

**THE CHILDREN'S MERCY HOSPITAL
ADMINISTRATIVE POLICY**

TITLE: Emergency Use of Investigational Drug or Biologic

EFFECTIVE: 5/23/05

REVISION DATE:

REVIEWED WITH NO CHANGES

RETIRED:

PURPOSE: To provide a description of the process for emergency use of an investigational drug or biologic in patients with life-threatening or severely debilitating conditions.

POLICY: In general, research involving human subjects must be reviewed and approved by the IRB in advance of initiation. In an emergency situation, an Investigator may be able to use an unapproved investigational drug or biologic without prior approval by the IRB if specific criteria are met. In such cases, the Office of Research Integrity (ORI) must be notified in advance of such uses whenever possible.

DEFINITIONS:

Emergency Use: 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.

Institutional Review Board (IRB): a committee designated by the hospital to review biomedical research involving humans as subjects.

Investigational New Drug (IND): an Investigational New Drug (IND) application is a request for FDA authorization to administer an investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug that is not the subject of an approved new drug application.

Investigator: an individual who actually conducts a clinical investigation (i.e. under whose immediate direction the drug is administered or dispensed to a subject).

Investigational Product: a drug or biologic in any of the clinical stages of evaluation which has not been released by the FDA for general use or cleared for sale in interstate commerce.

Legally Authorized Representative: an individual or judicial or other body who is authorized under applicable law for medical decision-making on behalf of a prospective subject to the subject's participation in the research. In the case of a minor child, this is likely, but not necessarily, the subject's parent(s).

Life-threatening: disease or condition where the likelihood of death or substantive permanent harm is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of the 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: diseases or conditions that cause major irreversible morbidity. Examples include blindness, loss of limb, loss of hearing, paralysis, or stroke.

Treatment IND: a mechanism for providing eligible subjects with investigational drugs for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. A Treatment IND will be granted only if the drug is already under investigation or trials have been completed and the trial sponsor is actively pursuing marketing approval. In addition, patients who receive a drug under a treatment IND are not eligible to be enrolled into the definitive clinical trials, which must be well underway, if not almost finished.

PROCEDURE:

1. If a member of the medical staff encounters a situation for which emergency use of an investigational product seems appropriate, they will determine whether the following required criteria are met:
 - a. the patient has a life-threatening or severely debilitating condition that needs immediate attention
 - b. there is no generally acceptable alternative for treating the patient, the patient is failing alternative treatment, or there is some compelling reason to believe that the experimental intervention has a substantive advantage over other available options
 - c. because of the immediate need to use the drug, there is no time to use existing procedures to get IRB approval for use of the drug.
2. If the required criteria are met and a decision is made to pursue emergency use, the basis for this decision must be documented. A member of the medical staff who is responsible for patient's treatment will be designated as the Investigator and will be responsible for conduct or oversight of the requirements of this policy. In these situations it is not required that the Investigator meet the human subjects education requirements defined by the Office of Research Integrity.
3. Emergency use of an unapproved investigational product must be done under an IND. If the intended subject does not meet the criteria of an existing study protocol at CMH the manufacturer of the investigational product ("Sponsor") must be contacted to determine if the investigational product can be made available for emergency use under the Sponsor's IND. The Investigator may contact the Investigational Drug Pharmacist for assistance in identifying the Sponsor, or obtaining additional information related to the investigational product.

4. If the Sponsor has a protocol under which the patient could be treated, the Investigator will work with the Sponsor to determine if the patient meets protocol inclusion criteria and is an appropriate candidate for use of the drug. If the manufacturer agrees to such use, the Investigator will work with them to get all manufacturer-required paperwork in place. The Investigator must notify Research and Grants Administration of this communication with the Sponsor as soon as possible. If a contract between the Hospital and Sponsor is required by the Sponsor, then the review and execution of this agreement will be coordinated by Research and Grants Administration in accordance with their policy titled “Contractual Documents” (RG100-002). Negotiation and execution of a contract will not delay obtaining the investigational drug unless Sponsor requires a contract prior to shipping drug.
5. If the Sponsor has no such protocol, the Investigator must contact the FDA in order to obtain FDA permission for use of the drug in this manner; however, the Sponsor must approve of such an approach. In such cases the FDA may authorize shipment of the investigational drug or biologic for a specified one-time use. Such authorization is usually conditioned upon the Investigator filing an Investigator IND application as soon as practicable after drug shipment. The sponsor should be able to provide FDA contact information. If not, some FDA contacts for obtaining an emergency IND are listed in Attachment A. The Investigator must notify Research and Grants Administration of communication with the FDA as soon as possible.
6. Although prior IRB approval is not required for emergency use of an investigational product, the Office for Research Integrity (ORI) must be notified prior to any such emergency uses, when at all possible, in order to assess that the required criteria have been met. If a member of the ORI staff is **unavailable** by phone or page, this step can be omitted.
7. The Investigator must complete and sign a “Request for Emergency Use of an Investigational Drug or Biologic” (Attachment B) and submit it to the Office for Research Integrity and the Investigational Drug Pharmacy prior to emergency use. If a member of the ORI staff is **unavailable** by phone or page, this form must be signed and submitted to ORI as soon as possible, but at least within five days of initiation of treatment with the investigational product.

This process should not be construed as IRB approval. If the form indicates that an IND must be filed, a copy of the form must be submitted to Research and Grants Administration so that they can track submission of the IND.

8. Some Sponsors may require an IRB approval letter before the test article will be shipped. Typically it is not possible to convene a quorum of the IRB within the time available and thus obtain such approval; however, the IRB will provide a written statement that the IRB is aware of the proposed use and considers the use to meet the requirements of 21 CFR 56.104(c). This sponsor requirement cannot be waived and must be satisfied before investigational drug can be administered.
9. The Investigator will work with the Investigational Drug Pharmacist to arrange for receipt, disposition, and accountability of the investigational drug in accordance with Hospital policies.

10. Even for emergency use, the investigator is required to obtain parental permission and/or subject assent to use the investigational drug or biologic (in accordance with IRB policies) unless both the Investigator and a physician who is not otherwise involved in the patient's care certify, in writing, the following:
 - a. the subject is confronted by a life-threatening situation necessitating the use of the investigational drug or biologic
 - b. informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject (when the subject is an adult)
 - c. time is not sufficient to obtain consent from the subject's legally authorized representative (when the subject is an adult or child)
 - d. no alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.

Such certification must be provided to the IRB within five (5) working days after initiation of treatment with the investigational drug.

11. Because of the emergent nature of this situation, the Investigator is not required to have the informed consent document approved by the IRB in advance of use. In most cases, the Sponsor will supply a consent form for emergency use of the investigational drug or biologic. In cases where the Sponsor's consent form is not available, the IRB's sample permission/assent form must be used as a template for developing an appropriate consent document. When informed consent is required, the pharmacy must be provided with a copy of the signed document before investigational product can be dispensed. Be certain that the informed consent includes the CMH approved HIPAA Authorization language. If a Sponsor's form is used, a separate CMH HIPAA Authorization form must be executed. This form is available on the CMH Research web page under ORI.
12. The investigational drug or biologic must be used in accordance with specifications supplied by the manufacturer.
13. This emergency use provision applies to the one course of treatment for one subject. If the investigator anticipates the enrollment of additional subjects in the future, or future treatment of the same subject, a full protocol must be submitted to the IRB for full review and action at a convened meeting.
14. If the Investigator is required to file an IND application for use of the investigational drug or biologic, this must be done as quickly as possible in accordance with the Administrative Policy entitled *Investigator Initiated Investigational New Drug (IND) Applications*. This policy also describes the process for maintenance and closure of an IND.
15. All adverse events must be reported to the Sponsor and IRB in accordance with their policies. Additionally, data must be collected and submitted to the Sponsor in accordance with their requirements and in accordance with the documented informed consent.

16. When treatment with the investigational product has been completed, the form titled “Final Report for the Emergency Use of An Investigational Drug or Biologic” (Attachment C) must be completed and submitted to the IRB for their review.

RELATED POLICIES:

Administrative Policy: Investigator Initiated Investigational New Drug (IND) Applications

REFERENCES:

21 CFR 50

21 CFR 56

21 CFR 312

FDA Information Sheets; Emergency Use of an Investigational Drug or Biologic

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REVIEW PERIOD:

According to Hospital Policy

APPROVED:

Medical Executive Committee: 05/04/2005

Administrative Council: 05/19/2005

Randall L. O'Donnell, Ph.D. 05/23/05
President and Chief Executive Officer Date

Attachment A

FDA contacts for obtaining an emergency IND

For drug products contact:

Drug Information Branch (HFD-210) 301/827-0473

For biologic blood products contact:

Office of Blood Research and Review (HFM-300) 301/827-3518

For biological vaccine product contact:

Office of Vaccines Research and Review (HFM-400) 301/827-0648

For a biological therapeutic product contact:

Office of Therapeutics Research and Review (HFM-500) 301/594-2860

Nights and weekends:

Division of Emergency and Epidemiological Operations (HFC-160) 202/857-8400

Attachment B

**Children's Mercy Hospital
Pediatric Institutional Review Board**

REQUEST FOR EMERGENCY USE OF AN INVESTIGATIONAL DRUG OR BIOLOGIC

Investigator: _____ Phone: _____ Fax: _____
Department: _____ Pager: _____

Please complete the following:

Does the patient meet the following criteria for emergency use of an investigational product?

1. the patient has a life-threatening condition that needs immediate attention Yes No
2. there is no generally acceptable alternative for treating the patient, the patient is failing alternative treatment, or there is some compelling reason to believe that the experimental intervention has a substantive advantage over other available options Yes No
3. because of the immediate need to use the drug, there is no time to use existing procedures to get IRB approval for use of the investigational product Yes No

What is the time frame within which the drug or biologic needs to be administered?

Under what conditions will the investigational product be used at CMH (choose one):

1. under an IRB approved protocol at CMH (specify protocol number _____)
2. under a manufacturer's protocol that has not been approved at CMH
3. under a new IND to be filed by the investigator

Does the sponsor require an acknowledgement letter from the Institutional Review Board prior to receiving the drug or biologic? Yes No

Please complete the following information which is relevant to the emergency situation:

Patient Initials _____ Age of Pt. _____ Sex of Pt. _____ Location of Pt. _____

Describe the life threatening situation and justification for use of investigational drug:

Name of product: _____ IND #: _____

This drug or biologic will be used according to the following dosage schedule:

Treating Physician's Signature

Date

FOR IRB USE ONLY:

I have reviewed the emergency request and agree the emergency use meets the requirements of regulation 21 CFR 56.104(c).

IRB Reviewer's Name

IRB Reviewer's Signature

Date

