

**INSTITUTIONAL REVIEW BOARD
HUMAN SUBJECTS PROTECTION OFFICE**

PENN STATE COLLEGE OF MEDICINE
PENN STATE MILTON S. HERSHEY MEDICAL CENTER

IRB Information Sheet
Emergency Uses of Investigational Test Articles
(Unapproved Drugs, Biologics or Devices)

The following information outlines the requirements for physicians to use a U.S. Food and Drug Administration (FDA)-regulated test article (i.e., unapproved drug, biologic, or device) to provide medical treatment to a single patient in a life-threatening situation.

NOTE: These related topics are addressed separately:

- **Emergency Protocol Deviations - IRB Information Sheet: Protocol Deviations**
- **Planned Emergency Research - Research Activities in Emergency Situations: Policy and Procedures**

Background

An exemption under FDA regulations (21 CFR 56.104) permits the emergency use of an investigational test article (i.e., unapproved drug, biologic or device) without prior IRB review and approval.

Emergency use is defined as a life-threatening situation in which: 1) no standard acceptable treatment is available and 2) there is not sufficient time to obtain IRB approval.

“Life-threatening” in the emergency use context includes both likelihood of death unless the course of the disease is interrupted and conditions with potentially fatal outcomes, as well as severely debilitating conditions, that cause major irreversible morbidity, e.g., blindness, loss of limb, loss of hearing, paralysis, stroke, etc.

The investigator must obtain the informed consent of the participant for such an emergency use, unless the emergency situation does not make it feasible to obtain informed consent prior to using the test article. In such a case, an exemption under FDA regulations (21 CFR 50.23) permits the emergency use of an investigational drug, device or biologic without informed consent if the investigator and an uninvolved physician certify in writing that certain conditions exist. (See below for the specific requirements.)

What should I do first if I need to use a test article in an emergency situation?

Whenever possible, investigators should consult an IRB Chair for guidance prior to the emergency use. IRB Chairs are listed on the IRB website, www.pennstatehershey.org/irb, under *About Us, IRB Contacts*.

In any case, all emergency uses of test articles must be reported in writing to the IRB within 5 weekdays of the event. See below for more details and a template for the report to the IRB.

What are the requirements for the emergency use of a test article without IRB review?

All of the following conditions must be met for this type of emergency use:

- A patient is in a life-threatening situation
- No standard acceptable treatment is available.
- There is insufficient time to obtain IRB approval.
- Ordinarily, the investigator must obtain the informed consent of the patient for such an emergency use, except as described in Emergency Use of a Test Article without Informed Consent below. For emergency use situations the consent form provided by the sponsor may be used for obtaining the informed consent of the patient.

The emergency use must be reported in writing to the IRB within five weekdays (such reporting should not be construed as IRB approval for emergency use).

This written report will include:

- a cover letter with the name of the investigational test article,
 - an explanation of the medical condition and its reason for use,
 - date and time administered,
 - any adverse events or unanticipated problems to the recipient or others and outcome if known;
 - a copy of the informed consent document; or if consent is not feasible provide:
 - documentation of the infeasibility of obtaining consent (see specific conditions below)
- and
- a report of concurrence from an independent physician (explained below)
 - and any manufacturer information available on the product (e.g., protocol, drug brochure or device information).

For a template see the 'Suggested Wording for Emergency Use Report'.

What are the requirements for the emergency use of a test article without informed consent?

In addition to meeting the requirements for emergency use, outlined above, the investigator and an independent physician who is not otherwise participating in the clinical investigation must certify in writing all four of the following specific conditions. (The IRB Chair making the determination about the emergency use is not eligible to serve as the independent physician whose concurrence is described below.) If time is not sufficient to obtain the independent physician determination before use of the test article, the actions of the investigator must be reviewed and evaluated in writing by an independent physician within five weekdays.

- The patient is confronted by a life-threatening situation necessitating the use of the test article.
- No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the patient's life.
- Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from the patient.
- Time is not sufficient to obtain consent from the patient's legally authorized representative.

What happens after the IRB receives the report of the emergency use of the test article?

Once the investigator has provided a written report, the emergency use is assigned an IRB tracking number. The IRB Chair or the Chair's designee determines whether the relevant regulatory and

institutional requirements appear to have been satisfied and responds in writing with his/her determination. The emergency use is reported at the next IRB meeting.

What if it is likely that I will have other patients that may benefit from the use of this test article in the future?

If it appears probable that similar emergencies will require use of the test article at PSU, the investigator should sign on to the sponsor's study or develop a protocol for future use of the test article. Either process would need to be prospectively reviewed and approved by the IRB. However, if a situation occurs whereby emergency use of the same test article for a second patient is requested, either by the same or a second physician, subsequent emergency use should not be withheld for the purpose of gaining IRB approval. This procedure is not intended to limit the authority of a physician to provide emergency care in a life-threatening situation.

May I publish or present the results of this emergency use of a test article?

The emergency use regulations may only be used to treat your patient in an emergency and may not be used as a mechanism to bypass the requirements for IRB review. Other than providing information to the sponsor and FDA, you may not use the data without prior review and approval by the IRB.

Are there any additional requirements for use of investigational drugs or biologics?

In addition to meeting the requirements for emergency use of a test article without IRB review, outlined above, the emergency use of an unapproved drug requires an Investigational New Drug review and number (IND) from the FDA applicable to the intended use. The sponsor (holder of the IND) should be consulted to verify such applicability. If no applicable IND exists, use of the drug in the emergency situation requires a request to the FDA to authorize shipment of the drug for emergency use. Such authorization is conditioned on the sponsor making an appropriate IND submission as soon as practicable (21 CFR 312.36).

Are there any additional requirements for use of devices?

In addition to meeting the requirements for emergency use of a test article without IRB review, outlined above, the emergency use of an unapproved device requires an Investigational Device Exemption review and number (IDE) or Humanitarian Device Exemption review and number (HDE) from the FDA applicable to the intended use. The sponsor (holder of the IDE/HDE) should be consulted to verify such applicability. Follow-up reports should be provided to the sponsor.

Where (1) an IDE/HDE for the device does not exist, or (2) a physician wants to use a device in a way not approved under an existing IDE/HDE, or (3) the physician is not an investigator under the existing IDE/HDE, the device may be used with the prior approval of the FDA. Follow-up reports should be provided to the FDA.

If there is not sufficient time to obtain FDA approval, the device may be used provided that the physician later justifies to the FDA that an emergency actually existed. Each of the following conditions must exist to justify emergency use:

- The patient is in a life-threatening condition that needs immediate treatment;
- No generally acceptable alternative for treating the patient is available; and

- Because of the immediate need to use the device, there is no time to use existing procedures to obtain FDA approval for the use.

In this situation, the physician must follow as many subject protection procedures as possible. These include: (1) obtaining informed consent of the patient or a legal representative; (2) notifying institutional officials as specified by institutional policies; (3) concurrence of an IRB Chair; (4) an independent assessment of an uninvolved physician; and (5) authorization from the IDE/HDE sponsor, if an IDE/HDE exists.

What if the situation is not an emergency? Can a patient with a serious illness or condition have access to an investigational device outside a study?

Yes, FDA recognizes that there are circumstances in which an investigational device is the only option available for a patient faced with a serious or life threatening condition (hereinafter referred to as compassionate use). Unlike emergency use of an unapproved device discussed above, prior FDA approval is needed before compassionate use occurs. In order to obtain FDA approval, the sponsor submits an IDE supplement requesting approval for a protocol deviation in order to treat the patient. (See 21 CFR 812.35(a)).

If the request is approved by the FDA, the attending physician must devise an appropriate schedule for monitoring the patient, taking into consideration the investigational nature of the device and the specific needs of the patient. The patient is monitored to detect any possible problems arising from the use of the device. Following the compassionate use of the device, a follow-up report is submitted to the FDA in which summary information regarding patient outcome is presented. If any problems occurred as a result of device use, they are discussed in the supplement and reported to the IRB as soon as possible.

IRB review and approval and informed consent of the patient (or legally authorized representative) are required for the compassionate use of a medical device. However, should medical necessity require the use of the device by a physician-investigator without IRB review and approval or without informed consent, the policies and procedures for the emergency use of test articles apply.

Where can I get additional information?

The following are links to the regulations and guidance for emergency use situations:

Federal Regulations:

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| FDA: | 21 CFR 50 – Protection of Human Subjects; Informed Consent |
| | 21 CFR 56 – Institutional Review Boards |
| | 21 CFR 312 – Investigational New Drug Application |
| | 21 CFR 812 – Investigational Device Exemptions |
| DHHS: | 45 CFR 46 – Protection of Human Subjects |

Guidance Documents:

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| FDA: | Emergency Use of an Investigational Drug or Biologic
Emergency Use of Unapproved Medical Devices |
| DHHS: | Emergency Research Informed Consent Requirements
Emergency Medical Care |