

SOP 502G: Emergency Use of FDA Regulated Products

1. POLICY

“Emergency use” is defined in 21 CFR 56.102(d)¹ as the use of a test article with a human participant in a life-threatening situation for which no standard acceptable treatment is available and there is not sufficient time to obtain IRB approval.

The HSC IRB allows a one-time emergency use of an investigational drug, device, or biologic test article by an investigator without prior IRB approval, as permitted under FDA regulations at 21 CFR 56.104(c), **provided that the emergency use is reported to the IRB within 5 University business days**. Any subsequent use of the test article requires prior IRB review.

The investigator must obtain written informed consent from each individual or legally authorized representative prior to the use of a test article, in accordance with FDA regulations at 21 CFR 50, unless the circumstances meet the exception to the requirement for consent at 21 CFR 50.23(a)-(c).

Under DHHS regulations, patients receiving a test article in an emergency use as defined by FDA regulations may not be considered to be a research participant and do not permit data obtained from patients to be classified as human participants research, nor permit the outcome of such care to be included in any report of a research activity subject to DHHS regulations. However, under FDA regulations, emergency use of a test article meets the FDA definition of a clinical investigation,² and the patient receiving the test article meets the FDA definition of a human participant.³ Therefore, a patient in such case is a research participant as defined by FDA regulations.

Specific Policies

1.1 Emergency Use of an Unapproved Drug or Biologic

A drug or biologic may be used in an emergency prior to IRB review, provided that the following criteria are met:

- The participant is in a life-threatening situation for which no standard acceptable treatment is available, and
- There is not sufficient time to obtain IRB approval, and
- The use will be reported to the IRB within five University business days as outlined in Section 1.5 of this SOP, and
- Any subsequent use of the test article by an investigator is subject to IRB review.

¹**Life threatening**, for the purposes of 21 CFR section 56.102(d), includes the scope of both life-threatening and severely debilitating, as defined as follows: **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 participants 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.

² 21 CFR 56.102(c).

³ 21 CFR 56.102(e).

If the intended participant does not meet the criteria for an existing research project protocol or if an approved research project protocol does not exist, the investigator must contact the manufacturer to determine if the drug or biologic can be made available for the emergency use under the manufacturer's IND.

If the manufacturer does not allow the investigator to reference its IND, the investigator must contact the FDA directly at 301-796-3400 for an IND (note that this phone number is subject to change). The FDA requires an Investigational New Drug number (IND) for emergency use and does not allow a waiver of its policy.

1.2 Emergency Use of an Unapproved Device

FDA guidance documents state that emergencies that qualify for use of an unapproved device exist where an unapproved device may offer the only possible life-saving alternative and (1) an IDE for the device does not exist, or (2) the proposed use is not approved under an existing IDE, or (3) the investigator or institution is not approved under the IDE.

An investigator may use an unapproved device in such an emergency, provided that each of the following requirements is met to justify the use:

- The patient is in a life-threatening condition that needs immediate treatment;
- There is no generally acceptable alternative available for treating the patient; and
- Because of the immediate need to use the device, there is not time to use existing procedures to obtain FDA approval for the use.

Prior to using the device, the investigator must obtain authorization from the IDE holder, if an approved IDE for the device exists. If an IDE does not exist or if the IDE holder does not authorize the use the investigator shall notify the FDA of the emergency use and provide FDA with a written summary of the conditions constituting the emergency, participant protection measures, and results. The contact telephone number for the Center for Devices and Radiological Health (CDRH) is 301-796-5640 (subject to change).

The FDA expects the physician to follow as many participant protection measures as possible. These include:

- Obtaining an independent assessment by a physician not involved in the patient's care; (see 1.3.2)
- Obtaining informed consent from the patient or a legal representative;
- Notifying institutional officials as specified by institutional policies;
- Notifying the Institutional Review Board (IRB); and
- Obtaining authorization from the IDE holder, if an approved IDE for the device exists.

1.3 Informed Consent

1.3.1 Informed Consent Requirements for Emergency Use Situations

The investigator shall obtain informed consent from the patient or the patient's legally authorized representative, as applicable, using a consent document that contains the elements of informed consent (as described in 21 CFR 50.25). The investigator is encouraged to utilize the Sample Consent Form for Emergency Use that is available on the IRB website. In emergent situations, unless the investigator has time to notify the IRB prior to the use of the test article, the informed consent document will not be reviewed or approved by the IRB.

1.3.2 Exception from Informed Consent Requirements⁴

If obtaining informed consent is not possible, both the investigator and a physician who is not participating in the research project must certify in writing all of the following:

- A. The patient is confronted by a life-threatening situation necessitating the use of the test article;
- B. Informed consent cannot be obtained because of an inability to communicate with or obtain legally effective consent from the patient;
- C. Time is not sufficient to obtain consent from the patient's legally authorized representative; and
- D. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the life of the patient.

If, in the investigator's opinion, immediate use of the test article is required to preserve the patient's life and time is not sufficient to obtain an independent physician's determination that the above four conditions apply, the investigator shall make the determination and, after the use of the test article, have the determination reviewed and evaluated in writing by a physician who is not participating in the research project.

The investigator must submit to the IRB a copy of the independent physician's evaluation within 5 University business days after the use of the test article.

1.4 Prior Notification to the IRB

The investigator should attempt to notify the IRB prior to an emergency use. If an investigator notifies the IRB of the intent to use a test article on an emergency basis in a life-threatening situation without prior IRB review, the IRB Chair or IRB designee shall review the use (including informed consent or the exception from

⁴ 21 CFR 50.23.

the requirement for informed consent) to determine whether the circumstances of the emergency comply with FDA regulations. However, this notification and subsequent IRB Chair acknowledgement should not be considered an IRB approval.

1.5 Reporting Requirements

1.5.1 Requirement for Five-Day Follow-up Report to the IRB

The emergency use **must be reported to the IRB within 5 University business days** after emergency use of a test article. Failure to comply with this requirement is considered non-compliance with the IRB. The report must include the following:

- One-time Emergency Use of a Test Article;
- Case history of the patient;
- Therapeutic protocol, including reference material and;
- Copy of the executed informed consent document or a copy of the independent physician's determination that the conditions for exception from informed consent as described in Section 1.3.2 above were met and the emergency use was necessary to preserve the participant's life.

1.5.2 Report of an Unapproved Device to the Sponsor or FDA

After using an unapproved device in an emergency, and if an IDE does exist, the investigator shall notify the sponsor of the emergency use.

After using an unapproved device in an emergency, and if an IDE does not exist, the investigator shall provide the FDA with a written summary of the conditions constituting the emergency use, the participant protection measures followed, and the results of the use. Note that the FDA requires that data generated from the use be used in reports of the research activity to the FDA.

1.6 Subsequent Use

FDA regulations allow for one emergency use (single use with one participant) of a test article without prospective IRB review, provided that the emergency use is reported to the IRB within five University business days after such use. Subsequent use is considered a second use with that participant or another participant. The investigator must evaluate the likelihood of a similar need and, if future use is likely, initiate efforts to obtain IRB approval and an approved IND or IDE from the FDA for subsequent use.

1.7 Planned Emergency Research

Planned emergency research is defined as planned research in a life-threatening emergency where the requirement to obtain prospective informed consent has

been waived as covered by 21 CFR 50.24. The research plan must be approved in advance by the FDA (or DHHS) and the IRB, and the project, as well as its results, must be publicly disclosed to the community in which the research is conducted.

Oklahoma law does not allow for an exception to the waiver of consent in emergency research. Therefore, the IRB cannot waive the requirement to obtain informed consent for planned emergency research, and no planned emergency research shall be conducted at OU.

Refer to SOP 701: Consent Process and Documentation, Section 1.4 C for more information regarding waiver of informed consent.

1.8 VA Requirements

A patient in a VA research project receiving a test article in an emergency use that is regulated by FDA is not considered to be involved in research and is not a research participant. VA regulations pertaining to research involving human participants do not permit data obtained from patients to be classified as human participants research, nor may the outcome of such care be included in any report of a research activity subject to VA regulations pertaining to research involving human participants.

2. SCOPE

This SOP applies to all emergency use protocols submitted to the IRB, whether prior or subsequent to the use.

3. RESPONSIBILITY

- 3.1 The investigator is responsible for consulting with the IRB Chair prior to use of the test article if time allows and must submit a One-Time Emergency Use of a Test Article Submission Form to the IRB within 5 University business days after emergency use of the test article.
- 3.2 The IRB staff is responsible for processing the submission and forwarding it to the appropriate IRB Chair for review and adding the item to the next available IRB meeting agenda.
- 3.3 IRB Reviewers are responsible for verifying that the use of the test article in an emergency falls within the emergency use criteria, conducting a thorough review of the use of the test article, securing appropriate consulting expertise as needed, and making appropriate approval recommendations for consideration by the IRB.

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 50.23, 50.24, 50.25

21 CFR 56.102(d)-(e), 56.104(c)

5. REFERENCES TO OTHER APPLICABLE SOPS

SOP 701: Consent Process and Documentation

SOP 903: Non-Compliance/Scholarly Misconduct

6. ATTACHMENTS

301-E HSC One-Time Emergency Use of a Test Article

203-A HSC Reviewer Checklist

502G-A Sample Consent Form for Emergency Use

7. PROCESS OVERVIEW

- 7.1 If time allows, an investigator shall notify the IRB of an intent to use a test article on an emergency basis in a life-threatening situation without prior IRB review and the IRB Chair or IRB designee shall review the use (including informed consent or the exception from the requirement for informed consent) to determine whether the circumstances of the anticipated emergency use will comply with applicable regulations. The IRB Chair may assist the investigator in efforts to follow as many participant protection measures as possible. However, this notification and subsequent IRB Chair acknowledgement or assistance will not be considered an IRB approval.
- 7.2 Within 5 University business days of the use of the test article, the physician shall submit a new application in the IRB electronic information system, indicating One-Time Emergency Use of a Test Article, and upload all applicable documents into the IRB electronic information system.
- 7.3 The submission is received in the IRB Office and processed (see SOP 301: Research Submission Requirements and SOP 403: Initial Review – Criteria for IRB Approval). The submission with all applicable documents is made available to all IRB members.
- 7.4 The IRB Administrator conducts a pre-review of the submission and verifies all necessary documents are received including: (1) New Application with the One Time Emergency Use of a Test Article subform, (2) documentation from the FDA authorizing the use of the test article for this single use, (3) copy of the consent form signed by the patient (or explanation of why consent could not be obtained in the emergency situation), and (4) assessment from an independent physician. The IRB Administrator also verifies that the report is received within 5 days of the use of the test article.
- 7.5 The IRB Administrator assigns the submission to the next appropriate Board agenda. The process follows SOP 403: Initial Review – Criteria for IRB Approval.
- 7.6 The IRB reviews the submission at the convened meeting to verify that the use falls within the criteria stated in the regulations and makes any recommendations necessary. The IRB may require the investigator submit a follow-up status report and to report unanticipated problems to the IRB.

- 7.7 Following review of the submission, the IRB Administrator updates the outcome of the IRB review and communicates the outcome and any stipulations to the physician / investigator.
- 7.8 If the use of the test article did not meet the emergency use criteria, or if the investigator fails to submit a New Application with the One Time Emergency Use of a Test Article sub-form to the IRB within five working days, this may represent reportable non-compliance subject to SOP 903, Non-Compliance / Scholarly Misconduct. The investigator, the Department Chair and the Director of Compliance will be informed in writing that the use of the test article did not meet the criteria and is subject to investigation.

APPROVED BY: _____ **DATE:** 09/09/2016

NEXT ESTABLISHED REVIEW DATE: AUGUST 2018