The Christ Hospital IRB **Number:** 1.11
Submitted By: Erica Jones, CIP **Effective Date:** 02/09
Approved By: Steve Roberts, MD **Revision Date:** 10/25

STANDARD OPERATING PROCEDURE

Expanded Access to Investigational New Drugs

1.0 POLICY

This policy outlines the IRB process for expanded access use of investigational new drugs (IND). Expanded access, sometimes called "compassionate use", refers to the use of an investigational drug or biologic when the primary purpose is to diagnose, monitor, or treat a patient rather than to obtain the kind of information about the drug that is generally derived from clinical trials. The expanded access 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 investigational medical product may provide a benefit in treating and/or diagnosing their disease or condition. This provision is typically approved for individual patients, but may be approved to treat a small group.

All Expanded Access to Investigational New Drugs (IND) must meet the following criteria in FDA regulation 21 CFR 312.305(a):

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;
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.

There are three categories of expanded access based on the number of people who need access and the level of risk. An expanded access IND submission is required to FDA for each type of expanded access. The submission may be a new IND or a protocol amendment to an existing IND.

Expanded access to investigational drugs for treatment use may be available in the following circumstances:

1.1 **Individual Patient IND** or **Protocol** including **Emergency Use IND** (21 CFR 312.310), commonly held by treating physician or investigator for treatment of an individual patient. The product may or may not be under development.

Additional Criteria for Individual Patient Access:

- The probable risk to the person from the investigational drug is not greater than the probable risk from the disease or condition; and
- The FDA must determine that the patient cannot obtain the investigational drug under another IND or protocol.

1.2 **Intermediate Population Treatment IND** or **Treatment Protocol** (21 CFR 312.315), commonly held by the sponsor (manufacturer) for use in population smaller than typical of 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.

Additional Criteria for Intermediate Population Access:

- The drug is being investigated in a controlled clinical trial under an IND designed to support a marketing application for the expanded access use, or all clinical trials of the drug have been completed;
- The sponsor is actively pursuing marketing approval of the drug for the expanded access use with due diligence; and
- When the expanded access use is for a serious disease or condition, there is sufficient clinical evidence of safety and effectiveness to support the expanded access use. Such evidence would ordinarily consist of data from phase 3 trials, but could consist of compelling data from completed phase 2 trials; or when the expanded access use is for an immediately life-threatening disease or condition, the available scientific evidence, taken as a whole, provides a reasonable basis to conclude that the investigational drug may be effective for the expanded access use and would not expose patients to an unreasonable and significant risk of illness or injury. This evidence would ordinarily consist of clinical data from phase 3 or phase 2 trials, but could be based on more preliminary clinical evidence.

1.3 **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.

Additional Criteria for Intermediate Population Access:

- 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 clinical evidence of effectiveness of the drug, or of a plausible pharmacologic effect of the drug to make expanded access use a reasonable therapeutic option in the anticipated patient population.

2.0 PROCEDURE

2.1 Sponsor-Investigator/Sponsor

2.1.1 Determine that the all Expanded Access criteria in FDA regulation 21 CFR 312.305(a) are met.

2.1.2 Submit IND Application to FDA on Form 1571 or 3926 (Individual Access only). FDA approval is required prior to IRB approval and before expanded access/compassionate use occurs (30 calendar day review timeframe). The convened IRB must review the submission. However, for an individual patient expanded access IND, a submitting physician may request a waiver under § 56.105 of the requirements in § 56.108(c) which relate to full IRB review. To request a waiver for convened IRB review, the submitting physician may either:

2.1.2.1 Select box 10(b) when using Form FDA 3926, or

2.1.2.2 Include a separate waiver request when using Form FDA 1571.

2.1.3 Submit a new Compassionate Use e-application to TCH IRB in Mentor IRB. The following documentation should be uploaded with the submission for IRB consideration:

2.1.3.1 FDA Approval letter, or notification that this is pending FDA review;

2.1.3.2 Expanded Access Protocol, if applicable;

2.1.3.3 Investigator Brochure or Package Insert, if applicable;

2.1.3.4 Authorization from the device manufacturer on the use of the drug;

2.1.3.5 Proposed Informed Consent Form.

Note: Submissions requiring convened IRB review must be received prior to the set meeting deadline to be reviewed at the next convened IRB meeting.

2.1.4 Submit IND safety reports and annual reports (when the IND continues for 1 year or longer) to the FDA as required by §§ 312.32 and 312.33.

2.1.5 Submit to the IRB any updates or changes including but not limited to:

2.1.5.1 Amendments to the protocol/treatment plan,

2.1.5.2 Written results of the use including safety information,

2.1.5.3 Notice of any problems that occurred as a result of use,

2.1.5.4 Changes to FDA approval status,

2.1.5.5 When the expanded access is completed, and

2.1.5.6 Continuing review report if treatment continues beyond the IRB approval date.

2.1.6 Submitting physician may request a waiver under § 56.105 of the requirements in § 56.108(c) which relate to full IRB review. To request a waiver for convened IRB review, the submitting physician may either:

2.1.6.1 Select box 10(b) when using Form FDA 3926, or

2.1.6.2 Include a separate waiver request when using Form FDA 1571.

2.2 **IRB Chair Review (For Individual Patient IND or Protocol, if waiver of requirement for convened IRB review is requested)**

2.2.1 Review the request for expanded access Individual Patient IND or Protocol and all submission documents utilizing the IRB: Compassionate Use/Expanded Access Checklist.

2.2.2 Ensure that a waiver for full review has been requested.

2.2.3 Confirm the medical evaluation of the patient's condition that there is no comparable or satisfactory alternative available, including already approved therapies or other clinical trials for which the patient might be eligible.;

2.2.4 Ensure that the informed consent or appropriate permissions will be obtained and documented per 21 CF 50.25.

2.2.5 Review the treatment plan to determine that it makes adequate provision for ensuring the safety of the patient, including adequate monitoring and appropriate plans for collecting and reporting the data, that the physician is qualified to administer the treatment, and that treatment facility is adequately equipped.

2.2.6 Either defer to convened board for full review or make a determination to concur with the use and determine review frequency. The IRB Chair may approve the expanded access use for up to 1 year. If treatment continues beyond 1-year, continuing review is required.

2.2.7 Perform continuing review for expanded access that continues beyond the approval period.

2.3 **CONVENED IRB REVIEW (for Intermediate Population Treatment IND, Large Access IND Protocols, and Deferred Access Individual Patient IND)**

2.3.1 Review the request for expanded access and all submission documents utilizing the IRB: Compassionate Use/Expanded Access Checklist.

2.3.2 Confirm the medical evaluation of the patient's condition that there is no comparable or satisfactory alternative available, including already approved therapies or other clinical trials for which the patient might be eligible.

2.3.3 Ensure that the informed consent or appropriate permissions will be obtained and documented per 21 CF 50.25.

2.3.4 Review the treatment plan to determine that it makes adequate provision for ensuring the safety of the patient, including adequate monitoring and appropriate plans for collecting and reporting the data, that the physician is qualified to administer the treatment, and that treatment facility is adequately equipped.

2.3.5 Vote to approve, approve with minor or major modifications, table, or disapprove the use. The IRB may approve the expanded access use for up to 1 year. If treatment continues beyond 1-year, continuing review is required.

2.3.6 Perform continuing review for expanded access that continues beyond the approval period.

2.4 **IRB Office**

2.4.1 Review the submission utilizing the IRB Office: Compassionate Use/Expanded Access Checklist to:

2.4.1.1 Ensure all ancillary reviews have been completed,

2.4.1.2 Ensure that all required documentation has been uploaded;

2.4.2 Communicate IRB decision to the investigator in writing. Approvals are given a 1-year approval, effective the date of the convened meeting, and expiring on the 1st day of the month, 12 months later.

2.4.3 Facilitate continuing review for expanded access that continues beyond the approval period.

3.0 REFERENCES

3.1 21 CFR 56: Institutional Review Boards

3.2 21 CFR 50: Protection of Human Subjects

3.3 21 CFR 312.310: Expanded Access for Individual Patients, Including for Emergency Use

3.4 21 CFR 312.315: Expanded Access for Intermediate Sized Patient Populations

3.5 21 CFR 312.320: Expanded Access for Widespread Treatment Use Through a Treatment IND or Treatment Protocol

3.6 FDA Guidance: Expanded Access to Investigational Drugs for Treatment Use — Questions and Answers Guidance for Industry (Updated October 2017)

3.7 IRB Reference Manual 13: Expanded Access to Investigational Medical Products

3.8 AAHRPP Domains and Elements: I.7.A; I.7.B