MCW Office of Research
Standard Operating Procedure

EXPANDED ACCESS USE OF AN INVESTIGATIONAL DRUG OR BIOLOGIC

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

Applies to: Faculty and Staff involved in human research

PURPOSE:
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 treatment IND or treatment protocol (designed for larger populations)

FDA has requirements that relates to all categories of expanded access [21 CFR 312.305]:

1) The patient(s) to be treated have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition.

2) The potential patient benefit justifies the potential risks of the treatment use and those potential risks are not unreasonable in the context of the disease or condition to be treated; and

3) Providing the investigational drug for the requested use will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use.

The MCW IRB is responsible to conduct initial reviews and maintain ongoing monitoring of all drugs or biologics used in human subjects under its jurisdiction. IRB approval is required to be in place before a patient is treated with an investigational drug/ biologic under expanded access for treatment use [21 CFR 312.305].

NOTE: 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. The treating physician should consult with the IRB office regarding the proposed treatment.

2. The treating physician should contact the Sponsor to determine if the Sponsor is willing to provide the investigational drug for expanded access, outside the context of a clinical trial, and then ask the Sponsor to submit or file for a Treatment Use IND with the FDA.
    a. The treating physician may need to contact FDA for a new expanded access IND if the Sponsor declines to be the sponsor of the expanded access use (typically seen with single patient expanded access). In this case, the treating physician must obtain a letter of authorization to cross-reference the Sponsor's existing IND for FDA to approve the new IND. The treating physician must obtain the IND to treat the patient prior to IRB approval.

3. When the treating physician wishes to utilize an investigational drug/biologic to treat a patient, an initial eBridge submission must be completed and submitted for IRB review. Refer to *IRB SOP: Submitting New Projects* for further information. Required documentation for submission in eBridge is outlined below, dependent on the type of expanded access request.

    a. *Individual patient expanded access IND*: Expanded access to an investigational product for treatment use by a single patient submitted under a new IND or as a protocol to an existing IND.
        i. Required documentation in eBridge includes:
            a. IND number
            b. FDA approval letter
            c. A consent form for the patient (See treatment use template available on the HRPP website)
            d. Approval from the Sponsor for the treatment use of the drug/ biologic
        ii. The completed Form FDA 3926 must also be submitted as part of the eBridge application for approval.

    b. *Intermediate-Size Patient Population Expanded Access*: Expanded access to an investigational drug for use by more than one patient, but generally fewer patients than are treated under a typical treatment IND or protocol, submitted under a new IND or as a protocol to an existing IND.
        i. Required documentation in eBridge includes:
            1. IND number
            2. Documentation from the Sponsor that an IND is in effect for the intermediate-size expanded access program.
            3. A consent form for the patient (See treatment use template available on the HRPP website)
            4. Sponsor provided protocol

    c. *Treatment IND or Treatment Protocol*: Expanded access to an investigational product for treatment use by a large (widespread) population, submitted under a new IND or as a protocol to an existing IND.
        i. Required documentation in eBridge includes:
            1. IND number
            2. Documentation from the Sponsor that an IND is in effect for the Treatment IND or Treatment Protocol.
            3. A consent form for the patient (See treatment use template available on the HRPP website)
            4. Sponsor provided protocol

4. Following the treatment use of an investigational drug/biologic the patient shall be monitored to detect any possible problems arising from the use of the investigational drug/biologic. If treatment is approved by FDA for a specific duration of treatment or chronic therapy, the treating physician must submit reports to FDA in accordance with 21 CFR 312.64, including safety reports and annual progress reports. At conclusion of the treatment, the treating physician must provide FDA with a written summary of the results of the expanded access, including adverse events.

5. MCW IRB requires follow-up reports to be submitted 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.

6. If any problems occur as a result of using the investigational drug/biologic these should be reported promptly to the IRB (via a Reportable Event), the Sponsor and/or FDA.

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

SUPPORTING DOCUMENTS:
IRB SOP: Submitting New Projects
IRB SOP: Continuing Progress Reports
IRB SOP: Emergency Use of Investigational Drugs or Biologics

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