# IRB Policy 20: Emergency Use
# Revision Date April 16, 2008, revised January 11, 2011, revised April 22, 2011, revised April 17, 2020, October 22, 2020

## I. Summary Policy

The policy of the East Tennessee State University/Veterans Affairs Institutional Review Board (ETSU/VA IRB) is that all applicable rules and regulations will be followed in the Emergency Use of a Test Article. This policy describes the process and procedure to assess the appropriateness of the emergency use of a test article, and the subsequent process for physicians and the IRB to obtain and review emergency use. This policy describes responsibilities of the physician/investigator when an emergency requires a patient be treated with an investigational test article such that there is not sufficient time to obtain IRB review and approval at a convened meeting. Expedited review of Emergency Use is not permitted.

## II. Scope and Responsibility

**A.** **Scope**: This policy applies to treating physicians affiliated with ETSU and JHQVAMC seeking to use investigational agents for the purpose of providing clinical treatment (non-research purposes), in an emergency context where there is insufficient time to obtain IRB review. This procedure also applies to OPHRS staff and the ETSU IRBs.

**B.** **Responsibility**: It is the responsibility of the IRB, OPHRS staff, and all physicians seeking to carry out procedures covered in this policy to understand and comply with this policy.

## III. Definitions

**A.** **Emergency use** is defined as the use of a test article (e.g., investigational drug, device or biologic) 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.

**B.** **Test Article:** Any drug, biological product, or medical device for human use [21 CFR 56.102(1)].

**C.** **Immediately life-threatening disease or condition (Drugs/Biologics Context)** means a stage of disease in which there is a reasonable likelihood

that death will occur within a matter of months or in which premature death is likely without early treatment.

**D.** **Investigational Device Exemption (IDE)**: An IDE requests FDA permission to use an investigational device in a patient.

**E.** **Emergency IDE** may be needed when an IDE for the device does not exist when a physician wants to use a device in a way not approved under an approved IDE; or when a physician is not an investigator under the relevant IDE (e.g., not participating in the clinical investigation of the device).

**F.** **Investigational New Drug Application (IND)**: An FDA submission that requests permission to use an investigational drug/biologic in a patient.

**G.** **Emergency IND** allows the FDA to authorize the use of an investigational drug/biologic in an emergency situation that does not allow time for prior submission of an IND application in accordance with FDA regulation. It is also used for patients who do not meet criteria of an existing study protocol, or if any approved study protocol does not exist for the drug/biologic.

**H.** **Life-threatening condition (Device Context)** includes serious diseases of conditions such as sight-threatening and limb-threatening conditions as well as other situations involving risk of irreversible morbidity (e.g., blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke). (http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM127067.pdf).

**I.** **Serious disease or condition (Drug/Biologics Context)** means a disease or condition associated with morbidity that has substantial impact on day to day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors survival, day to day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one. 21 CFR 312.300(b)

## IV. Emergency Use Requirements

The FDA regards emergency use of a test article, other than a medical device, as a clinical investigation and may require data from an emergency use to be reported in a marketing application. However, emergency uses are for the purpose of providing clinical treatment and are not considered to be research according to DHHS regulations at 45 CFR 46.102(d). DHHS states, “emergency care may not be claimed as research, nor may the outcome of such care be included in any report of a research activity.” Thus, a patient receiving an emergency use of a test article is not considered a research participant by DHHS

regulation, and such emergency use is not "research" as covered under 45 CFR 46.

The investigator is still required to obtain prior informed consent from the patient, or his/her legally authorized representative (LAR) under these circumstances.

The 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)).

VA research (see VHA Handbook 1108.04):

- Emergency use of test articles must meet FDA regulations.
- Emergency medical care is not research and does not need to be approved by an IRB.
- Emergency use of test articles cannot be claimed as research, and the outcome of such care cannot be included in any report of research activity.

**NOTE:** Emergency use of a test article is different than using a test article for a single patient under an Expanded Access Treatment Use IND. If there is sufficient time to obtain IRB review, or the patient is not in an Immediate Life-Threatening Situation, then the Expanded Access IND path may be followed. Prospective IRB review of the treatment plan and other materials is required prior to administering an investigational agent under the Expanded Access Treatment Use IND program.

# V. Emergency Use Procedure for Physician/Investigator

**Step 1: The Physician/Investigator and FDA determines if an emergency use is appropriate.**

| For Drugs/Biologics (IND) | For Devices (IDE) |
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| The **treating physician determines** that all the following are met:<br>(1) Life-threatening or serious disease or condition that needs immediate treatment;<br>(2) No generally acceptable alternative for treating the patient is available; and<br>(3) Due to immediate need to use the test article, there is no time to follow existing procedures to obtain IRB approval prior to the use.<br>(4) The FDA also expects the physician | The **treating physician determines** that all the following are met:<br>(1) The patient has a life-threatening condition that needs immediate treatment;<br>(2) No generally acceptable alternative treatment for the condition exists; and<br>(3) Because of the immediate need to use the device, there is no time to use existing procedures to get IRB and FDA approval for the use. |

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| to make the determination that the probable risk to the person from the investigational test article is not greater than the probable risk from the disease or condition. 21 CFR 312.310(a)(1). | (4) The FDA also expects the physician to assess the potential for benefit from the use of the unapproved device, and to have substantial reason to believe that benefits will exist. |
| **FDA must determine** based on information provided by physician that:<br>(1) The patient to be treated has a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition (21 CFR 312.305(a)(1);<br>(2) The potential patient benefit justifies the potential risks of the treatment use and those potential risks are not unreasonable in the context of the disease or condition to be treated (21 CFR 312.305(a)(2);<br>(3) Providing the investigational test article for the requested use will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use (21 CFR 312.305(a)(3));<br>(4) The patient cannot obtain the test article under another IND or protocol. (21 CFR 312.310(a)(2). | An **uninvolved physician (not participating in the emergency use) determines** that all of the above emergency use criteria are met.<br><br>AND<br><br>The **treating physician**:<br>(1) Obtains **documentation** of the uninvolved physician's determination whenever possible (e.g., via email).<br>(2) If it is not possible to obtain a second opinion from an uninvolved physician (and/or documentation), the treating physician should make the determination and proceed with the emergency use process. |

**<u>Step 2</u>: The Physician/Investigator takes steps to obtain the investigational test article.**

| For Drugs/Biologics (IND) | For Devices (IDE) |
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| (1) <u>Identify the sponsor:</u><br>• Manufacturer may have the IND and serves as the "sponsor" of emergency use<br>• Manufacturer has no plans to get an IND and the treating physician | (1) <u>Identify the sponsor:</u><br>• Generally, there will be a manufacturer who has applied for an IDE and will serve as the "sponsor" of the emergency use. |

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| serves as the "sponsor-investigator"<br>(2) Contact the manufacturer/sponsor:<br>• Determine if they are willing to provide the investigational drug/biologic.<br>(3) Contact the FDA for an Emergency IND:<br>• If the manufacturer will serve as the "sponsor" they will usually contact the FDA on the physician's behalf for approval of the emergency IND. If the physician will serve as the "sponsor-investigator" the physician contacts the FDA directly to obtain an emergency IND. An emergency use may be requested by telephone, fax, or other means of electronic communication. Contact information is listed below.<br>• The physician or sponsor must explain how the expanded access use will meet the criteria listed above for emergency use.<br>(4) FDA will usually provide a new IND number for the specific emergency use. | (2) Contact the sponsor:<br>• Determine if they are willing to provide the investigational device. Obtain authorization from the IDE sponsor if an approved IDE exists for the device.<br>(3) Advance contact to FDA is NOT required for Emergency IDE:<br>• Prior FDA approval for shipment or emergency use of an investigational device is NOT required. 21 CFR 812.35(a)(2). Treating physician may contact the Office of device Evaluation (ODE) at FDA to discuss his/her patient's condition (ODE as advisory role vs. approving use). Contact information listed below.<br>• The responsibility of making the decision as to whether the situation meets the emergency use criteria and whether the investigational device should be used lies with the treating physician.<br>• If no IDE exists the physician should follow the above procedures and report the emergency use to CDRH as directed in Step 6. |

**FDA Contact Information**

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| **Drugs (CDER):** | **Division of Drug Information**<br>**310-796-3400 or 301-827-4570**<br>**Email: druginfo@fda.hhs.gov**<br>See FDA Guidance, Physician Request for an Individual Patient IND under Expanded Access for Emergency Use |
| **Biologics (CBER):** | **Office of Communication, Outreach and Development**<br>**310-827-1800 or 1-800-835-4709**<br>**ocod@fda.hhs.gov** |
| **Devices (CDRH):** | **Office of Device Evaluation, Program Operations Staff**<br>**301-796-5640**<br>**Email: dsmica@fda.hhs.gov** |
| **All Products After Business Hours** | **FDA Emergency Call Center**<br>**1-866-300-4374 or 301-796-8240 or 301-443-1240** |

| Email: emergency.operations@fda.hhs.gov |
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**Step 3: The Physician/Investigator takes as many patient protection measures as possible.**

Please note: patient care should not be compromised if there is not sufficient time to complete all these measures.

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| Obtain Concurrence from the IRB Chair or Representative. | (1) Email the Emergency Use Report Form to the ETSU/VA IRB Chair (youngber@etsu.edu) **AND** IRB Office (IRB@etsu.edu) on **high priority**.<br>(2) Contact the IRB Chair or Representative in the following order of availability:<br>1. IRB Chair: **George Youngberg, MD** 423-439-6793 youngber@etsu.edu<br>2. IRB Director: **Katie Sellers** 423-439-6054 sellerskm@etsu.edu |
| Either:<br>Obtain written informed consent from the patient or their legally authorized representative, | (1) Informed Consent* may be obtained with:<br>• ETSU IRB *Informed Consent Document* template<br>• Informed Consent document provided by the manufacturer or sponsor. The informed consent process should include obtaining a signed Patient' Bill of Rights form.<br>**Please note: There is no requirement to obtain IRB approval of the Informed Consent document prior to use.* |
| **OR**<br>Determine the criteria are met to waive consent for emergency use. | (2) To Waive Informed Consent (21 CFR 50.23) the following criteria should be determined met and, if possible, **documented (writing/email)**, by the **treating physician and an independent physician**** before using the test article:<br>• The patient is confronted with a life-threatening situation necessitating the use of the test article;<br>• Informed consent cannot be obtained from the patient because of an inability to communicate with, or obtain legally effective consent from, the patient;<br>• Time is not sufficient to obtain consent from |

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| | the patient's legally authorized representative; and<br>• No alternate method of approved or generally recognized therapy is available that provides equal or greater likelihood of saving the patient's life. |
| **Please note: If immediate use of the test article is needed to preserve the patient's life and there is not sufficient time to secure an independent physician's determination that the conditions to waive informed consent as described above apply, the treating physician should make a determination that consent cannot be obtained and proceed in the best interest of the patient, but must have his/her written determination reviewed by an independent physician within five working days after the emergency use of the test article. ((21 CFR 50.23(b) & (c); 21 CFR 812.150(a)(5)). | |

## Step 4: Deliver treatment with the investigational agent.

| For Drugs/Biologics (IND) | For Devices (IDE) |
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| Treatment may begin when the emergency use is authorized by the FDA reviewing official (21 CFR 312.305(d)(2)(i)). | Emergency use of the device may begin when the use is authorized by the IDE sponsor per. |

## Step 5: Submit a final report to the IRB and FDA or Sponsor after treatment.

### A. The IRB Report:

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| The IRB report must be submitted **within 5 days** of initiating treatment of the investigational agent and should include: | • Emergency Use Report Form<br>• All attachments and documentation requested in the report form<br>• If the treating physician uses an investigational device without obtaining informed consent, this information must be reported to the IRB and Sponsor within **5 working days** after the use occurs (21 CFR 812.150(a)(5)). |

### B. The FDA Report:

| For Drugs/Biologics | For Devices |
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| Physicians must submit an expanded access submission **within 15 days** of FDA authorizing the emergency use (21 CFR 312.310(d)(2)). | The treating physician must notify the IDE sponsor (who will then notify the FDA) of the deviation from the investigational plan to protect the life or well-being of the subject in an emergency.<br>The follow-up notice to the Sponsor*** must be given within **5 working days** of the emergency use (21 CFR |

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| See Form FDA 1571 application and instructions. | 812.35(a)(4).<br>The Sponsor report should contain the following:<br>• Summary of conditions constituting the emergency;<br>• The patient protection measures that were followed; and<br>• Patient outcome information;<br>****Please note: If no IDE exists, the physician should follow these procedures and report the emergency use to CDRH or CBER.*<br>If the treating physician uses an investigational device without obtaining informed consent, this information must be reported to the IRB and Sponsor within **5 working days** after the use occurs (21 CFR 812.150(a)(5)). |

**Step 6: The ETSU/VA IRB Chair will review the emergency use report as described in Section VI of this policy.**

# VI. Emergency Use Procedure for IRB Review

When a physician/investigator identifies a need for emergency use of a test article, the following procedures for IRB review will be followed:

The ETSU/VA IRB Chair or Vice Chair, or in their absence, a physician member of the IRB should be contacted prior to the treatment, if possible. If the Chair is not an M.D., the Chair will make immediate contact with a qualified physician who is either 1) a member of the IRB, or 2) referred to the Chair by the member-physician as a qualified consulting-physician for concurrence on the emergency use approval. Prior IRB notification is preferable, so that the IRB can provide support to the physician/investigator to ensure compliance with regulatory requirements and this policy. However, patient care should not be compromised. This prior notification of the IRB is not meant, in any way, to be construed as an IRB approval.

The physician/investigator must report the emergency use of the test article to the IRB within five (5) working days of treatment by submitting the following documentation via email:

- Emergency Use Report Form, and

- All documentation and attachments requested in the report form

When the IRB receives a report of emergency use from a physician/investigator, the IRB Chair, or designee, will examine each case and receive a collaborating statement from a physician associated with neither the patient nor the current attending physician (consult) supporting the emergency use. The IRB will review whether the emergency use criteria were satisfied, the physician followed reasonable patient protection measures given the circumstances, patient outcome information, and if future uses of the investigational test article are anticipated such that an application to the IRB should be submitted.

The IRB Chair will also determine if the activity was a systematic investigation designed to develop or contribute to generalizable knowledge. If the physician/investigator reports that informed consent was not sought, the Chair will determine if the criteria for the exception to the requirement for consent were met in accordance with and to the extent required by FDA regulations and will be appropriately documented, in accordance with and to the extent required by FDA regulations.

The IRB Chair reviews the report using the Emergency Use Report Checklist and determines whether the circumstances of the emergency use complied with regulatory requirements. If the use meets the regulatory requirements, the investigator is notified of this determination in writing. If the use does not meet the regulatory requirements, the investigator is notified in writing and the action will be handled according to IRB Policy 25 Non-compliance.

The Emergency Use will be reported to the convened IRB at its next regularly scheduled meeting following review by the IRB Chair.

## VII. Subsequent Use

The FDA regulations (21 CFR 56.104(c)) allow for **one** emergency use of a test article at an institution. Any subsequent use of the investigational product at the institution is subject to prospective IRB review and approval. Should the investigator or IRB anticipate a subsequent need to use the test article, a complete formal application must be made for IRB review at a convened meeting. However, the 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. (FDA Information Sheet, 2003 Update)

If an IND or IDE application for subsequent use has been filed with the FDA and FDA disapproves the application, the investigational agent may not be used even if an emergency exists.

## VIII. Emergencies for which Informed Consent is not Feasible

In some emergency circumstances, it may not be feasible to obtain informed consent prior to using the test article. The regulations [21 CFR 50.23(a)(1-4)and (b-c)], [.116(d)(3) and.116(d)(4)(f)], therefore provide an exception for informed consent requirements for such situations. Except as stated below, in order for the exception to apply, both the investigator and an independent physician who is not otherwise participating in the clinical investigation must certify in writing all of the following:

(1) The subject is confronted by a life-threatening or severely debilitating situation necessitating use of the test article;
(2) Informed consent cannot be obtained from the patient (because the patient cannot communicate or is incompetent to give consent);
(3) There is insufficient time in which to obtain consent from the subject's legally authorized representative; and
(4) There is no available alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the patient's life.

If, in the investigator's opinion, immediate use of the test article is necessary and there is insufficient time to obtain the independent certification, the investigator is to make his or her own written determinations as outlined above, and within five (5) working days after the use of the test article, obtain the written review and evaluation by an independent physician.

Documentation, in both instances, must be submitted to the IRB within (5) working days after the use of the test article. The ETSU/VA IRB Chair, or designee, reviews the report as described in Section VI of this policy.

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
45 CFR 46.116
Emergency Use of an Investigational Drug or Biologic [FDA]
Form FDA 1571 and Instructions - Investigational New Drug Application
Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors - Frequently Asked Questions About Medical Devices
Physician Request for an Individual Patient IND under Expanded Access for Non-emergency or Emergency Use

IDE Early/Expanded Access [FDA] - Emergency Use of Unapproved Medical Devices
Exception from Informed Consent Requirements for Emergency Research
VHA Handbook 1108.04
FDA Information Sheets: Frequently Asked Questions: IRB Procedures
OHRP Compliance Activities: Common Findings and Guidance #13, 41, and 72
Informed Consent Requirements in Emergency Research (OPRR Letter, 1996)