Emergency Use of a Test Article

Background & Summary

Emergency Use: 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 [21 CFR 56.102(d)].

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

**Life-threatening* includes both life-threatening and severely debilitating:

Life-threatening: Diseases or conditions where 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 IRB meeting is feasible.

Severely debilitating: Diseases or conditions that cause major irreversible morbidity e.g., blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

Criteria for Emergency Use – Drugs

Emergency use must meet the definition above and FDA must determine: [21 CFR 312.305(a)]

(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;

(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;

(3) Providing the investigational drug 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.

Also, the following must be determined: [21 CFR 312.310(a)]

(4) The physician must determine that the probable risk to the person from the investigational drug is not greater than the probable risk from the disease or condition;

(5) FDA must determine that the patient cannot obtain the drug under another IND or protocol.

Contact sponsor

Most sponsors agree to ship the test article by referencing the relevant IND/IDE. Some sponsors may require an acknowledgement from the IRB "that the proposed use meets the requirements of 21 CFR 56.104(c)".

Contact FDA

(1) Emergency use may be requested by telephone, facsimile, or other means of electronic communications. See FDA guidance.

(2) The licensed physician or sponsor must explain how the expanded access use will meet the requirements (of 312.305 and 312.310) and must agree to submit an expanded access submission within 15 working days of FDA's authorization of the use. See Form FDA 1571 and Instructions.

Criteria for Emergency Use – Devices

Must meet all of the following:

- Life-threatening or serious disease or condition
- No alternative
- No time to obtain FDA approval

Exemption from Prior IRB Approval

Emergency Use of a test article is exempt from prior IRB review and approval, provided that such emergency use is reported to the IRB within 5 working days *after the use*.

Expedited IRB approval is not permitted in emergency use.

Investigators might wish to contact the IRB about their intent to use a test article in an emergency or to invoke the exception to the requirement to obtain consent. A staff member in the Office of Human Subjects Protection will advise whether the circumstances follow FDA regulations.

One Emergency Use per Test Article

The FDA regulations [21 CFR 56.104(c)] allows 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***. *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)

Note: For devices, if an IDE application for subsequent use has been filed with FDA and FDA disapproves the IDE application, *the device may not be used even if the circumstances constituting an emergency exist*.

Informed Consent

Informed consent (and HIPAA Authorization) must be obtained from the subject (or the legally authorized representative), unless the requirements of an exception from the informed consent requirement [21 CFR 50.23(a)] are satisfied. The investigator may use the MD Anderson consent form and HIPAA Authorization template, or adapt a consent form from a previously approved research study involving the use of the same investigational drug or biologic. Alternatively, the investigator may develop a new consent form that includes all required elements (see General Requirements for Informed Consent).

Exception from Informed Consent Requirement

FDA regulations [21 CFR 50.23] permit emergency use of a test article without informed consent where the investigator and an independent physician, who is not otherwise participating in the clinical investigation, certify in writing:

1. The patient is confronted by a life-threatening or severely debilitating situation, necessitating the 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. Time is not sufficient to obtain consent from the patient's legally authorized representative
4. No alternative method of approved or generally recognized therapy is available 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 required and if time is not sufficient to obtain the independent physician determination, the 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 an independent physician.

Submission and Reporting to IRB and FDA

The following documentation of the emergency use must be submitted to the IRB ***within 5 working days*** after the use of the test article:

(i) Emergency Use of a Test Article – Notification to the IRB
(ii) Confirmation of permission from the manufacturer/sponsor for the Emergency Use of the test article
(iii) Confirmation of the FDA authorization for Emergency Use IND
(iv) Signed Consent Form, with HIPAA unless meets Exception from Informed Consent Requirement

Drugs: Physician or sponsor must agree to submit an expanded access submission to FDA **within 15 working days** of FDA's authorization of the use. [21 CFR 312.310]

Devices with no IDE: Physician must report the use to FDA (CDRH or CBER) ***within 5 working days*** after the use.

Devices with an IDE: IDE sponsor must report the use to FDA ***within 5 working days*** from the time the sponsor learns of the use.

IRB Review (Retrospective)

A medical IRB Chair or designated IRB member will review the documentation submitted. IRB review includes an assessment of whether or not the conditions for the emergency use were satisfied; the reviewer completes the Exemption from IRB Review: Emergency Use of a Test Article. A copy of this form is sent to the investigator. If the emergency use did not meet the criteria allowing an exemption from prior IRB review and approval, the action will be handled according to HRPP non-compliance policy.

The Office of Human Subjects Protection is responsible for maintaining all relevant documentation on emergency uses of test articles in the IRB records.

Emergency Use is not "Research" under DHHS Regulation

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, 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.

Resources: Regulations and Guidance

AAHRPP

Element I.7.C

FDA

- 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
- 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

Product	FDA/Office Division to Contact	Phone
Drug	Division of Drug Information	301-827-4750 310-827-1501
Biological Blood	Office of Blood Research and Review	301-827-3518
Biological Vaccine	Office of Vaccines Research	301-827-3070
Device	Center for Devices and Radiological Health (CDRH) http://www.fda.gov/cdrh	301-594-1190 800-638-2041
All Products: Nights & weekends	Office of Emergency Operations emergency.operations@fda.hhs.gov	866-300-4374 301-796-8240 301-443-1240

Resources: Other References

MD Anderson HRPP

- **Chapter 5.9** Emergency Use of a Test Article (Drugs and Devices)
- **Emergency Use of a Test Article – Notification to the IRB**
- **Exemption from IRB Review: Emergency Use of a Test Article**

MD Anderson HRPP Guidance	General Requirements for Informed Consent 45 CFR 46.116 [OHRP] 21 CFR 50.25 [FDA]	THE UNIVERSITY OF TEXAS MD Anderson Cancer Center Making Cancer History®

Except as provided elsewhere in this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

45 CFR 46.116 (a) Basic elements of informed consent. Except as provided in paragraph (c) or (d) of this section, in seeking informed consent the following information shall be provided to each subject:

Study involves research; study description	(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;
Reasonably foreseeable risks	(2) A description of any reasonably foreseeable risks or discomforts to the subject
Benefits	(3) A description of any benefits to the subject or to others which may reasonably be expected from the research;
Alternative procedures or treatment	(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
Confidentiality of records	(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;*[FDA regulated research only: "and that notes the possibility that the Food and Drug Administration may inspect the records"]*
Compensation and treatment for injury	(6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
Contact information	(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and
Voluntary participation	(8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

45 CFR 46.116(b); 21 CFR 50.25(b) **Additional elements** of informed consent.
When appropriate, one or more of the following elements of information shall also be provided to each subject:

Risks which are currently unforeseeable	(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;
Investigator may terminate participation	(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
Additional costs	(3) Any additional costs to the subject that may result from participation in the research;
Consequences of subject's withdrawal	(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
Significant new findings	(5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and
Number of subjects	(6) The approximate number of subjects involved in the study.
Clinical trial registration	A statement that a description of the trial will be available on http://www.ClinicalTrials.gov

Versions

Date	Version Number	Action	Initials	Description
11/1/2018	1	New	MT	New document created

MD Anderson HRPP	**Emergency Use of a Test Article** [Investigational drug, device, or biologic; FDA regulations 21 CFR 56.104(c)] **Notification to the IRB**	THE UNIVERSITY OF TEXAS MD Anderson Cancer Center Making Cancer History®

INSTRUCTIONS

Questions? Contact the IRB at 713-792-2933 or IRB_Help@mdanderson.org

See guidance HRPP Policy Manual Chapter 5.9.

Report to IRB

The Principal Investigator (PI) must submit the following to the IRB within five (5) working days following the emergency use of the test article: 1. This form completed as follows: **- Sections A, B, C**

- arrange for an independent physician to complete **Section D *if informed consent was not obtained*** from the participant or their legally authorized representative.

2. ***If obtained:*** Signed Consent Form

Submit: Email to IRB_Help@mdanderson.org; or FAX: 713-794-4589; or hardcopy to:
IRB – Mailing Address: 7007 Bertner Ave., Houston, TX 77030 (Unit 1637)

Report to FDA

- Drugs: Physician or sponsor is responsible for submitting a new IND, or an amendment to an existing IND, to FDA **within 15 working days** of FDA's authorization of the use. *Clearly mark as "Emergency IND".* See FDA website for Physician Request for a Single Patient IND for Compassionate or Emergency Use
- ***Devices when no IDE:*** the physician should submit a follow-up report on the use of the device (description of device used, details of the case, and the patient protection measures that were followed) to CDRH.
- ***Devices when IDE:*** The IDE sponsor must notify the FDA of the emergency use within 5 days through submission of an IDE Report (§812.35(a)(2)).

Section A

Principal Investigator		**Degree: MD/PhD**	**Title**	
Dept/Div	**Unit**	**Phone**	**Fax**	**E-mail**
Has the Principal Investigator completed the Required Human Subjects Protection Training? **Yes** **No**				
Protocol Title: include name of test article				
Alternate Contact (*e.g.,* Admin Contact)		**Phone**	**Fax**	**E-mail**
Confirm: ☐ This emergency use of the test article was not a systematic investigation designed to develop or contribute to generalizable knowledge.				

Subject Populations: *check all applicable:*

☐ Child (under 18)
☐ Pregnant Woman/Fetus
☐ Neonate
☐ Prisoner
☐ Other_____

Location:

☐ MD Anderson Cancer Center
☐ Proton Therapy Center
☐ Houston Area Locations (HALs)
- Sugarland Regional Care Center
- Katy Regional Care Center
- Woodlands Regional Care Center
- Bay Area Regional Care Center

Will the drug or device be provided at cost or free of charge? **Yes** **No**

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Section B

Investigational Drug or Biologic? **Yes** **No**

Name:

IND#:

Manufacturer: _____

1) Has sponsor agreed to the use of this drug or biologic for this subject?
2) Has FDA given permission for this use and this subject? If "yes", provide FDA IND letter.

Investigational Device?

Has sponsor agreed to the use of this device for this subject?

If there is an existing IDE# for this device, please list: _____

☐ If there is an IDE for the device, the IDE sponsor must notify the FDA of the emergency use within 5 days through submission of an IDE Report (§812.35(a)(2)).

☐ If no IDE exists, the physician should submit a follow-up report on the use of the device (description of device used, details of the case, and the patient protection measures that were followed) to CDRH.

Section C

Principal Investigator Certification: Emergency Use of a Test Article

Date of Use of Test Article: _____

1. I certify that all of the following statements are true:

☐ The participant was confronted by a life-threatening or severely debilitating situation necessitating the use of the Test article.

Explain the nature of the life-threatening or severely debilitating situation and why use of the test article was necessary:

2. ☐ No alternative method of approved or generally recognized therapy was available that provides an equal or greater likelihood of saving the participant's life.

Describe available alternative treatment methods:

3. ☐ There was not sufficient time to obtain IRB approval in advance of the use of the test article.

Explain why there was not sufficient time to obtain IRB approval of the Emergency Use of the Test Article

4. **Do you intend to use this test article in the future?** No **OR** Yes

Any subsequent use of the test article at MD Anderson is subject to full and prospective IRB review.

If you intend to use the test article in the future, you must submit a Standard Protocol Application to the IRB.

Informed Consent

5. Was informed consent obtained from the participant or the participant's legally authorized representative?

Yes Date of Informed Consent Obtained:

☐ Documentation of Informed Consent is attached.

OR

No If informed consent was **NOT** obtained from the participant or the participant's legally authorized representative, you **MUST:**

- answer the following questions,
- arrange for an independent physician to complete **Section D** below

6. Informed consent could not be obtained from the participant because of an inability to communicate with, or obtain legally effective consent from, the participant

Explain why the participant was unable to provide informed consent:

7. Time was not sufficient to obtain informed consent from the participant's legal representative. **Explain why there was insufficient time, and describe efforts made (if any) to contact the participant's legally authorized representative and obtain informed consent:**

_____ _____

Signature of Principal Investigator ***Date***

Section D

Independent Physician Certification: Emergency Use of a Test Article Without Informed Consent

Certification of Independent Physician Who is Not Otherwise Participating in the Clinical Investigation of the Test Article:

I have reviewed the information provided and certifications made by the Principal Investigator and certify that all of the following statements are true:

☐ The participant was confronted by a life-threatening or severely debilitating situation necessitating the use of the test article

☐ Informed consent could not be obtained from the participant because of an inability to communicate with, or obtain legally effective consent from, the participant

☐ Time was not sufficient to obtain consent from the participant's legal representative.

☐ No alternative method of approved or generally recognized therapy was available that provided an equal or greater likelihood of saving the life of the participant.

Name of Independent Physician:

Signature of Independent Physician

Date

Versions

Date	Version Number	Action	Initials	Description
11/1/2018	1	New	MT	New document created

MD Anderson HRPP	**Exemption from IRB Review: Emergency Use of a Test Article**	THE UNIVERSITY OF TEXAS MD Anderson Cancer Center Making Cancer History®

Principal Investigator (PI):

Protocol:

Name of Test Article:
include IND/IDE Number, if applicable

Date of Use of Test Article:

Date of Submission by PI:
(Must be within 5 working days of the Emergency Use of the Test Article)

Verification of IRB Chair or Designated Member of the IRB

Complete the information in one or both columns, as appropriate:

Emergency Use of a Test Article With Informed Consent	Emergency Use of a Test Article Without Informed Consent
I verify that all of the following statements are true: ☐ The participant was confronted by a life-threatening or severely debilitating situation. ☐ No standard acceptable treatment was available. ☐ There was not sufficient time to obtain IRB approval in advance of the use of the test article.	I verify that all of the following statements are true: ☐ The participant was confronted by a life-threatening situation necessitating the use of the test article. ☐ Informed consent could not be obtained from the participant because of an inability to communicate with, or obtain legally effective consent from, the participant. ☐ Time was not sufficient to obtain consent from the participant's legal representative. ☐ No alternative method of approved or generally recognized therapy that provided an equal or greater likelihood of saving the life of the participant was available. Independent Physician Certification

_____
Name of IRB Chair or Designated IRB Member

_____ _____
Signature of IRB Chair or Designated IRB Member Date

Versions

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11/1/2018	1	New	MT	New document created