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?
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 at:
[http://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/investigationalnewdrugindapplication/ucm107434.htm](http://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/investigationalnewdrugindapplication/ucm107434.htm)

**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. The consent form should contain all the standard elements of informed consent.

If the subject is unable to sign the consent, it may be signed by either a legal guardian or an attorney-in-fact with the authority to make health care decisions. If a person fulfilling those requirements is not available, Kansas law allows for the consent to be signed by a family member in the following order:

1. The adult or emancipated minor’s spouse, unless they are legally separated;
2. An adult child;
3. A parent;
4. Adult sibling (for Missouri campuses only);
5. An adult relative by blood or marriage.

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. The letter will note the date of the next convened IRB meeting at which the emergency use will be reviewed.
**Notification to the full IRB**

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

1. A letter to the Committee stating the reason for the emergency use. That letter must specifically state that the subject was (or is) “in a life-threatening situation,” that “no standard acceptable treatment” was (or is) available for the subject’s condition, and that “there was [or is] not sufficient time to obtain approval” from the Human Subjects Committee prior to the use. The letter should include sufficient details about the patient’s condition and the available treatments to permit a determination of the correctness of the above statements.

2. A protocol for such use of the product.

3. A copy of the consent form that is being used. That consent form should include information on all of the usual elements of informed consent, and should in general conform to the model consent form adopted by the Committee.

4. A report indicating the current status of the subject.

A primary and secondary reviewer will review all the above documentation. At the 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.

**How to submit the follow up information to the IRB**

The five-day report and other follow-up information can be submitted on paper. Please submit one hard copy of the documents listed above to the IRB office at Sudler G006.

**Questions or concerns**

Please contact the IRB office at 8-1240 or humansubjects@kumc.edu should you have any questions about the emergency use of an investigational agent at KUMC.