

<b>Expanded Access Use of an Investigational Medical Product (Investigational Drug, Device, or Biologic)</b>	Effective Date	08.22.2023
	Revision Date	

- 1.0 Purpose:** This standard operating practice (SOP) establishes guidelines for expanded access use of an investigational drug, device, or biologic according to federal guidelines and in accordance with ECU’s University and Medical Center Institutional Review Board (UMCIRB) practice. This SOP will address the treating provider/investigator’s responsibilities in the expanded access use of an investigational drug, device, or biologic as well as IRB responsibility for review of the expanded access use of investigational drugs, devices, or biologics.
- 2.0 Persons Affected:** Treating providers/investigators who wish to utilize an investigational drug, device, or biologic in an expanded access situation, UMCIRB staff, and the IRB chairperson or designee.
- 3.0 SOP:** Sometimes called “compassionate use”, expanded access is a potential pathway for a patient with a serious or immediately life-threatening disease or condition to gain access to an investigational medical product (drug, biologic, or medical device) for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available. The expanded access use of an investigational drug, device, or biologic must meet applicable federal and institutional IRB criteria for such use and, except in emergency situations, must obtain approval by a convened committee of the UMCIRB or concurrence from the UMCIRB chair (or the chair’s designee). The treating provider/ investigator needs to make sure the following criteria apply:
- 3.1** The patient or patients 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.
  - 3.2** 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.
  - 3.3** Providing the investigational medical product 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.
- 4.0 Definitions:**
- 4.1 Investigational Medical Product:** Includes investigational new drugs and biologics, and investigational devices. Investigational new drug means a new drug or biological drug that is used in a clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes. The terms “investigational drug” and “investigational new drug” are deemed to be synonymous. Investigational device means a device, including a transitional device, that is the object of an investigation.
  - 4.2 Expanded Access:** Refers to a potential pathway for a patient with an immediately life-threatening condition or serious disease or condition to gain access to an investigational medical product (drug, biologic, or medical device) for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available.

- 4.3 **Life-threatening:** Refers to 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 does not require the condition be immediately life-threatening or to immediately result in death. Rather, the participants must be in a life-threatening situation requiring intervention before review at a convened meeting of the UMCIRB is feasible.
- 4.4 **Severely Debilitating:** Refers to diseases or conditions that cause major irreversible morbidity; examples being blindness, loss of limb, loss of hearing, paralysis, or stroke.
- 4.5 **Letter of Authorization (LOA):** Refers to a letter permitting FDA to refer to the company's IND or IDE file to provide certain necessary information about the investigational medical product (e.g., chemistry, manufacturing, controls) for the individual patient expanded access IND or IDE submitted by the treating provider/investigator. The company should include the IND or IDE number for its investigational medical product in the LOA.
- 4.6 **Sponsor:** Refers to the party who submits a request to open an expanded access IND application and receives FDA's authorization to use the investigational product. In the absence of any other sponsor (e.g., pharmaceutical company), the treating physician is the sponsor of the expanded access IND application.
- 4.7 **Sponsor-Investigator:** Refers to an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. The term does not include any person other than an individual. The requirements applicable to a sponsor-investigator under this part include both those applicable to an investigator and a sponsor.
- 4.8 **Types of Expanded Access Investigational New Drugs (INDs) and Investigational Device Exemptions:**
  - 4.8.1 Individual (or single) Patient IND/IDE: Expanded access to an investigational drug or investigational device for treatment use by a single patient submitted under a new IND/IDE.
  - 4.8.2 Intermediate Size Population IND/IDE: Access to an investigational drug (including biologic) or investigational device for use by more than one patient.
  - 4.8.3 Widespread Treatment IND/IDE: Access to an investigational drug (including biologic) or investigational device for treatment use by a large widespread population.

**5.0 Procedures/Responsibilities**

**5.1 Treating provider/Investigator (or designee) responsibilities for obtaining an Individual Patient IND/IDE include:**

- 5.1.1 Notifying the UMCIRB as soon as the treatment provider identifies a patient and determines that the patient meets the criteria for expanded access.
- 5.1.2 Contacting sponsor/manufacturer to ensure that the manufacturer has the investigational product available and is willing to provide it.
- 5.1.3 Determining from the product manufacturer who will be submitting the IND or IDE application. The application will either be submitted by:
  - 5.1.3.1 Sponsor who is willing to provide the investigational medical product and either submits the expanded access to the FDA and allows the FDA to cross-

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reference to their industry IND (for drugs and biologics) or IDE (medical devices) on behalf of the expanded access sponsor-investigator through the use of a Letter of Authorization (LOA), or

- 5.1.3.2** Sponsor-Investigator who is the treating provider submits the expanded access request to the FDA. The product manufacturer provides the necessary investigational medical product information for the sponsor-investigator to submit to support an expanded access request. In this case, the sponsor-investigator will hold the IND or IDE.
- 5.1.4** Requesting authorization from the FDA by calling the FDA main line then completing form FDA 3926 and submitting it either electronically or by fax.
  - 5.1.4.1** A physician using Form FDA 3926 may choose to request authorization to obtain concurrence by the IRB chairperson or by a designated IRB member before the treatment use begins, in lieu of obtaining IRB review and approval at a convened IRB meeting at which a majority of the members are present. This is done by checking box 10b on the 3926 FDA form.
- 5.1.5** If time permits, the expanded access request for a single patient should be submitted via ePIRATE using the “New Study” function. Time sensitive uses may necessitate submission of information via a worksheet available on the UMCIRB website.
- 5.1.6** Whether a full ePIRATE submission or the worksheet are used, treating providers must submit all applicable documents to the UMCIRB for review. These may include (but are not limited to):
  - 5.1.6.1** An acknowledgement letter or email documentation of FDA approval. Unless the FDA notifies the sponsor (e.g., the patient’s physician) that treatment may begin earlier, there is a 30-day period from the date the FDA receives the IND/IDE before treatment with the drug may begin.
  - 5.1.6.2** LOA from the manufacturer.
  - 5.1.6.3** FDA form 3926.
  - 5.1.6.4** Investigator Brochures for any investigational drugs/biologics or instructions for use for any investigational devices.
  - 5.1.6.5** CV of treating provider.
  - 5.1.6.6** Formal treatment plan.
  - 5.1.6.7** UMCIRB worksheet.
  - 5.1.6.8** Informed consent document for treatment with the investigational medical product and HIPAA Authorization. These may be merged into a single document.
  - 5.1.6.9** Supporting documentation for the use of the product for the expanded access use.
- 5.1.7** Once UMCIRB approval is secured, the treating provider/investigator is responsible for:
  - 5.1.7.1** Facilitating the process and managing use of the investigational medical product and the patient’s medical care.
  - 5.1.7.2** Obtaining informed consent and HIPAA Authorization of the participant or the participant’s legally authorized representative.
  - 5.1.7.3** Beginning treatment 30 days after application is received by FDA (or earlier if notified by FDA).

- 5.1.7.4 Reporting SAEs to UMCIRB and the FDA.
- 5.1.7.5 Providing a summary report to UMCIRB on an ongoing basis. This would include when the treatment begins and ends as well as any SAEs or significant developments.
- 5.1.7.6 Submitting annual reports as necessary to the FDA.
- 5.1.7.7 Formally close out IND/IDE with the FDA when treatment is complete.
- 5.1.7.8 Maintaining accurate and complete treatment and regulatory documentation.

**5.2 Treating provider/Investigator’s (or designee) responsibilities for obtaining an Intermediate Size Population IND and Widespread Treatment IND include:**

- 5.2.1 Treatment provider/investigator identifies more than one patient and determines that the patients meet the criteria for expanded access.
- 5.2.2 Treating provider contacts the manufacturer to inquire if they have an intermediate or broad IND and if they have a compassionate use program.
- 5.2.3 If manufacturer holds an IND or IDE and has a compassionate use program, the treating provider needs to submit an application in ePIRATE to obtain prospective IRB approval of the expanded access program owned by the manufacturer. The application needs to be reviewed by the full board.
- 5.2.4 Treatment provider submits the consent and HIPAA Authorization to the UMCIRB for review.
- 5.2.5 Manufacturer works closely with the treating provider to submit the application to the FDA.
- 5.2.6 Once the expanded access program is approved by the full board, the treating provider has the same responsibilities described under section 5.1.7

**5.3 University and Medical Center Institutional Review Board (UMCIRB) responsibilities include:**

- 5.3.1 Acknowledging the use of the investigational medical product meets the federal criteria for expanded access in accordance with FDA regulations.
- 5.3.2 Reviewing the documents indicated under 5.1.6 and submitting them to the chair for review.
- 5.3.3 Providing an approval letter to the treating physician once UMCIRB receives concurrence from the chair (for individual access IND).
- 5.3.4 Assigning a primary and secondary reviewer for the application for prospective approval of the expanded access program to be reviewed by the full board (for intermediate and widespread INDs).
- 5.3.5 Conducting annual continuing reviews for the prospective expanded access program.
- 5.3.6 Ensuring that the treating provider meets the regulatory requirement for submission of safety reports to UMCIRB and the FDA, provides monthly updates on the condition of the patient to the IRB, and submits a summary when treatment is complete.

**5.4 UMCIRB Administrative Director or designee responsibilities include:**

- 5.4.1 Ensuring compliance with this SOP.
- 5.4.2 Ensuring appropriate tools/resources are available for review of expanded access of investigational medical products based on new and evolving applicable regulations and guidelines.
- 5.4.3 Assisting the UMCIRB committee/chair in the review of the expanded access

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material as needed.

- 5.4.4 Providing written documentation of IRB determinations.
- 5.5 **The IRB Chairperson or designee responsibilities include:**
  - 5.5.1 Reviewing expanded access documentation material to be shared with the convened UMCIRB if applicable.
  - 5.5.2 Providing acknowledgement for use if required by manufacturer of the investigational medical product.
  - 5.5.3 Reviewing expanded access applications and providing concurrence when all required elements have been satisfied.

## References

<https://www.fda.gov/news-events/public-health-focus/expanded-access>

<https://www.fda.gov/news-events/expanded-access/expanded-access-how-submit-request-forms>

<https://www.fda.gov/drugs/investigational-new-drug-ind-application/ind-applications-clinical-treatment-expanded-access-overview>

<https://www.fda.gov/drugs/investigational-new-drug-ind-application/physicians-guide-non-emergency-single-patient-expanded-access-submissions>

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