POLICY

1. Purpose

This policy establishes the requirements for the emergency use of investigational drugs, biologics, and medical devices.

Note: This policy is not intended to limit the authority of a treating physician to provide emergency medical care, to the extent the treating physician is permitted to do so under applicable Federal, State and Local law, for patients who need such care.

2. Scope

This policy applies to the use of investigational drugs, biologics, and medical devices in an emergency setting by employees or agents of the University of Rochester.

Note: Emergency use of an unapproved test article is not considered research.

3. Definitions

3.1. *Emergency Use* – The use of an unapproved (investigational) test article in 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.

3.2. *Immediately Life Threatening Disease or Condition* – Stage of disease in which there is the reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment, inclusive of sight-threatening or limb-threatening conditions, as well as other situations involving risk of irreversible morbidity, or the patient is in the stage of disease that requires intervention before review at a convened meeting of the IRB is feasible.

3.3. *Serious Disease or Condition* – 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.

3.4. *Test Article* – Any drug, biologic, or medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the Food, Drug and Cosmetics Act or under sections 351 or 354-360F of the Public Health Service Act.

4. References

4.1. FDA 21 CFR 50.23; FDA 21 CFR 56.102(d); FDA 21 CFR 56.104(c); FDA 21 CFR 312; FDA 21 CFR 812

4.2. FDA Guidance IDE Policies and Procedures (Jan 1998);
FDA Emergency Use of Investigational Drug or Biologic Information Sheet

4.3. Emergency Use Physician Checklist;
Emergency Use Report to RSRB;
Emergency Use Follow-Up Report;
Emergency Use Consent Template

5. Responsibilities

5.1. The treating physician is responsible for determining that an emergency use of an unapproved test article (i.e., drug, biologic, or device) may be applied according to the criteria listed in Sections 6 – 8, as applicable, and to report such use to the RSRB, the sponsor, and FDA, as applicable. The treating physician may use the *Emergency Use Physician Checklist* for assistance in making determinations and fulfilling responsibilities associated with an emergency use of an unapproved test article.

5.1.1. If requesting emergency use before treatment, the treating physician is responsible for following the steps noted under Section 7 below.

5.1.2. If reporting emergency use after treatment, the treating physician is responsible for following the steps under Section 8 below.

5.2. The treating physician is responsible for the following additional activities once determining that emergency use of an unapproved test article may be applied:
Note: If the sponsor/manufacturer requires a letter from the RSRB prior to shipping an unapproved test article, the RSRB Chair will review the materials provided by the treating physician and can provide the *Emergency Use Chair Review Memo* (Appendix 1) indicating the RSRB is aware of the proposed use and, based upon the information provided, considers the use to meet FDA requirements. This will not constitute RSRB review and acknowledgement and will still require a report to the convened board.

5.2.1. For emergency use of drugs/biologics, contact the sponsor/manufacturer to determine whether the unapproved test article can be made available for the emergency use through the company's IND.

5.2.1.1. If an unapproved test article will not be provided under sponsor's IND, the treating physician must contact the FDA and submit the form to the FDA to obtain an IND for this emergency use and to provide authorization for the sponsor/manufacturer to ship the test article. The CTSI Office of Regulatory Support can provide assistance in the FDA process.

5.2.1.2. Notify University of Rochester Investigational Drug Services (IDS) of the intended emergency use. All investigational drugs and biologics utilized in an emergency setting must be dispensed through IDS.

5.2.2. For emergency use of devices, when possible, contact the sponsor/manufacturer to obtain authorization for use of the device. FDA authorization prior to use or shipment of the device is not required when the patient meets the criteria for emergency use.

5.3. The treating physician is responsible for obtaining informed consent from the patient and/or the patient's legally authorized representative unless there is written confirmation that all qualifying criteria described in Section 9.1.1 were met to waive consent before treatment. If the criteria to waive consent are met before treatment and the administration of the unapproved test article requires continued/repeat administration or procedures, consent to continue treatment should be obtained.

5.4. The RSRB staff is responsible for reviewing information about the emergency use provided by the treating physician for completeness, reviewing the Emergency Use Treatment log to ensure that the unapproved test article has not been previously used for the specified indication in an emergent situation, and reporting such use to the convened board for review.

5.5. The RSRB convened board is responsible for review of the information related to the emergency use provided by the treating physician to ensure that the emergency use is in compliance with FDA provisions, and must acknowledge the use in writing.

6. Requirements for Emergency Use of Any Unapproved Test Article (Drug, Biologic, Device)

6.1. FDA regulations [21 CFR 56.104(c)] allow for **one** emergency use of an unapproved test article for a particular indication without prospective RSRB approval, provided it is not possible to convene a board meeting within the time available and the emergency use of the unapproved test article is reported to the RSRB **within 5 working days** of the treatment date. Any subsequent similar use of the unapproved test article must have prior RSRB review and approval before treatment. Refer to the FDA Emergency Use of Investigational Drug or Biologic Information Sheet or FDA's information regarding Expanded Access for Medical Devices for additional guidance.

6.1.1. FDA acknowledges that such emergency treatment will not be denied to a second patient if the only obstacle is that the RSRB does not have sufficient time to convene a meeting to review the emergency use request.

6.2. The treating physician must determine that all of the following criteria apply for emergency use of an unapproved test article according to 21 CFR 56.102(d):

6.2.1. The patient has a serious or immediately life-threatening disease or condition (e.g., a serious disease, or a sight-threatening or limb-threatening condition, other situations involving risk of irreversible morbidity) that requires immediate treatment,

6.2.2. There is no standard or generally accepted therapy or alternative to treat the disease or condition,

6.2.3. The probable risk to the patient from use of the unapproved test article is not greater than the probable risk from the disease or condition [21 CFR 312.310(a)(1)], and,

6.2.4. There is not sufficient time to obtain an IND/IDE or RSRB approval of a protocol at a convened board meeting.

6.2.5. For emergency use of an **unapproved medical device**, the treating physician must also:

6.2.5.1. Determine there is substantial reason to believe that benefit will exist from the use of the unapproved medical device; and,

6.2.5.2. Obtain a written independent assessment for each of the items noted in Sections 6.2.1 – 6.2.4 and 6.2.5.1 above by a physician who is not otherwise participating in the emergency treatment. If there isn't time to obtain this assessment, the treating physician makes the determinations. The independent assessment is obtained as soon as possible after the treatment and is included in the report to the RSRB (see Section 8.1.4 below).

6.3. The RSRB must grant acknowledgement for emergency use of an unapproved test article at a convened meeting. Expedited review procedures will not be utilized for emergency use requests.

7. Requirements for RSRB Notification Before Treatment

7.1. The treating physician will complete the following activities when notifying the RSRB of emergency use of an unapproved test article before treating the patient:

7.1.1. Submit a report of the intended emergency use to the RSRB using a Report of New Information through the IRB Review System. The report should be titled "Emergency Use of [INSERT NAME of DRUG/BIOLOGIC/MEDICAL DEVICE] in [INSERT DISEASE/DISORDER]" and include the *Emergency Use Report to RSRB*. This report should include:

- Name of the unapproved test article to be used;
- Conditions under which the unapproved test article will be used;
- Confirmation that all qualifying criteria described in Section 6.2 are met to justify the emergency use;
- Copy of the informed consent document (refer to the *Emergency Use Consent Template*, alternately the sponsor/ manufacturer may provide a

consent form) *or* confirmation that all qualifying criteria described in Section 9.1.1 were met to waive consent prior to treatment;

7.1.2. Evaluate the likelihood of a similar use for the unapproved test article. If future use is likely, immediately initiate efforts to obtain RSRB approval and FDA clearance (IND or IDE) for such future use. *Note:* It may be necessary to consult with other individuals within the University to make this determination.

7.2. The RSRB will conduct the following activities when receiving a report of emergency use provided by a treating physician before administration:

7.2.1. Review the Emergency Use Treatment log to check whether the unapproved test article was previously used for a similar indication.

7.2.2. Review documents provided by the treating physician and complete the *Emergency Use RSRB Checklist* (sample checklist in Appendix 3).

7.3. The treating physician will complete the following activities once the unapproved test article has been administered:

7.3.1. Submit a follow-up report to the RSRB **within 5 working days** using the previously submitted Report of New Information through the IRB Review System. The *Emergency Use Follow-Up Report* should be submitted and include the date of administration and the outcome of the emergency use (including any reportable events, if applicable).

7.3.1.1. If the outcome of the emergency use is not available at the time of the initial report, the follow-up may be provided once the information is available.

7.3.2. If an IND/IDE exists, the sponsor must be notified and provided any follow-up information **within 5 working days** of the treatment date (for IDEs, the sponsor is then required to submit a report to the FDA within 5 working days).

7.3.2.1. For IDEs, This follow-up report should include a summary of the conditions constituting the emergency, the patient protection measures that were followed, and patient outcome information.

7.3.3. If an IND was obtained by the treating physician, the treating physician must submit a follow up report to the FDA within 15 working days of the emergency use. The notification report (Form 3926) is the same form used to obtain the emergency IND from the FDA.

7.3.4. If no IDE exists, the treating physician should submit to the FDA a follow-up report within 5 days on the use of the device including: a description of device used, details of the case, and the patient protection measures that were followed.

The CTSI Office of Regulatory Support can provide assistance in the FDA process.

7.4. The RSRB will schedule the emergency use as a review item at the next available convened board meeting once the 5-day follow-up report is received from the treating physician. Review by the board that reviews for the treating physician's department is

preferable; however, if this is not possible, the report may be scheduled for review at the next available biomedical convened board meeting.

7.4.1. After board review, written acknowledgment of the convened board's review of the emergency use will be provided to the treating physician using the *Emergency Use RSRB Acknowledgment Memo* (Appendix 2).

7.4.2. The emergency use will be documented by RSRB staff in the Emergency Use Treatment log.

8. Requirements for RSRB Review and Acknowledgement After Treatment

8.1. The treating physician will complete the activities listed under Section 7.3 after treatment of the patient with the unapproved (investigational) test article, in addition to:

8.1.1. Evaluate the likelihood of a similar use for the unapproved test article. If future use is likely, immediately initiate efforts to obtain RSRB approval and FDA clearance (IND or IDE) for such future uses. *Note:* It may be necessary to consult with other individuals within the University to make this determination.

8.2. The RSRB is responsible for the activities listed under Sections 7.2 and 7.4 above when receiving a report of emergency use provided by a treating physician after treatment.

9. Requirements for Obtaining Informed Consent

9.1. The treating physician must obtain informed consent (refer to the *Emergency Use Consent Template*) from the patient or the patient's legally authorized representative before emergency use of an unapproved test article.

9.1.1. In a medical emergency, it may not be possible to obtain informed consent prior to treatment. If both the treating physician and a physician who is not otherwise participating in the emergency treatment certify all of the following in writing, consent may be waived on a case-by-case basis [21 CFR 50.23(a)]:

9.1.1.1. The patient is confronted by a life-threatening situation necessitating the use of the unapproved test article;

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

9.1.1.3. Time is not sufficient to obtain consent from the patient's legally authorized representative; and

9.1.1.4. There is no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the patient's life.

9.1.2. If immediate use of the unapproved test article is, in the treating physician's opinion, required to preserve the patient's life, and if time is not sufficient to obtain an independent physician's determination that the four conditions of section 9.1.1

above apply prior to treatment, the treating physician should make and document the determination.

9.1.2.1. **Within five working days** after the treatment date, the treating physician's determination must be reviewed and evaluated in writing by a physician who did not participate in the emergency use [21 CFR 50.23(b) & 21 CFR 50.23(c)].

9.2. The treating physician must provide documentation required under sections 9.1.1 or 9.1.2 regarding consent to the RSRB **within 5 working days** after the treatment date.

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Appendices:

Appendix 1: Emergency Use Chair Review Memo Template
Appendix 2: Emergency Use RSRB Acknowledgement Memo Template
Appendix 3: Emergency Use RSRB Checklist – Sample

Revision History:

01/2018: Sect 4.2 and 4.3 hyperlinks added; Sections 7.2.3 – 7.2.5 moved as revised Sect 7.4; editorial changes
08/2021: Update with current FDA process for obtaining an emergency IND; update hyperlinks;

Supersedes Date:

01/10/2018

Approved By:

Kelley A. O'Donoghue
_____ 09/08/2021

Kelley A. O'Donoghue Date
Director, OHSP

Appendix 1 - Emergency Use Chair Review Memo Template

OFFICE FOR HUMAN SUBJECT PROTECTION

Research Subjects Review Board

UNIVERSITY of ROCHESTER

NOTE: FOR USE WHEN SPONSOR/MANUFACTURER REQUIRES RSRB CHAIR REVIEW PRIOR TO SHIPMENT

Date: [Enter date]

To: [Enter treating physician's name]

From: [Enter reviewing chair's name]
RSRB Chair, Board 0X

Re: Emergency Use of [Drug/Biologic/Device]

I am writing in response to your request for the emergency use of the investigational [drug/biologic/device], XX, for patient XX.

I reviewed the material submitted related to the emergency use noted above. Based upon this information, it appears to meet the conditions for emergency exemption as described in 21 CFR 56.102(d) and 21 CFR 56.104(c). As documented, written consent will be obtained from the patient (or the legally authorized representative) [OR: As documented, I understand that you will not be able to obtain consent and will comply with the requirements of 21 CFR 50.23(a-c).]

Please note that according to FDA regulations [21 CFR 56.104(c)] and OHSP Policy 607 Emergency Use of Investigational Drugs, Biologics, and Medical Devices you are required to submit the outcome of this emergency use on the Emergency Use Report to RSRB **within five working days** of administration. This information should be submitted to the RSRB via a Report of New Information in the IRB Review System. The information will be presented to the convened board for review and acknowledgement.

Should you have any questions, please contact the RSRB office at (585) 275-2398.

Appendix 2 - Emergency Use RSRB Acknowledgement Memo Template

OFFICE FOR HUMAN SUBJECT PROTECTION

Research Subjects Review Board

UNIVERSITY of ROCHESTER

Date: [Enter date]

To: [Enter treating physician's name]

From: [Enter reviewing chair's name]
RSRB Chair, Board 0X

Re: Emergency Use of [Drug/Biologic/Device]

BEFORE TREATMENT NOTIFICATIONS TO CONVENED BOARD:

The Research Subjects Review Board (RSRB) received your notification of the emergency use of the investigational [drug/biologic/device], XX, for patient XX.

The emergency use materials were presented to the convened board on {DATE} and the board confirmed that the conditions for emergency exemption as described in 21 CFR 56.102(d) and 21 CFR 56.104(c) have been met.

The notification you provided to the RSRB meets the requirements of OHSP Policy 607 Emergency Use of Investigational Drugs, Biologics, and Medical Devices and federal regulations for emergency use. Please note FDA regulations [21 CFR 56.104(c)] allow for **one** emergency use of an unapproved test article for a particular indication without prospective RSRB approval. If you anticipate any subsequent similar use of [drug/biologic/device], submit a treatment use protocol for review and approval by the convened board.

Please be reminded that:

- A follow-up report of the outcome of the emergency use (including any reportable events) should be submitted to the RSRB using the previously submitted Report of New Information through the IRB Review System after the test article has been administered to the patient using the Emergency Use Follow-Up Report to RSRB.
- Data pertaining to the emergency use may be provided to the sponsor but may not otherwise be used as part of a research study.

Should you have any questions, please contact the RSRB office at (585) 275-2398.

AFTER TREATMENT NOTIFICATIONS TO CONVENED BOARD:

The Research Subjects Review Board (RSRB) received your notification of the emergency use of the investigational [drug/biologic/device], XX, for patient XX.

The emergency use materials were presented to the convened board on {DATE} and the board confirmed that the conditions for emergency exemption as described in 21 CFR 56.102(d) and 21 CFR 56.104(c) were met.

The notification you provided to the RSRB meets the requirements of OHSP Policy 607 Emergency Use of Investigational Drugs, Biologics, and Medical Devices and federal regulations for emergency use. Please note FDA regulations [21 CFR 56.104(c)] allow for **one** emergency use of an unapproved test article for a particular indication without prospective RSRB approval. If you anticipate any subsequent similar use of [drug/biologic/device], submit a treatment use protocol for review and approval by the convened board.

Please be reminded that:

- [INSERT IF NOT ALREADY PROVIDED] A written follow-up reporting the outcome of the emergency use (including any reportable events) should be submitted to the RSRB using the previously submitted Report of New Information through the IRB Review System using the Emergency Use Follow-Up Report to RSRB.
- Data pertaining to the emergency use may be provided to the sponsor but may not otherwise be used as part of a research study.

Should you have any questions, please contact the RSRB office at (585) 275-2398.

Appendix 3 - Emergency Use RSRB Checklist Sample

EMERGENCY USE RSRB CHECKLIST

Upon receipt of an Emergency Use Report to RSRB from a treating physician, either before or after treatment, the RSRB Director (or designee) will review the information received to verify that the test article is/was used in compliance with FDA regulations.

[For RSRB Internal Uses Only]

BASIC INFORMATION:				
Date Report Received:				
Type of Report:	☐ Before Treatment ☐ After Treatment			
Treating Physician Name:				
Name of Test Article:				
Patient Initials:				
Physician provided report to RSRB <u>within 5 business days</u> of treatment date: ☐ N/A – Before treatment report ☐ Yes ☐ No – Add Comment:				
EMERGENCY USE INFORMATION:				
Emergency use applies based on the qualifying criteria (all must be "YES"):		YES	NO	N/A
1. The patient has a serious or immediately life-threatening disease or condition.		☐	☐	
2. There is **<u>NO</u>** standard or generally accepted therapy or alternative to treat the disease or condition.		☐	☐	
3. The probable risk from the disease or condition is greater than the probable risk from use of the unapproved test article.		☐	☐	
4. There is/was insufficient time to obtain an IND/IDE or RSRB approval of a protocol at a convened board meeting.		☐	☐	
5. For medical devices, there is substantial reason to believe that benefit will exist from the use of the unapproved medical device.		☐	☐	☐
☐	Emergency Use Treatment Log indicates <u>prior use</u> of this test article by this physician: ☐ No ☐ Yes – Add Comment:			
ADMINISTRATIVE PROCEDURES:				
Review the documents submitted by the treating physician for completeness.				
☐	The treating physician reported the emergency use to the sponsor/manufacturer (if IND/IDE exists), or the FDA (if IND/IDE does not exist).			
☐	The treating physician evaluated the likelihood of a future similar need for the test article. ☐ Future use is likely (file treatment documentation in Emergency Treatments log and initiate efforts to obtain RSRB approval). ☐ No future use is anticipated (file treatment documentation in Emergency Treatments log).			

☐	☐	The treating physician will obtain the informed consent of the patient or the patient's authorized representative, ***or*** (continued next page)
☐	☐	Written certification by the treating physician and a physician not otherwise participating in the emergency treatment confirms: ☐ The patient is/was confronted by a life-threatening condition necessitating the use of the test article; ☐ Informed consent cannot be/could not be obtained because of an inability to communicate with, or obtain legally effective consent from, the patient; ☐ Time is not/was not sufficient to obtain consent from the patient's authorized representative; and ☐ No alternative method of approved or generally recognized therapy is/was available that provides an equal or greater likelihood of saving the patient's life.
☐	RSRB acknowledgement memo provided for the sponsor/manufacturer: ☐ N/A ☐ Yes	
☐	Schedule the report for convened board review. Meeting Date:	
☐	RSRB acknowledgement memo of the convened board's review provided to treating physician.	
☐	Document the emergency use in the Emergency Use Treatment Log.	
☐	All documents pertaining to this report filed in the Emergency Use Treatment binder.	

Additional Comments:

Request reviewed by: _____ _____
RSRB Executive Director or Designee **Date**