SOP		
Department	**Title**	**Dates**
Institutional Review Board	Treatment use of Investigational Drug, Biologic or Device, including Emergency Use	Effective: 10/23/17
		Approved: 12/3/2018
SOP ID		Last Revised: 11/28/2018
IRB-SOP-602		Expiration: n/a

PURPOSE

The FDA has various mechanisms and regulations available to allow a physician to use a drug, biologic or device to treat a patient faced with a serious and/or life-threatening condition when the drug, device or biologic is not otherwise approved for marketing by the FDA.

This document describes the process for Investigators who wish to request Treatment Use of an investigational drugs, biologics or device.

SCOPE

This SOP applies to the non-research, treatment use of any investigational drug, biologic or device at any Ascension Wisconsin site.

This SOP does not apply to "off label" use of approved drugs, devices, or biologics.

This SOP does not apply to the non-emergency use of Humanitarian Use Devices (HUD), because the FDA has granted a type of approval for the devices. See SOP Humanitarian Use Device.

DEFINITIONS

Compassionate use: Compassionate use is one of several "expanded access" mechanisms established by the FDA to allow access to an investigational device outside of a clinical trial and before the device has been approved by the FDA for marketing for patients were the treating physician believes the device may provide a benefit in treating and/or diagnosing their serious (albeit not life-threatening) disease or condition.

Emergency Use of an Investigational Drug: Emergency Use refers to the one-time use by a single physician or Investigator of an Investigational Drug on a patient who is suffering from a life-threatening condition for which no standard acceptable treatment is available.

Emergency Use IND: If a patient is facing a life-threatening condition and he or she does not meet the inclusion criteria of an existing Research Project or if an approved Research Project does not exist, the physician/Investigator should contact the manufacturer and determine if the Investigational Drug can be made available for the Emergency Use under an existing IND. If the Sponsor refuses or there is no IND and, because of the patient's life-threatening condition, the physician/Investigator does not have time to submit an IND application, the physician/Investigator may contact the FDA to obtain authorization to ship the Investigational Drug in advance of the IND submission under an Emergency Use IND.

Emergency Use of an Investigational Device: When, in a physician's judgment, an Investigational Device offers the only alternative to save the life of a patient who is suffering from a condition for which there exists no other alternative therapy and (i) an Investigator wants to use an Investigational Device to treat

the patient in a way that is not approved under the IDE, (ii) the physician who wants to use the Investigational Device to treat the patient is not an Investigator under the IDE, or (iii) no IDE exists for the Investigational Device; the FDA may make the Investigational Device available to the physician/Investigator pursuant to the Emergency Use regulations. Emergency Use of an Investigational Device may occur before or after the initiation of a Research Project when: (i) the IDE Sponsor permits the Investigator to deviate from the Research Project protocol; (ii) the IDE Sponsor permits a physician who is not an Investigator under an IDE to use the Investigational Device in accordance with the Research Project protocol; or (iii) the FDA approves shipment of the device, although no IDE exists.

Expanded access: The FDA has several specific mechanisms and regulations that allow use of an investigational product outside of a formal clinical trial. These include mechanisms such as compassionate use, treatment use IND or single patient use requests, continued access or single patient emergency use.

Investigational: This term is used to refer to an item is not FDA-approved for marketing in the United States, or to an item that is being evaluated for a new and not-yet-approved indication, dosage, or formulation.

Life threatening: With regards to 21 CFR 56.1 02(d), Life-threatening means diseases or conditions where 1) the likelihood of death is high unless the course of the disease is interrupted and 2) 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 subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible

Off-label use: The clinical use of an FDA-approved drug, device or biologic for a purpose or population that has not been approved by the FDA, or in a route or dose that has not been approved by the FDA. Off-label use is not regulated by the IRB or the FDA; it is subject only to any policies and procedures of the clinician's institution.

Severely debilitating: With regards to 21 CFR 56.1 02(d), severely debilitating means 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.

Treatment Use: Treatment use is a mechanism defined in the federal regulations to allow the use of a drug, biologic or device in the treatment of patients not in a clinical trial under the provisions of a treatment investigational device exemption (IDE) or treatment investigational new drug (IND).

PROCESS

1. **Emergency Use of and Investigational Drug, Biologic or Device or Humanitarian Use Device (HUD)**
   - **1.1.** Whenever possible physicians are to notify the IRB of a proposed emergency use in advance of the use.
   - **1.2.** When a Physician has used an investigational drug, biologic or device to treat a patient with a life threatening event, the Physician must notify the IRB of the use within 5 working days of the use, per federal regulations.
   - **1.3.** The submission should be completed using the Emergency Use Submission Form for either Investigational Drug, Biologic or Devices, or Humanitarian Use Device (HUD). This can be submitted via email, fax or using the electronic IRB system.
     - **1.3.1.** The submission must include the following:
       - Emergency Use IND/IDE number or authorization for shipment from the FDA
       - Sponsor approval to use the drug, biologic or device
       - Consent form used to consent the patient (does not need to follow requirements at 21 CFR 50)

- If informed consent was unable to be obtained from the patient or his/her legally authorized representative, an Independent Physician's Assessment, from a physician not otherwise participating in the intervention certifying that:
    - The patient was confronted by a life-threatening situation necessitating the use of the test article
    - Informed consent could not be obtained because of an inability to communicate with or obtain legally effective consent from the patient
    - Time was not sufficient to obtain consent from the patient's legal representative
    - No alternative method of approved or generally recognizable therapy was available that would provide an equal or greater likelihood of saving the patient's life

1.3.2. Follow-up reports should be submitted to the IRB, the Sponsor and/or the FDA in which summary information regarding the patient outcome is presented. The IRB follow up reports must be completed and submit an Emergency Use submission in Mentor.

1.4. IRB Review

1.4.1. Research Integrity and Protection (RI&P) staff review the submission to determine whether the use meets/met the FDA requirements. This review is documented on the applicable checklist in Mentor and "WORKSHEET: Emergency Use (WRK-1701) or WORKSHEET: Compassionate Use of a Device (WRK-1702) may be referenced.

1.4.2. The staff creates a submission in Mentor, if not initially submitted through Mentor.

1.4.3. If the event does not meet the FDA requirements, staff will stop processing the submission and notify the submitter or work with the submitter to have the use comply with FDA requirements.

1.4.4. For requests meeting all FDA requirements, the IRB Chair evaluates the notification materials against the FDA criteria described on the form, to determine whether the compassionate use met the eligibility criteria and complied with the regulatory requirements.

1.4.4.1. If the notice is in advance of the use, inform the IRB staff (or physician if time sensitive) that the physician can proceed with the use or work with the physician to identify what additional information/procedures the physician needs to follow.

1.4.5. IRB staff notify the physician of the IRB determination through Mentor and set a 5-day reminder to request the 5-day report.

1.4.6. Follow-up reports should be submitted to the IRB, the Sponsor and/or the FDA in which summary information regarding the patient outcome is presented. The IRB follow up reports must be completed and submit an Emergency Use submission in Mentor.
If a use was carried out and did not meet the IRB or FDA requirements, it is handled as Noncompliance, using SOP: New Information/ Reportable Events.

2. Treatment Use Requests via other Expanded Access Mechanisms

2.1. FDA approval and Sponsor agreement is required before use.

2.2. IRB approval is required before use, when an investigator wishes to use an investigational drug, device or biologic to treat a patient clinically, other than the instances described above.

2.3. All treatment use requests, other than those described above, must be completed and submitted as an Initial New Protocol submission in Mentor.

2.4. The IRB is responsible to conduct initial reviews, grant approvals and maintain ongoing monitoring of all drugs, devices or biologics, used in human subjects under its jurisdiction. IRB Review is conducted following standard review mechanisms, in accordance with applicable SOPs.

3. Data Usage

3.1. Data collected for uses described in this SOP cannot be used in a non-exempt systematic investigation designed to develop or contribute to generalizable knowledge

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

3.3. Under DHHS regulations, a patient may not be considered to be a research subject whenever emergency care is initiated without prior IRB review and approval.

REFERENCES

- 21 CFR §50.23; 21 CFR §50.24; 21 CFR §56.102(d); 21 CFR §56.104(c).
- 21 CFR §812.36; 21 CFR §812.47
- FDA Information Sheet Guidance for IRBS, Clinical Investigators, and Sponsors: Frequently Asked Questions About Medical Devices
  http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM127067.pdf

RELATED MATERIAL

- IRB FORM: Emergency Use of Investigational Products
- IRB FORM: Emergency Use of an HUD
- IRB FORM: Compassionate Use of an Investigational Device
- IRB TEMPLATE: Example Consent Form for Emergency/Treatment Use

REVISION HISTORY

Version #	Date Revised	Reason for/Brief Description of Change	Revised By
01	4/11/2017	New- Initial Integration Update	J. Blundon
02	10/23/2017	Addition of Related Material, References and Revision History sections.	J. Blundon
03	11/28/2018	Combination of Emergency and Compassionate Use sections; clarification of process for reporting emergency use to the IRB.	J. Blundon-Kirchen