

Emergency Use of a Test Article

SOP 121

Approved: December 18, 2015

Purpose and Scope

This standard operating procedure establishes the process to review notifications of emergency uses of test articles (drug, biologic, or device) in life-threatening situations. This includes compassionate use of an unapproved device without an IDE for a serious condition.

This SOP applies to all HSP staff, IRB members, and Investigators/ Treating Physicians who may be involved in the conduct or process of emergency use of a test article.

Definitions

- **Emergency Use of a Test Article:** the use of a test article on a human patient 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.

Under the HHS Regulations

Under the HHS regulations, emergency use of a test article does not constitute research; the patient may not be considered as a research subject; and any data derived from the use may not be included in any report of research activities. This is because HHS regulations do not permit research activities to be initiated without prior IRB review and approval, even in emergency.¹

Under the FDA Regulations

FDA regulations allow emergency use of a test article when the human subject have been 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.² A clinical investigation involving emergency use is still a clinical investigation under the FDA regulations. FDA may require data from emergency use to be included in marketing applications.³

Emergency use involves four major issues:

- (1) approval by or notification to FDA;
- (2) exemption from prospective IRB approval;
- (3) waiver or alteration of informed consent requirements in emergency research; and
- (4) emergency exception from informed consent requirements.

- **Designated Reviewer:** The Cooperative IRB Chair, Biomedical IRB Chair or an IRB member

¹ 45 C.F.R. § 46.103(b) (2014); [HHS on Emergency Care](#), *supra* note **Error! Bookmark not defined.**

² 21 C.F.R. § 56.102(d).

³ 21 C.F.R. §§ 314.50, 814.20(b)(2) (2014).

designated by the IRB Chair qualified to make determination on emergency use of test article requests.

Procedures

Approval by or Notification to FDA

Drugs

Emergency use generally requires an IND. But if the emergency use does not fall under the existing IND and the emergency does not allow time for submission of a new IND, the Investigator or the sponsor may seek authorization from FDA on the emergency use.⁴

Devices

An Investigator may deviate from the investigational plan under an existing IDE in an emergency to protect the life or well-being of a human subject. But the Investigator or the sponsor must report the emergency use to FDA no later than five (5) working days after the sponsor learns of the use.⁵

Exemption from Prospective IRB Approval

Under 21 C.F.R. § 56.104(c), emergency use is exempted from prospective IRB approval only if:

- (1) the human subject is in a life-threatening situation;
- (2) standard acceptable treatments are not available for the situation;
- (3) there is not sufficient time to obtain IRB approval; and
- (4) the emergency use is reported to the IRB no later than five (5) working days after the use.⁶

Communicating with the IRB

- I. **Before the Use.** Whenever feasible, physicians are to notify the IRB Chair (via Human Studies Program) of a proposed emergency use of a drug, biologic, or device in a life-threatening situation prior to the use.
 - a. The treating physician should use **APP 11** or **APP 12 Emergency Use Checklist** to determine whether the circumstances will meet the regulatory and guidance criteria.
 - i. The physician providing the assessment of the patient's condition must not be participating in the investigation of the experimental drug, biologic or device. If the treating physician is also an Investigator of the test article, the assessment must be conducted by an independent physician.
 - b. The Designated Reviewer *may* use **APP 11** or **APP 12 Emergency Use Checklist** to determine whether the circumstances will meet the regulatory and guidance criteria.
 - i. If met, the reviewer informs the physician that the physician can proceed with the use.

⁴ 21 C.F.R. § 312.310(d); Emergency Use of an Investigational Drug or Biologic—Information Sheet, FDA, <http://www.fda.gov/RegulatoryInformation/Guidances/ucm126491.htm> (last updated June 25, 2014) [hereinafter FDA Information Sheet on Emergency Use].

⁵ 21 C.F.R. § 812.35(a)(2); Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors, Frequently Asked Questions About Medical Devices, FDA, 10 (Jan. 2006),

<http://www.fda.gov/downloads/regulatoryinformation/guidances/ucm127067.pdf>.

⁶ 21 C.F.R. §§ 56.102(d), 56.104(c).

- ii. If not met, reviewer informs the physician that if the physician proceeds with the use, the IRB will consider that action to be “Non-Compliance.”

II. Acknowledgment Letter.⁷

- a. If the proposed use meets the exemption requirements under 21 C.F.R. § 56.104(c), the IRB Chair may provide an acknowledgment letter. Although the letter is not an “IRB approval,” manufacturers may accept the letter and allow the shipment of test articles.

III. Notifying the IRB. The physician must notify the IRB no later than five (5) working days after the emergency use.⁸

- a. The treating physician must use **APP 13 Post-Emergency Use Report Form** to determine whether the circumstances met the regulatory and guidance criteria and to report on the use of the test article to the IRB.
- b. Notification should include the following:
 - i. The drug or device name;
 - ii. Provider or sponsor of the drug or device;
 - iii. IND or IDE number;
 - iv. Subject’s initials;
 - v. Details about the subject’s disease or condition;
 - vi. Copy of the consent form; and
 - vii. Justification or rationale for the emergency use.

IV. HSP’s Action. The HSP will send a written statement to the Investigator acknowledging that the IRB is aware of the use and, if appropriate, considers it to have met the exemption requirements under 21 C.F.R. § 56.104(c).

V. Subsequent Use. Subsequent use of the test article in similar circumstances is subject to IRB review.⁹ But FDA acknowledges that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is lack of time for the IRB to convene and review the issue.¹⁰ In that scenario, the Investigator still must notify the IRB no later than five (5) working days after the emergency use.

Exception to the Informed Consent Requirements in an Emergency

Again, informed consent is generally required. FDA regulations provide an exception to this requirement for emergencies.

To meet the exception,

⁷ See [FDA Information Sheet on Emergency Use](#), *supra* note 4.

⁸ 21 C.F.R. § 56.104(c).

⁹ *Id.*

¹⁰ [FDA Information Sheet on Emergency Use](#), *supra* note 4.

- (1) the Investigator and a physician not participating in the clinical investigation must certify in writing all of the following¹¹:
 - (a) The human subject is confronted by a life-threatening situation necessitating the use of the test article;
 - (b) Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject;
 - (c) Time is not sufficient to obtain consent from the subject's legally authorized representative; and
 - (d) There is no approved or generally recognized alternative that provides an equal or greater likelihood of saving the subject's life.

AND

- (2) the Investigator or the sponsor must submit those documents to the IRB no later than five (5) working days after the use.¹²

Materials

- APP 11 Emergency Use Checklist – Device
- APP 12 Emergency Use Checklist – Drugs
- APP 13 Post-Emergency Use Report Form

References

- 21 CFR 50.23 – Exception to informed consent
- 21 CFR 56.102(d) – Emergency Use definition
- 21 CFR 56.104 – Exception to IRB review
- 21 CFR 312.300 (Subpart I) - Expanded Access to Investigational Drugs for Treatment Use
- 21 CFR 812.35 – Exception to IDE requirement
- Emergency Use of an Investigational Drug or Biologic [FDA]
- Form FDA 1571 and Instructions - Investigational New Drug Application
- The Organization has and follows written policies and procedures for compliance with legal and regulatory requirements governing emergency use of an investigational or unlicensed test article. (AAHRPP Standard I.7.C)

¹¹ 21 C.F.R. § 50.23(a).

¹² 21 C.F.R. § 50.23(c).