HUMAN RESEARCH PROTECTION PROGRAM DEPARTMENTAL POLICY AND PROCEDURE

7.4 EXPANDED ACCESS TREATMENT USE OF AN UNAPPROVED DRUG/BIOLOGIC

RESPONSIBLE OFFICE: Human Research Protection Program Department (HRPPD) **EFFECTIVE DATE: June 7, 2021**

I. POLICY STATEMENT

A. **Nothing in this policy is intended to prevent a physician from preserving life.** If in the investigator's opinion, immediate use of the test article is required to preserve the patient's life, and time is not sufficient to obtain IRB Approval or notify the IRB, the investigator or physician should make the determination and then follow the procedures outlined in the Emergency Use of an Unapproved Investigational Drug Policy and Procedure [21 CFR 50.23(c)].

B. This policy describes the procedures for utilizing the Food and Drug Administration (FDA) Expanded Access Program (EAP) including individual patient and intermediate or large population treatment investigational new drug (IND) applications

C. Expanded access, sometimes called "compassionate use," is the use of an investigational test article outside of a clinical trial to treat a patient with a serious or immediately life-threatening disease or condition who has no comparable or satisfactory alternative treatment options.

D. The compassionate use provision allows access for patients who do not meet the requirements for inclusion in the clinical investigation but for whom the treating physician believes the test article may provide a benefit in treating and/or diagnosing their disease or condition.

II. SCOPE

A. This policy and these procedures apply to investigators or physicians requesting approval for one of the following categories of EAP:

a Individual patient IND, including emergency use IND (21 CFR 312.310) commonly held by treating physician or investigator for treatment of an individual patient.

b Intermediate population treatment IND (21 CFR 312.315) commonly held by the sponsor (manufacturer) for use in a population smaller than a typical treatment IND or treatment protocol. The investigational drug for intermediate population treatment INDs may be in active development or may be an FDA approved drug that is unavailable or in limited supply.

c Large population treatment IND or treatment protocol (21 CFR 312.320) commonly held by the sponsor for widespread treatment use. For a large population treatment INDs, the sponsor must be pursuing marketing approval.

III. PROCEDURES FOR POLICY IMPLEMENTATION

A. Before submitting an Individual Patient IND to FDA, a physician or PI must confirm the manufacturer will provide the drug. If a large or intermediate scale EAP is available through the

manufacturer, the PI may coordinate access to the drug through the manufacturer's approved Treatment IND rather than filing a separate Individual Patient IND.

B. FDA regulations require prospective review by the convened IRB or by physician request (Form FDA 3926) for alternate review via IRB Chair Concurrence.

C. FDA policy specifies that "the provision for emergency use would rarely apply to a treatment protocol or treatment IND because these are planned uses of the test article and sufficient time is available to obtain IRB review and approval." In rare cases in which emergency use does apply for individual patients, administration takes place according to emergency use federal regulations (21 CFR 56.104) following procedures in the 7.5 EMERGENCY USE OF AN INVESTIGATIONAL DRUG OR DEVICE POLICY AND PROCEDURE.

D. The FDA identifies special considerations when a patient is to be treated under an EAP:

   a **Drug Development:** In considering EAP use, individual needs must be balanced against societal needs. The FDA stipulates that expanded access use should not compromise enrollment or interfere with active clinical investigations that could support approval of the drug.

   b **Informed Consent:** Informed consent is especially important in expanded access use situations because the subjects are desperately ill and particularly vulnerable. They will receive medications which have not been proven either safe or effective in a clinical setting. Both the setting and their desperation may work against their ability to make an informed assessment of the risk involved. Therefore, the PI or physician must ensure that potential subjects are fully aware of the risks involved in the participation.

   c **Charging for Treatment INDs:** The FDA permits charging for the drug, agent, or biologic when used in an EAP when regulatory criteria are met. Therefore, the IRB must pay particular attention to EAPs in which the subjects will be charged for the cost of the drugs. If subjects will be charged for use of the test article, economically disadvantaged persons may inadvertently be excluded from participation. Charging for participation may preclude economically disadvantaged persons as a class from receiving access to test articles. The IRB must balance this interest against the possibility that unless the sponsor can charge for the drug, it will not be available for treatment use until it receives full FDA approval.

   d **Regulatory Responsibilities:** Per FDA a licensed physician under whose immediate direction an investigational drug is administered for an expanded access use is considered an investigator assuming applicable regulatory responsibilities. An individual who submits an IND for expanded access use is considered a sponsor-investigator, assuming applicable responsibilities for sponsors and investigators (21 CFR 312.305(c)).

E. Individual Patient IND

   a The physician or PI submits the following for review by the convened IRB:

i. a completed application;

ii. individual patient IND approval letter from FDA;

iii. investigator's brochure if applicable;

iv. Form FDA 3926 (signed version submitted to FDA) which includes a brief description of patient situation and treatment plan; and

v. copy of the appropriate informed consent form.

b HRPPD staff screen the IRB submission and verify the IND number according to procedures described in the 7.1 DRUG RESEARCH POLICY AND PROCEDURE.

c The IRB reviews the submission as outlined in 2.1. INITIAL REVIEW OF RESEARCH and according to federal regulations.

d At the conclusion of treatment, the physician or PI reports a written summary of the results of the expanded access use, including any safety related information, to the IND sponsor or FDA and the IRB.

F. Individual Patient IND in an Emergency Situation

a In the rare cases in which an emergency requires that the patient be treated before a written IND submission can be made, the PI obtains authorization for individual use from FDA by telephone or electronic communication with subsequent submission of IND paperwork (21 CFR 312.310).

b The PI follows procedures described in the 7.5 EMERGENCY USE OF AN INVESTIGATIONAL DRUG OR DEVICE, and submits documents outlined above (E.a)

c The IRB Chair, HRPPD staff, and the IRB follow review procedures as described in the 7.5 EMERGENCY USE OF AN INVESTIGATIONAL DRUG OR DEVICE.

G. Intermediate or Large Population Treatment IND

a The PI follows procedures described in 2.1. INITIAL REVIEW OF RESEARCH with the following additions and provisions:

i. a completed eIRB application;

ii. documentation of FDA treatment IND approval (i.e., correspondence from FDA or commercial sponsor, IND number printed on sponsor protocol); and

iii. related materials including the treatment protocol, investigator's brochure, informed consent form, and potential investigational drug costs.

b HRPPD staff screen the IRB submission following procedures described in 2.1. INITIAL REVIEW OF RESEARCH.

c The convened IRB reviews the protocol as outlined in 2.1. INITIAL REVIEW OF RESEARCH and according to federal regulations.

d At the conclusion of treatment, the physician or PI reports a written summary of the results of the expanded access use, including any safety related information, to the IND sponsor or FDA and the IRB.

H. See 8.1 IRB MINUTES for details concerning documenting Treatment Use Protocols.

IV. DEFINITIONS

SEE GLOSSARY OF HUMAN RESEARCH TERMS

V. REFERENCES

Resource
21 CFR 50 – PROTECTION OF HUMAN SUBJECTS
45 CFR 46 – PROTECTION OF HUMAN SUBJECTS
45 CFR 164 – SECURITY AND PRIVACY (HIPAA PRIVACY RULE)
21 CFR 56 – INSTITUTIONAL REVIEW BOARDS

VI. REVISION AND REVIEW HISTORY

Revision Date	Author	Description
June 2021	HRPP	Separated policy from P&P manual. Updated references to AVPHRA and IRB Director. Minor administrative edits.
August 2017	HRPP	New Policy Development
March 2012	IRB Office	IRB Written Procedures