Fact Sheet on Emergency Use of an Investigational Drug or Biologic

This fact sheet discusses the process of submitting an Emergency Use to the KUMC IRB and provides investigators with information on how to request the use of an investigational agent when the standard IRB submission process is unavailable due to time or urgency. Please note that Emergency use situations are limited to **life-threatening** or **severely debilitating** situations as outlined in 21CFR56.102(d):

- **Life-threatening** 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** 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

The first step is to determine whether an Emergency Use submission is appropriate.

Emergency Use Requirements

1. **Is this situation life-threatening or severely debilitating?**
2. **Have standard therapies failed?**
3. **Is the holder of the IND or drug manufacturer willing to provide the drug/biologic?**
4. **Call FDA (http://www.fda.gov/regulatoryinformation/guidances/ucm126491.htm) – Will they issue an emergency use IND?**
5. **Do you have time to get informed consent? If not, is another physician available to provide concurrence?**

If the answers to the above questions are all **YES**, then follow the instructions below to submit an Emergency IND request to the KUMC IRB.

Emergency Use of Investigational Drugs or Biologics

Emergency Use requirements apply to the use of an investigational drug or biologic product that is not yet approved by the Food and Drug Administration. Emergency use is defined as their use on 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 for the use.

The basic steps for emergency use of an investigational drug or biologic are as follows:

1. Confirm the willingness of the holder of the drug/biologic to provide the product.
2. Obtain an IND number or other permission from FDA
3. Consult with the KUMC Investigational Pharmacy about any requirements related to the shipment or receipt of the drug.

4. Obtain written acknowledgement from the KUMC Institutional Review Board (IRB) prior to the use. Acknowledgement is contingent on submission of the following documents:
    a. Submit a letter to the IRB chair, discussing the six justifications for the emergency use, as outline in the ***Justification for Emergency Use*** section below
    b. Submit information about the source, nature and use of the drug (drug label or Investigational Brochure)
    c. Submit an informed consent document to be signed by the patient or legally authorized representative, as outlined below.
    d. Within 5 days after the emergency use, file a formal notification to the IRB.
    e. Adhere to the federal rules on use of the data and subsequent emergency uses

FDA Permission

The emergency use of an unapproved investigational drug or biologic requires an IND. If the intended subject does not meet the criteria of an existing study protocol, or if an approved protocol does not exist at KUMC, investigators should contact the manufacturer and determine if the drug or biologic can be made available for the emergency use under the company's IND. Investigators then consult with FDA to obtain an emergency IND number specific to the use.

For an emergency IND number, investigators should be prepared to submit documentation to the FDA. Documentation will include: FDA forms 1571 and 1572, clinical history to justify the emergency use in the patient, and a proposed treatment plan. The treatment plan should include dose, route, planned duration; detailed plans to monitor the safety of the patient after drug administration; assessment of side effects, events that would be considered an adverse reaction to the drug and plans to address an adverse reaction; criteria for stopping, reducing or pausing the medication. Additionally, investigators must include a drug supply reference statement, a proposed informed consent document, and a curriculum vitae. These documents are outlined on the FDA's website.

Pharmacy Requirements

The investigator should contact the hospital's Investigational Pharmacy as early as feasible in the planning process. This applies both to oral medications and infusions. The Investigational Pharmacy will ensure appropriate receipt, distribution, dosing and storage.

Justification for Emergency Use

Emergency use can occur prior to review by the IRB if all the following conditions exist:

1. The subject must be in a life-threatening condition;
2. No standard treatment is acceptable;
3. The condition of the subject requires intervention before review at a convened meeting of the IRB is feasible;
4. The investigator agrees to provide a report of the use to the IRB within five working days;
5. The investigator agrees that any subsequent use of the investigational drug or biologic will be subject to IRB review;

6. Informed consent will be sought from the subject or the subject's legally authorized representative, unless circumstances exist as described below in Informed Consent section to justify the waiver of the consent requirement.

Whenever feasible, the IRB must be notified prior to the emergency use. At that time, the investigator must affirm that the six above criteria are met. The investigator also must inform the IRB about the source of the drug, and the investigator must notify the Investigational Drug Service in advance.

Drug/Biologic Information

Information about the drug will be needed. Investigators should receive the Investigational Brochure from the Sponsor who will supply the drug or biologic product. This Brochure will need to be submitted to the IRB with your initial acknowledgement letter.

Informed Consent

Informed consent must be sought from the subject or the subject's legally authorized representative. Investigators are asked to use the consent template specific to emergency use, posted on the IRB website.

The requirement for informed consent can be waived if there is no ability to get the consent of the subject (e.g., the subject is incompetent) and there is not enough time to get consent from a legally authorized representative. In this case, both the investigator and a physician who is not otherwise participating in the investigation must certify in writing that:

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

Acknowledgement Letter

If the investigator provides the information described above, the Chairperson or designee will, under appropriate circumstances, issue a letter stating that the IRB is aware of the proposed use for a single patient.

Notification to the full IRB

Within five working days after the emergency use, the investigator must supply the following documentation to the IRB within the myIRB system:

1. Emergency Use Notification Form posted on the IRB website.
2. A protocol for such use of the product.
3. Documentation of the IND number.
4. A copy of the subject's signed consent form with patient name and signature redacted.

At a convened meeting, the IRB will confirm that the emergency use was justified and met the six regulatory criteria. As needed, additional information may be requested prior to that determination. The IRB will inform the investigator by letter of the final determination on the emergency use. If the regulatory requirements were not met, the emergency use will be referred to the Institutional Official as non-compliance. The incident will be handled according to SOP 17.1.

Use of Data

Information from the emergency use cannot be used as research data.

Future Uses of the Investigational Drug

FDA's emergency use provisions allow only one use of the investigational drug. Any subsequent use must occur under a standard IRB-approved research protocol. The IRB may make an exception to the requirement for prior approval if a second individual meets the emergency criteria before IRB review can take place.

Questions or concerns

Please email the IRB office or call 913-588-1240 with any questions about the emergency use of an investigational agent at KUMC.