Guidance on Expanded Access and Emergency Use

Overview

This document is intended to serve as a guidance to assist physicians in following the appropriate regulatory pathways to provide patients with serious or life-threatening conditions with access to *investigational* (unapproved) products (drugs, biologics, and devices) for the purposes of treatment when FDA-approved treatments are not working or not available and when the patient is not eligible or able to participate in a clinical trial. These uses of investigational products (referred to generally as expanded access) are regulated and require IRB oversight. There are different pathways for these therapeutic uses of investigational products and different mechanisms for drugs and biologics and for devices that will be described in this document. Please note that these uses are not the same as the "off label" use of an *approved* drug, device, or biologic.

This document provides an overview of definitions and descriptions of the various mechanisms for therapeutic use of investigational products, including expanded access and emergency use with instructions on how regulatory approval should be managed in these situations. These provisions provide support for a physician to treat a patient using investigational products that would otherwise be inaccessible. Contrary to common usage, the terms "emergency use," "compassionate use," and "expanded access" are not synonymous, and each has specific, separate standards that will be described in this document.

Finally, because the investigational products have not yet been approved by FDA as generally safe and effective, it is important to remember that the product may not be effective and there may be unexpected serious adverse effects and to take appropriate measures to ensure that this is understood by the patient or their representative and to monitor for safety.

What is expanded access?

Investigational drugs, biologics, and devices regulated by the FDA may normally only be used in human subjects through an approved clinical trial in which the subjects meet prescribed criteria following an approved protocol by a clinical investigator. The use of an investigational drug or biologic by a patient as part of a clinical trial is preferable because clinical trials can generate data about safety and efficacy that can lead to approval and wider availability. However, when patient enrollment in a clinical trial is not possible, a physician may be in a situation with a patient in which an investigational product may help save a life or relieve suffering when there is no effective alternative therapy.

Expanded access involves regulatory pathways for the therapeutic use of unapproved investigational products available outside of clinical trials. These pathways have the following general requirements under FDA regulations:

- The use is required to diagnose or treat a serious or immediately life-threatening disease or condition as defined by the FDA;
- No comparable or satisfactory alternative is available;
- For drugs and biologics: The potential patient benefit justifies the potential risks and the treatment use and those potential risks are not unreasonable in the context of the disease or condition to be treated and providing 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 categories for widespread treatment, intermediate-sized patient groups, and single patients available as non-emergency use and emergency use;

- For devices: the device is under investigation in a controlled clinical trial for the same use under an approved IDE or clinical trials have been completed and the sponsor is pursuing marketing approval/clearance with due diligence.

What are the differences among expanded access, compassionate use, and emergency use?

Expanded access is the overarching category for access to unapproved investigational products available outside of clinical trials for therapeutic use. The other situations depend on what type of investigational product is used:

For investigational drugs and biologics, emergency use means that there is not sufficient time to obtain standard IRB review and approval before the drug must be used. There is no recognized concept of compassionate use for drugs and biologics by the FDA. If the use does not fit the criteria for emergency use, the physician must obtain standard IRB approval. Though emergency use exempts the physician from obtaining prospective IRB approval, an IND is required, and the FDA must be contacted prior to use.

For investigational devices, emergency use means that there is not sufficient time to obtain FDA approval (an IDE) before the device is used and prior IRB approval. Compassionate use of the device means that the use does not fit the criteria for emergency use and an IDE is required before the device can be used.

For criteria and processes for the emergency use of investigational products at Allina Health, please see the following documents: **Information Sheet for the Emergency Use of Investigational Drugs or Biologics** or **Information Sheet for the Emergency Use of Investigational Devices.**

Expanded Access for Non-Emergency Use of Drugs & Biologics

Allina Health requires that expanded access protocols are reviewed by the IRB at a convened meeting unless emergency use conditions permit an exemption from prospective review or if a physician submitting an individual patient expanded access IND selects the appropriate box on Form FDA 3926 to request a waiver of full IRB review. In the latter case, the protocol must be submitted to the IRB for Chair concurrence (see 14.7.1 in the Allina Health HRPP/IRB Standard Operating Procedures). Consult with the Research Integrity Director or IRB Manager to determine if the use of an external IRB for an expanded access protocol is acceptable in time-sensitive but not emergency use circumstances. In all other circumstances, the FDA requires a physician to obtain prior IRB approval for nonemergency expanded access mechanisms in addition to obtaining informed consent when using an investigational product for therapeutic use. Steps to supply an investigational product to patients outside of an ongoing clinical trial in non-emergent situations and/or for more than one use of an investigational product in one person at Allina Health:

- ☐ Contact the manufacturer for permission to use and to obtain the investigational product.
- ☐ Contact the FDA to obtain an expanded access IND or IDE under treatment protocol.
- ☐ Obtain IRB approval from the Allina IRB following the process in this guidance.
- ☐ Follow reporting and monitoring requirements based on the type of expanded access program.

Expanded Access for Non-Emergency Use of Devices (Compassionate Use)

Compassionate use refers to the use of an investigational *device* used to treat or diagnose an individual or small group of patients with a serious disease or condition with no available alternative options under FDA regulations. The compassionate use provision is a pathway to accessing investigational devices that have not received FDA approval or clearance when a physician believes the device may provide a benefit in diagnosing, monitoring, or treating a patient's disease or condition, however, compassionate use does not meet the definition of emergency use. The FDA describes the processes for approving Compassionate Use for individual patients and small group access. At Allina Health, the physician must obtain IRB approval or concurrence by the IRB Chair or designee before

treatment use begins. Notify the Allina Health IRB Office and create a submission in IRBNet following the procedures below.

IRB Submission Process for Expanded Access Protocols at Allina Health

Though expanded access is not research, the FDA considers expanded access a "clinical investigation" and the review requirements are similar to those of a new research submission. The following submission requirements are required regardless of whether obtaining chair concurrence or review at a convened IRB meeting, each is described with more detail on the Read Me First – IRBNet Researcher Guide available in the Forms & Templates Library on IRBNet (with parenthetical references to this document below):

- ☐ Create a new project submission in IRBNet selecting "Submission for Expedited or Convened (Full) IRB Review by Allina IRB" when completing Allina Health – Application Part 1
- ☐ Study Personnel Requirements including the Principal Investigator (PI)'s current CV, biosketch, or resume and CITI training (VI, 1a and 1b)
- ☐ Conflict of Interest Review is required (VI, 1c)
- ☐ Application Part 2: Expedited or Full Board Review (VI, 2b)
- ☐ HIPAA Authorization Form (VI, 2c)
- ☐ PI granted full access to the IRBNet project (VI, 2d)
- ☐ PI signature on the IRBNet package (I, 4 and VI, 2e)

If you have any questions about the information in this document, please contact the Allina Health IRB Office at 612-262-4920 or irb@allina.com and review the FDA resources listed below:

Resources

FDA Expanded Access Information (March 2021)

FDA Expanded Access Information for Physicians (September 2020)

FDA Expanded Access How to Submit a Request | Forms (September 2019)

FDA Expanded Access for Medical Devices (June 2019)

FDA Information Sheet: Emergency Use of an Investigational Drug or Biologic (January 1998)