i.e., clinical investigation) that is exempt from the requirements for IRB review.*

**Unapproved Medical Device:** A device used for a purpose or condition for which the device would require but does not have premarket approval or an approved investigational device exemption (IDE) from FDA.

**Investigational Device Exemption (IDE):** An application that permits a medical device that would otherwise be required to comply with an existing performance standard or to have premarket approval by FDA to be legally shipped for a clinical investigation.

**Investigational New Drug Application (IND):** An application that permits an investigational drug that would otherwise be required to have premarket approval by FDA to be legally shipped for a clinical investigation.

**Compassionate Use:** Use of an investigational drug or biologic or unapproved medical device for a single subject (or small group of subjects) with a serious disease or condition, who does not meet the requirements for inclusion in a clinical investigation, and for whom no standard acceptable treatment is available. Prior FDA and IRB approval are required for compassionate use. *Note: The terms compassionate use and emergency use are not synonymous.*

**Life-threatening:** Refers to diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted; also diseases or conditions with potentially fatal outcomes.



**Severely Debilitating:** Refers to diseases or conditions that cause major irreversible morbidity (e.g., blindness, loss of limb, loss of hearing, paralysis, or stroke).

### 3. General Information

- A.** The emergency use of an investigational drug or biologic or unapproved medical device is research involving human subjects as defined by FDA regulations. All emergency uses are subject to the requirements of The Ohio State University Human Research Protection Program (HRPP), except as described by this policy. Note: The emergency use of a drug, biologic, or device does not meet the DHHS definition of research involving human subjects. For more information on activities that are defined by FDA and DHHS regulations as “research involving human subjects,” see HRPP policy [[Research Involving Human Subjects](#)].
- B.** The use of a marketed drug, biologic, or medical device for an indication that is not listed in the FDA-approved product labeling (i.e., “off label” use) for an individual in a life-threatening situation does not constitute an emergency use as defined by FDA regulations and HRPP policy. Regulations and university policy do not limit the authority of physicians to provide such emergency “medical care” to patients in life-threatening situations; however, physicians and other healthcare providers are responsible for complying with applicable state laws and other institutional requirements (e.g., The Ohio State University Wexner Medical Center policies) regarding all uses of drugs, biologics, and medical devices.
- C.** FDA requirements for emergency uses of investigational drugs and biologics differ slightly from the requirements for emergency uses of unapproved medical devices, as described below. For more information on research involving investigational drugs and medical devices, see HRPP policies [[Research Involving Investigational Drugs](#)] and [[Research Involving Medical Devices](#)].

### 4. Criteria for Emergency Use

According to FDA regulations, the emergency use exemption may be used if all of the following conditions are met:

- The use involves an investigational drug or biologic, unapproved medical device, or other “test article” as defined by FDA
  - A test article is any drug, biologic, or medical device for human use, or human food additive, color additive, electronic product, or any other article subject to FDA regulations
- The individual for whom the test article is intended is in a life-threatening situation
  - To meet the criteria for life-threatening a condition does not have to be *immediately* life-threatening or *immediately* resulting in death
  - Life-threatening also includes “severely debilitating”
  - Severely debilitating does not include “pre-existing” (e.g., chronic) diseases or conditions with major morbidity
- No standard acceptable treatment is available
  - Also, the individual for whom the test article is intended does not meet the enrollment criteria for an existing IRB-approved study or an approved study does not exist



- There is not sufficient time to obtain IRB approval
  - An intervention is needed before review at a convened meeting of the IRB is feasible.

## 5. Prior Notification of Emergency Use

- A.** The IRB Chair (or physician designee) of the appropriate IRB will be notified of an investigator's intent to use an investigational drug or biologic or unapproved medical device for emergency use. Notification may be made in person, electronically (e.g., by telephone, fax, or email), or in writing. Investigators will provide the following information to allow the IRB Chair to determine that FDA requirements for emergency use are met:
- Explanation of the life-threatening situation necessitating the emergency use
  - Description of standard treatment(s) previously used and/or why available options are not acceptable
  - Investigational drug or biologic or unapproved medical device to be used
  - If available, IND or IDE number of the drug, biologic, or device. *Note: It is important to distinguish between emergency use INDs or IDEs and other types of expanded access that do require prospective IRB review and approval (e.g., single-patient access, humanitarian use devices, etc.).*
- B.** An IRB Chair's acknowledgment of the emergency use does not constitute an IRB approval of the clinical investigation. The investigator's notification is used by the IRB and the Office of Responsible Research Practices (ORRP) to confirm that the proposed use meets FDA requirements and to assist the investigator with filing the required report within the five-day timeframe required by FDA regulations.
- C.** Emergency uses of investigational drugs and biologics and unapproved medical devices in The Ohio State University Wexner Medical Center must comply with applicable policies (e.g., The Department of Pharmacy Investigational Drug Service Policies and Procedures). The Investigational Drug Service will be notified (as applicable) of the intended emergency use of an investigational drug or biologic to arrange for the product's shipment and proper storage, dispensing, and accountability.

## 6. Informed Consent Requirements

Investigators are required to obtain the informed consent of the subject or the subject's legally authorized representative in an emergency use situation. Consent form templates containing the basic elements of informed consent are available on the ORRP website. Alternatively, the product manufacturer or sponsor may provide a consent form for emergency use. All of the basic elements of informed consent (and any applicable additional elements) are to be provided, unless the situation meets the conditions for exception described below.

## 7. Exception to the Requirements for Informed Consent

- A.** When informed consent cannot be obtained, both the investigator and a physician who is not otherwise involved in the emergency use must confirm in writing that all of the following conditions apply:



- The subject is confronted by a life-threatening situation necessitating the use of the investigational drug or biologic or unapproved medical device
  - Informed consent cannot be obtained because of an inability to communicate with or obtain informed consent from the subject
  - Time is not sufficient to obtain informed consent from the subject's legally authorized representative
  - No alternative method of approved or "generally recognized therapy" is available that provides an equal or greater likelihood of saving the subject's life.
- B.** If time is not sufficient to obtain an independent physician's determination that the criteria for an exception to the requirements for informed consent (described above) are met, and in the investigator's opinion the *immediate* use of the investigational product is required to preserve the subject's life, the investigator must do both of the following:
- Verify in writing that the four conditions for an exception to the requirements for informed consent apply
  - Obtain an independent review and evaluation of the investigator's determination in writing within five working days by a physician who is not otherwise involved in the emergency use.
- C.** The IRB must be notified of the exception within five working days after the emergency use, as described below (see "Five-Day Reporting").

## 8. IND Requirements for Emergency Uses of Drugs and Biologics

- A.** The emergency use of an investigational drug or biologic requires an IND. To obtain an emergency use IND, an investigator should contact the product manufacturer or sponsor to determine if the investigational drug or biologic can be made available for the emergency use under the company's IND.
- B.** Alternatively, if the manufacturer/sponsor will not provide the investigational product under its IND, an investigator may contact FDA directly to obtain authorization for the company to ship the drug or biologic for the specific emergency situation in advance of an IND submission. For more information, see ["FDA Contacts for Obtaining an Emergency IND."](#)
- C.** Some manufacturers or sponsors will agree to the emergency use of an investigational drug or biologic, but require an "IRB approval letter" before shipping the product. When necessary, following the IRB Chair's review of the emergency use as described above ("Prior Notification of Emergency Use") ORRP staff will provide the investigator with documentation acknowledging that the IRB is aware of the intended emergency use and considers the use to meet FDA requirements.

## 9. Additional Requirements for Emergency Uses of Unapproved Medical Devices

- A.** FDA approval prior to emergency use or shipment of an unapproved medical device is not required. The emergency use may involve a device that does not have an existing IDE, a device used in a way that is not approved under an existing IDE, or a physician who is not named as an investigator on the IDE. Whenever possible, authorization



should be obtained from the sponsor (if an IDE exists for the device) before the emergency use.

- B.** In addition to determining that the criteria for emergency use are met, investigators are required by FDA to assess the potential for benefit from the use of an unapproved device and to have “substantial reason” to believe that benefits will occur. Whenever possible, an independent assessment of the circumstances prior to the emergency use should also be obtained from a physician who is not otherwise involved in the emergency use.
- C.** If the device has an existing IDE and the investigator could not obtain authorization from the sponsor prior to the emergency use, the investigator is responsible for reporting to the sponsor within five working days. The emergency use of an unapproved device must be reported to FDA by the sponsor (if an IDE exists for the device) within five working days of the time the sponsor learns of the use. If no IDE exists, the investigator is responsible for reporting the emergency use directly to FDA. The investigator’s follow-up report should contain the information described below.

## 10. Reporting Requirements

- A.** Investigators are responsible for notifying the IRB in writing within five working days after the emergency use of an investigational drug or biologic or unapproved medical device. Reports should be sent to the Office of Responsible Research Practices with the following information:
- Investigational drug or biologic or unapproved medical device used
  - IND number of the drug or biologic or IDE number (if one exists) of the device
  - Date(s) of administration of the investigational product
  - Explanation of the life-threatening situation necessitating the emergency use
  - Demographic information of the subject (e.g., age, gender, etc.), without personally identifiable information
  - Outcome(s) of the emergency use
  - An unsigned copy of the consent form that was used
    - Alternatively, if consent was not obtained, either of the following as described above (“Exception to the Requirements for Informed Consent”):
      - The investigator’s and independent physician’s verification prior to the emergency use that the conditions were met for the exception to the requirements for informed consent
      - The investigator’s verification that the conditions for exception were met and independent physician’s review and evaluation (within 5 working days of the emergency use) of the investigator’s determination.
- B.** The IRB Chair (or physician designee) will review emergency use reports within 14 days of receipt to determine that the circumstances met FDA requirements. If the IRB Chair (or physician designee) determines that the use failed to meet regulatory requirements, the Chair will determine if noncompliance occurred as described in HRPP policy [\[Noncompliance\]](#). Investigators will be notified by ORRP staff of the outcome of the Chair’s review within 14 days of the review.



- C. Investigators are also responsible for reporting the circumstances of the emergency use to the product manufacturer or sponsor of the investigational drug or biologic or unapproved medical device when the emergency use was performed under the manufacturer's/sponsor's IND or IDE. Otherwise, the emergency use is reported directly to FDA. The follow-up report should contain the following information:
- Summary of the conditions constituting the emergency
  - Acknowledgment by the IRB Chair of prior notification of the emergency use
  - Whether informed consent was obtained or the conditions were met for the exception to the requirements for informed consent
  - Independent assessment by a physician not otherwise involved in the emergency use (when applicable)
  - Outcome(s) of the emergency use
  - Other information as required by the product manufacturer or sponsor.
- D. Investigators and IRBs are responsible for reporting and review of any adverse events, unanticipated problems involving risks to subjects or others, or other events associated with the emergency use, as described by HRPP policies [[Event Reporting – Unanticipated Problems Involving Risks to Subjects or Others, Adverse Events, and Other Problems](#)] and [[IRB Reporting – Unanticipated Problems, Noncompliance, Suspensions, and Terminations](#)].
- E. Investigators who obtain an IND or IDE for the emergency use or subsequent use of the investigational drug or biologic or unapproved medical device are responsible for complying with FDA requirements for the use of investigational drugs and devices, including providing progress and/or final reports. For more information, see FDA regulations at [Investigational New Drug Application: 21 CFR Part 312](#) and [Investigational Device Exemptions: 21 CFR Part 812](#).

## 11. Limitations of Emergency Use

- A. The emergency use exemption allows for a single use or single “course of treatment” (e.g., multiple doses of an antibiotic) of an investigational drug or biologic or unapproved medical device without prior IRB review. FDA regulations require that any subsequent use of the investigational product at the same institution receive IRB review and approval before the product is used again.
- B. FDA guidance 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 request. Investigators are encouraged to evaluate the likelihood of a similar need occurring again, and if future use is likely, immediately initiate efforts to obtain IRB review and approval of a protocol to permit further use of the investigational drug, biologic, or device.
- C. Emergency use of an investigational drug or biologic or unapproved medical device must be differentiated from “planned emergency research” in life-threatening situations. Planned emergency research is research conducted in emergency settings with subjects who cannot provide informed consent because of their life-threatening medical



conditions (e.g., comparison of methods for providing cardiopulmonary resuscitation) and who do not have an available legally authorized representative. Unlike emergency uses, planned emergency research must be approved in advance by FDA (or DHHS) and the IRB and publicly disclosed to the community in which the research will be conducted. For more information about the requirements for planned emergency research, see HRPP policy [[Planned Emergency Research](#)].

## 12. Applicable Regulations/Guidance

21 CFR 50.23, 21 CFR 56.102, 21 CFR 56.104, FDA Information Sheets: "Emergency Use of an Investigational Drug or Biologic," "Frequently Asked Questions About Medical Devices," and Frequently Asked Questions: "IRB Procedures"

## 13. History

Issued: 10/20/2008

Revised: 04/28/2009, 06/04/2012

Edited: 08/08/2014