Policies and Procedures

<table>
<thead>
<tr>
<th>SECTION:</th>
<th>NUMBER:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human Research Protection Program</td>
<td>127</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CHAPTER:</th>
<th>ISSUED:</th>
<th>LAST REVIEWED/REVISED:</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>POLICY:</th>
<th>PAGE:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emergency Use of Unapproved Drugs/Devices/Biologics</td>
<td>1 OF 6</td>
</tr>
</tbody>
</table>

1. **PURPOSE**

This policy describes the process for emergency use of investigational drugs, devices, or biologics. Emergency use of unapproved drugs or biologics is considered research under the FDA regulations. However, as adequate time usually is not available for a prospective IRB review in accordance with policies and procedures, this activity may not be considered research at Creighton University and shall not be included on any research reports. However, comprehensive records must be retained regarding the administration and monitoring of any unapproved article. Standard IRB reporting requirements and deadlines apply, as do any sponsor requirements for monitoring and sharing safety information. Emergency use of a test article shall not be used to circumvent the general requirement for prior IRB review and approval.

2. **DEFINITIONS**

2.1. *Emergency use* is defined as the use of an investigational drug or biological product 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 IRB approval [21 CFR 56.102(d)]. The Food and Drug Administration (FDA) regulations do not provide for expedited IRB review in emergency situations. Therefore, “interim,” “compassionate,” “temporary,” or other terms for an expedited approval process are not applicable.

2.2. An *unapproved medical device* is defined as a device used for a purpose or condition for which the device requires, but does not have, an approved application for pre-market approval under section 515 of the Federal Food, Drug, and Cosmetic (FD&C) Act [21 U.S.C. 360(e)]. An unapproved device may be used in human subjects only if it is approved for clinical testing under an approved application for an Investigational Device Exemption (IDE) under section 520(g) of the FD&C Act [21 U.S.C. 360(j)(g)] and 21 CFR part 812. Medical devices that have not received marketing clearance under section 510(k) of the FD&C Act are also considered unapproved devices that require an IDE. The FDA recognizes that emergencies arise in which an unapproved device may offer the only possible life-saving alternative but an IDE for the device does not exist, or the proposed use is not approved under an existing IDE, or the physician or institution is not approved under the IDE. In these instances, justification to the FDA that the emergency existed is subsequently required.

2.3. *Life-threatening*, for the purposes of section 56.102(d), includes the scope of both *life-threatening* and *severely debilitating*, as defined below.
2.3.1. *Life-threatening* diseases or conditions are those in which the likelihood of
death is high unless the course of the disease is interrupted, as well as
diseases or conditions that have potentially fatal outcomes for which 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.

2.3.2. *Severely debilitating* diseases or conditions are defined as those that cause 
major irreversible morbidity. Examples of severely debilitating conditions include 
blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis, and stroke.

2.4. Emergency Use Provision: The “Emergency Use Provision” in the FDA 
regulations [21 CFR 56.104(c)] is an exemption from prior review and approval 
by the IRB. The exemption, which may not be used unless all of the conditions 
described in 21 CFR 56.102(d) exist, allows for one emergency use of a test 
article without prospective IRB review. FDA regulations require that any 
subsequent use of the investigational product at the institution have prospective 
IRB review and approval. FDA acknowledges, however, 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.

2.5. 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 to be reported in a marketing application.

3. **CONDITIONS FOR THE EMERGENCY USE PROVISION (EXEMPTION FROM PRIOR REVIEW)**

3.1. Prospective IRB Review Not Possible: If Creighton University’s IRB review and approval at a convened meeting is possible, the responsible individual (medical professional) should pursue the prospective IRB review. The Emergency Use Provision (Exemption from Prior IRB Review and Approval) applies ONLY IF treatment of a life-threatening condition is necessary before the IRB approval is made.
3.2. IND Required for Drugs/Biologics: The emergency use of an unapproved investigational drug or biologic requires an IND. If the intended subject does not meet the inclusion criteria for an existing study protocol, or if an approved study protocol does not exist, the usual procedure is to contact the manufacturer and determine whether the drug or biologic can be made available for the emergency use under the manufacturer’s IND.

3.3. The need for an investigational drug or biologic may arise in an emergency situation that does not allow time for submission of an IND or amendment of the manufacturer’s IND. In such a case, only the FDA may authorize shipment of the test article in advance of the IND submission (or amendment). Requests for such authorization may be made by telephone or other rapid communication means to the FDA [21 CFR 312.36].

4. INFORMED CONSENT REQUIRED

4.1. Even for an emergency use, the physician is required to obtain informed consent of the patient or the patient’s legally authorized representative, in accordance with and to the extent required by 21 CFR 50 [The consent process needs to disclose all required and appropriate additional elements of consent disclosure.] and informed consent is appropriately documented, in accordance with and to the extent required by 21 CFR 50.27. In addition to other exceptions to the requirement for informed consent, informed consent is not required if all of the following are true (both the treating physician and a physician who is not otherwise participating in the patient’s care certify in writing all of the following [21 CFR 50.23(a)]:

4.1.1. Immediate use of the test article is, in the investigator’s opinion, required to preserve the life of the participant.
4.1.2. Time is not sufficient to obtain the independent determination a physician who is not otherwise participating in the clinical investigation.
4.1.3. Before the use of the test article the investigator will certify in writing all of the following:
   4.1.3.1. The participant is confronted by a life-threatening situation necessitating the use of the test article.
   4.1.3.2. Informed consent cannot be obtained from the participant because of an inability to communicate with, or obtain legally effective consent from, the participant.
   4.1.3.3. Time is not sufficient to obtain consent from the participant’s legal representative.
4.1.3.4. 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 participant.

4.1.4. After the use of the test article a physician who is not otherwise participating in the clinical investigation will certify in writing within five working days after the use of the article all of the following:

4.1.4.1. The participant is confronted by a life-threatening situation necessitating the use of the test article.

4.1.4.2. Informed consent cannot be obtained from the participant because of an inability to communicate with, or obtain legally effective consent from the participant.

4.1.4.3. Time is not sufficient to obtain consent from the participant’s legal representative.

4.1.4.4. 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 participant.

4.1.5. The above written certification will be submitted to the IRB within five working days after the use of the test article. The IRB Chair will review the five-day reports.

5. PROMPT IRB REPORTING REQUIRED

5.1. If, in the physician’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 five 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. The physician shall notify the IRB in writing within five working days after the use of the test article [21 CFR 50.23(c)].

5.2. Creighton University’s IRB Required Reporting/Review Procedures

5.2.1. Pre-Emergency Use Notification: The physician seeking to provide life-saving treatment with an investigational drug, device, or biologic should notify the Creighton University IRB that he or she is prepared to exercise the “Emergency Use Provision” (when possible, using any available means, such as fax, phone, email, or other method).
5.2.2. This notification should not be construed as an IRB approval. Rather, the Creighton University IRB uses the prior notification to initiate tracking to ensure the investigator files a report within the five-day timeframe required by 21 CFR 56.104(c).

6. PRE-EMERGENCY USE RESEARCH SUBJECT PROTECTIONS

6.1. Creighton University’s IRB requires the physician authorizing the use of the device follow as many subject protection procedures as possible, including:

6.1.1. obtaining an independent assessment by an uninvolved physician;

6.1.2. obtaining informed consent from the patient or a legal representative;

6.1.3. notifying institutional officials as specified by clinical/institutional policies;

6.1.4. notifying the Creighton University IRB, and

6.1.5. obtaining authorization from the IND/IDE holder (as appropriate)

6.2. Post-Emergency Use Report: Following the treatment of an individual under the “Emergency Use Provision,” the treating physician must justify the “Emergency Use” as follows:

6.2.1. Describe how the individual treated was in a life-threatening situation in which no standard acceptable treatment was available and in which there was not sufficient time to obtain Creighton University’s IRB approval;

6.2.2. Document when contact was made to the IRB and what information was transmitted;

6.2.3. Justify why prospective IRB review was not possible;

6.2.4. Identify how the requirements for an IND were met (if applicable; see several options, above); and

6.2.5. Identify the informed consent process used (see options, above)
6.3. Subsequent Use: Any subsequent use of the test article is subject to prospective Creighton University IRB review.

7. **IRB CHAIR OR DESIGNEE REVIEW**

7.1. The IRB Chair or knowledgeable designee shall review reports of “Emergency Use” (both prospective reports and retrospective reports) to determine whether the circumstances meet the regulatory requirement and to determine whether informed consent was obtained or waived in accordance with FDA regulations.

7.2. Concerns: If the IRB Chair or designee has concerns regarding failure to follow regulations, the matter shall be referred to the Institutional Official.

8. **SPECIAL ISSUES**

8.1. The FDA notes in the event that a device is to be used in circumstances meeting the criteria listed above, the device developer must notify the Center for Devices and Radiological Health (CDRH) Program Operation Staff immediately after shipment is made. [Note: an unapproved device may not be shipped in anticipation of an emergency.] Nights and weekends, contact the Division of Emergency and Epidemiological Operations.

8.2. Some manufacturers will agree to allow the use of the test article, but their policy requires “an IRB approval letter” before the test article will be shipped. If it is not possible to convene a quorum of the IRB within the time available, the Creighton University IRB may send the sponsor a written statement that the IRB is aware of the proposed use and considers the use to meet the requirements of 21 CFR 56.104(c). Although, this is not an “IRB approval,” the acknowledgment letter has been acceptable to manufacturers and has allowed shipment to proceed.