1. POLICY

The FDA allows the use of investigational drugs and biologics or devices for the treatment of serious or life-threatening conditions for a single patient when no effective alternative treatment exists outside of a clinical trial ("Emergency Use", 21 CFR 56.104(c)). Although not research, human subjects protection regulations (21 CFR 50 & 56) apply due to the use of an investigational product.

An exemption under Food & Drug Administration (FDA) regulations at 21 CFR 56.104(c) allows for the emergency use of an investigational drug, device, or biologic on a one-time basis per institution without Institutional Review Board (IRB) review and approval when all of the following conditions are met:

- A patient (subject) is in a life-threatening situation.
- No standard acceptable treatment is available.
- There is insufficient time to obtain IRB approval.
- The emergency use is reported to the IRB within five (5) working days. (This report is not to be construed as an IRB approval for the emergency use).
- The Physician/Investigator obtains informed consent from the patient or legally authorized representative for such emergency use, except when there are circumstances that prevent obtaining consent.

Nothing in this Policy or in the federal regulations intends to place a limit on the authority of the physician to provide emergency care to the extent the physician is permitted to do so under applicable federal, state, or local law. This policy does NOT apply when using a marketed product for an indication not in the approved labeling ("off-label use") when the intent is the practice of medicine.

Department of Health and Human Services (HHS) regulations do not permit the commencement of research activities, even in an emergency, without prior IRB review and approval. Therefore, when emergency medical care is initiated without prior IRB review and approval, the patient may not be considered a subject in the HHS–supported research. The emergency care cannot be claimed as research nor can any of the data regarding such care be included in any report of HHS–supported research, except where required by FDA regulations, even if the emergency protocol is identical to that of a research protocol subsequently approved by the IRB.

When emergency use of a investigational article takes place pursuant to 21 CFR 56.104(c), any subsequent use of the investigational article will require full board approval.

Specific Policies

The following definitions are for key terms used in this policy. Other terms not defined herein shall have the meanings set forth in the Glossary.
1.1. Definitions

“Emergency Use” means the use of an investigational product with a human subject in a "life-threatening"or "severely debilitating" situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval.

“Life-threatening” means diseases or conditions where the 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 patients must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

“Severely Debilitating” means “Life-threatening” also includes 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.

“Independent Physician” means a physician not otherwise participating in the single time use of the investigational article's care.

1.2. Individual Patient Emergency Use

1.2.1. Physicians must contact the RSPP office to determine whether a full board meeting can be convened before use of the investigational drug, biologic or device is necessary. Expedited review procedures may not be used to grant approval of an expanded access emergency use.

1.2.2. In situations where time does not allow for review by the convened IRB, a one-time Emergency Use of an investigational product is allowed without prior IRB approval provided that such emergency use is reported to the IRB within 5 working days. The report should contain the following information:

- The name of the physician responsible for administering the investigational product;
- The name of the investigational product;
- The initials of the patient who received the investigational product;
- The date the investigational product was administered;
- A summary of the conditions that constituted the emergency use (i.e., lifethreatening or severely debilitating situation in which no standard acceptable treatment is available);
• The outcome;

• A copy of the informed consent document used or a signed attestation as noted below under "Informed Consent"; and

• A signed attestation by the physician indicating that the situation under which the investigational product was used met the definition of an "emergency use."

Any subsequent use of the same investigational product by the same physician must have prior IRB approval.

1.1.1. Under FDA regulations, 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 permit. DHHS regulations do not permit data obtained from patients to be classified as human participant research, nor permit the outcome of such care to be included in any report of a research activity subject to DHHS regulations.

1.1.2. Some manufactures may request RSPP Office acknowledgement prior to emergently shipping the investigational drug, biologic or device. If there is not time to convene a meeting of the full board to review the emergency use, the IRB Chair or designee will issue a letter indicating that the IRB is aware of the proposed use under the provisions at 21 CFR 56.104(c).

1.1.3. FDA Approval and Reporting

Specific approvals by and reporting to the FDA may also be required, including requirements to obtain verbal authorization by a reviewing FDA official and to submit an expanded access IND or protocol within 15 working days of FDA’s authorization of the use. Physicians should consult the FDA or 21 CFR 312 (drugs and biologics) and 21 CFR 812 (devices) for these requirements.

1.1.4. Informed Consent

A. Even in emergency use situations, informed consent must be obtained whenever feasible. If time does not allow for a convened meeting, the consent form, whenever possible, should be reviewed by RSPP staff. If there is no time to seek RSPP staff review, the physician is responsible for ensuring that appropriate elements of informed consent (as noted at 21 CFR 50.25) are included.

B. An exception from the requirement to obtain informed consent is allowed only when both the physician responsible for the emergency use and an independent physician (defined above), before use of the investigational article, certify in writing that all of the following conditions exist:
• The patient is confronted by a "life-threatening" or "severely debilitating" situation necessitating the use of the investigational product.

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

• Time is not sufficient to obtain consent from the patient's legal representative.

• No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the patient's life.

C. If, in the physician's opinion, immediate use of the investigational product is required to preserve the patient's life, and if time is not sufficient to obtain an independent physician's determination, the physician responsible for the emergency use may alone make the certification prior to administering the investigational product. The situation must then be reviewed and evaluated by a physician who is not involved in the patient's care, and this individual should certify that the above listed conditions were met.

The certifications noted above must be submitted to the RSPP office along with the Emergency Use Report within 5 working days from the use of the test article.

1.1.1.1. Review of Emergency Use Report

The IRB Chair will review the Emergency Use report and certifications regarding exception to obtain informed consent. The IRB will be notified of the emergency use at a convened IRB meeting. The meeting minutes will document IRB notification.

1.2. Emergency IND for Drugs and Biologics

The emergency use of an unapproved investigational drug or biologic requires an Investigational New Drug Exemption (IND) from the FDA. If the intended patient does not meet the criteria for an existing study protocol, or an approved study protocol does not exist, the usual procedure is to contact the manufacturer, verify that an IRB exists, and determine if the drug or biologic can be made available for the emergency use under the company's IND.

If no IND exists or if manufacturer denies permission or cannot be reached, a request must be made to the FDA to authorize shipment of the drug for emergency use in advance of the IND submission. These requests may be made by phone or other communication means (per FDA regulations 21 CFR 312.36).
1.3. — Emergency Investigational Device Exemption (IDE) for Devices

The Physician/Investigator should contact the sponsor to determine whether an IDE is required, and, if so, whether the device could be made available under the sponsor’s IDE. Where an IDE for the device does not exist or the sponsor denies permission or cannot be reached, a physician wants to use a device in a way not approved under an existing IDE, or the physician is not an investigator under the existing IDE, the device may be used without the prior approval of the FDA. Follow-up reports must be provided to the FDA that justify the emergency use of the device.

If there is not sufficient time to obtain FDA approval, the device may be used with the following protections in place:

- Informed consent of the patient;
- Clearance from the institution;
- Concurrence of the Senior IRB chair;
- Independent Physician assessment; and
- Authorization from the IDE holder (if an IDE exists).

1.4. — Informed Consent for Emergency Use of Any Investigational Article

In an emergency use situation, the Physician/Investigator is required to obtain informed consent of the patient or the Legally Authorized Representative (LAR) unless both the Physician/Investigator and an Independent Physician certify ALL of the following in writing:

- The patient is confronted by a life-threatening situation where the use of the investigational article is necessary;
- Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from the patient;
- Time is not sufficient to obtain consent from the patient’s legally authorized representative; and
- 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 immediate use of the investigational article is required to preserve life and there is insufficient time to obtain an Independent Physician’s determination that the four conditions above apply, the Physician/Investigator should make the determination and within 5 working days after use of the investigational article, have the use reviewed and evaluated in writing by an Independent Physician. The Physician/Investigator must notify the IRB within 5 working days after the use of the investigational article [21 CFR 50.23 (c)]. All documents will be maintained per Aurora IRB Policy EO 305.

1.5. IRB Notification and Review of Emergency Use Request

If full IRB approval cannot be obtained and use of the investigational drug, biologic or device meets the criteria for emergency use, the following steps must be completed prior to the use:

1. The Aurora IRB requires notification prior to the single time emergency use of a investigational article whenever possible. This notification should not be considered IRB approval. Notice must be made by calling or paging the Senior Aurora IRB Chair or RSPP Manager before the investigational article is administered or used in the patient. The Senior IRB Chair or RSPP Manager will use Form EU 1301-A to determine that the regulatory criteria will be met.

Notification is used to track the use in order to ensure that the Physician/Investigator submits a report within the five day time-frame required by 21 CFR 56.104(c).

2. The Senior IRB Chair or the RSPP Manager shall notify the Chief Medical Officer, the Site Administrator, the Institutional Official, or Vice President of Medical Affairs, as appropriate. This notification is to prohibit such use if the patient's condition does not qualify for Emergency Use or the risk to the patient outweighs any benefit related to the Emergency Use.

3. Unless immediate use of investigational article is required to preserve the life of the patient, verbal or written acknowledgement from the Senior IRB Chair or the RSPP Manager of the acceptance of the one-time use should be secured prior to use.

4. Regardless of whether the RSPP Office was notified prior to use, the Physician/Investigator is always required to submit a written report to the RSPP Office within 5 working days after emergency use of the investigational article. The report must document compliance with the specific FDA requirements for emergency use, indicating that a life-threatening situation existed in which no standard acceptable treatments were available, and that the investigational article needed to be used expeditiously, meaning insufficient time was available to convene a quorum for full board IRB approval. If informed consent was not obtained prior to the use, the report should indicate that the requirements in section 1.4 were satisfied.

5. If a investigational article was used in a life-threatening situation without full committee approval, or prior notification of the Senior IRB Chair or RSPP Manager, an Independent Physician must certify in writing that all of the criteria...
for single time emergency use were met. All documentation must be reviewed by the IRB Chair to determine/verify that the circumstances of the emergency use followed FDA regulations.

Any subsequent use of the investigational article will require submission of a research protocol for full IRB review and approval.

1.6. Use of Data Generated Prior To IRB Approval

Whenever emergency use is initiated without prior IRB review and approval, the patient may not be considered to be a research subject. HHS regulations do not permit research activities to be started, even in an emergency, without prior IRB review and approval. The physician may, without prior IRB approval, treat the patient using an investigational article (if the situation meets the FDA requirements as noted in this policy), but the patient may not be considered a research subject and data derived from use of the investigational article may not be used in the study.

1.7.1.3. Institutional and Aurora Patient Accounts Department Notification of Emergency Use

The RSPP office will notify the Institutional Official and the Aurora Specialty Patient Accounts Representative of the Emergency Use as soon as possible so appropriate billing procedures may be followed.

2. SCOPE

This policy/procedure applies only to single time emergency use of FDA regulated investigational articles without IRB review and approval and with or without informed consent. This policy/procedure does not apply when using an approved agent/device for non-marketed (off-label) purpose when the goal is medical treatment or "compassionate use" for drugs or devices. The RSPP Office should be consulted when "compassionate use" is being considered to ensure compliance with federal regulations.

3. APPLICABLE REGULATIONS, GUIDELINES AND STANDARDS

21 CFR 50.23 (a), (b) & (c)
21 CFR 56.102 (d)
21 CFR 56.104 (c)
21 CFR 312.36
FDA IRB Information Sheets/Guidance 1998
OHRP Guidance on Written IRB Procedures (January 15, 2007)
OHRP Report, Emergency Medical Care (May 15, 1991)

AAHRPP Element I.7.C.

4. REFERENCES TO OTHER APPLICABLE SOPS

None