

Title:	Emergency Use of an Investigational Drug or Biological Product, or Unapproved Medical Device
Department:	Human Research Affairs
Policy Type:	<input checked="" type="checkbox"/> Partners System-wide <input type="checkbox"/> Partners System-wide Template <input type="checkbox"/> Partners HealthCare <input type="checkbox"/> Partners HealthCare Departmental <input type="checkbox"/> Institution
Applies to:	Employees, Professional Staff or Other Agents of Brigham and Women's Hospital (BWH), Faulkner Hospital (FH), Massachusetts General Hospital (MGH), McLean Hospital (McLean), and North Shore Medical Center (NSMC)
Approved by:	Chief Academic Officer
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Contact Person:	Director, Human Research Review and Compliance

KEYWORDS:

IRB, Institutional Review Board

PURPOSE:

The purpose of this policy is to define the applicability of the Food and Drug Administration (FDA) emergency exemption from prospective IRB approval for use of an investigational drug or biological product, or unapproved medical device with 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)] and the procedures for reporting such emergency uses to the Partners Human Research Committees (PHRC) and to the Food and Drug Administration (FDA).

DEFINITIONS:

See Definition of Human-Subjects Research

Emergency use of an investigational drug or biologic product as defined by FDA means the use of an investigational drug or biological product with 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.

Emergency use of an unapproved device as defined by FDA means the use of an unapproved medical device with a human subject in a life-threatening situation in which no standard acceptable treatment is available.

Life-threatening as defined by FDA 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.

Severely debilitating as defined by FDA 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.

POLICY STATEMENT:

The FDA regulations allow for the emergency use of an investigational drug or biological product, or unapproved medical device with 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.

The emergency use of an investigational drug or biological product, or unapproved medical device does not meet the DHHS definition of *research involving human subjects*; however, the emergency use of a drug or biological product meets the FDA definition of *clinical investigation*. As such, the patient is a participant, and the FDA may require data from an emergency use to be reported in a marketing application.

Medical staff, not residents, fellows, or trainees, who propose to use an investigational drug or biological product, or unapproved medical device, must comply with all applicable FDA regulations. Whenever possible, investigators should notify the PHRC of a proposed emergency use of an investigational drug or biological product, or unapproved medical device prior to such emergency use; however such notifications do not constitute PHRC approval. When it is not possible for the investigator to notify the PHRC before the emergency use of the investigational drug or biological product, or unapproved medical device, the investigator must notify the PHRC of such use within 5 working days.

PROCEDURES:

When a member of the medical staff of the applicable Partners-affiliated entities, not including residents, fellows, or trainees, proposes to use an investigational drug or biological product, or unapproved medical device, he/she must comply with FDA regulations and institutional policies and procedures, as described below:

Whenever possible, the investigator proposing to use an investigational drug or biological product, or unapproved medical device in an emergency situation should contact the Partners Human Research Office for guidance.

Whenever possible prior to the proposed use, the investigator should complete and submit the Insight/eIRB Emergency Use Form to the Partners Human Research Office to document in writing the emergency exemption from prospective IRB approval for use of an investigational drug or biological product, or unapproved medical device with 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.

The reviewing PHRC Chairperson is responsible for either concurring with the emergency exemption or for finding that the proposed use does not meet the criteria for an emergency exemption from prospective IRB approval.

The reviewing PHRC Chairperson may request additional information or review by an independent physician when determining whether or not the criteria for an emergency exemption are met.

The reviewing PHRC Chairperson is responsible for informing the investigator of his/her concurrence or disagreement with the emergency exemption.

When the reviewing PHRC Chairperson disagrees with the emergency exemption, the proposed use will be scheduled for review at the next available convened meeting of the PHRC.

When time is not sufficient for the investigator to notify the PHRC of the proposed use, the investigator must notify the PHRC within 5 working days after the use of the investigational drug or biological product, or unapproved medical device.

All emergency uses are reported to the PHRC at a convened meeting, at which time the PHRC reviews and determines whether the FDA requirements for emergency exemption from prospective IRB approval were met and, when appropriate, requires additional follow-up information.

The Partners Human Research Office is responsible for notifying the investigator of PHRC review of the reported emergency use. The notification includes the requirement for prospective PHRC review and approval of any subsequent use of the investigational drug or biological product, or unapproved medical device.

Although the FDA requires prospective IRB review and approval prior to subsequent uses of the investigational drug or biological product, or unapproved medical device, the FDA 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 protocol.

1. Investigational Drugs or Biological Products

FDA regulations permit a physician to treat a patient with an investigational drug or biological product if he/she concludes that:

- the subject has a disease or condition which is life-threatening (e.g., the likelihood of death is high) or severely debilitating (e.g., may cause irreversible morbidity, such as blindness, loss of limb, loss of hearing, paralysis or stroke);
- the subject's disease or condition requires intervention with the investigational drug or biological before review at a convened meeting of the IRB is feasible; and
- no standard acceptable treatment is available.

In such cases, the physician (also referred to as the “investigator”) is responsible for contacting the manufacturer to determine whether the investigational drug or biological product can be provided under an existing IND.

When the investigational drug or biological product is not available under an existing IND, the investigator is responsible for contacting the FDA to obtain an emergency IND.

Once an IND is in place, the investigator may administer the investigational drug or biological product with the informed consent of the subject or the subject’s legally authorized representative.

An exception to the requirement for informed consent may be made if both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:

- The subject is confronted by a life-threatening (or severely debilitating) situation necessitating the use of the investigational drug or biologic;
- Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject;
- Time is not sufficient to obtain consent from the subject's legal representative; and
- No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the life of the subject.

If, in the investigator's opinion, immediate use of the investigational drug or biological product 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 above apply, the investigator should make the determination and, within 5 working days after the use of the investigational drug or biological product have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

The investigator is responsible for alerting the relevant pharmacy of the proposed emergency use and arrangements for drug shipment.

2. Unapproved Medical Devices

FDA regulations permit a physician to treat a patient with an unapproved medical device in an emergency situation if he/she concludes that:

- The patient has a life-threatening condition that needs immediate treatment;
- No generally acceptable alternative treatment for the condition exists; and
- Because of the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use.

FDA expects investigators to follow as many of the patient protection procedures listed below as possible:

- Informed consent from the patient or a legal representative;
- Clearance from the institution;
- Concurrence of the IRB chairperson;
- An assessment from a physician who is not participating in the study; and
- Authorization from the IDE sponsor, if an IDE exists for the study.

When an unapproved medical device is not available under an existing IDE, the investigator is responsible for reporting the emergency use to the FDA Center for Devices and Radiological Health (CDRH) or Center for Biologics Evaluation and Research (CBER) within 5 working days of the use. The report should contain a summary of the conditions constituting the emergency, patient outcome information, and the patient protection measures that were followed (e.g., informed consent from the patient or the patient's legal representative; clearance from the institution as specified by institutional policies; concurrence of the IRB chairperson; and an assessment from a physician who is not participating in the study).

When applicable, the investigator is responsible for alerting the operating room or other facility of the proposed emergency use and arrangements for device shipment.

REFERENCE:

21 CFR 50, 56, 312, 812

DEVELOPMENT AND CONSULTATION

Human Research Office
Office of the General Counsel

Reviewed by:	Original Review Date:	Revision Approval Dates:
Dennis A. Ausiello, MD, Chief Scientific Officer	December 16, 2010	
Anne Klibanski, MD, Chief Academic Officer		May 5, 2015