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## 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 senior staff member in the Research Compliance Office 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 Stanford [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](#) [APP-11m]
- (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 Research Compliance Office (RCO) is responsible for maintaining all relevant documentation on emergency uses of test articles in the IRB records.

### Emergency Use is not “Research” under DHHS or VA 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.

**VA research** (see [VHA Handbook 1200.05](#), section 41):

- Emergency medical care is not research and does not need to be approved by an IRB.
- Emergency use of test articles must meet FDA regulations.

**Resources: Regulations and Guidance**

<b>AAHRPP</b>	<ul style="list-style-type: none"> <li>• <a href="#">Element I.7.C</a></li> </ul>																		
<b>FDA</b>	<ul style="list-style-type: none"> <li>• <a href="#">21 CFR 50.23</a> – Exception to informed consent</li> <li>• <a href="#">21 CFR 56.102(d)</a> – Emergency Use definition</li> <li>• <a href="#">21 CFR 56.104</a> – Exception to IRB review</li> <li>• <a href="#">21 CFR 312.300 (Subpart I)</a> - Expanded Access to Investigational Drugs for Treatment Use</li> <li>• <a href="#">21 CFR 812.35</a> – Exception to IDE requirement</li> <li>• <a href="#">Emergency Use of an Investigational Drug or Biologic</a> [FDA]</li> <li>• <a href="#">Form FDA 1571</a> and <a href="#">Instructions</a> - Investigational New Drug Application</li> <li>• <a href="#">Information Sheet Guidance For IRBs, Clinical Investigators, and Sponsors - Frequently Asked Questions About Medical Devices</a></li> <li>• <a href="#">Physician Request for an Individual Patient IND under Expanded Access for Non-emergency or Emergency Use</a></li> <li>• <a href="#">IDE Early/Expanded Access</a> [FDA] - Emergency Use of Unapproved Medical Devices</li> <li>• <a href="#">Medical Devices- Guidance on IDE Policies and Procedures</a> [FDA] - Guidance on IDE Policies and Procedures</li> </ul> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="text-align: center;">Product</th> <th style="text-align: center;">FDA Office/Division to Contact</th> <th style="text-align: center;">Phone</th> </tr> </thead> <tbody> <tr> <td style="text-align: center;">Drug</td> <td style="text-align: center;">Division of Drug Information</td> <td style="text-align: center;">301-827-4570 310-827-1501</td> </tr> <tr> <td style="text-align: center;">Biological Blood</td> <td style="text-align: center;">Office of Blood Research and Review</td> <td style="text-align: center;">301-827-3518</td> </tr> <tr> <td style="text-align: center;">Biological Vaccine</td> <td style="text-align: center;">Office of Vaccines Research</td> <td style="text-align: center;">301-827-3070</td> </tr> <tr> <td style="text-align: center;">Device</td> <td style="text-align: center;">Center for Devices and Radiological Health (CDRH) <a href="http://www.fda.gov/cdrh">http://www.fda.gov/cdrh</a></td> <td style="text-align: center;">301-594-1190 800-638-2041</td> </tr> <tr> <td style="text-align: center;"><b>All products: Nights &amp; weekends</b></td> <td style="text-align: center;">Office of Emergency Operations <a href="mailto:emergency.operations@fda.hhs.gov">emergency.operations@fda.hhs.gov</a></td> <td style="text-align: center;">866-300-4374 301-796-8240 301-443-1240</td> </tr> </tbody> </table>	Product	FDA Office/Division to Contact	Phone	Drug	Division of Drug Information	301-827-4570 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) <a href="http://www.fda.gov/cdrh">http://www.fda.gov/cdrh</a>	301-594-1190 800-638-2041	<b>All products: Nights &amp; weekends</b>	Office of Emergency Operations <a href="mailto:emergency.operations@fda.hhs.gov">emergency.operations@fda.hhs.gov</a>	866-300-4374 301-796-8240 301-443-1240
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**Resources: Other References**

<b>Stanford HRPP</b>	<ul style="list-style-type: none"> <li>• <a href="#">Chapter 5.9</a> Emergency Use of a Test Article (Drugs and Devices)</li> <li>• Human Subjects Research web page <a href="#">Emergency Use</a></li> <li>• <a href="#">Emergency Use of a Test Article – Notification to the IRB</a> [APP-11m]</li> <li>• <a href="#">Exemption from IRB Review: Emergency Use of a Test Article</a> [RPT-6m]</li> <li>• Human Subjects Research web page <a href="#">Consent Form and HIPAA Templates</a></li> </ul>
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