

SPECIFIC INFORMATION

Regulations pertaining to emergency use of a test article (FDA-regulated investigational drug, biologic or device) are those of the US Food & Drug Administration (FDA), published as part of the Code of Federal Regulations (CFR) 21 CFR 50 and 21 CFR 56. Emergency use of a test article in a life-threatening condition is not considered research; nevertheless, it is under the purview of the IRB, because the use of an investigational test article not yet approved by the FDA is involved. The investigational drug or biologic must have received an IND (Investigational New Drug) approval, or the investigational device an IDE (Investigational Device Exemption) from the FDA for clinical testing, to be eligible for use in an emergency setting. Usually, IND or IDE acquisition is conducted by the manufacturer. If IND or IDE approval by the FDA is not available, the Investigator must contact the FDA on an emergency basis.

For emergency use of a test article, all of the following criteria must be met:

1. The subject is facing a life-threatening condition, for which there is no conventional treatment, or conventional treatments have failed.
2. The physician has access to a test article, and believes that there is a reasonable likelihood that the article will help save the subject's life, and that there is no approved treatment that has equal or greater likelihood of helping the subject.
3. Comprehensive written informed consent is to be executed prior to initiation of the administration of the test article.

Certain emergency circumstances may not permit the execution of the standard informed consent process prior to administration of the test article. FDA regulations provide an exemption from the informed consent requirement, if the subject is unable to provide effective consent, and there is insufficient time in which to obtain consent from the subject's legal representative. Under these circumstances, the opinion of another impartial physician is required on the expected benefit from the use the test article; please refer to the "Definitions and interpretations of the Federal rules on Emergency Use of A Test article, prepared by the Office for Human Research Protections of the US Department of Health and Human Services"

The test article is expected to be administered to a single subject as a single course (may involve multiple dosing to achieve maximal efficacy). The subject to receive the test article should not be enrolled in a research study related to the test article. If subsequent use of the test article is contemplated in the same subject or in others, a new project application to the IRB is required in advance of that use.

The use of a test article in an investigation designed to be conducted under emergency conditions (e.g. emergency room research) usually does not qualify for the emergency use exemption.

Emergency use is defined as the use of a test article 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 Investigator is still required to obtain informed consent under these circumstances.

FDA exempts from IRB review the emergency use of a test article so long as the emergency use is reported to the IRB within five working days of its occurrence. Any subsequent use of the test article is subject to IRB review [21 CFR 50.23; 21 CFR 56.104(c)]. "Subsequent use" means any use of the test article that occurs after its initial emergency use. When an IRB receives a report by a clinical Investigator of an emergency use, the IRB must examine each case to assure itself and the institution that the emergency use was justified.

Although 21 CFR 56.104 is designed to permit only a single emergency use of a test article for the treatment of one patient by one physician within an institution, the regulation is not intended to limit the authority of a physician to provide emergency care in a life-threatening situation. Should a situation arise which would require the emergency use of the test article for a second patient, either by the same or a second physician, subsequent emergency use should not be withheld for the purpose of gaining IRB approval. If it appears probable that similar emergencies will require subsequent use of the test article at the institution, every effort should be made either to sign on to the Sponsor's protocol or to develop a protocol for future emergency use of the article at the institution. Either of these protocols would need to be prospectively reviewed and approved by the IRB for future use of the test article.

In emergency circumstances, it may not be feasible to obtain informed consent prior to using the test article. The regulations therefore provide an exemption from the informed consent requirement for such situations. Emergencies qualifying for this exemption are defined as:

- (1) life-threatening situations necessitating use of the test article;
- (2) where the subject is unable to provide effective consent;
- (3) there is insufficient time in which to obtain consent from the subject's legal representative; and
- (4) there is no available alternative method of approved or generally recognized therapy of equal or greater likelihood of saving the subject's life [21 CFR 50.23(a)(1)-(4)].

Special procedures for documenting the unfeasibility of obtaining consent apply as follows:

- (1) The Investigator and another physician, who is not participating in the clinical investigation, must certify in writing the existence of all four conditions listed above before use of the test article [21 CFR 50.23(a)].
- (2) If in the Investigator's opinion,
 - (a) immediate use of the test article is necessary to save the life of the subject; **and**
 - (b) there is insufficient time to obtain the independent determination required by 21 CFR 50.23(a) before using the test article;
 - (c) the Investigator is to make his or her own written determinations, then obtain the written review and independent evaluation of a physician who is not participating in the clinical investigation within five working days after the use of the test article [21 CFR 50.23(b)].

The documentation required by either 21 CFR 50.23(a) or 50.23(b) must be submitted to the IRB **within five working days** after the use of the test article [21 CFR 50.23(c)]