



MCW Office of Research Standard Operating Procedure

EXPANDED ACCESS USE OF AN INVESTIGATIONAL DRUG, DEVICE 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, device, or 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:

- Treatment Use.
- Compassionate Use.
- Intermediate-Size Patient Population Expanded Access
- Single patient Expanded Access
- Open Label Protocol/IND
- Humanitarian Use Devices

This policy only addresses these pathways which still require 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, Devices or Biologics*.

DEFINITIONS:

Expanded Access: The use outside of a clinical trial of an investigational medical product (i.e., one that has not been approved by FDA). This term is used broadly by the FDA. It can cover treatment use and emergency use. It is often used by the device arm of the FDA synonymously with compassionate use. It is often used by the drug arm of the FDA to address intermediate-size patient population expanded access and single patient expanded access.

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.

Treatment Use: The use of an unapproved drug, biologic or device when the primary purpose is to diagnose, monitor, or treat a patient's disease or condition rather than to obtain information in support of a clinical trial.

Treatment IND/IDE: There are four requirements that must be met before the FDA will issue a treatment IND/IDE:

1. The product is intended to treat a serious or immediately life-threatening disease;
2. There is no satisfactory alternative treatment available;
3. The product is already under investigation, or trials have been completed; and
4. The trial sponsor is actively pursuing market approval.

Compassionate Use: This term is used primarily by the device arm of the FDA. Compassionate use can be for devices that are being studied in a clinical trial under an IDE for patients who do not meet the requirements for inclusion in the clinical investigation but for whom the treating physician believes the device may provide a benefit in treating and/or diagnosing their disease or condition. It can also be used for devices that are not being studied in a clinical investigation (i.e., an IDE for the device does not exist). This provision is typically approved for individual patients but may be approved to treat a small group.

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.

Open Label Protocol or Open Protocol IND: These are usually uncontrolled studies, carried out to obtain additional safety data (Phase 3 studies). They are typically used when the controlled trial has ended and treatment is continued so that the subjects and the controls may continue to receive the benefits of the investigational drug until marketing approval is obtained. These studies require prospective Institutional Review Board (IRB) review and informed consent.

Humanitarian Use Device (HUD): A medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the United States per year.

PROCEDURE:

1. When an Investigator wishes to utilize an investigational drug, device or biologic to treat a patient; the Investigator must complete and submit an initial eBridge submission for IRB review. Refer to *IRB SOP: Submitting New Projects* for further information. The MCW IRB is responsible to conduct initial reviews, and maintain ongoing monitoring of all drugs, devices or biologics used in human subjects under its jurisdiction. This includes the following FDA expanded access pathways:
 - Treatment Use
 - Compassionate Use
 - Intermediate-Size Patient Population Expanded Access
 - Single Patient Expanded Access requests
 - Open Label Protocols
 - *Humanitarian Use Devices – see HUD section of this document*
 2. The Investigator must include the following information in the eBridge submission:
 - IND or IDE number and;
 - Approval Letter from the FDA; and
 - A consent form for the patient based on the MCW/FH research intervention consent template; and
 - Approval from the Sponsor for the treatment use of the device or the single patient use of the drug or biologic.
 3. Unlike an emergency use of an investigational drug, device or biologic, FDA approval is required before the treatment use occurs. To obtain FDA approval to use an
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Investigational Drug, Device or Biologic for a single patient, the Investigator or Sponsor must:

- a. For Devices: Submit an IDE supplement requesting approval for a deviation from the IDE investigational plan in order to treat the patient.
 - i. For approval to treat a few patients, the Investigator must request access to the Investigational Device through the IDE Sponsor, who must submit an IDE supplement indicating the total number of patients to be treated.
 - ii. A follow-up report must be submitted to the MCW IRB and the FDA in the form of an IDE supplement in which summary information regarding the patient outcome is presented. MCW IRB requires follow-up reports to be submitted at 30 days and 90 days post use via eBridge CPR submission.
 - iii. If any problems occur as a result of using the investigational device these should be discussed in the supplement.
 - b. For Drugs or Biologics:
 - i. The Investigator should contact the Sponsor to submit or file for a Treatment Use IND with the FDA.
 1. *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.
 2. *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/IDE or as a protocol to an existing IND.
 3. *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.
4. Following the treatment use of an investigational drug, device, or biologic the patient should be monitored to detect any possible problems arising from the use of the investigational drug or biologic. 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.
 5. If any problems occur as a result of using the investigational drug or biologic these should be reported promptly to the IRB, the Sponsor and/or FDA.

Humanitarian Use Devices (HUD)

1. To be considered for HUD status, an investigator or the device sponsor must submit a request for HUD designation to the FDA. The FDA will determine if it should grant a Humanitarian Device Exemption (HDE) for use of the device.
2. The FDA requires IRB review and approval for local use of an HUD, including convened Committee review and, at a minimum, annual continuing review, which may be expedited. This is the only situation where federal regulations require IRB approval and monitoring of an activity that is clearly not research. However, if the HUD is being used in research or in a clinical investigation, the IRB must comply with all FDA regulations related to IRB review of research.
3. FDA regulations require that the investigator and/or sponsor clearly state that the device is an HUD and that the effectiveness of the device has not been demonstrated.
4. When an Investigator wishes to utilize a HUD to treat a patient population; the Investigator must complete and submit an initial eBridge submission for IRB review. Refer to *IRB SOP: Submitting New Projects* for further information. The MCW IRB is

responsible to conduct initial reviews, grant approvals and maintain ongoing monitoring of all HUD devices, used in human subjects under its jurisdiction.

5. The Investigator must include the following information in the eBridge submission:
 - generic and trade name of the device
 - FDA HDE #
 - date of HUD designation
 - indications for the use of the device
 - description of the device
 - contraindications, warnings, and precautions for use of the device
 - adverse effects on health
 - alternative practices and procedures
 - marketing history
 - summary of projects using the device
 - A clinical consent form for the patient that includes a clear statement that the device has not been proven safe or effective in the way most devices are approved.
6. The MCW IRB will review the submission and issue an approval letter if the criteria for the use of HUD have been met.
7. Investigators are required to submit continued progress reports to the IRB to continue the use of an HUD once approval has been obtained. See *IRB SOP: Continuing Progress Reports* for additional information.

REFERENCES:

21 CFR 312 subpart I
21 CFR 812.36
FDA website and guidance documents

SUPPORTING DOCUMENTS:

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

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Approved By	
HRPP Authorized Official:	David Clark, PhD, Director, HRPP Human Research Protections Program (HRPP) Office of Research Medical College of Wisconsin