Emergency Use of a drug or device

Overview
The FDA defines "emergency use" as the use of a test article (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 [21CFR 56.102 (d)]. The FDA regulates use of all investigational drugs and devices, including emergency use. The IRB must be notified of all emergency use, even though it is not considered research.

Any subsequent use of the test article is subject to IRB review and approval. Only one emergency use of the test article is permitted at a given institution and any subsequent use needs to have an IRB approved protocol in place for the use. However, 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.

What Does "Life-Threatening" Mean?
Life-threatening, for the purposes of the above section [21 CFR 56.102(d)] includes the scope of both life-threatening and severely debilitating as defined below:

- FDA definition of "life-threatening": 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.
- FDA definition of "severely debilitating": 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.

Responsible Physician requirements for review by and reporting to the IRB
The FDA allows for use of a test article (an unapproved drug or device) without IRB approval [21 CFR 56.104(c)] which allows an exception from prospective review by the IRB. Emergency use of a test article as defined above does not require review by a convened IRB. The IRB Chair or designee will determine whether the use complies with the regulatory requirements.

1. The treating physician must notify the IRB before the emergency use of the test article. If immediate use of the test article is required to save the life of the participant and there is not sufficient time to contact the IRB, the treating physician may proceed with the emergency use.

2. The investigator must submit:
   a. Summary of the patient’s condition and indication about the life-threatening or severely debilitating condition
b. Explanation as to why the drug or device, including dosage and route of administration, are necessary

c. Written permission from the manufacturer (may be by email) for the use of the test article under their IND/IDE.

d. Completed worksheet, W317 - Emergency Use of a Test Article.

e. Concurrence from an independent physician that the use is appropriate and necessary to save the life of the patient.

3. The use must be reported to the IRB five (5) days from the use, regardless if the use was reported to the IRB before the use occurred.
   a. Submit the 'Certification for Emergency Use of a Test Article' for determination that the use complies with the regulatory requirements.
   b. Signed informed consent, or if consent was not obtained, certification by an Independent Physician
   c. Provide an update on the outcome of the use and patient's condition, including any adverse events related to the use.

Notifying the IRB of the emergency use should not be construed as IRB approval. A letter will be issued stating whether the use complies with the regulatory requirements. If the use does not comply with the regulatory requirements, the use will be considered non-compliance and handled as such.

If the IRB can reasonably hold a convened meeting to review all prepared emergency use materials prior to the use of the test article, it is not considered exempt from prospective review by the IRB. The HSPP should be contacted as soon as possible to facilitate review at a convened meeting.

**Informed Consent**

Even for emergency use, the treating physician is required to obtain informed consent of the subject or the subject’s legally authorized representative. An informed consent must be submitted to the IRB. Although emergency use is not research, a research consent template may be used to create a consent form for emergency use situations. The drug/device manufacturer may possibly have a consent template available. The IRB consent template may also be used. Language in the consent form must reflect that the treatment is not FDA-approved and the treatment is an option for treating the patient’s life-threatening condition. The consent form must state that the patient is not receiving treatment as part of research. Additionally, the FDA provides an exception from the requirements of informed consent [21 CFR 50.23] when consent cannot be obtained:
Before the use of the test article, both the treating physician and a physician who is not otherwise participating in the clinical investigation must certify all of the following:

1. The human subject is confronted by a life-threatening situation necessitating use of test article.
2. Consent cannot be obtained because of an inability to communicate with or obtain consent from the subject.
3. Time is not sufficient to obtain consent from subject's legal representative.
4. No alternative generally approved method is available.
5. If immediate use of the test article is required to save the life of the subject and time is not sufficient to obtain independent determination by another physician, a determination by the treating physician shall be made. This determination is to be reviewed and evaluated in writing by a physician who is not participating in the investigation within 5 days after use of article.

Emergency Use of an Investigational Drug
The emergency use of an unapproved investigational drug or biologic requires an Investigational New Drug (IND) number. For more information, please refer directly to the Emergency Use of an Investigational Drug or Biologic - Information Sheet found on the FDA website. Obtaining access to an IND number can be accomplished in two ways:

- Contact the manufacturer (or IND holder) of the product to determine if the drug or biologic can be made available for the emergency use under the existing IND. There may or may not be an existing, approved study (at any of the manufacturer’s study sites) using the IND. The manufacturer may be required to contact the FDA to obtain permission for the emergency use to occur using the existing IND.
- A treating physician may request an emergency IND from the FDA specific to the emergency use case. An emergency use IND number is not associated with another other clinical trial or another emergency use case. In some cases, the need for an investigational drug or biologic may be a situation that does not allow time for a submission of an emergency IND and the FDA may authorize shipment of the test article in advance of the IND submission.

Emergency Use of an Unapproved Device
The FDA provides guidance that defines an unapproved medical device as a device that is utilized for a purpose, condition, or use for which the device requires, but does not have, an approved application for premarket approval under section 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360e)(the act) or an approved IDE under section 520(g) of the act (21 U.S.C. 360j(g)).

An unapproved device should normally only be used in human subjects if it is approved for clinical testing under an IDE and if it is used by an investigator for the sponsor in accordance with the terms and conditions of the application. Emergency use of an unapproved device,
however, may also occur when: (i) an IDE for the device does not exist, (ii) when a physician wants to use the device in a way not approved under the IDE, or (iii) when a physician is not an investigator under the IDE.

A physician who intends to treat a patient with an unapproved medical device in an emergency situation should conclude that:

1. The patient has a life-threatening condition that needs immediate treatment.
2. No generally acceptable alternative treatment for the condition exists; and
3. Because of the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use.

FDA expects the physician to make the determination that the patient’s circumstances meet the above criteria, to assess the potential for benefit from the use of the unapproved device, and to have substantial reason to believe that benefits will exist.

The emergency use of an investigational device must be reported to the FDA by the IDE sponsor within 5 working days. If no IDE exists, the physician should follow the above procedures and report the emergency use to CDRH or CBER. For additional information on the procedures physicians should follow in an emergency situation, see chapter 3 of the guidance entitled IDE Policies and Procedures on the FDA website.

**Is the emergency use of a test article considered "research?"**
Emergency use of a test article (21 CFR 56.104(c)) is considered by FDA to be human research. It meets the FDA definition of clinical investigation and requires regulation under the Food, Drug and Cosmetic Act. It also involves the administration of a test article to a human, so it involves human subjects. Therefore under FDA regulations, it is human research.

The research typically is not subject to DHHS regulation since DHHS. In other words, the data from an emergency use may not be reported in a way that implies that the activity was a prospectively planned systematic investigation designed to develop or contribute to generalizable knowledge. If the data are intended to be used as 'research' with 'human subjects' per DHHS then prospective IRB approval is required.

**IRB requirements for emergency use**
The IRB and the Human Subjects Protection Program track all requests for emergency use of a test article. Each request for emergency use is reviewed to determine:

1. Has the test article been used