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**Boston
Children's
Hospital**

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Applicability Boston Children's
Hospital- Policies
& Procedures

Expanded Access – Investigational Drugs Policy/Procedure

Internal Approval

SVP, Research

EVP & Chief Scientific Officer, Research

Scope

This policy describes the various regulatory mechanisms for obtaining and using investigational drug (IND) and biologic products for the treatment of patients under expanded access mechanisms in compliance with federal and state regulations pertaining to clinical investigations. The mechanisms that are described, include:

1. Individual Patient Expanded Access (emergency and non-emergency requests)
2. Intermediate-Size Patient Population Access
3. Treatment IND/Protocol

Definitions

Investigational use: Suggests the use of an approved product in the context of a clinical study protocol [21 CFR 312.3(b)]. When the principal intent of the investigational use of a test article is to develop information about the product's safety or efficacy, submission of an Investigational New Drug (IDE) may be required.

Sponsor-Investigator: An individual who both initiates and conducts an investigation, and under whose immediate direction an investigational drug is administered or dispensed. The term does not include any person other than an individual.

Policy Statements

Research at Boston Children's Hospital that involves the **investigational use** of drugs, biologics, and dietary supplements must conform to U.S. Food and Drug Administration (FDA) regulations, Department of Health and Human Services (HHS) regulations, and Massachusetts state laws (94C MGL 8).

Massachusetts General Law:

1. 94C MGL 8: Requires the registration of investigators who use investigational and Schedule II drugs in research protocols

FDA Regulations:

Expanded Access of Investigational Drugs

The use of investigational drugs and biologics is usually limited to subjects enrolled in clinical trials under an Investigational New Drug (IND). However, test articles may show some promise before the trials are completed. When there is no satisfactory standard treatment for a serious, life-threatening, or a debilitating condition, the FDA has a mechanism that allows expanded access to the drugs before the clinical trials are complete. When no satisfactory alternative treatment exists, subjects are generally willing to accept greater risks from test articles that may treat life-threatening and debilitating illnesses. The following mechanisms expand access to promising therapeutic agents without compromising the protection afforded to human subjects, or the thoroughness and scientific integrity of product development and marketing approval.

1. 21 CFR 312 Subpart I: Expanded access use of an Investigational New Drug (IND)
2. 21 CFR 314: Drug products
3. 21 CFR 600: Biological products

Emergency Use INDs

In instances where a patient needs to be treated before a written application can be submitted, the FDA can grant an emergency IND. Researchers should use the FDA's website for the comprehensive process.

1. Once an Emergency Use IND is granted, the physician-sponsor has 15 calendar days to submit the written application to the FDA.
2. The Emergency Use IND must be reported to the Boston Children's Hospital IRB within 5 working days.
 - a. Any subsequent use of the test article is subject to IRB review prior to initiation of treatment.

The emergency use of a test article, other than a medical device, is a clinical investigation, the patient is a participant, and the FDA may require data from an emergency use to be reported in a marketing application.

However, HHS regulations do not permit data obtained from patients to be classified as research involving human participants, nor permit the outcome of such care to be included in any report of a

research activity subject to HHS regulations.

FDA Exemption

Federal law requires that a drug be the subject of an approved marketing application before it is transported or distributed across state lines. Because there is likelihood that a sponsor will want to ship the investigational drug to clinical investigators in other states, the investigator must seek an exemption from that legal requirement. The Investigational New Drug (IND) is the means through which the sponsor technically obtains this exemption from the FDA (21 CFR 312). This requirement applies to any expanded access mechanism obtaining the drug/biologic.

Informed Consent

The FDA requires informed consent to be obtained from the subject or the subject's legally authorized representative, unless both the physician-investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following (21 CFR 50.23(a)):

1. The subject is confronted by a life-threatening situation necessitating the use of the test article.
2. Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject.
3. Time is not sufficient to obtain consent from the subject's legal representative.
4. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.

Intermediate-Size Patient Population Access

In cases where more than a single patient will be treated with an investigational product (but fewer than a treatment IND/protocol), an intermediate-size patient population expanded access IND or protocol can be submitted to the IRB via CHERP as a New Research Activity.

- a. An intermediate-size patient population IND is traditionally submitted by a single physician to treat multiple patients.
- b. The investigational product may or may not be under development for marketing.

Treatment IND/Protocol

A treatment IND (21 CFR 312.34 and 312.35) is a mechanism for providing eligible subjects with investigational drugs for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments.

A treatment IND may be granted after sufficient data have been collected to show that the drug "may be effective" and does not have unreasonable risks. Data related to safety and side effects are collected, treatment INDs also serve to expand the body of knowledge about the drug.

There are four requirements that must be met before a treatment IND can be issued:

1. The drug is intended to treat a serious or immediately life-threatening disease.

2. There is no satisfactory alternative treatment available.
3. The drug is already under investigation, or trials have been completed.
4. The trial sponsor is actively pursuing marketing approval.

A sponsor may apply for a waiver of local IRB review under a treatment IND, if justified to be in the best interest of the subjects and if a satisfactory alternate mechanism for assuring the protection of human subjects is available (i.e. review by a central IRB). Such a waiver does not apply to the informed consent requirement. An IRB may still opt to review a study even if FDA has granted a waiver.

It is also possible for a treatment protocol to be submitted under an existing IND for that investigational product. The same requirements are required for a treatment protocol.

Treatment INDs and treatment protocols should be submitted to the IRB in CHERP as New Research Activity.

Sponsor-Investigators Holding Patient Expanded Access INDs Responsibilities

A **Sponsor-Investigator** is responsible for all requirements as both a sponsor and an investigator. Regulatory responsibilities for investigators and sponsors are detailed in 21 CFR 312 subpart D.

Dispensing and Storage of Investigational Drugs and Drugs Used in Expanded Access Mechanisms

All investigational drugs and drugs used for expanded access must be stored and dispensed from the pharmacy and used only under the direct supervision of the Principal Investigator (PI).

1. Investigational drugs must be shipped to the pharmacy and should not be stored in offices and clinic areas.
2. In all cases where study drugs are to be dispensed, the PI or a designee must contact the Pharmacy's Investigational Drug Study Service (ext. 2014 or 6803) to plan for:
 - a. shipping location
 - b. storage
 - c. dispensing instructions
 - d. compounding, blinding procedures
 - e. record keeping
 - f. other areas of pharmacy involvement.

Procedures

Individual Patient Expanded Access Investigational New Drug (IND) Application Process

FDA Submission

An individual patient can access an investigational drug/biologic through either:

1. An individual patient expanded access protocol that is submitted to an existing IND for that drug/biologic or
2. Through an individual patient expanded access IND.

Individual patient expanded access INDs are usually submitted by the physician treating the patient, and therefore, that physician becomes an IND holder.

In either case, an emergency protocol/IND can be submitted and granted by the FDA in situations where the patient needs to be treated before a written submission can be made and reviewed under the traditional 30-day review timeframe.

The Individual Patient Expanded Access IND application must contain:

- a. **FDA Form 3926:** This form includes questions where the physician must describe the clinical history of the patient and proposed treatment plan. It is possible to attach a separate document if more information is needed.
- b. **Physician qualification statement:** This information is usually provided in the format of the physician's curriculum vitae and medical license.
- c. **Letter of Authorization:** An IND traditionally requires information about the toxicology studies and manufacturing information about the investigational product.
 - a. A Letter of Authorization signed by the manufacturer enables the FDA to cross-reference the Drug Master File, rather than having the physician resubmit information.
 - b. Usually, a Drug Master File by the manufacturer of the investigational product has been submitted to the FDA

Information to be submitted with the IRB Application:

Whenever possible, the IRB requests a research protocol submission before the use of an investigational product. This request can be submitted in CHERP, using the Individual Patient Expanded Access form.

This form will ask for:

- a. A description of the clinical history
- b. Treatment plan of the patient
- c. Any documentation available from the FDA
- d. Written consent form.

It is also possible for treatment with an investigational product to begin prior to authorization from the IRB. This is in situations where there is not sufficient time to obtain IRB approval. If this occurs, the use of the investigational product must be reported to the IRB within 5 working days of the treatment initiation. This can also be reported in CHERP with the Individual Patient Expanded Access form.

Related Content

- U.S. Food & Drug Administration
 - 21 CFR.312: Investigational New Drug Applications
 - **FDA Form 3926**
- Massachusetts General Law
 - Chapter 94C Section 8: Research projects and studies
- IRB Policy
 - Drugs, Biologics, and Dietary Supplements
 - Requirements for Investigators Who are Also Considered Sponsors of New Drugs
- Boston Children's Hospital Guidance
 - [Office of Regulatory Affairs: Regulatory Resources](#)

Approval Signatures

Step Description

Approver

Date

Applicability

Boston Children's Hospital- Policies & Procedures