

## **EMERGENCY USE OF AN INVESTIGATIONAL DRUG OR BIOLOGIC (From FDA information sheets)**

The emergency use of test articles frequently prompts questions from Institutional Review Boards (IRBs) and investigators. This information sheet addresses three areas of concern: emergency Investigational New Drug (IND) requirements; IRB procedures; and informed consent requirements.

### **Obtaining an Emergency IND**

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 study protocol does not exist, the usual procedure is to contact the manufacturer and determine if the drug or biologic can be made available for the emergency use under the company's IND.

The need for an investigational drug or biologic may arise in an emergency situation that does not allow time for submission of an IND. In such a case, FDA may authorize shipment of the test article in advance of the IND submission. Requests for such authorization may be made by telephone or other rapid communication means [21 CFR 312.36].

### **Emergency Exemption from Prospective IRB Approval**

Emergency use is defined as 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 [21 CFR 56.102(d)]. The emergency use provision in the FDA regulations [21 CFR 56.104(c)] is an exemption from prior review and approval by the IRB. The exemption, which may not be used unless all of the conditions described in 21 CFR 56.102(d) exist, **allows for one emergency use of a test article without prospective IRB review.**

FDA regulations require that any subsequent use of the investigational product at the institution have prospective IRB review and approval. FDA acknowledges, however, 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.

**Life-threatening**, for the purposes of section 56.102(d), includes the scope of both life-threatening and severely debilitating, as defined below.

**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.

FDA requires the investigator to report the emergency use to the IRB within five working days 21 CFR 56.104(c).

The FDA regulations do not provide for expedited IRB approval in emergency situations. Therefore, "interim," "compassionate," "temporary" or other terms for an expedited approval process are not authorized. An IRB must either convene and give "full board" approval of the emergency use or, if the conditions of 21 CFR 56.102(d) are met and it is not possible to convene a quorum within the time available, the use may proceed without any IRB approval.

Some manufacturers will agree to allow the use of the test article, but their policy requires "an IRB approval letter" before the test article will be shipped. If it is not possible to convene a quorum of the IRB within the time available, some IRBs have sent to the sponsor 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). Although, this is not an "IRB approval," the acknowledgment letter has been acceptable to manufacturers and has allowed the shipment to proceed.

**HOWEVER, the National Institutes of Health's Office For Human Research Protections (OHRP) does not permit patients to be considered research subjects without prior IRB review and approval. Emergency care may not be claimed as research, nor may the outcome of such care be included in any report of a research activity.**

#### **Exception From Informed Consent Requirement**

Even for emergency use, the physician is required to obtain informed consent of the subject or the subject's legally authorized representative unless both the investigator and a physician who is not otherwise participating in the clinical trial certifies in writing to all of the following [21 CFR 50.23(a)]:

- (a) The subject is confronted by a life-threatening situation necessitating the use of the test article.
- (b) Informed consent cannot be obtained because of inability to communicate with, or obtain legally effective consent from the subject.

- (c) Time is not sufficient to obtain consent from the subject's legal representative.
- (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.

If, in the investigator's opinion, immediate use of the test article is required to preserve the subject's life, and if time is not sufficient to obtain an independent physician's determination that the four conditions above apply, the clinical investigator should make the determination and, within 5 working days after the use of the article, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. The investigator must notify the IRB within 5 working days after the use of the test article [21 CFR 50.23(c)]. **The documentation of this determination shall be submitted to the IRB within 5 working days after the use of the test article [21 CFR 50.23(c)].**

**Notification/Reporting to Upstate IRB:**

1. If possible, the physician who will be using the investigational product should notify the IRB Chairperson that an Emergency Use of an investigational product has occurred or will occur.
  - (a) Notification does **not** constitute IRB approval.
  - (b) Notification initiates tracking to insure that the investigator files a report within the 5-day time frame required by 21 CFR 56.104(c).
2. **Within 5 working days**, the emergency use must be reported to the IRB.
  - a. The *Emergency Use Report Form* (available on IRBNet) may be used to fulfill this requirement.
  - b. A copy of the completed consent form or a copy of the written determination/certification required for exception from informed consent (described above).