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

Content Applies To

Mayo Clinic Human Research Protection Program

Flowchart

Purpose

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.

Key Words

Test Article: Any investigational drug, biologic product (i.e. blood, vaccine), or medical device for human use.

Clinician: Licensed physician

Human Subject: Patient

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 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.

Investigational New Drug (IND): FDA grants permission so that a new drug, agent or biologic product may be used in humans prior to FDA review of clinical data that shows that the new drug, agent, or biologic product is safe and effective for a specific use. This FDA permission is evidenced by the assignment of an IND number by the FDA or the granting of an IND exemption.

Investigational Device Exemption (IDE): 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.

Policy

- The emergency use of a test article is permitted provided 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 him/her that the emergency use criteria specified in this document have been met.
- At the earliest opportunity, the clinician will notify the IRB of his/her intent to use or use of a test article in an emergency.
- Informed consent will be obtained from the patient or his/her legally authorized representative unless the Federal requirements for waiver or exception from the informed consent requirement are satisfied.
- The emergency use will be reported to the IRB, using the IRB Emergency Use Follow-Up application, within **5** working days.
- A convened IRB will review the IRB Emergency Use Follow-Up application.
- Expedited IRB approval is not permitted with emergency use.
- The emergency use will be reported to the holder of the IND/IDE. If there is no IND or IDE, the emergency use will be reported 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 a first-time emergency use.

EMERGENCY USE OF AN INVESTIGATIONAL DEVICE, DRUG or BIOLOGIC

Clinician/Physician	IRB	Related Documents
A Clinician/Physician identifies a qualifying emergency situation where the use of an investigational device, drug or biologic may be a treatment option		Emergency Use of an Investigational Device, Drug or Biologic
The Clinician obtains an independent physician's written assessment indicating his/her concurrence with the need for emergency use.		
The Clinician contacts the manufacturer of the test article		
If the manufacturer/sponsor **AGREES** to the use of the investigational drug, biologic or device, the clinician notifies the IRB by contacting the On-Call Chairperson through the Mayo Clinic Operator: (507) 284-2511 At this time, and if needed, the clinician may request an IRB letter directed to the manufacturer, which serves as documentation that the FDA provisions for emergency use of a test article without prior IRB review and approval appear to be met.	**IRB Consultation** The IRB Chair/Vice Chair-on-call will guide the clinician to assure adherence to FDA regulations and Mayo Clinic policies and procedures.	Emergency Use of Investigational Device, Drug or Biologic – Guidance for IRB Chair or Vice-Chair Emergency Use Letter to Manufacturer
If the manufacturer/sponsor **DOES NOT AGREE TO THE USE OF A DRUG OR BIOLOGIC,** the clinician may contact the FDA to obtain an EMERGENCY approval: Investigational biologics: 301-827-3518 (blood) or 301-827-3070 (vaccine) Investigational drugs 301-796-3400 After working hours (EST) 301-796-8240 If the clinician receives an Emergency IND he/she proceeds to the next step		
Clinician obtains the investigational device, drug or biologic		
Clinician obtains informed consent from the patient or their legal representative by using an EMERGENCY USE AUTHORIZATION form (IRB Forms Library). If the clinical situation or patient condition does not allow for informed consent – the clinician must obtain an independent physician's concurrence/written assessment affirming the reasons a consent could not be obtained.		Emergency Use Patient Authorization
Emergency Use Occurs		
Within **5 DAYS** of the emergency use the clinician notifies the IRB by either submitting an IRBe Emergency Use follow-up form or if the clinician has no access to IRBe, contacting the IRB Service Center at 266-4000 for assistance.	**Convened IRB Review** A convened IRB reviews the Emergency Use follow-up form and related documents in IRBe.	IRBe Emergency Use Follow-Up application.
The IRBe Emergency Use Follow-up application must include: 1) a written assessment by an independent physician indicating concurrence with the need for emergency use and, 2) if the Emergency Use Authorization could not be obtained from the patient or their legally authorized representative, an independent physician's assessment confirming reasons why.		
The clinician reports any serious, unanticipated problems related to the use of the investigational drug, device or biologic to the IRB using the IRBe Reportable Event form.	**Investigator Notification** The IRB notifies the clinician of the outcome of the Convened IRB review	IRBe: Reportable Event Application (if applicable)

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:

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 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 5 working days after the use of the article, have the determination reviewed and evaluated in writing by an independent physician.

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 ORRS@mayo.edu for assistance.

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

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

Criteria

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.

Clinician Responsibilities

Prior to Emergency Use

1. 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 company's IND (drug, biologic product) or IDE (device).
2. 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. FDA contact information is provided at the end of this document.
3. The clinician notifies an IRB on-call Chairperson to inform him/her of the intended emergency use and, as may be required by the manufacturer, request an Emergency Use Letter to Manufacturer 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.
4. Prior to the use of the investigational drug, agent, or biologic, the clinician is responsible to obtain a written assessment from a physician not involved in the emergency use with 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 submitted to the IRB via the IRBe system (by accessing the Emergency Use Follow-up Form) within 5 working days of the emergency use of the drug, agent, or biologic.
5. When informed consent can be obtained, the clinician uses the Emergency Use Authorization form to document authorization from the patient or their legally authorized representative (LAR). The clinician provides a copy to the patient or his/her legally authorized representative.
6. When informed consent cannot be obtained, both the clinician and an independent physician, who is not otherwise participating in the clinical investigation, 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 legal representative.
    - No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.
7. 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 clinical investigator should make the determination and, within 5 working days after the use of the test article, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

After Emergency Use

1. The clinician completes the IRB Emergency Use Follow-up application and submits it to the IRB within 5 working days of the emergency use of the test article.
2. The IRB Emergency Use Follow-up application 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).
3. The clinician reports any unanticipated adverse event or problem related to the emergency use of the test article to the IRB as an IRB Reportable Event.

Use of Patient Data - Drug 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 - 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).

Contacts

Test Article	FDA	Phone
Drug	Division of Drug Information	888-463-6332 301-796-3400
Biologic-Blood	Office of Blood Research and Review	301-827-3518
Biologic Product-Vaccine	Office of Vaccines Research	301-827-3070
Device	Center for Devices and Radiological Health (CDRH)	301-796-5640

All products Nights & weekends	FDA Office of Emergency Operations 866-300-4374 301-796-8240 e-mail: emergency.operations@fda.hhs.gov

Related Documents

Emergency Single-Case Use of an Investigational Device, Drug or Biologic - Guidance for the IRB Chair

Emergency Use - IRB Letter to Manufacturer *(IRB10048)*

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

IRB Emergency Use Follow-up application

References

FDA Guidance: Emergency Use of an Investigational Drug or Biologic

FDA Website: Emergency Use of a Device

21 CFR 50.23 – Exception from general requirements for informed consent

21 CFR 56.102(d) – Emergency Use definition

21 CFR 56.104 – Exemptions from IRB Requirement

21 CFR 812.36 – Treatment Use of an Investigational Device

Effective Date

September 16, 2013