Marshfield Clinic

Expanded Access to Investigational Drugs, Biologics or Devices (Individual Patient, Including Emergency Use, Intermediate Size Populations, Treatment IND and Treatment Protocol)

1. SCOPE

1.1. System Wide

2. DEFINITIONS & EXPLANATIONS OF TERMS

2.1. Emergency Use
- 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.

2.2. Life-threatening
- 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 patient must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

2.3. 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.

3. PROCEDURE BODY

The FDA sometimes allows the use of investigational drugs and biologics or devices for the treatment of serious or life-threatening conditions either for a single patient (including emergency use) or for a group of patients (intermediate size patient populations or larger patient populations under a treatment IND or protocol) when no effective alternative treatment exists. The revision to 21 CFR 312 subpart I was finalized in 2009 to clarify existing regulations and add new types of expanded access for treatment use. The final rule is, "Intended to improve access to investigational drugs (and biologics) for patients with serious or immediately life-threatening diseases or conditions who lack other therapeutic options and who may benefit from such therapies." Corresponding regulations regarding devices is found at 21 CFR 812.36. The FDA also released a guidance, "Expanded Access to Investigational Drugs for Treatment Use – Qs & As" which clarified that expanded access uses are not primarily intended to obtain information about the safety or effectiveness of the drug, and clarified in detail the allowable expanded access uses.

Expanded Access exists for treatment outside of a clinical trial. Although not research, human subjects protection regulations (21 CFR 50 & 56) apply due to the use of an investigational product.

3.1. Individual Patient Emergency Use

a. Physicians must contact the IRB 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.

b. In situations where time does not allow for review by the convened IRB, a one-time emergency use (see definition above) 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:

(1) The name of the physician responsible for administering the investigational product;

(2) The name of the investigational product;

(3) The initials of the patient who received the investigational product;

(4) The date the investigational product was administered;

(5) A summary of the conditions that constituted the emergency use (i.e., life-threatening or severely debilitating situation in which no standard acceptable treatment is available);

(6) The outcome;

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

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

The IRB form entitled "Emergency Use Reporting Form" is available to facilitate this reporting. Any subsequent use of the same investigational product by the same physician must have prior IRB approval.

c. 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.

d. Some manufactures may request IRB 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).

e. 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 21

CFR 312 (drugs and biologics) and 21 CFR 812 (devices) for these requirements.

f. Informed Consent:

- 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 IRB staff. If there is no time to seek IRB staff review, the physician is responsible for ensuring that appropriate elements of informed consent (as noted at 21 CFR 50.25) are included.
- An exception from the requirement to obtain informed consent is allowed only when both the physician responsible for the emerging use and a physician who is not otherwise involved in the patient's care*, before use of the investigational product, 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.

*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 IRB office along with the Emergency Use Report within 5 working days from the use of the test article. IRB form entitled "Emergency Use – Exception From Informed Consent" is available to assist the physician in certifying that all requirements for an exception from obtaining informed consent have been met.

3.2. **Individual Patient Treatment Use, Intermediate-Size Patient Populations and Treatment INDs, Treatment Protocols and Continued Access (Sometimes referred to as "Compassionate Use")**

a. Prospective review and approval by the convened IRB is required before a patient can be treated under these expanded access options. The convened

IRB will evaluate whether the expanded access to an investigational drug, biologic or device is acceptable after review of the submitted materials and consideration of FDA research approval criteria listed at 21 CFR 56.111.

The following must be submitted to the IRB using the IRB Expanded Access Request form:

- Approval from the sponsor for the proposed use;
- Description of the patient's condition and the circumstances necessitating treatment;
- Treatment plan or protocol;
- Patient protection measures that will be followed;
- IDB;
- Informed consent document. (Written informed consent is required of all patients receiving expanded access treatment under this policy.)

b. Upon approval, all reporting that is required on IRB approved research also applies to expanded access uses (amendments, unanticipated problems, continuing review).

4. ADDITIONAL RESOURCES

4.1. IRB Forms for Submission: (found in Policy & Handbook Library [Forms])

- Emergency Use – Exception From Informed Consent
- IRB Expanded Access to Investigational Drug Request
- IRB Emergency Use Report

5. DOCUMENT HISTORY

Version No.	Revision Description
1.0	New Document in Document Control transferred from Policy & Handbook Library - #3889.7 (no changes made)
2.0	Add hyperlink to IRB Expanded Access Forms for submission

6. DOCUMENT PROPERTIES

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