MCW IRB Committee Procedures

REVIEW OF EXPANDED ACCESS USE REQUESTS – DRUGS OR BIOLOGICS

Unit: Human Research Protections Program (HRPP), Office of Research

Applies to: Institutional Review Board Committees

PURPOSE:
To outline the process and steps the IRB Committee takes in reviewing and evaluating requests for expanded access use of an investigational drug or biologic by a physician.

When a patient has a serious or life-threatening condition that is not addressed by current approved treatments, options may exist to use an investigational medical drug/ biologic (i.e., one that has not been approved or cleared by FDA) to treat the patient. A variety of FDA mechanisms exist to grant this expanded access, including:

- Expanded access for individual patients
- Expanded access for intermediate-size populations
- Expanded access for widespread use via a treatment IND or treatment protocol (designed for a larger population)

This policy only addresses these pathways which still require both IRB and FDA approval prior to expanded access. If a physician needs to treat a patient in an emergency capacity in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB or FDA approval, please see *IRB SOP: Emergency Use of Investigational Drugs or Biologics.*

DEFINITIONS:

Expanded Access for Treatment Use [21 CFR 312.300]: The use of an investigational drug in the context of expanded access is to diagnose, monitor, or treat a patient's disease or condition rather than to obtain data about the drug usually derived from clinical trials. This term is used broadly by the FDA. It can cover treatment use and emergency use. The terms expanded access, access, and treatment use are all used interchangeably.

Clinical Trial: A research project in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

Immediately Life-Threatening Disease: A stage of a disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.

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

Individual Patient Expanded Access [21 CFR 312.310]: In addition to FDA required criteria above, the treating physician must determine that the probably risk to the person from the investigational drug is not greater than the probable risk from the disease or condition and must determine that the patient cannot obtain the drug under another IND or protocol.

Intermediate-size Patient Population Expanded Access [21 CFR 312.315]: In addition to FDA required criteria above, FDA must determine there is enough evidence that the drug is safe at the dose and duration proposed for expanded access use to justify a clinical trial of the drug in the approximate number of patients expected to receive the drug under expanded access and there is at least preliminary evidence of effectiveness of the drug, or a plausible pharmacological effect of the drug in the anticipated patient population.

There are a number of reasons an intermediate-size expanded access program may be needed: 1) A drug is not being developed because the disease or condition is so rare that the sponsor is unable to recruit patients for a clinical trial. 2) The drug is being studies in a clinical trial, but patients requesting the drug for expanded access are unable to participate in the trial (such as due to a different disease state, enrollment is closed, or geographical restrictions). 3) A drug is an approved drug that is no longer marketed for safety reasons.

Treatment IND or Treatment Protocol [21 CFR 312.320]: In addition to FDA criteria required above, FDA must determine: 1) The drug is being investigated in a clinical trial under an IND designed to support a marketing application for the expended access use or all clinical trials of the drug have been completed and 2) The sponsor is actively pursuing marketing approval of the drug for the expanded access use with due diligence

PROCEDURE:

1. Under Federal Regulations, the IRB Committee is charged to review a physician's application for expanded access use of an investigational drug or biologic, prior to the use.
2. For the review of the expanded use submission, the HRPP office will assign IRB Reviewers in accordance with *Staff: Assigning Primary Reviewers and Use of Consultants*
3. The IRB Committee Chair, designated IRB member, or Full Committee will review the submission to ensure the appropriate regulatory elements are addressed per the federal regulations. The IRB Committee will complete the *IRB Member Form: Expanded Access Reviewer's Checklist.*
    i. Note: The MCW IRB allows waivers of the requirement for review and approval at a convened IRB meeting for individual patient expanded access INDs where the IRB chairperson or another designated IRB member provides concurrence before treatment use begins. This must be noted in the completed Form FDA 3926 with the box in Field 10.b selected and the form signed by the physician to be a request for a waiver under § 56.105 of the requirements in § 56.108(c), which relates to full IRB review. Please see the *IRB Staff: C2 Checklist for Treatment Use Submissions* for details and reviewer section.
4. The IRB Committee Chair, designated IRB member, or Full Committee will determine if the submission meets the criteria for approval, per the federal regulations. An IRB

decision letter will be issued to the Investigator, along with the consent form in accordance with *Staff: Creation and Processing of IRB Meeting Minutes and Decision Letters.* The IRB Decision Letter will include instructions to the Investigator to file follow up reports regarding the patient's outcome at the end of the treatment period or no later than 12 months after the initial approval was granted. The follow up must be submitted via eBridge CPR submission.

REFERENCES:
21 CFR 312 subpart I
FDA website and guidance documents

SUPPORTING DOCUMENTS:
IRB Member SOP: Emergency Use of Investigational Drugs or Biologics
IRB Member Form: Expanded Access Reviewer's Checklist
IRB Staff: C2 Checklist for Treatment Use Submissions
Staff: Assigning Primary Reviewers and Use of Consultants
Staff: Creation and Processing of IRB Meeting Minutes and Decision Letters

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Effective Date:	04/28/2023
Version number:	4.0
Previous Version/date:	3.0, 06/15/2018
Responsible Office:	HRPP Office
Approval Date:	04/14/2023

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