



POINTS FOR PATIENTS TO CONSIDER:

Clinical Trials and/or Expanded Access to Experimental Drugs or Devices (Single Patient INDs or IDEs)



Clinical Research
PATHWAYS 

Opening Access. Advancing Treatments.



When you or a family member is diagnosed with a serious or life-threatening disease, you have choices to make about your treatment once standard treatment options are exhausted. Two important options are clinical trials and expanded access to experimental products. This document is intended as a quick reference guide to provide a simple, concise overview of these options. See the glossary at the end for definitions of terms with which you might not be familiar.

CLINICAL TRIALS

A clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes.

Why should I consider a clinical trial?

There are many reasons that patients consider enrolling in a clinical trial, such as:

- Standard treatments are no longer working.
- Standard treatments cause intolerable adverse effects.
- There are no approved therapies available.
- An investigational drug, biologic, or medical device is available that might help to supplement standard treatment.
- Your physician recommends a clinical trial.

Clinical trials are preferable to no treatment when there is no standard treatment available because patients who enroll in a trial are carefully monitored for their safety as well as for whether and how well the drug, biologic, or medical device is working. Be aware that clinical trials are designed to study a new drug, biologic, or medical device. This means that patients are randomly assigned to the experimental group (the investigational product) or to a control group (standard treatment or no treatment) in what is known

as a phase 3 trial—which is conducted when previous phases have shown positive results. You will have an equal chance of being in the experimental group or in a group that is receiving standard treatment or no treatment. In other words, you are not guaranteed to receive the experimental treatment.

How do I start the process to find a clinical trial?

Before you go too far in looking for a clinical trial, discuss your desire to enroll in a clinical trial with your physician. If your physician is unable to help you identify or enroll in a trial, he or she might be able to refer you to another physician who can help you.

How do I find out more about clinical trials?

Here are the most common options:

- Visit ClinicalTrials.gov.
- Contact the voluntary health organization that represents your disease.
- Ask your physician.

Ask lots of questions so that you fully understand the risks and potential benefits associated with the clinical trial. Be sure to ask about the costs—what your insurance company

will cover, what the company who sponsors the trial will cover, and what will be your out-of-pocket expenses.

Note: Companies (commercial sponsors and here called product manufacturers) that manufacture new drugs, biologics, or medical devices list their clinical trials of investigational products on [ClinicalTrials.gov](https://www.clinicaltrials.gov). You can search the site by disease and geographic region to see what clinical trials are being conducted for a disease or condition, and where.

Am I eligible to participate in a clinical trial?

Each clinical trial has specific qualifications for enrolling in the trial. These are called inclusion and exclusion criteria. To learn about eligibility for a specific clinical trial, visit [ClinicalTrials.gov](https://www.clinicaltrials.gov) and read the list of criteria. They can include:

- Age.
- Gender.
- Types and stage of a disease.
- Previous treatment history.
- Other medical conditions that you have.
- Your location relative to the trial site.
- Ability to follow the trial protocol.

The best way to determine if you are eligible and if you want to participate in a trial is to discuss the clinical trial with your physician, who knows your medical condition and can find out more to help you consider the trial.

You can find additional information about clinical trials at <https://www.fda.gov/ForPatients/ClinicalTrials/default.htm> or <https://clinicaltrials.gov/ct2/about-studies/learn>.



EXPANDED ACCESS

Sometimes, patients cannot wait for an investigational drug, biologic, or medical device to complete the approval process and have no standard options of treatment left. In these cases, patients may consider a special program that grants access to investigational products. Overseen by the U.S. Food and Drug Administration (FDA), the expanded access program (sometimes called compassionate use) involves investigational products—i.e., investigational new drugs (INDs) or investigational device exemptions (IDEs)—used outside of a clinical trial for the purpose of treatment, rather than research. Patients are not eligible for expanded access if they qualify and are able to participate in a clinical trial for their disease or condition.

There are two categories of expanded access, based on urgency. Emergency expanded access is available when a patient must be treated immediately and therefore there is not enough time for the treating physician to complete the paperwork that must be submitted to FDA. In these situations, FDA will determine that the treatment is an emergency and work with the physician to grant approval by telephone or fax. Most treatment situations fall into the other category, which is non-emergency expanded access, explained below. Even in non-emergency cases, every day is precious so it's important to understand the expanded access process to avoid delays.

Recently, a federal right-to-try law was passed that will create a second pathway to access investigational products. This pathway will be discussed at the end of the document.

Should I consider expanded access?

FDA regulates the use of investigational products outside of clinical trials. You can learn more about FDA's expanded access program at <https://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/ucm20080392.htm>.

You must meet the following requirements to qualify for expanded access:

- Your disease or condition is “serious or life-threatening.”***

A serious disease or condition is associated with illness that has substantial impact on day-to-day functioning. Short-lived and self-limiting illness will usually not be sufficient, but the illness need not be irreversible if it is persistent or recurrent. 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.

Life-threatening means a disease or condition where the likelihood of death is high unless the course of disease is interrupted.

- There is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition.***
- You cannot obtain the drug, biologic, or medical device under another IND or protocol. (This means that you are not eligible or able to enroll in a clinical trial. For example, you do not meet the inclusion criteria or you live too far from a trial site.)***
- The potential benefit to you justifies the risks of the treatment use and those risks are not unreasonable in the context of the disease or condition to be treated.***
- Providing the investigational drug 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.***

You can use [ClinicalTrials.gov](https://clinicaltrials.gov) to see what products are in development, where study sites are located, and whether you qualify for a clinical trial. If the company has an expanded access program for a product in which you are interested, it will likely be listed on the site. You can use “Advanced Search” to search for expanded access programs under “Study type.”

In addition to considering whether you are eligible for expanded access, you should consider the costs both in terms of the time it takes to receive all the necessary approvals and the expenses. Insurance companies and Medicare generally do not reimburse for experimental treatments. Although companies typically do not charge for the experimental product, they are permitted to charge the direct costs if approved by FDA. Hospital and physician expenses are likely to be your responsibility. Explore what expenses will be your responsibility as you decide whether to seek an expanded access treatment use.

For approval, there are four steps, involving the following:

- 1) **Physician**
 - 2) **Product Manufacturer**
 - 3) **FDA**
 - 4) **IRB**
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In each case, you will need to get answers to the questions posed below.

1 Physician

Is the investigational (experimental) product a drug/biologic or a medical device?

If you are unsure what type of product you are seeking access for, ask your physician or contact the FDA Office of Health and Constituent Affairs online at patientaffairs@fda.hhs.gov or at 301-796-8460.

This is an important first step because FDA regulations and the approval process for access

are different for drugs and biologics versus medical devices. Further, if you are seeking treatment involving a medical device and there is no IDE, you might be able to access the product under the FDA regulations for humanitarian use device.

Will my physician agree to treat me with the investigational product?

Your physician or another physician must agree to request the treatment involving the investigational drug, biologic, or medical device because only a licensed physician may apply to the product manufacturer (commercial sponsor) and FDA for expanded access. Treatment with an investigational product must be supervised by a licensed physician.

First, talk with your physician about your desire to seek treatment under FDA's expanded access program and the product that you are interested in trying. If he or she agrees to treat you, then find out if your physician knows about the process to apply for expanded access. If not, you might have to work with your physician's staff to help them learn about the process. Your physician can learn more about the approval process at <https://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/ucm20080392.htm> or on the website of the Reagan-Udall Foundation for the FDA (<http://navigator.reaganudall.org>).

If your physician does not agree to treat you with the investigational product, you can try to find another physician who is willing to treat you.

2 Product Manufacturer

Does the product manufacturer (commercial sponsor) offer the investigational product under an expanded access program?

If your physician agrees to treat you with the investigational product, the next step is to seek approval from the company that manufactures the product. Companies are required to publicly post their expanded access policy. This does

not, however, mean they are required to provide access to their investigational products.

Information about which investigational products are available through an expanded access program can be found on the commercial sponsor's website. Search using terms such as "expanded access" or "compassionate use." The website will also describe how your physician requests a single-patient use from the company.

You may also find a company's expanded access policy posted on the Reagan-Udall Foundation for FDA's Expanded Access Navigator Company Directory. Companies with active expanded access programs usually list their programs on <https://clinicaltrials.gov/> as well. Use Advanced Search and select "Expanded Access Studies" under the "Study type" drop-down menu.

Will the product manufacturer/commercial sponsor approve the single patient expanded access request?

Approval by the commercial sponsor is the next step in the approval process after you and your physician decide expanded access is an option for you. Your physician must make the request to the company; you cannot do this.

The commercial sponsor must agree to the use and to supply the investigational product before FDA can act on the request. Your physician must follow the company's instructions for submitting a request (usually available on the company's website). If the company agrees to provide its product, the company will provide your physician with a Letter of Authorization (LOA), which your physician will submit to FDA indicating that the company is allowing the expanded access use.



3 FDA

Will FDA approve the single-patient request?

To request FDA approval, your physician must submit Form 3926 when requesting an investigational drug or biologic, describing:

- Your medical history.
- Current medical status.
- Rationale for use of the investigational product.
- Any available supplementary information about the investigational product's safety and efficacy.
- The LOA is also submitted as part of the application.

To request FDA approval for access to an investigational medical device, your physician must submit a treatment plan that includes the same type of information. Form 3926 may only be used when requesting access to drugs or biologics.

The LOA is also submitted as part of the application.

For information about the FDA process for submitting a request, your physician should refer to the FDA website providing Expanded Access Information for Physicians.

FDA generally reviews requests within a few days of receiving them and approves more than 99 percent of requests.

4 IRB

Will an IRB approve the single patient request?

IRB review is the final step. Ask your physician if there is an IRB (institutional review board) that he or she uses. If not, contact Clinical Research Pathways at info@clinicalresearchpathways.org to find an IRB that can review the expanded access request for your physician at no charge.



An IRB is a committee that reviews research (clinical trials) proposals to ensure that participants are protected. IRBs perform a similar function for expanded access. For these requests, an IRB determines that patients are not exposed to unreasonable risks, and that the treatment has some likelihood of being successful for the patient. The IRB also reviews the informed consent process and document, and ensures that the patient is informed about the known risks and told that there might be unknown risks, potential benefits of the treatment use, and alternatives that might be available to the patient.

Most large IRBs are aware of FDA's expanded access program and review requests within a few days.

What happens after all the approvals are obtained?

Once your physician has obtained approvals from the product manufacturer, FDA, and IRB, your physician should notify the product manufacturer so that the product can be shipped to your physician. Once the product is received, treatment may begin.

RIGHT-TO-TRY LEGISLATION

On May 29, 2018, a new federal law went into effect, creating an alternative pathway for patients to obtain access to investigational products outside of a clinical trial. The law is called the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017.

Under this law, patients with life-threatening diseases or conditions may obtain access to investigational drugs or biologics that are not approved, are in the clinical trial approval process, and have completed the phase 1 clinical trial. As with the current expanded access process, your physician must agree to the treatment use, certify that you meet the conditions for treatment, and obtain your written consent. The physician must also obtain approval from the product manufacturer. What's different is that the new law exempts the requirements for FDA and IRB approvals before treatment is permitted. Note, though, that your physician or the product manufacturer may still request that FDA and an IRB approve the treatment use.

GENERAL RESEARCH TERMS

Clinical trial: Refers to research on promising new therapies or procedures involving people. Clinical trials are conducted in phases. During a trial, more information is gained about an experimental treatment, its risks, and its efficacy (how well it works). Some studies involve promising new treatments that may directly benefit participants. Others do not directly benefit participants but may help scientists learn better ways to help future patients.

Expanded access: Sometimes referred to as “compassionate use” or “pre-approval access,” this process allows the use, in limited circumstances, of unapproved investigational products, outside of a clinical trial for the purpose of treatment. You can learn more about expanded access on the FDA website.

Human participants: Also called human subjects. These terms refer to individuals who enroll in studies who receive specific interventions according to the research plan or protocol created by the investigators. Interventions may involve medical products, such as drugs, biologics, or medical devices; procedures; or changes to participants’ behavior, such as diet. Clinical trials may compare a new medical product or approach to a standard one that is already available, to a placebo that contains no active ingredients, or to no intervention. Some clinical trials compare interventions that are already available to each other. When a new product or approach is being studied, it is not usually known whether it will be helpful, harmful, or no different than available alternatives (including no intervention). The investigators try to determine the safety and efficacy of the intervention by measuring certain outcomes (endpoints) in the participants. For example, investigators may give a drug or treatment to participants who have high blood pressure to see whether their blood pressure decreases.

IRB: Stands for “institutional review board,” a group that has been formally designated to review and monitor research involving human participants. Though primarily involved in clinical trials, because expanded access involves investigational medical products, FDA requires IRB review and approval before treatment can begin. This group review serves an important role in the protection of the rights, safety, and welfare of people who participate in research studies, both in advance and by periodic review. IRBs review research protocols and related materials (e.g., informed consent documents). The IRB must monitor and review a study throughout its duration. A study may not begin until it is approved by an IRB. For single-patient expanded access, the IRB chair or a designee who serves on the IRB may review the request.

Products Regulated by Food and Drug Administration (FDA)

Drug: A chemical used to treat, cure, prevent, or diagnose a disease or to promote well-being. Drugs are metabolized in the body. They may be used for a limited duration or on a regular basis for chronic disorders. Unapproved drugs that are tested in clinical trials are called investigational new drugs. Because unapproved investigational drugs cannot be shipped for sale via interstate commerce, they are shipped under an “investigational new drug application” (IND) for the purpose of research or expanded access treatment.

Biologics: Products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins that are isolated from a variety of natural sources—human, animal, or microorganism—and include gene-based and cellular therapies. Biologics are complex mixtures. They are sometimes referred to as “large molecule” products. By contrast, most conventional drugs (sometimes referred to as small molecule products) are chemically synthesized. Unapproved biologics that are tested in clinical trials are called INDs.

Medical device: An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent (or other similar or related article) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease in humans or other animals, or intended to affect the structure or any function of the body of humans or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes. Unapproved devices that are tested in clinical trials are called investigational device exemptions (IDEs).

QUESTIONS? MORE INFORMATION?

Please contact Clinical Research Pathways at info@clinicalresearchpathways.org.

About Clinical Research Pathways: Clinical Research Pathways works to improve health and well-being for all by creating pathways to new medicines. The 501(c)(3) organization develops programs that increase diversity in research and expand access to experimental drugs. By opening access and advancing treatments, Clinical Research Pathways helps make new, effective medicines available to the public. For more information, go to www.clinicalresearchpathways.org. To sign up to receive news, go to: <http://clinicalresearchpathways.org/news-and-blog/sign-up-to-receive-news/>