“Exemptions from IRB requirement. The following categories of clinical investigations are exempt from the requirements of this part for IRB review: ...(c) Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review.” 21 CFR 56.104

“Emergency use means the use of a test article (investigational drug or device) 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)”

“Immediately life-threatening disease or condition means a stage of disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.” 21 CFR 312.300(b)

“Serious disease or condition means a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one.” 21 CFR 312.300(b)

U.S. Food and Drug Administration (FDA) regulations provide an exemption from prior Institutional Review Board (IRB) review and approval for emergency use of an investigational drug or device if the use meets the criteria for exemption under 21 CFR 56.104(c), the definition of emergency use under 21 CFR 56.102(d), and if the investigator obtains informed consent in accordance with regulations or laws such as 21 CFR 50 or meets the criteria for exception from informed consent under 21 CFR 50.23(a)-(c). For emergency use of an investigational drug with a single patient, the investigator is also required to comply with 21 CFR 312 Subpart I, Expanded Access to Investigational Drugs.

The investigator should notify the IRB prior to any emergency use so that the IRB chair or designated physician IRB member may determine if the emergency use exemption criteria are met. Notification may include justification for use, the consent document, and for investigational drugs, documentation of FDA authorization pursuant to 21 CFR 312
Subpart I. The IRB chair or a physician IRB member evaluates whether the circumstances meet the criteria for the emergency use exemption and whether the informed consent process meets regulatory criteria. The IRB chair or a physician IRB member will review the information provided for compliance with the regulations and document their findings.

An activity must meet all of the following criteria for an emergency use exemption:
1. Life-threatening situation or severely debilitating situation
2. No standard acceptable treatment available
3. Not sufficient time to obtain IRB approval
4. Report to the IRB within 5 working days of use
5. Any subsequent use of the test article is subject to IRB review
6. The activity is not a systematic investigation designed to develop or contribute to generalizable knowledge

The IRB chair or designated physician IRB member evaluates and documents his or her determination regarding whether the emergency use met all applicable criteria. The IRB chair, designated physician IRB member, or IRB administrator may communicate with the investigator to obtain clarification. The IRB chair, physician IRB member, or an IRB administrator notifies the investigator of the determination once made. This notification should not be construed as IRB approval. The investigator must report to the IRB within 5 working days of the emergency use, even if the investigator notified the IRB prior to use. Upon notification, the IRB chair, designated physician IRB member, or IRB administrator will initiate tracking to follow-up with the investigator to assure that the investigator files a report to the IRB within five working days.

If the investigator is not able to notify the IRB prior to emergency use of an investigational drug or device, the investigator is responsible for assuring that the emergency use exemption criteria have been met and must report to the IRB within 5 working days of the emergency use. The investigator is also responsible for assuring that the requirements for investigational drugs under 21 CFR 312 Subpart I have been met. The investigator’s report must document why the prospective reporting to the IRB was not feasible and document how the use met the criteria for the emergency use exemption and the process for obtaining informed consent including the consent document and for investigational drugs, documentation of FDA authorization pursuant to 21 CFR 312 Subpart I. The IRB will review the report to determine that the circumstances of the emergency use met FDA regulations.

The investigator is required to obtain informed consent of the subject or the subject's legally authorized representative in compliance with regulations and laws such as 21 CFR 50. If the investigator is not able to obtain informed consent of the subject or the subject's legally authorized representative prior to emergency use of a test article, the investigator’s report must include a certification from a physician who is not otherwise participating in the clinical investigation as to how the use met the criteria for exception from informed consent in 21 CFR 50.23(a) – (c). See details below under “Exception from Informed Consent Requirement.”
Upon receipt of the investigator's report within 5 working days of the emergency use, the IRB chair or designated physician IRB member evaluates and reviews the 5 working day report and documents his or her determination regarding whether the emergency use met all applicable criteria. Reports of emergency use will be provided to the IRB at a regularly scheduled IRB meeting. Any noncompliance with the criteria for emergency use will be reviewed in accordance with the Human Research Protection Program Manual 9-2 “Noncompliance.”

If the activity is subject to U.S. Department of Health and Human Services regulations:
- Patients receiving a test article in an emergency use as defined by FDA regulation may not be considered a research subject
- Data obtained from patients cannot be classified as human subject research
- Outcome of such care cannot be included in any report of research activity

If the activity is subject to FDA regulations, emergency use of the test article is considered to be a clinical investigation, the patient is a subject, and the FDA may require data from an emergency use to be reported in a marketing application.

If the investigator plans subsequently to use the test article, he or she must submit an initial application to the IRB for review and approval prior to such use. Any subsequent use of the test article is subject to IRB review. See HRPP Manual 7, “Research Involving Investigational Drugs and Devices” for policies and procedures.

**Exception from Informed Consent Requirement**

Even for an emergency use, the investigator is required to obtain informed consent from the subject or the subject's legally authorized representative in accordance with 21 CFR 50 (such as providing all required and appropriate additional elements of disclosure) and document consent in writing in accordance with 21 CFR 50.27 (obtaining a signed and dated consent document consistent with the short or long form regulatory requirement) 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 human 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 consent from the subject’s legal representative.
4. There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.

A report by the investigator and a physician who is not otherwise participating in the clinical investigation’s written certification must be submitted to the IRB within 5 working days after the use of the test article. The IRB chair or designated physician IRB member
will review the five working day report to determine if the regulatory requirements in 21 CFR 50.23(a) have been met.

If, in the investigator’s opinion, immediate use of the test article is required to preserve the subject’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 article, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. 21 CFR 50.23(b). The independent evaluation must be submitted to the IRB within the 5 working days time period. 21 CFR 50.23(c). The IRB chair or designated physician IRB member will review the 5 working day report to determine if the regulatory requirements in 21 CFR 50.23(a) – 21 CFR 50.23(c) have been met.