Emergency Single-Case Use of an Investigational Device, Drug or Biologic Product Policy

Scope

Applies to personnel of Mayo Clinic and Relying Organizations for which the Mayo Clinic Institutional Review Board (IRB) is the Reviewing IRB.

Purpose

To provide instruction to clinicians about the use of an investigational device, drug or biologic product in an emergency use situation. Federal regulations do not limit or interfere with the authority of a clinician to provide emergency medical treatment using an investigational device, drug, or biologic product for one patient in a life-threatening medical emergency, where there is no standard acceptable treatment available and insufficient time to obtain IRB approval. In this circumstance, Federal regulations grant an exemption from prior review and approval by the IRB.

Policy

- The emergency use of an unapproved (investigational) medical product (medical device, drug, or biologic) is permitted when a patient is in a life-threatening situation in which no standard acceptable treatment is available, and when there is not sufficient time to obtain IRB review and approval.
- The clinician will consult with an independent clinician (not involved in the patient's care) and obtain a written assessment from them that the emergency use criteria specified in this document have been met.
- At the earliest opportunity, and no later than 3 working days following the emergency use, the clinician must notify the IRB of the intent to use, or of the completed use of an unapproved medical product.
- Informed consent must be obtained from the patient or their Legally Authorized Representative (LAR) unless the Federal requirements for exception from the informed consent requirement are satisfied, as noted below in this policy.
- The clinician must report the emergency use to the IRB within 3 working days of the emergency use to meet the Food and Drug Administration (FDA) and IRB reporting requirements. Three working days includes the day of the emergency use and the day of submission to the IRB. The clinician must complete and submit the Emergency/Compassionate Clinical Use Follow-up Report in the IRB's electronic system (IRBe) within 3 working days of the emergency use.
- The IRB will review the Emergency/Compassionate Clinical Use Follow-up Report to assess compliance with emergency use requirements. The clinician will report the emergency use to the holder of the product's Investigational New Drug (IND), Investigation Device Exemption (IDE) or Humanitarian Device Exemption (HDE). The holder is responsible for reporting the emergency use, as required, to the FDA.

- The clinician will consult with the Mayo Clinic Office of Research Regulatory Support (ORRS) to identify and fulfill Federal regulatory requirements following the Emergency Use. The Mayo Clinic Office of Research Regulatory Support (ORRS) can be contacted by phone at 507-266-0022 (internal: [77]6-0022), or by email: ORRS@mayo.edu.
- The Mayo Clinic IRB and FDA acknowledge that it is inappropriate to deny
 emergency treatment to a second qualified individual if the only obstacle is that
 the IRB has not had sufficient time to convene a meeting to review the issue. Any
 emergency treatment to a second qualified individual must follow the same
 process as the first-time emergency use.

Exception From Informed Consent Requirement

FDA regulations permit emergency use of a test article without informed consent where the clinician and an independent physician certify in writing:

- The patient is confronted by a life-threatening or severely debilitating situation, necessitating the use of the test article;
- Informed consent cannot be obtained from the patient (because the patient cannot communicate or lacks capacity to give informed consent);
- Time is not sufficient to obtain consent from the patient's LAR; and
- 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 clinician's opinion, immediate use of the test article is required and if time is not sufficient to obtain the independent physician determination, the clinician should make the determination and, **within 3 working days** after the use of the article, have the determination reviewed and evaluated in writing by an independent physician. This is in addition to submitting the Emergency/Compassionate Clinical Use Follow-up Report to IRB **within 3 working days** of initiating use of the test article.

Clinician Responsibilities

The clinician must determine the following:

- The patient to be treated has a serious or immediately life-threatening disease or condition;
- There is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition;
- 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:
- The probable risk to the person from the test article is not greater than the probable risk from the disease or condition; and
- The provision of the 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.

Prior to Emergency Use

- The clinician is responsible for contacting the manufacturer or sponsor to determine if the test article can be made available for the emergency use under the test article's IND (drug, biologic product), or IDE or HDE (device).
 - If the manufacturer does not permit use of the test article under their IND/IDE, the clinician may request emergency use from the FDA by telephone, facsimile, or other means of electronic communication. Mayo Clinic clinicians may contact the Office of Research Regulatory Support (ORRS) if assistance is needed with the Emergency IND or IDE submission to the FDA. The ORRS may be contacted by internal telephone (77)6-0022 or email to ORRS@mayo.edu.
- The clinician notifies an IRB on-call Chairperson to inform them of the intended emergency use (prior to the emergency use if possible) and, as may be required by the manufacturer, request an Emergency Use IRB Concurrence Letter from the IRB.
 - To notify the on-call IRB Chairperson, call the Mayo Clinic (Rochester) main number at 507-284-2511 or (77) 4-2511 requesting the IRB Chairperson on-call.
 - Prior to the use of the test article, the clinician is responsible to obtain a
 written assessment from a physician not involved in the emergency use as
 documentation that the proposed emergency use is appropriate (i.e., the
 conditions for emergency use are met).

Note: The physician's independent assessment must be included in the Emergency/Compassionate Clinical Use Follow-up Report submitted to the IRB via IRBe within **3 working days** of the initial use of the product (i.e. the date of device use or implant or initial drug administration, specifically, the first dose of a multi-dose treatment). **Three working days includes the day of the emergency use and the day of submission to the IRB.**

- When informed consent can be obtained, the clinician uses the Emergency Use Authorization form to document authorization from the patient or their LAR. The clinician provides a copy to the patient or his/her LAR.
- When informed consent cannot be obtained, both the clinician and an independent physician, who is not involved in the patient's clinical care and management, must certify in writing all of the following [(21 CFR 50.23[a]):
 - The subject is confronted by a life-threatening situation necessitating the use of the test article.
 - Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject.
 - Time is not sufficient to obtain consent from the subject's LAR.
 - No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.
- If, in the clinician's opinion, immediate use of the test article is required to preserve the patient's life, and if time is not sufficient to obtain an independent physician's determination that the four conditions above apply, the clinician

should make the determination and, **within 3 working days** after initiating use of the test article, have the determination reviewed and evaluated in writing by a physician who is not participating in the patient's clinical care and management.

After Emergency Use

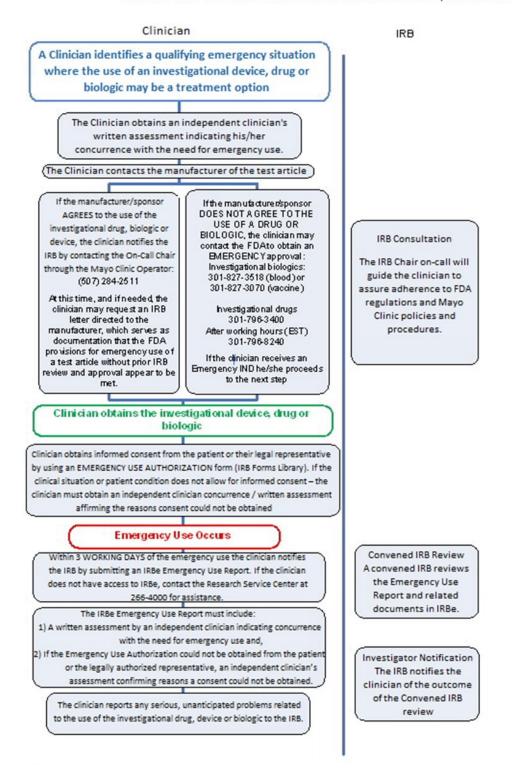
- The clinician completes the Emergency/Compassionate Clinical Use Follow-up Report and submits it to the IRB within 3 working days of initiating use of the test article (i.e. the date of device use/implant or initial drug or biologic administration, specifically, the first dose of a multi-dose treatment). Three working days includes the day of the emergency use and the day of submission to the IRB.
 - The IRB Emergency/Compassionate Clinical Use Follow-up Report will include:
 - The independent physician's assessment of the patient's need for emergency treatment with the test article.
 - Confirmation of permission from the manufacturer/sponsor for the Emergency Use of the test article, if applicable.
 - Signed Emergency Use Authorization form (unless the Exception from Informed Consent Requirement is met).
 - If applicable, written certification from the clinician and an independent physician who is not otherwise participating in the patient's clinical care and management, documenting that the Exception from Informed Consent Requirement is met.
- The clinician reports any unanticipated adverse event or problem related to the emergency use of the test article to the IRB in the Emergency Use Report.

Use of Patient Data Related to Emergency Use of aDrug or Biologic Product

- Emergency use of the investigational drug or biologic product is limited to a single patient and data from the single patient use may not be used as part of a prospective research study conducted by the clinician or sponsor of the drug or biologic without IRB approval (Mayo Clinic Legal communication: 12/16/2009).
- However, when following FDA regulations and guidance, the emergency use of a
 test article, other than a medical device, is a clinical investigation, the patient is a
 participant, and the FDA may require data from an emergency use reported in a
 marketing application (AAHRPP I.7.C).

Use of Patient Data Related to Emergency Use of a Device

 Emergency use of the investigational device is limited to a single patient and data from the single patient use may not be used as part of a prospective research study conducted by the clinician or sponsor of the device without IRB approval (Mayo Clinic Legal communication: 12/16/2009).



Policy Notes

Assistance

The clinician may contact the on-call IRB Chairperson for guidance by calling Mayo Clinic Rochester at 507-284-2511 (internal: (77)4-2511) and requesting the IRB Chairperson on-call.

The clinician may contact the Mayo Clinic Office of Research Regulatory Support (ORRS) at 507-266-0022, (77)6-0022, or <u>ORRS@mayo.edu</u> for assistance.

The clinician may contact the Research Service Center at 507-266-4000, Monday-Friday, 8 am - 5 pm central time.

Related Procedures

N/A

Related Documents

Emergency Use Authorization Form - Patient or Legally Authorized Representative (10346)

Emergency/Compassionate Clinical Use Follow-up Report Sample IRBe application

Definitions

Clinician: Licensed physician or other licensed authorized prescriber with a regular (standing) institutional appointment.

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)].

- Life-threatening includes both life-threatening and severely debilitating 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
 endpoint of clinical trial analysis is survival.
- The criteria for life-threatening do not require the condition to be immediately lifethreatening 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, such as blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis, or stroke.

Investigational New Drug (IND): Application document submitted to the FDA proposing human clinical research to study an unapproved drug, or an approved product for a new indication or in a new patient population in a research study. The FDA permission is evidenced by the assignment of an IND number by the FDA or the granting of an IND exemption.

Additionally, individual patient INDs (Form FDA 3926) are used to request expanded access to an investigational drug outside of a clinical investigation, or to an approved drug where availability is limited by a risk evaluation and mitigation strategy (REMS), for an individual patient who 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.

Investigational Device Exemption (IDE): Application document submitted to the FDA proposing human clinical research to study an unapproved significant risk device, or a cleared or approved device for use other than its approved indication or intent. FDA grants permission so a device that otherwise would be required to comply with a performance standard or to have pre-market approval can be shipped lawfully for the

purpose of conducting investigations of that device. This FDA permission is evidenced by the assignment of an IDE number.

Additionally, the FDA may authorize investigational devices to be used under emergency use circumstances. Emergency use may apply if the device is being studied in clinical trials under an IDE such as when a physician who is not part of the IDE clinical study wishes to use the device to treat a patient in an immediately life-threatening situation. The IDE sponsor and/or the FDA may require consultation prior to the emergency use and follow-up reporting after the use.

Test Article: Any investigational drug, biologic product, such as blood or a vaccine, or medical device for human use.

References

21 CFR 50.23 – Exception from general requirements for informed consent

21 CFR 56.102(d) - Emergency Use definition

21 CFR 56.104(c) – Exemptions from IRB Requirement

21 CFR 312 Subpart I - Expanded Access to Investigational Drugs for Treatment Use

21 CFR 812.36 – Treatment Use of an Investigational Device

<u>Expanded Access Categories for Drugs (Including Biologics) - Food and Drug</u> Administration

Expanded Access for Medical Devices - Food and Drug Administration

Owner

Michelle Daiss on behalf of the Office for Human Research Protections

Contact

Michelle Daiss

Revision History

Date	Synopsis of Change
03/13/2023	Scheduled review. Converted to policy at recommendation of Policy Office. Updated Owner and Contact. Updated general terminology, Definitions, Related Documents and References.
09/06/2017	Minor revision. Updated the following definitions per Glossary review: Emergency Use, Investigational Device Exemption (IDE), Investigational New Drug (IND), and Test Article.
05/22/2017	Changed the reporting requirement to the IRB from 5 working days to 3 working days and defined 3 working days. Clarified definition of "clinician". Added that the IND, IDE, or HDE holder is responsible for reporting emergency use, as required, to the FDA. Updated the flowchart embedded in the policy. Updated to the new Policy template.

Content Information Stamp

Title:

Emergency Single-Case Use of an Investigational Device, Drug or Biologic Product Policy

Content ID:

DOCMAN-0000127707

Effective Date of Current Version:

02/12/2024 05:23:57 PM

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Arizona

Florida Sites:

Florida

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Reviewer(s):

Approver(s):

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