

HAC Policies and Procedures

Emergency Use Exemption from Prospective HAC Approval

The emergency use provision in the Food and Drug Administration (FDA) regulations [21CFR56.102 (d)] is an exemption from prior review and approval of the HAC. The exemption, which may not be used unless all of the conditions described in 21CFR56.102 (d) exist, allows for a one time emergency use of a test article without prospective HAC review. This emergency use is to fulfill the physician's obligations to treat a seriously ill patient with all available modalities. This use allows physicians to have access to experimental or investigational treatments that would be prohibited in other settings. FDA regulations require that any subsequent use of the investigational product at the institution have prospective HAC approval.

NOTE: The HAC cannot approve a waiver of written informed consent for planned emergency research that is subject to Veterans Health Administration (VHA) regulations. For more information, please see the Augusta VAMC section.

What Is Emergency Use?

Emergency use is defined as the use of an investigational drug or biologic product (i.e., test article) with 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 full Human Assurance Committee (HAC) approval [21CFR56.102(d)]. Unless it is an area that the chair has particular expertise in, he will consult with members of the committee who have such expertise. The exemption is granted by the HAC Chairperson or his designee. It is not a systematic investigation designed to develop or contribute to generalized knowledge.

What is a Life-Threatening Situation?

A situation in which a patient has a disease or condition 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 subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

Is Notification to the HAC of the Emergency Use of a Test Article Required Prior to Its Use?

Yes, the physician is required to notify the HAC prior to the emergency use of a test article so that it can be reviewed by the HAC Chair or their designee to determine that the circumstances follow FDA regulations, however, notification of emergency use of a test article to the HAC chairperson should not be construed as HAC approval.

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The investigator is required to submit a report on the use of the test article within five working days. This report will be reviewed by the HAC Chair or their designee.

How Do I Request Emergency Use Exemption Review from the HAC?

Telephone the MCG paging operator to have the HAC Chairperson paged and provide the following information:

- Name of the investigator.
- Telephone number of the investigator.
- Name of test article.
- Patient's name, sex, age, date of birth, medical record number and diagnosis.
- Is the patient enrolled in another research study?

What About Waiver Of Informed Consent For An Emergency Use?

Even for an emergency use, the investigator is required to obtain informed consent of the subject or the subject's legally authorized representative unless both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following [21 CFR 50.23(a)]:

1. The subject is confronted by a life-threatening situation necessitating the use of the test article.
2. Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject.
3. Time is not sufficient to obtain informed consent from the subject's legal representative.
4. There is no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.

When Is This Information Required to be Submitted to the HAC?

Complete the [HAC Form 101EMG](#), Emergency Exemption from Prospective HAC Approval, and return it to the HAC within five working days of the test article use in order for the HAC to determine that the circumstances met FDA regulations.

What if the HAC Chairperson or Designee Disagrees with the Emergency Use?

The HAC Chairperson or his designee will have discussed the use with members of the HAC who have expertise in the area. If the use is not deemed appropriate by the Chairperson and members, the HAC will work with the clinician to determine an alternative method of treatment.

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What If I Think That This Situation May Happen Again Within the Next Few Months?

The regulation, 21 CFR 56.104(c), allows one use (i.e., one course of treatment) without prior approval by the HAC. If it is anticipated that the situation may occur with other patients, the FDA suggests the HAC review a protocol (in this case, a plan for use in an emergency, not necessarily a research project) and an informed consent document so that a HAC-approved plan for use is in place when the next patient presents.

However, since life-threatening emergencies cannot always be planned, the FDA has allowed that if the only obstacle is lack of HAC approval, the product may be used a second time without the PI's submission of a full review protocol to the HAC for approval. This situation is discussed under the heading "Emergency Exemption from Prospective IRB Approval" in the sheet "Emergency Use of an Investigational Drug or Biologic" in the FDA Information Sheets for IRBs and Clinical Investigators.

What Documentation Does The Sponsor Usually Need to Release the Test Article to the Physician?

Sponsors (e.g., pharmaceutical companies or device manufacturers) usually require written documentation of HAC approval before shipping an investigational drug, even in emergency situations. Many sponsors will accept a statement from the HAC that the use meets the 21CFR56.104(c) requirements for emergency use without HAC approval.

Is Emergency Use and Compassionate Use the Same?

No.

What is Compassionate Use?

Physicians may use the term "compassionate use" to refer to the treatment of a seriously ill patient using an unapproved test article when all other available treatments have failed or are inappropriate.

Compassionate use of an investigational drug, biologic, or device is correctly channeled as one treatment mechanism that is only allowed after prospective review and approval by the HAC. The FDA must also approve these types of use as well in most instances. Prospective HAC approval is required even if the treatment only involves one patient.

What is Expanded Access with Treatment INDs or Individual Patient Access to Investigational Drugs/Devices for Serious Diseases?

The primary intent of these types of treatments is to give seriously ill patients access to experimental drugs or devices where no comparable or satisfactory alternative treatment is available. Expanded access studies involve systematic use of experimental treatments. These types of treatments are considered research and require both HAC approval and

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FDA approval in the form of an IDE (medical device) or an IND (drug/biologic). The sponsor of the test article is still required to conduct clinical trials and obtain marketing approvals in compliance with the regulations for non-expanded access trials.

Is Research Conducted in the Emergency Medicine Department (ED) or Emergency Room (ER) Considered to be Emergency Use Research?

Although research may be conducted in the ED or ER and is designed to evaluate emergency care treatments, this does not constitute “emergency use.” As with all other clinical research, prospective HAC review and approval are required before research in the ED or ER can start. The unique exception from informed consent for these studies is provided by federal regulations enforced by the FDA [21 CFR 50.24] and the Department of Health and Human Services (DHHS) Office for Human Research Protections [45 CFR 46.101(i)]. The waiver of written informed consent is described in the section on Informed Consent.

Is It Research If I, As A Clinician, Use Innovative Treatment, or Off-Label Use, of An Approved Drug?

Emergency use provisions apply to investigational drugs, biologics, and devices. The off-label use or innovative use of a marketed drug or device for an individual patient treatment rather than for research purposes does not require HAC approval. However, treating a series of patients in a novel or innovative manner and analyzing the results for publication is considered to be research and requires prior HAC approval. A planned chart review that looks at the data obtained during the off-label use is also considered to be research and must be approved by the HAC prior to its use.