POLICY:

I. The stipulation for emergency use of a test article (i.e., investigational drugs, agents, biologics, or medical devices) in the FDA regulations represents an exemption from prospective IRB review and approval for the use in a single patient of an investigational drug, biologic or medical device that does not have premarket approval or other approval. Any subsequent use of the test article at the institution requires prospective convened IRB review and approval, unless emergency treatment to a second individual arises before the IRB has had sufficient time to convene a meeting to review the issue. (Refer to FDA Information Sheets: Emergency Use of an Investigational Drug or Biologic, 1998 Update). The IRB Chair (or designee) determines whether or not this condition has been met.

II. The UIC IRB manages the emergency use of investigational drugs, biologics and medical devices in accordance with FDA regulations and UIC policies and procedures. The FDA and UIC policy exempt the requirement for review by the convened IRB in emergency use situations.

III. UIC policy requires the investigator to notify the IRB and receive acknowledgement of the emergency use from the IRB Chair (or designee) before administering the test article. The IRB Chair (or designee) reviews the application for emergency use and acknowledges whether or not they concur that administering the test article in this situation meets the emergency use requirements at 21 CFR 56.102(d). The acknowledgement by the IRB does not represent approval as FDA regulations do not allow expedited approval of research in emergency situations. It should be noted that manufacturers’ policies typically require an acknowledgement or approval letter from the IRB before the test article will be shipped.

IV. Criteria for Emergency Use.
   A. The emergency use exemption for an investigational drug, biologic or medical device requires that each of the following criteria in 21 CFR 56.102(d) are satisfied:
      1. A life-threatening situation exists requiring treatment with the test article;
      2. No standard acceptable treatment is available;
3. Insufficient time is available to obtain IRB approval at a convened meeting; and
4. The activity is not a systematic investigation designed to develop or contribute to generalizable knowledge.

B. The term “life-threatening” encompasses conditions that are both:

1. Life-threatening: diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subject must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

2. Severely debilitating: diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness; loss of arm, leg, hand or foot; loss of hearing; paralysis or stroke.

V. Representation of the activity as research.

A. Under FDA regulations, emergency use of a test article meets the FDA definition of a clinical investigation, and the patient receiving the test article meets the FDA definition of a human subject. Therefore, this activity qualifies as human subjects research under FDA regulations and the FDA may require data from emergency use of a test article to be reported in a marketing application.

B. This activity does not however meet the DHHS criteria for human subjects research, as DHHS regulations at 45 CFR 46 do not allow research involving human subjects to be initiated without prior IRB review and approval. Therefore, UIC policy is that data from emergency use of a test article may not be reported as part of a prospective systematic investigation designed to develop or contribute to generalizable knowledge. Similarly, this FDA exemption from IRB review is not recognized as VA-regulated human subjects research.

C. The above policy does not prevent the retrospective use of the data, provided appropriate IRB review and approval of this use has occurred, or the publication of a single patient case history.

VI. Requirement for Five-Day Follow-up Report. The emergency use of a test article must be reported to the IRB within five business days of administration of test article. The report is presented to the IRB at the next convened meeting. The IRB reviews the initial notification, five-day follow-up report, and other relevant information provided by the PI. The IRB Chair (or designee) serves as the primary reviewer on this meeting agenda item. The IRB acknowledges whether or not the emergency use of the test article meets the requirements of 21 CFR 56.102(d) and whether there are any further issues related to the treatment of the subject. The IRB’s determination is documented in the meeting minutes and communicated in writing to the investigator.
VII. Requirement for an IND for an Investigational Drug or Biologic. The emergency use of an investigational drug or biologic that does not have premarket approval or other approval requires an IND. The investigator must contact the manufacturer and determine if the drug or biologic can be made available for emergency use under the company's IND. When an IND does not exist and the situation does not allow time for submission of an IND, the FDA may authorize the shipment of the test article in advance of the IND submission. The request for such authorization may be made by telephone or other rapid communication means.

VIII. Requirement for an IDE for an Investigational (Unapproved) Medical Device. An unapproved device may be used in human subjects only if it is approved for clinical testing under an approved application for an IDE. However, the FDA recognizes that emergencies arise where an unapproved device may offer the only possible life-saving alternative, but an IDE for the device does not exist, the proposed use is not approved under an existing IDE, or the physician or institution is not approved under the IDE. Using its enforcement discretion, the FDA has not objected if a physician chooses to use an unapproved device in such an emergency, provided that the physician later justifies to the FDA that an emergency actually existed.

A. The requirements for emergency use of an unapproved device are similar to those for an investigational drug:
   1. The patient is in a life-threatening condition that requires immediate treatment;
   2. No generally acceptable alternative for treating the patient is available; and
   3. Because of the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use.

B. The FDA expects the physician/investigator to follow as many human subjects protection procedures as possible, including:
   1. Obtaining an independent assessment by an uninvolved physician;
   2. Obtaining informed consent from the patient or a legal representative in accordance with, and to the extent required by, 21 CFR 50;
   3. Documenting informed consent in writing in accordance with, and to the extent required by, 21 CFR 50.27;
   4. Notifying institutional officials as specified by institutional policies;
   5. Notifying the IRB; and
   6. Obtaining authorization from the IDE holder, if an approved IDE for the device exists.

C. After an unapproved device is used in an emergency use situation, the investigator should:
   1. Report to the IRB within five business days of administration and otherwise comply with provisions of the IRB regulations (21 CFR 56);
   2. Evaluate the likelihood of a similar need for the device occurring again, and if future use is likely, immediately initiate efforts to obtain IRB approval and an approved IDE for subsequent use of the device; and
3. If an IDE for the use does exist, notify the sponsor of the emergency use, or if an IDE does not exist, notify the FDA of the emergency use (CDRH Program Operation Staff 301-594-1190) and provide the FDA with a written summary of the conditions constituting the emergency, subject protection measures, and results. While prior approval for shipment or emergency use of the investigational device is not required, the use must be reported to the FDA by the IDE sponsor within five business days from the time the sponsor learns of the use.

IX. Informed Consent in an Emergency.

A. Even for emergency use of a test article, the physician/investigator is required to obtain and document informed consent from the subject or the subject's legally authorized representative in accordance with FDA regulations (21 CFR 50 subpart B) and Illinois state law. Therefore, a physician/investigator must prepare and submit a consent document with the request to the IRB Chair (or designee) for emergency use of the test article. The UIC OPRS Emergency Use of an Investigational Drug/Biologic/Device consent form template should be utilized.

B. An exception to the requirement for informed consent is allowed if the physician/investigator and a physician who is not otherwise participating in the clinical investigation certify in writing that all of the criteria at 21 CFR 50.23(a) are met before (and/or after) the use of the test article:
   1. The subject is confronted by a life-threatening situation necessitating the use of the test article;
   2. Informed consent cannot be obtained 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; and
   4. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.

C. If, in the physician/investigator's opinion, immediate use of the test article is required to preserve the subject's life, and time is not sufficient to obtain an independent physician's determination that the four conditions above apply, the physician/investigator should make the determination as to the above four items and, within five business 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.

D. In the five day follow-up report notifying the IRB of the emergency use of a test article, the physician/investigator must also inform and provide documentation to the IRB of any exceptions to the requirement for consent if this was not done at the time of notification of emergency use. The IRB will subsequently review and determine if the criteria for an exemption from IRB review and the exception for the requirement from consent has been met.

X. Consequence of failure to comply with this policy or FDA requirements. If notification is not obtained prior to emergency administration of the test article or the five-day
follow-up report is not submitted, the IRB may determine that the use of the test article did not meet the criteria for exemption from prospective IRB approval and represents serious and reportable noncompliance to the FDA. The IRB may also decide that the use represents reportable noncompliance when, after reviewing the report, it concludes that the requirements of 21 CFR 56.102(d) for emergency use or 21 CFR 50.23(a) for exception of informed consent are not met.

PROCEDURE:

This procedure describes the submission, IRB review, and OPRS staff processing of requests for emergency use of a test article (i.e., investigational drug, biologic or device).

I. A physician/investigator seeking acknowledgment for emergency use of a test article telephones the OPRS Front Desk (312-996-1711) to alert the staff that an Emergency Use Determination application is forthcoming. During non-office hours or if no one is available at the OPRS front desk, the clinician should use the dedicated email address (uicirb@uic.edu). (Refer to UIC HSPP policy Instructions for Requesting and Reporting the Emergency Use of a Test Article.) OPRS staff evaluates the criteria for emergency use with the physician/investigator and conducts a search in the OPRS database (RiSC) to verify that the test article has not been used previously at UIC.

   A. When the test article has been used previously and is not eligible for additional emergency use, OPRS staff informs the physician/investigator, Investigational Drug Service (IDS) at University of Illinois Hospital & Health Sciences System (UI Health) Pharmacy, and the OPRS Director that the test article is not eligible for emergency use.

   B. When the test article may be eligible for emergency use, OPRS staff guides the physician/investigator to the UIC OPRS form Notification of Emergency Use of a Test Article and the UIC OPRS Emergency Use of an Investigational Drug/Biologic/Device consent form template on the OPRS website.

   C. OPRS staff also alerts an IRB Chair (or designee) of the impending submission.

II. The clinician submits to OPRS the following:

   A. UIC OPRS form Notification of Emergency Use of a Test Article and applicable appendices;

   B. Informed consent document; or

   C. If the physician/investigator ascertains that informed consent cannot be obtained prior to administration of the test article, the physician/investigator:

      1. Attests on the UIC OPRS form Notification of Emergency Use of a Test Article that the four conditions in 21 CFR 50.23(a) apply; and

      2. Has a physician who is not otherwise participating in the clinical investigation complete the UIC OPRS form Independent Physician Certification: Emergency Use of a Test Article Without Informed Consent, or
3. If immediate use of the test article is required to preserve the subject's life and time is not sufficient to obtain an independent physician's determination, the physician/investigator makes the determination himself/herself and, within five business days after the use of the article, has the determination reviewed and evaluated in writing by an independent physician and submits this determination to the IRB.

D. Investigational Drug Brochure or Device Manual (if available);
E. Treatment Protocol;
F. Authorization from the sponsor to allow use of the test article by the physician/investigator or an approved IND/IDE or letter verifying exemption of IND/IDE from the FDA; and
G. Appendix A1 if the test article is a drug or biologic or Appendix A2 if the test article is a device.

III. The physician/investigator must notify the IDS at UI Health Pharmacy of the intended shipment and emergency use of the test article.

IV. Upon receipt of the Emergency Use Application and supporting documents, OPRS staff conducts a pre-review to ensure that the submission is complete and all necessary documentation is included. OPRS staff then provides the submission and Emergency Use of a Test Article review guide to the IRB Chair, Chair's designee, or OPRS Director.

V. The Chair, designee, or OPRS Director reviews the submission to determine whether the request qualifies for emergency use under 21 CFR 56.102(d). The Chair, or designee completes the review guide, and provides one of the following determinations:
   A. Acknowledge based on the information provided by the physician/investigator that the proposed emergency use meets the requirements of 21 CFR 56.102(d) and, when applicable, the requirements of 21 CFR 50.23(a) for exception from informed consent.
   B. Revisions or additional information are required.
   C. Proposed use does not qualify as Emergency Use.

VI. After making a determination, the OPRS staff then processes the submission as follows:
   A. Completes data entry of the submission in RiSC.
   B. Enters the review action and generates a letter in RiSC.
   C. Stamps the informed consent document. The stamp used for HIPAA Authorizations is used, since the document is used only once and no expiration date is needed.
   D. Emails the letter and consent document to the physician/investigator.
   E. Faxes a copy of the determination letter to the IDS at UI Health Pharmacy.
   F. The IRB is notified of the Emergency Use by the inclusion of the event on the next convened meeting agenda.
VII. The physician/investigator must submit the UIC OPRS form *Five-Day Follow-Up Report of Emergency Use of a Test Article* to the IRB within five business days of administration of the test article. In the *Five-Day Follow-Up Report of Emergency Use of a Test Article* form, the physician/investigator must also inform and provide documentation to the IRB of any exceptions to the requirement for informed consent if this was not done at the time of notification. The previously submitted *Notification of Emergency Use of a Test Article* form and any information listed in Step II (see above) that was not provided with the *Notification of Emergency Use of a Test Article* form should also be submitted.

VIII. The IRB reviews the initial *Notification of Emergency Use of a Test Article* form, *Five-Day Follow-Up Report of Emergency Use of a Test Article*, informed consent document, and any other information provided by the physician/investigator at the next available meeting. The IRB Chair or designee serves as the primary reviewer. The IRB determines if the criteria for an exemption from IRB review and, when applicable, the exception for the requirement of informed consent are met, and whether there are any further issues related to the treatment of the subject. The IRB’s determinations (as outlined in step V) are documented in the meeting minutes and communicated in writing to the physician/investigator. The follow-up report and IRB communication are added to the protocol file.

IX. The acknowledgement informs the physician/investigator that the exemption from IRB review and approval allows for one emergency use of a test article without prospective IRB review at an institution. Any subsequent use of the test article at the institution requires prospective convened IRB review, and the physician/investigator should evaluate the likelihood of similar need for the drug, biologic or device. If future use is likely, the physician/investigator should promptly prepare and submit a protocol and *Health and Biological Sciences Initial Review application* for submission for convened IRB review.

X. Failure to notify the IRB prior to emergency use of the test article, provide a five-day follow-up report to the IRB, or meet the requirements of 21 CFR 56.102(d) for emergency use or 21 CFR 50.23(a) for exception of informed consent is considered non-compliance and is evaluated by the IRB as described in the UIC HSPP policies, including but not limited to, *Handling Complaints and Allegations of Potential Non-Compliance with Human Subject Protection Regulations* and *Reporting of Unanticipated Problems, Suspensions, Terminations, and Non-Compliance*.

REFERENCES:

21 CFR 50.23(a)-(c), 21 CFR 56.102(d), 21 CFR 56.104(c), 21 CFR 312.36, 21 CFR 812.35(a)(2), 21 CFR 812.150(a)(4)

FDA. Emergency Use of an Investigational Drug or Biologic. FDA Information Sheets, 1998 Update.


FDA Guidance: Expanded Access to Investigational Drugs for Treatment Use, dated June 2016
Expanded Access for Medical Devices, FDA website

REVISION LOG:

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