The Christ Hospital IRB
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Number: 1.10
Effective Date: 02/09
Revised/Reviewed Date: 03/25

STANDARD OPERATING PROCEDURE

Emergency Use Of An Investigational Drug, Biological Product, or Device

POLICY:

This policy does not limit the authority of a physician to provide emergency medical care outside of the research context.

The Institutional Review Board (IRB) must approve the use of a test article in human subjects research except when:

- The patient has a life-threatening condition that requires immediate treatment,
- No generally acceptable alternative treatment is available, and
- Because of the immediate need to use the drug or device, there is insufficient time to convene a quorum for full IRB board approval.

In an emergency situation, prior IRB approval is not required for use/provision of the test article to the patient, but the FDA requires that the IRB is notified within 5 working days of the emergency use of the test article. The FDA does not allow any type of expedited or subcommittee review and approval in its regulations. Any subsequent use of the test article at The Christ Hospital is subject to IRB review.

DEFINITIONS

Note: Emergency uses and device uses cannot be claimed as research.

Emergency Use: Emergency use is the use of an investigational device in an emergency situation. It is intended to provide patients and physicians with access to devices intended to treat life-threatening or serious diseases or conditions when there is no available alternative and no time to obtain FDA approval. Emergency use may apply even if the investigational device is being studied in a clinical trial under an IDE: if a physician needs to use the device in a manner inconsistent with the approved investigational plan; or a physician who is not part of the clinical study, wishes to use the device to treat a patient with a life-threatening or serious disease or condition. Emergency use of an investigational device may occur before an IDE is approved and when a device is not being studied under an IDE [21 CFR 56.102(d)].

Unplanned Emergency: The presentation of a patient suffering an unexpected life-threatening event.

Planned Emergency Research: A research study that will include participants in life-threatening situations, where a test article must be used before consent can be obtained, and the researcher cannot know in advance who the participants will be.

Test Article: Any drug, biological product or medical device intended for human use that is subject to FDA regulations.

IND: Investigational New Drug

IDE: Investigational Device Exemption

Requirements for an Investigational New Drug Exemption (IND) or an Investigation Device Exemption (IDE):

1. Investigational Drug or Biologic: The emergency use of an unapproved investigational drug or biologic requires an IND exemption. If the intended subject/emergency use does not meet the criteria or methods of a research protocol being conducted under a currently approved IND for the drug or biologic, the investigator must contact the FDA to obtain, prospectively, an Emergency IND number (see list of FDA contacts for obtaining an Emergency IND under "Procedure" below). Alternately, the emergency use may be conducted under an existing Treatment IND or Parallel Track IND.
2. Investigational Device: The emergency use of an unapproved investigational device does not require an IDE for such use, provided that the physician subsequently provides written justification to the FDA that an emergency actually existed.
3. General Requirements: In requesting an emergency use of a drug or biologic under an existing IND or an Emergency IND number, or notifying the FDA of the emergency use of an investigational device, the FDA expects the physician to determine whether the criteria for emergency use have been met, to assess the potential for benefits from the emergency use of the drug or device, and to have substantial reason to believe that benefits will exist. The physician may not conclude that an "emergency" exists in advance of the time when the treatment may be needed based solely on the expectation that IND or IDE approval procedures require more time than available. Physicians should be aware that the FDA expects them to exercise reasonable foresight with respect to potential emergencies and to make appropriate advance arrangements under Treatment IND, Parallel Track IND, or IDE procedures to avoid creating a situation where such arrangements are impracticable.
4. When Following FDA Requirements: The emergency use of a test article, other than a medical device, is a clinical investigation, the patient is a subject, and the FDA may require data from an emergency use to be reported in a marketing application.
    - DHHS regulations do not permit data obtained from patients to be classified as research involving human subjects, nor permit the outcome of such care to be included in any report of a research activity subject to DHHS regulations.

References: Federal regulations related to Emergency Use Exemption are in 21 CFR 56.102(d); 21 CFR 56.104©, 21 CFR 50.23, 21 CFR 50.24; 21 CFR 312. Also referenced FDA Emergency Use Guidance. (Please see Reference Manual Section Chapter 13 in the IRB Office for more information).

PROCEDURE:

INVESTIGATIONAL DRUG OR BIOLOGIC

Investigator Responsibilities

1. Contact the manufacturer of the investigational drug or biologic to determine if the manufacturer has in place a Treatment IND or a Parallel Track IND that will permit emergency treatment of the patient outside a controlled clinical trial.

    a. If yes, request inclusion of the patient in the Treatment IND or Parallel Track IND, request a supply (or a replacement supply if currently available under a controlled clinical study) of the drug for the emergency use, and obtain the Treatment or Parallel Track IND number.

    b. If no, inquire if the manufacturer will provide a supply (or replacement supply) of the drug subsequent to obtaining FDA approval of the emergency use (i.e., if there is currently an approved IND for the drug or biologic) or an Emergency IND number (i.e., if there is no approved IND for the drug or biologic). Note that the manufacturer will likely require the attending physician to contact the FDA to obtain emergency use of the Emergency IND approval, with subsequent notification of the manufacturer. To facilitate this process, request that the manufacturer identify the specific FDA Division which is currently reviewing the drug or biologic.

    To obtain an emergency use approval under an existing IND or to obtain an Emergency IND number, call the appropriate office as follows:

Drug products:	Division of Drug Information (HFD-240) (888) 463-6332 | (301) 796-3400
Biologic blood products:	Office of Blood Research & Review (HFM-300) (240) 402- 8360
Biological vaccine products:	Office of Vaccines Research (HFM-400) (240) 402-7800
On nights and weekends:	Office of Crisis Management & Emergency Operations (HFC-160) (301) 796-8240

2. Notify the IRB chair and IRB Office at 513-585-2298 or IRB_Office@thechristhospital.com of the intended emergency use of the unapproved investigational drug or biologic. This notification should occur prior to implementation of the emergency use. Provide the IND number under which this use is authorized (e.g., Treatment IND, Parallel Track IND, other currently approved IND, or Emergency IND). NOTE: If the unapproved investigational drug or biologic emits ionizing radiation, the Radiation Safety Officer (513-585-1197) must also be notified.

3. Obtain written confirmation from a physician independent of the clinical investigator that confirms that an emergency situation exists.

4. Obtain written informed consent from the patient or the patient's legally authorized representative.

   NOTE: The patient must understand the investigational nature of the test article. Informed consent must be obtained; however, the consent form is not a standard research consent form. In most cases, the sponsor will supply a consent form. The IRB is not involved in the review or approval of the consent form if the situation meets the criteria for emergency use. The FDA describes the "Exception from informed consent requirements" in 21 CFR 50.23(a).

   a. Even for an emergency use, there is a provision for waiver of informed consent 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 situation necessitating use of the test article.
      - Informed consent cannot be obtained because of an inability to communicate with, or obtain a legally effective consent from, the subject.
      - Time is not sufficient to obtain consent from the subject's legal 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, in the investigator's opinion, there is not sufficient time to obtain an independent physician's determination that the four criteria are met, the investigator should make the determination and subsequently obtain (i.e., within five working days) a review of his/her determination by a physician not participating in the investigation.

5. Post-implementation of the Emergency Use:

   a. Within five working days of initial notification of the IRB Chair, an Emergency Use application must be submitted in Mentor IRB. The following documentation should be uploaded with the submission for IRB consideration:
      - FDA Form 1572 or Form 3926. [Note: On Form 3926, Box10.b. Request for Authorization to Use Alternative IRB Review Procedures should be checked if requesting authorization to obtain concurrence by the Institutional Review Board (IRB) before the treatment use begins, in order to comply with FDA's requirements for IRB review and approval. This concurrence would be in lieu of review and approval at a convened IRB meeting.]
      - Letter of confirmation from an independent physician of the clinical investigator that an emergency existed.
      - The Emergency Use Consent Form signed and dated by the patient or the patient's legally authorized representative or written documentation from both the investigator as well as a physician independent of the clinical investigator that a waiver of consent was necessary based on the four points noted above.

b. Submit promptly any documents that may be required by the manufacturer or FDA as a result of emergency use. Submit a copy of all such documents to the IRB Office.

c. Submit follow-up reports with respect to the subsequent outcome of the emergency use, including the occurrence of adverse events, promptly to the IRB, manufacturer, and/or FDA.

d. Evaluate the likelihood of a similar need for emergency use of the unapproved investigational drug or biologic, and if probable, immediately initiate efforts to obtain prospective FDA (if not already in existence) and IRB approval of a Treatment IND or Parallel Track IND (if applicable).

NOTE:

1. FDA regulations and Christ Hospital policy require that any subsequent emergency use of the investigational drug at the Institution have IRB (i.e., full board) review and approval.
2. When following FDA requirements, the emergency use of a test article, other than a medical device, is a clinical investigation, the patient is a subject, and the FDA may require data from an emergency use to be reported in a marketing application.
    - DHHS regulations do not permit data obtained from patients to be classified as research involving human subjects, nor permit the outcome of such care to be included in any report of a research activity subject to DHHS regulations.

IRB Chair Responsibilities

The IRB Chair or designee reviews the submitted documents and confirms that:

1. An emergency situation exists, and
2. There is not sufficient time to convene a quorum for full board consideration.

IRB Staff Responsibilities

The IRB office generates a letter acknowledging notification of emergency use of the test article for the Chair's signature. **This is not a letter of approval.**

All subsequent uses of the test article should be reviewed using standard full IRB board review process. If another request for use is anticipated, the full board process should be initiated.

INVESTIGATIONAL DEVICE

Investigator Responsibilities

1. Contact the manufacturer of the investigational device to determine if it has in place an Investigational Device Exemption (IDE) that will permit emergency use of the device on a patient outside of a controlled clinical trial.

a. If yes, request inclusion of the patient in this emergency use IDE, request immediate shipment of the device if not already available, and obtain the corresponding IDE number.
b. If no, inquire if the manufacturer will ship the device for emergency use if not already available. If the device is available, inform the manufacturer of the intended emergency use of the device outside of the approved clinical protocol. NOTE: The manufacturer should contact the FDA upon such notification, however, the manufacturer may require the attending physician to initiate FDA contact (Center for Devices and Radiological Health, Program Operation Staff, (301) 796-7100).

2. Notify the IRB in writing at IRB_Office@thechristhospital.com of the intended emergency use of the unapproved investigational device. This notification should occur prior to implementation of the emergency use. Provide the IDE number under which this use is authorized, if available, from the manufacturer.

   NOTE: If the unapproved investigational device emits ionizing radiation, the Radiation Safety Officer (513-585-1197) must also be notified.

2. Obtain written confirmation from a physician independent of the clinical investigator that confirms that an emergency situation exists.

3. Obtain written informed consent from the patient or the patient's legally authorized representative.

   NOTE: The patient must understand the investigational nature of the test article. Informed consent must be obtained; however, the consent form is not a standard research consent form. In most cases, the sponsor will supply a consent form. The IRB is not involved in the review or approval of the consent form if the situation meets the criteria for emergency use. The FDA describes the "Exception from informed consent requirements" in 21 CFR 50.24(a).

   a. Even for an emergency use, there is a provision for waiver of informed consent 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 situation necessitating use of the test article.
      - 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.
      - 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, in the investigator's opinion, there is not sufficient time to obtain a physician independent of the clinical investigator's determination that the four criteria are met, the investigator should make the determination and subsequently obtain

(i.e., within five working days) a review of his/her determination by a physician not participating in the investigation.

4. Post-implementation of the emergency use:

    a. Within 72 hours of initial notification of the IRB Chair, an Emergency Use application must be submitted in Mentor IRB. The following documentation should be uploaded with the submission for IRB consideration:
        - Letter of confirmation from a physician independent of the clinical investigator that an emergency exists.
        - The completed Emergency Use Consent Form signed and dated by the patient or the patient's legally authorized representative.

    b. If the manufacturer does not currently have in place an emergency use IDE for the device, notify (within 1 working day) the FDA (if not previously done) of the emergency use of the unapproved device. Submit promptly any documents that may be required by the manufacturer and/or FDA as a result of such emergency use. Submit a copy of all such documents to the IRB Office.

    c. Submit promptly to the IRB, manufacturer, and/or FDA follow-up reports with respect to the subsequent outcome of the emergency use, including the occurrence of adverse events.

    d. Evaluate the likelihood of a similar need for emergency use of the unapproved investigational device, and if probable, immediately initiate efforts to obtain prospective FDA (if not already in existence) and IRB approval of an emergency use IDE.

    If no IDE exists, the physician should submit a follow-up report on the use of the device (description of device used, details of the case, and the patient protection measures that were followed) to:

    Food and Drug Administration
    Center for Devices and Radiological Health
    10903 New Hampshire Ave
    Document Control Center
    WO66 Rm G-609
    Silver Spring, MD 20993

    NOTE: FDA regulations and Christ Hospital policy require that any subsequent emergency use of the investigational device at the Institution have IRB (i.e., full board) review and approval.

IRB Chair Responsibilities

The IRB Chair or designee reviews the submitted documents and confirms that:

1. An emergency situation exists, and
2. There is not sufficient time to convene a quorum for full board consideration.

IRB Staff Responsibilities

The IRB Office generates a letter in Mentor IRB acknowledging notification of emergency use of the test article for the Chair's signature. **This is not a letter of approval.**

All subsequent uses of the test article should be reviewed using standard full IRB board review process. If another request for use is anticipated, the full board process should be initiated.