

# Considering the Clinical Trial Option



## Learning Objectives

**After reading this Guide, you will be able to:**

- Approach the prospect of clinical trial with a better sense of what is involved
- Reflect on what is important to you and your family as you consider enrolling in a trial

## Introduction

Very few families are prepared for the news that a child has a rare and/or life-threatening condition. You likely feel that you have been plunged into a bewildering, overwhelming new world. In this new reality, you probably feel pressure to quickly absorb information and make critical decisions that may affect not just your child but your entire family unit.

Many children are living with rare conditions for which there are not yet treatments. Fortunately, the evolving landscape of potential new therapies and associated clinical trials offers great hope. But, like all of the other topics that may require your attention, the prospect of clinical trial comes along with the need to learn many new terms and concepts, some complicated decision-making, and the potential for disappointment and grief. Advocating for your child is both a privilege and a great responsibility. The more you understand about clinical trials, the better equipped you will be to navigate this landscape.

## Why Consider Participating in a Clinical Trial?

The answer to this question may seem obvious to you. A parent seeks to enroll their child in a clinical trial with the hope of a cure or, at the very least, improvement in their child's condition. However, whether your participation is through an actual trial, a natural history study, or adding your child to a patient registry, **your participation also helps advance science, build stronger communities, and impact the lives of children with serious illness.** In other words, there are many ways in which your participation, whatever the outcome of the research, can help.

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As you consider clinical trial you may encounter strong opinions. The Principal Investigator (PI) may urge you to enroll. You, your pediatrician, specialists or even family members may have concerns about the potential risks. The decision is yours, and yours alone, to make; there is no one way, no right way. Keep in mind that even if you wish to participate in a trial, you are not in complete control—because admission to a trial involves a rigorous process involving researchers, industry and regulators like the FDA that have the final say.

## Goals of the Clinical Trial

Before a clinical trial begins, the anticipated or hoped for outcomes or benefits from a treatment or drug are identified. These are called **endpoints**. These endpoints are part of the clinical trial protocol or study design. Endpoints must be objectively measurable to determine if the treatment or drug being tested is safe and beneficial to patients.

Some examples of endpoints are:

- Reduction in pain
- Oxygen level in the blood
- Ability to complete a physical task

While determining the clinical trial protocol and defining the outcomes, researchers diligently try to determine realistic, valuable, measurable endpoints and predict outcomes supported by preclinical data. However, a clinical trial is by nature an experiment. Scientists are testing something they have not tried before and so the actual outcomes, those determined when the trial has concluded, are not always what they predicted or what families who participate hoped for.

The ultimate goal of any clinical trial is to show that the drug or treatment has **efficacy**, which is a **measure** of how well a drug or treatment achieves its aim. Think of it as the ability to get the job done satisfactorily resulting in sufficient beneficial effects.

As you consider participating in a trial, it is important to understand the endpoints and outcomes as identified. It is equally as important for you to explore how you will feel if the actual outcomes are different from those predicted. Think about answering the question, “How will I feel, if this treatment does not help my child in a significant way?”

## Trial Phases

At every phase, the goal is to determine if a treatment or drug is both **safe** and **effective** for humans.

In addition, each phase has specific goals and asks different questions. Each builds upon what was learned in the earlier phase(s) and plays a key role in determining if the drug or treatment will become approved by a regulatory body and be made available for patients.

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There are typically **four phases** of clinical trials.

### Phase I

Validates how and where the treatment distributes in the body, and tests to ensure that the treatment is **safe in humans**. Phase I includes a very limited number of patients and often involves a low dose level of the treatment being tested.

### Phase II

Expands the number of patients receiving the treatment, and often is used to determine the most **efficacious, or effective**, dose level while still monitoring for safety. In some cases, the early phases (I/II) may be combined.

### Phase III

Further expands the number of trial participants to determine that the treatment would be safe and effective for a **wide variety of people**. Phase III sometimes also involves a control group.

### Phase IV

Tracks and evaluates **longer-term effects**, including potentially serious adverse events, after the treatment has been approved by the FDA. Often referred to as post-market surveillance (PMS).

The clinical research or trial process can take many years--on average, eight years. Many patients and their families feel frustration at this timeframe, especially for those conditions that progress rapidly and when time feels especially precious. Thus, it is often the protocols of a clinical trial that cause patients and families the greatest frustration. Understanding how and why these protocols exist can help lessen the frustration and increase your confidence in the clinical trial process. The Principal Investigator is responsible for responding to your questions.

It is important and helpful to remember that every medication currently available to patients passed through this critical learning process. The process is designed to keep patients safe.

## How Clinical Trials are Organized

There are five key players (organizations or individuals) involved in the clinical trial process:

- Regulatory bodies, such as the **US Food and Drug Administration (FDA)**. These agencies ensure that safe and effective drugs are available to improve people's health.
- The **Institutional Review Board (IRB)**, an independent committee responsible for reviewing the clinical trial design or protocols before the trial begins. It is the IRB's role to make sure the protocol protects the rights of the participants and that the trial is being done in a safe and ethical manner. The IRB also monitors the progress of the trial while it is underway.

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- The **Sponsor** of a clinical trial is an individual, company, institution, or organization that takes responsibility for the management and financing of the trial. It is typically the sponsor's responsibility to move the trial through the IRB, work with the FDA, and pay for the costs of the trial.
- The **Principal Investigator (PI)** is the physician, or a qualified individual supervised by a physician, responsible for conducting the clinical trial. The Principal Investigator reviews all the details about the trial with you, including the possible risks and potential benefits.
- The **Study or Research Coordinator** works under the direction of the Principal Investigator to facilitate and coordinate the daily clinical trial activities, such as appointments, scheduling tests, and conducting screening calls and visits.

Each clinical trial has a unique protocol or study design/plan that is determined by the Principal Investigator (often with input from the Sponsor) and approved by the FDA before the clinical trial can begin. The protocol typically includes:

- Who qualifies to participate in the trial (inclusion/exclusion criteria)
- The number of people that will participate in each phase of the trial
- How the drug or treatment will be administered to the patient
- At what dose level the drug or treatment will be delivered to the patient
- How long the trial will last
- If the trial will include a control or placebo group
- What data will be collected and when; the methods for collecting and how the data will be analyzed

A Phase I trial focuses primarily on the safety of the drug or treatment; thus, a lower dose of the drug may be part of the protocol. Once safety has been established, a later phase trial may include a higher dose that researchers think may be more effective or beneficial to patients. For gene therapy treatments, where the patient usually receives the treatment one time, the dosage level question is just one part of what makes the decision-making more complicated.

An **arm** of a clinical trial is a group of patients within the trial design who receive a specific treatment. The arm is also sometimes called a cohort. Some trials involve different arms or **cohorts**, so that researchers can compare medical outcomes between the groups to better measure the benefit or effectiveness of the treatment.

One of the most common groups is a placebo arm. If a trial includes a placebo arm, it is called a placebo-controlled trial. In a placebo-controlled trial, one group of patients receives the drug being tested (the treatment group) and the other group receives an inactive or placebo drug, often called a "sugar pill" (the control group). For both groups, the treatment is administered in the same way and therefore, in a placebo-controlled trial, the participants do not know their assigned group or arm. The people administering the drug or placebo also may not know. This helps researchers make the best comparisons between the groups.

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Some placebo-controlled trials will include a **rescue clause**, which allows for the administration of the drug or treatment to a patient in the placebo group if it is found that their condition is worsening during the trial. If a trial contains a rescue clause, it will be outlined in the Informed Consent documents you will be asked to review and sign (see below). In some cases, there is a crossover of patients initially selected to receive a placebo to eventually receive the therapy.

The inclusion of a placebo arm often troubles patients and families. Families may feel that they have wasted precious time and effort when after the trial they discover that their child has not been receiving the drug or treatment being tested. This disappointment and frustration is legitimate and understandable. But it is important to remember that at each step of a clinical trial something is learned. Participation in a placebo arm is a valuable and required part of the learning process.

In recent years, the FDA has allowed some investigational therapies to go forward without placebo control arms. This generally is true for diseases where there is a fairly rapid and consistent deterioration among affected children who are not treated.

Once all of the details and protocols of a US study are in place and have been approved by the regulatory agency, the trial and all the protocols are posted on [clinicaltrials.gov](https://clinicaltrials.gov). The Investigator then begins recruiting possible trial participants.

## The Trial Participation Recruitment and Selection Process

The process of finding participants for a trial is called **screening**. During the screening process, potential participants are evaluated to determine if they meet the **eligibility criteria**, which are the characteristics or factors that a participant must meet or be able to do in order to participate in the trial. The criteria help minimize risks and maximize success of the trial, by identifying a group of patients who are most likely to show a measurable benefit from the drug or treatment. The criteria are different for every trial.

Eligibility criteria can be broken down into two categories:

**Inclusion criteria** are the characteristics that a patient must meet in order to participate in a trial. In other words, the things a person must have so they can participate in a trial. Examples of inclusion criteria include:

- Falling within a particular age range (e.g., 6 months to 2 years old)
- The ability to complete a physical or cognitive test at a certain level

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**Exclusion criteria** are the characteristics that prevent a patient from participating in a trial. In other words, the things a person must not have or they cannot participate in a trial. Examples of exclusion criteria include:

- Having an allergy to the drug being tested
- Having a pre-existing condition that is different or separate from the condition or disease that is being treated/tested in the clinical trial. Called comorbidity, it is the presence of two chronic diseases or conditions in a patient

**Always remember that the goal of any trial is to bring a drug or treatment to market as safely and quickly as possible.** The eligibility criteria for each trial are designed for the trial to hopefully succeed. This may mean that the criteria for participation does not match your child's condition. The hard truth is that very few individuals will be given an opportunity to participate, especially in the early phases. There are good and practical reasons for this, but that does not change the emotional impact of the process on you and your family. It is a natural thing to desire every chance for your child and to advocate for them. However, remember that most of the clinical trial selection process is out of your control. If your child is excluded from a trial, it does not mean you have not been a good parent or advocate. Understanding how and why inclusion and exclusion criteria are established, and the critical role they play in the success of a trial, will hopefully help you come to accept and make peace with the design of the trial you have been considering.

It is also important to remember that each trial is unique and will have its own eligibility criteria, so participation in a different trial may be possible.

## Informed Consent

Probably the most important—and helpful—tool to support you in information-gathering and decision-making is **informed consent**. This is an agreement to participate in research. It is not just a document to be signed; it is a process during which the patient or their parent/guardian is walked through the study to get an understanding of the research, responsibilities, and risks. Review of the informed consent documents occurs during screening and before you have agreed to participate in the trial.

The research team (usually the Principal Investigator and Study Coordinator) will explain the key elements of the study and what participation will involve. They should review all of the planned procedures and the risks associated with each one. It is important to remember that at the start of a trial, it is not yet known if the new treatment or drug will be of benefit. Likewise, it may not be known if the new treatment or drug will cause side effects.

The informed consent document should outline all the logistical requirements for participation, including the number of site visits, if relocation to a study site is expected, and any financial responsibility you might face as a result of participating. The document should make clear that

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participating in clinical trials is voluntary and that you have the right not to participate, or to end your participation in the trial at any time. It will also include a statement informing you that the Sponsor or Principal Investigator may discontinue the trial at any time.

This is your opportunity to ask questions and make certain that you understand all of the possible benefits and potential risks of participation. You may wish to have a friend or relative accompany you to meet with the team, or to record the session. Do not feel rushed to sign the informed consent document. It is often long and will be written with legal terms. Take your time and read it carefully. You may wish to consult an attorney for guidance in understanding the language of informed consent. Only sign the document when you feel that you fully understand what is involved. This will make you more confident and comfortable with your decision to proceed.



CPN's printable [Guide to Informed Consent](https://courageousparentsnetwork.org/guides/guide-to-informed-consent/) offers questions to ask during the process of reviewing informed consent documents. <https://courageousparentsnetwork.org/guides/guide-to-informed-consent/>

## How Does a Parent Decide?

As a parent, you want to do anything possible to make your child's life better. This sense of responsibility can make navigating the landscape of a clinical trial very challenging and sometimes emotionally painful. It is important to anticipate that participating in a trial may have a wonderful outcome—and it may open up new ways to be disappointed and saddened. For example, there is the grief of not qualifying for the trial. This grief can feel especially mean and painful if the trial has opened after your child's condition has progressed past the point where they are able to meet the screening criteria. There is also the grief that can arise if the therapy does not have the desired effect.

Along the way there are many nuanced considerations. What if there are two affected children in a family, and only one qualifies for the trial? What if the expense of participating in the trial will deprive a sibling of the chance to pursue an important experience or goal? Or an adult the opportunity to advance in their career, possibly bringing greater financial stability to the family?

There are practical issues to consider as well. Participating in a clinical trial may have an impact on your life that goes beyond the medical changes it will bring for your child. Many clinical trials require long-distance travel and being away from home for long periods of time. Participating may mean that you have to spend a significant amount of time apart from your partner or other children, your extended family and friends—possibly even relocating for a period of time.

## Questions to Ask

Some questions to guide your thinking might include:

- What are your personal goals for your child and family—to have more time with your child? To manage symptoms?

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- How great is your sense of urgency?
- How will you feel if you decide not to participate, and then your child is not eligible for a later phase of the trial?
- Do you believe that “something” is better than “nothing” for your child?
- Are there other ways to help your child that are not treatment-specific, but might be acceptably effective?



The CPN Guide [“Questions to Consider”](https://courageousparentsnetwork.org/guides/clinical-trial-unit-questions-to-consider) explores these questions and more.  
<https://courageousparentsnetwork.org/guides/clinical-trial-unit-questions-to-consider>

## Feeling Confident with Your Choice

Courageous Parents Network does not presume to know what will help you find your way through this very personal process. You may wish to review these, and any other considerations you may have, with a trusted person: a provider on your child’s medical team, a therapist, chaplain, family member or friend. Devising a plan for how you could meet the requirements of the trial will help with the decision-making process and, if you decide to move forward, the participation period will be smoother thanks to your advance planning.

Finally, it is important to say that it is acceptable to conclude that the burden of participation will be too much and to decide not to participate. With time and space to really consider everything, you will know what is ultimately best for everyone. **The goal is to feel confident that whatever decision you make on your child’s behalf, you have done the best you can with the information you have, in a complex situation.**

## During the Trial and Beyond

It is not uncommon for families participating in clinical trials to feel unsure of their role or standing within their patient community. They may be faced with the reality that their child is improving while a peer’s condition is worsening. They may have feelings of guilt, and they may have to face (or sense) the anger and jealousy of others. A common response is to begin to withdraw from others. Many clinical trials include restrictions on sharing your experiences while you are participating in a trial, which may increase, or even worsen, the feeling of isolation.

These experiences are a natural by-product of the clinical trial experience, and they deserve to be acknowledged and addressed. Increasingly within patient disease groups involved in clinical trials, the Director of Family Services role can be a source of support.

If your child has participated in a trial, you and they are now in yet another uncharted territory. The introduction of a new drug or treatment may change the disease progression

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from one that is familiar to something unpredictable. On one hand, this is exciting. On the other hand, it can also be unnerving. It is hard not to have any visibility into what lies ahead.

This is where it is helpful to return to your original goals of participation. What was it that you had hoped for? An improvement in symptoms, greater comfort, a delay in disease progression, more time with your child? If you can focus on these things, it will help you feel that you are where you need to be and to live with the unknown.



## Conclusion

The prospect of participating in a clinical trial offers hope for the possibility to extend a life or even find a cure. But there are no guarantees. The process can lead to cause for celebration, as science advances in its understanding of disease. It can also lead to disappointment and even heartbreak.

Understanding the process itself is a first step toward making a decision that's right for your child and your family. Never hesitate to gather as much information as you can—from your medical team, from the researchers, and from other families you meet or whose stories you can view in this unit. The more you know, the better you will be able to navigate all that is involved in evaluating the clinical trial option.

## Related Resources



### Courageous Parents Network Section on Clinical Trial

This section is devoted to the lived experience of considering participation in a clinical trial.

<https://courageousparentsnetwork.org/medical-complexity/journey-topics/clinical-trial/>