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I. PURPOSE

The purpose of this SOP is to outline the investigator’s responsibilities, IRB submission requirements and review process for non-emergency 1) expanded access/treatment use of a drug for individual patients, and 2) compassionate use of a device.

II. POLICY STATEMENT

An investigator may use an unapproved test article for individual patient treatment use (drug) or compassionate use (device) after obtaining concurrence from the IRB Chair, Vice Chair (or another designated IRB member, as appropriate).

III. SCOPE

This policy applies to use of investigational drugs, biologics, diagnostics, devices or other interventions that are regulated by the FDA. This policy does not regulate or interfere with the clinical practice of medicine.

IV. DEFINITIONS


Chair, CPHS: The Chair functions as the executive chair of all of the IRB committees and subcommittees and provides input for IRB policies and educational training requirements. The Chair works with the Director, Human Subjects Research and the VP, Research Compliance and Regulatory Affairs on procedural matters pertaining to the IRB. The Chair serves as Chair or Vice-Chair for one or more of the CHOP IRBs.

Emergency Use: The use of a test article with a human subject in a life-threatening situation in which no standard approved or generally acceptable treatment is available and in which there is not sufficient time to obtain IRB approval or concurrence by the IRB chair or other IRB member [21 CFR 56.102(d)].

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

IND: An Investigational New Drug Application (IND) is a request for authorization from the Food and Drug Administration (FDA) to administer an investigational drug or biological product to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug or biological product that is not the subject of an approved New Drug Application or Biologics/Product License Application.

Investigational Device Exemption (IDE): IDE refers to the regulations under 21 CFR 812. An approved IDE means that the IRB (and FDA for significant risk devices) has approved the sponsor’s study application and the requirements under 21 CFR 812, as applicable, are met. An investigational device exemption (IDE) allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data. An approved IDE permits a device to be

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shipped lawfully for the purpose of conducting investigations of the device without complying with other requirements of the Food, Drug, and Cosmetic Act (FD&C Act) that would apply to devices in commercial distribution.

Reviewer: The Chair or Vice Chair, CPHS or their designee who is responsible for providing a review of all submitted materials, documenting the review on the appropriate evaluation form, and taking an action on behalf of the IRB.

- For the review of individual patient expanded access for drugs/biologics, the reviewer will be the chair or a designee (who must be an experienced IRB member/alternate).
- For the review of compassionate use of a device, the reviewer will be the Chair or Vice-Chair.

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 (e.g., blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke). 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.

Test Article: A drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the jurisdiction of the Food and Drug Administration.


Vice-Chair, CPHS: The Vice-Chair is responsible for assisting the Chair, CPHS and serving as a Chair or Vice-Chair of one or more of the CHOP IRBs.

V. PROCEDURES


A. Expanded Access for Drugs/Biologics – Non-Emergency Individual Patient Expanded Access

Expanded access refers to the use of an investigational drug when the primary purpose is to use the drug to diagnose, monitor, or treat a patient's disease or condition rather than to generate scientific information intended to characterize the safety and effectiveness of a drug. There are three categories:

- Expanded access for individual patients, including for emergency use;
 - Note: The requirements and investigator responsibilities for emergency use of a drug are outlined in **SOP 802**.
- Expanded access for intermediate-size populations

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- Will be referred for review and approval by the convened board in accordance with **SOP 105**.
 - Expanded access for widespread treatment use through a treatment IND or treatment protocol
 - Will be referred for review and approval by the convened board in accordance with **SOP 105**.
1. An investigator, who must be a licensed physician, may want to treat a patient with an investigational drug if they conclude that: (1) the patient has a serious or life-threatening condition and has no other comparable or satisfactory therapeutic options; and (2) the patient cannot obtain the drug under another IND or protocol.
 2. A licensed physician who submits a non-emergency individual patient expanded access IND may request a waiver from the requirement for full IRB review from the FDA. The waiver may be requested using Form FDA 3926 (by selecting the appropriate box on that form to request a waiver under § 56.105 of the requirements in § 56.108(c), which relate to full IRB review). A physician submitting an individual patient expanded access IND using Form FDA 1571 may include a separate waiver request with the application.
 - (a) If such a waiver is requested, the physician (sponsor-investigator) will need to obtain concurrence from the IRB chairperson or another designated IRB member before treatment use begins.
 - (b) If such a waiver is not requested, the single subject use will be referred for review and approval by the convened board (in accordance with **SOP 105**) before treatment use begins.
 3. The IRB can provide concurrence by the chair, or qualified member, for the single subject use provided the investigator holds the IND and the FDA has granted a waiver under § 56.105 of the requirements in § 56.108(c).
 - (a) Individual patient INDs and individual patient protocols submitted to an existing IND by a commercial sponsor will be referred for review by the convened board in accordance with **SOP 105**.
 4. **Requirements for Submission to the IRB to obtain concurrence of the Chair or Vice-Chair CPHS before treatment use begins:**
The investigator must submit (in the electronic system):
 - (a) A thorough patient history and treatment plan, included in the Form FDA 3926 or in another document; which should include
 - (1) The proposed daily dose, route, and frequency of administration, duration of planned treatment, criteria for discontinuation of treatment, and planned dose modifications for adverse events;

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- (2) The planned monitoring for adverse events, response to treatment, and changes in clinical status, as well as proposed modifications to the treatment plan to mitigate risks to patients if appropriate;
- (3) The key details of the patient’s history, including diagnosis and summary of prior therapy (including response to such therapy), the reason for request, including an explanation of why the patient lacks other therapeutic options; and information regarding a patient’s relevant clinical characteristics (such as comorbid conditions and concomitant medications) that is necessary to assess the potential for increased risks of the drug;
- (4) A summary of known risks of the drug (this information may be included in the consent form or the IB, rather than the treatment plan, as applicable), and
- (5) An assessment that the probable risk to the patient from the investigational drug is not greater than the probable risk from the disease or condition.

Note: The information provided to the IRB should match what was/will be submitted to the FDA.

- (b) A consent form that contains the information required under 21 CFR 50.25;
- (c) The Investigator’s Brochure (if available);
- (d) The FDA-issued individual patient expanded access IND.

5. **Post Approval Requirements:**


- (a) The investigator is responsible for complying with FDA and other regulatory requirements and policies, including, but not limited to, obtaining prospective IRB approval of proposed modification to the treatment plan (unless necessary to eliminate apparent immediate hazard to the participant; **SOP 403**), prompt reporting of unanticipated problem (**SOP 408**), non-compliance (**SOP 901**), submitting continuing reviews (**SOP 404**) and study closure (**SOP 405**), as applicable.

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B. Expanded Access for Medical Devices – Compassionate Use

Expanded access is a potential pathway for patients with a serious or life-threatening disease or condition to access an investigational medical device that has not been approved or cleared by the FDA for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available. There are three categories:

- Emergency Use
 - The use of an investigational device when an individual patient is in a life-threatening situation and needs immediate treatment; there are no alternative options; and no time to use existing procedures to get FDA approval for the use.
 - The requirements and investigator responsibilities for emergency use of a device are outlined in **SOP 802**.
 - Compassionate Use (or Individual Patient/Small Group Access)
 - Treatment Investigational Device Exemption (IDE)
 - The use of an investigational device to treat or diagnose a group of patients with a serious or immediately life-threatening disease or condition when the device is also being studied for the same use under an approved Investigational Device Exemption.
 - Treatment investigational device exemptions will be referred for review and approval by the convened board in accordance with **SOP 105**.
1. An investigator, who must be a licensed physician, may want to access an investigational device that has not received FDA approval or clearance if they conclude that: (1) the patient has a life-threatening or serious condition; (2) no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition exists; and (3) the potential patient benefit justifies the potential risks of the investigational device.
 2. Unlike emergency use of an unapproved device, prior FDA approval is needed before compassionate use occurs.
 3. Prior to compassionate use, an investigator must obtain concurrence of the Chair or Vice-Chair CPHS (Note: At CHOP, the concurrence of the Chair or Vice-Chair CPHS satisfies the requirement to obtain clearance from the Institution (See **Institutional Clearance for the Emergency Use of an Investigational Device** policy **SOP 802**).

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4. Requirements for **Submission to the IRB** (via the electronic system) **before compassionate use**, regardless of whether there is an IDE for the device or not
- The investigator must submit (in the electronic system):
- (a) A description of the patient's condition and the circumstances necessitating treatment;
 - (b) A discussion of why alternative therapies are unsatisfactory and why the probable risk of using the investigational device is no greater than the probable risk from the disease or condition;
 - (c) An identification of any deviations in the approved clinical protocol that may be needed to treat the patient;
 - (d) The patient protection measures that will be followed:
 - (1) A consent form that contains the information required under 21 CFR 50.25;
 - (2) An independent assessment of a physician who is not participating in the study or in the care of the patient that concurs with the planned usage;
 - (3) Authorization from the device manufacturer on the use of the device.
 - (e) An appropriate schedule for monitoring the patient to detect any possible problems arising from the use of the device, taking into consideration the investigational nature of the device and the specific needs of the patient.
 - (f) Evidence of FDA approval of the compassionate use;
 - (g) If there is an IDE for the device, confirmation of the IDE by the sponsor
 - (h) If there is no IDE for the device: A description of the device provided by the manufacturer
5. **Post Approval Requirements:**
- (a) Following the compassionate use of the device, a follow-up report should be submitted by whoever submitted the original compassionate use request to FDA within 45 days of using the investigational device. The report should present summary information regarding patient outcome. If any problems occurred as a result of device use, these should be discussed and also reported to the reviewing IRB as soon as possible.
 - (b) The investigator is responsible for complying with FDA and other regulatory requirements and policies, including, but not limited to, obtaining prospective IRB approval of proposed modification to the treatment plan (unless necessary to eliminate apparent immediate hazard to the participant; **SOP 403**), prompt reporting

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of unanticipated problem (**SOP 408**), non-compliance (**SOP 901**), submitting continuing reviews (**SOP 404**) and study closure (**SOP 405**), as applicable.

6. If there is an IDE for the device, the above compassionate use criteria and procedures can also be applied when a physician wishes to treat a few patients rather than an individual patient suffering from serious disease or condition for which no alternative therapy adequately meets the medical need. In this case, the IDE supplement (also submitted to FDA) should include the information identified above and indicate the number of patients to be treated. The supplement should also include the protocol to be followed or should identify deviations from the approved clinical protocol. As with single patient compassionate use, a monitoring schedule should be designed to meet the needs of the patients while recognizing the investigational nature of the device.

C. IRB Responsibilities


1. IRB Review of Individual Patient Expanded Access/Compassionate Use

- (a) Pre-review procedures to ensure completeness of the submission will be followed in accordance with **SOP 105**.
- (b) The reviewer will have access to all materials submitted in eIRB as described in **SOP 301**.
- (c) The reviewer discloses conflicting interest with any submission sent for review. If there is a conflict of interest the submission will be reassigned to another member.
- (d) The reviewer will:
 - (1) Assess the risks and benefits of treatment for the particular patient involved, whether risks to the patient have been minimized and that such risks are reasonable in relation to anticipated benefits;
 - (2) When the request is for a pediatric patient, confirm that adequate provisions are included for soliciting age-appropriate assent from children and permission from a parent or guardian, as required under 21 CFR 50.55;
 - (3) Confirm that the informed consent document contains the information required under 21 CFR 50.25;
 - i. Given that the drug/device used under expanded access is investigational, a statement in the informed consent document indicating that although the primary use of the drug/device is for treatment, the drug/device is investigational and FDA has not determined that the drug/device is safe or effective for use in treating the condition, will satisfy the requirement under 21 CFR §50.25(a)(1) that the informed

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consent provide a statement that the use of the product “involves research.”

- (4) Confirm the validity of the IND or IDE (if applicable) number in accordance with IRB **SOP 409**.
- (5) The qualifications of the physician submitting the individual patient expanded access request will be confirmed by the Department/Division approver prior to IRB submission in the electronic system.
- (e) The reviewer documents their review and determinations.
- (f) The reviewer establishes the continuing review frequency.
- (g) The Chair or Vice Chair CPHS will provide a statement of concurrence to the investigator via the electronic submission system.
- (h) Continuing review and the review of amendments and reportable events may also occur via the concurrence pathway.
- (i) At any time, the reviewer may forward the submission to the full board.


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VI. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 50	21 CFR 56
21 CFR 312	21 CFR 812
FDA Guidance for IRBs and Clinical Investigators: Institutional Review Board (IRB) Review of Individual Patient Expanded Access Submissions for Investigational Drugs and Biological Products 2023	FDA Guidance for Industry: Expanded Access to Investigational Drugs for Treatment Use— Questions and Answers: Guidance for Industry. October 2017
Form FDA 3926, and Instructions for Filling Out Form FDA 3926 – Individual Patient Expanded Access, Investigational New Drug Application (IND)	FDA Guidance on Expanded Access for Medical Devices. June 2016

VII. REFERENCES TO OTHER APPLICABLE SOPS

SOP 105: IRB Review Processes	SOP 301: Research Submission Requirements
SOP 403: Amendments and Reports of New Findings to Approved Research	SOP 404: Continuing Review of Approved Research
SOP 405: Study Closure	SOP 408: Unanticipated Problems Involving Risks to Subjects
SOP 409: Determination of IND/IDE Requirement	SOP 802: Exemption to the Requirement for Prior IRB Approval for Emergency Use of Investigational Drugs, Biologics, or Devices
SOP 901: Non-Compliance with Human Subjects Research Policies	Institutional Clearance for the Emergency Use of an Investigational Device

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VIII. RESPONSIBILITIES

Title	Responsibility
Director, HSR	The Director, HSR (or designee) is responsible for monitoring changes to regulations and communicating such changes to IRB staff, IRB members, and investigators.
Chair, CPHS	The Chair or Vice-Chair is responsible for ensuring compliance with regulations pertaining to expanded access of unapproved drugs, biologics, or devices including issuing concurrence.
Investigator	Responsible for securing the sponsors approval (as applicable), the FDA's approval, IRB Chair concurrence and the informed consent of the patient or the permission of the parent/guardian prior to using the test article.

IX. ATTACHMENTS:

X. REVISIONS:

06-25-2021: Initial approval date

06-07-2022: Editorial changes

12-12-2023: Edits to reflect FDA September 2023 Guidance on Institutional Review Board (IRB) Review of Individual Patient Expanded Access Submissions for Investigational Drugs and Biological Products

XI. APPROVAL:

Approval Indicator: Approved by Amy Schwarzhoff and Barbara Engel on 12/12/2023
Amy Schwarzhoff, Senior Director, Human Subjects Research and Barbara Engel, Chair, CPHS