AAH RSPP GUIDANCE
Emergency Use of a Test Article

PURPOSE
The purpose of this guidance document is to outline when a test article (investigational drug, device or biologic) may be used in an emergency use situation and the process to notify the Advocate Aurora IRB of the emergency use.

Definitions of italicized words can be found in the AAH RSPP Glossary.

GUIDANCE
What is an Emergency Use of an investigational article?
Emergency use is defined as the use of a test article (ie. investigational drug, device or biological product) 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 [21 CFR 56.102(d)].

- Emergency use of a test article is exempt from prior IRB review and approval, provided that such emergency use is reported to the IRB within 5 working days after the use.
- Expedited IRB approval is not permitted in emergency use.
- Consent of the subject (or legally authorized representative) is required unless an exception can be justified by the treating physician and an independent physician (see below).

How many times may the test article be used at the institution under the exception for IRB approval?
The FDA regulations [21 CFR 56.104(c)] allows for one emergency use of a test article at an institution. Any subsequent use of the investigational product at the institution is subject to prospective IRB review and approval. However, the FDA acknowledges that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue.

Note: For devices, if an IDE application for subsequent use has been filed with FDA and FDA disapproves the IDE application, the device may not be used even if the circumstances constituting an emergency exist.

What are the criteria for emergency use?
Drugs/biologics
Emergency use must meet the definition above, and FDA must determine [21 CFR 312.305(a)]:
- (1) The patient to be treated has a serious or immediately life-threatening disease or condition and there is no comparable or satisfactory alternative therapy to diagnose, monitor or treat the disease or condition;
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. 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.

Criteria for Emergency Use – Devices

The emergency use must meet all of the following:

- Life-threatening or serious disease or condition
- No alternative
- No time to obtain FDA approval

What is the process if I want to use a test article in an emergency use situation?

1. If the proposed emergency use of the test article meets the above criteria, the treating physician should first contact the drug/biologic/device manufacturer and FDA (see below) to ensure that the test article is available to use, and to begin, as necessary, the IND/IDE process.

   After initial contact with the manufacturer and the FDA, the treating physician should contact the RSPP office to determine if there is sufficient time to obtain IRB approval of the intended use.

   If there is not sufficient time to obtain IRB approval, the use may proceed without prospective IRB approval. However, a report to the IRB must be provided in writing within 5 working days of the use (see below).
2. Some manufacturers will agree to allow the use of the test article, but wish for “an IRB approval letter” before the test article will be shipped. If it is not possible to obtain IRB approval within the time available, the AAH IRB is willing send an acknowledgment letter to the drug/device/biologic manufacturer noting that the IRB is aware of the proposed use and considers the use to meet the requirements of 21 CFR 56.104(c). Although, this is not an "IRB approval," this acknowledgment or concurrence letter has been acceptable to manufacturers and has allowed the shipment to proceed.

In order to obtain an IRB acknowledgment/concurrence letter, information on the intended emergency use must be provided to the RSPP. The physician must provide the RSPP with information on the intended use in order for the IRB Chair or designated IRB member to consider whether the use meets the definition of ‘emergency use’. The information may be submitted on an Emergency Use Report (found on the AAH RSPP website) or by providing comparable information.

- NOTE that the submission of this initial information does not eliminate the need for the treating physician from submitting a report to the IRB within 5 working days from the use (see below).

An IRB Chair or designee will review the information and determine if the use meets the emergency use criteria. If the IRB Chair concurs that an emergency condition exists, the RSPP office will generate an IRB acknowledgment/concurrence letter which may be provided to the test article manufacturer to get the test article shipped to the institution.

Is informed consent required in emergency use situations?
Informed consent of the subject or the subject’s legally authorized representative is required in an emergency use situation. The process of informed consent must meet FDA requirements [21 CFR 50.25].

Whenever possible, a copy of the consent form intended to be used with the subject should be provided to the RSPP office in advance of the emergency use so that it can be determined that all applicable elements of informed consent are present.

In order to assist physicians in creating an appropriate emergency use consent, the AAH RSPP has created an emergency use consent template (located on the RSPP website). Note that the emergency use consent template does not include research authorization language as this use of the test article is seen as ‘treatment’ rather than ‘research’.

The treating physician is expected to retain a copy of the signed informed consent for his/her records. You may be asked to provide this document to an FDA auditor or the IRB at a later date.

What if informed consent cannot be obtained from the subject?
FDA regulations [21 CFR 50.23] permit emergency use of a test article without informed consent where the treating physician and an independent physician (one who is not otherwise participating in the emergency use), certify in writing:
1. the patient is confronted with a life-threatening situation;
2. informed consent cannot be obtained from the patient (because patient cannot communicate or is incompetent to give consent);
3. consent cannot be obtained from the legally authorized representative (unavailable or unknown); and
4. no alternative approved treatment/therapy is available that provides an equal or greater likelihood of saving the patient’s life. (21 CFR 50.23(2)).

If, in the treating physician’s opinion, immediate use of the test article is required to preserve the subject’s life, and time is not sufficient to obtain an independent physician’s determination that the four conditions above apply, the treating physician may make the decision him/herself. Within 5 working days after the use of the article, an independent physician must determine that the above conditions existed. This evaluation must be in provided in writing to the IRB.

What must be reported to the IRB after the emergency use?
Per FDA regulation, the treating physician must submit, within 5 working days of the emergency use of the test article, a written report to the IRB. The RSPP Emergency Use Report form, found on the RSPP website or obtained by contacting the AAH RSPP office, should be completed and forwarded to the RSPP office within this timeframe.

If the exception to the informed consent provision of the emergency use regulations was used, the written assessment by an independent physician assessment should accompany the Emergency Use Report. The Emergency Use Report also includes a place for an independent physician to attest to the patient’s condition if the independent physician’s assessment was not obtained prior to the use.

An IRB Chair or designated IRB member will review the report and document via signature that the federal regulations (21 CFR 56.104(c)) were satisfied. A copy of the completed report will be returned to the treating physician for his/her records.

If the emergency use did not meet the criteria allowing an exemption from prior IRB review and approval, OR the required follow-up report was not received by the RSPP within 5 working days of the emergency use, the action will be handled according to Noncompliance SOPs (AAH RSPP SOP #5 & 6).

The RSPP will retain copies of the relevant documentation of the emergency use as required by regulation. The IRB will be notified of the emergency use of the test article via an IRB meeting agenda of a future meeting.

Is the emergency use “Research”?
The FDA regards emergency use of a test article, other than a medical device, as a “clinical investigation” and may require data from an emergency use to be reported in a marketing application. However, DHHS states, “emergency care may not be claimed as research, nor may the outcome of such care be included in any report of a research activity.” Thus, a patient receiving an emergency use of a test article is not considered a research participant by DHHS regulation, and such emergency use is not “research” as covered under 45 CFR 46.
How do I obtain permission for use of an investigational drug or biologic in an emergency use situation?

- The treating physician should contact the drug/biologic manufacturer who will determine if the drug or biologic can be made available for the emergency use under the company’s IND. If the company only allows cross-referencing to their IND, declines permission or cannot be reached, the treating physician should contact the FDA directly to obtain an Emergency Use IND. The FDA may authorize shipment of the test article in advance of the IND submission.
- If the drug cannot be made available under the manufacturer’s current IND, the treating physician and/or manufacturer should contact the FDA to obtain and emergency IND. Information can be found in FDA guidance entitled: Emergency Use of an Investigational Drug or Biologic.

How can I obtain permission to use an investigational device in an emergency use situation?

The FDA allows two procedures for emergency use of an investigational device.

The first scenario involves securing an emergency IDE from the FDA. The treating physician should contact the manufacturer who will determine if the device can be made available for the emergency use under the company’s IDE.

If the device cannot be made available under the manufacturer’s current IDE, the treating physician and/or the manufacturer should contact the FDA directly. Information can be found in FDA guidance entitled: Expanded Access for Medical Devices.

The second scenario involves using an investigational article in an emergency situation without prior approval of the FDA.

In these circumstances, the treating physician must make the determination that an emergency situation exists (see criteria above). The treating physician must then assess the potential for benefit from the use of the unapproved device, and have substantial reason to believe that benefits will exist.

In the event that an investigational device is used without prior FDA approval, the physician should follow as many patient protection procedures as possible. Such patient protection procedures include obtaining:

1. Informed consent from the patient or a legal representative;
2. Clearance from the institution as specified by their policies;
3. Concurrence of the Institutional Review Board (IRB) chairperson;
4. An independent assessment from an uninvolved physician; and
5. Authorization from the device manufacturer.

In addition, if the investigational device is used without prior FDA approval, ie. *no IDE is issued*, the use must be reported to the FDA within 5 working days. **NOTE** the FDA reporting requirement is *in addition to* the emergency use reporting to the IRB required by regulation. The report to the FDA should contain a summary of the conditions constituting the emergency, patient outcome information, and the patient protection measures that were followed. The treating physician can contact the FDA for guidance.

**REQUIREMENTS**

- FDA Regulations: 21 CFR 50.23; 50.25; 56.102; 56.104; 312.304(a); 312.305(a); 312.310(a)
- FDA guidance: Emergency Use of an Investigational Drug or Biologic; Expanded Access for Medical Devices
- AAHRPP Accreditation Standards/Elements: I.7.C
- AAH RSPP SOPs: 1, 2, 5