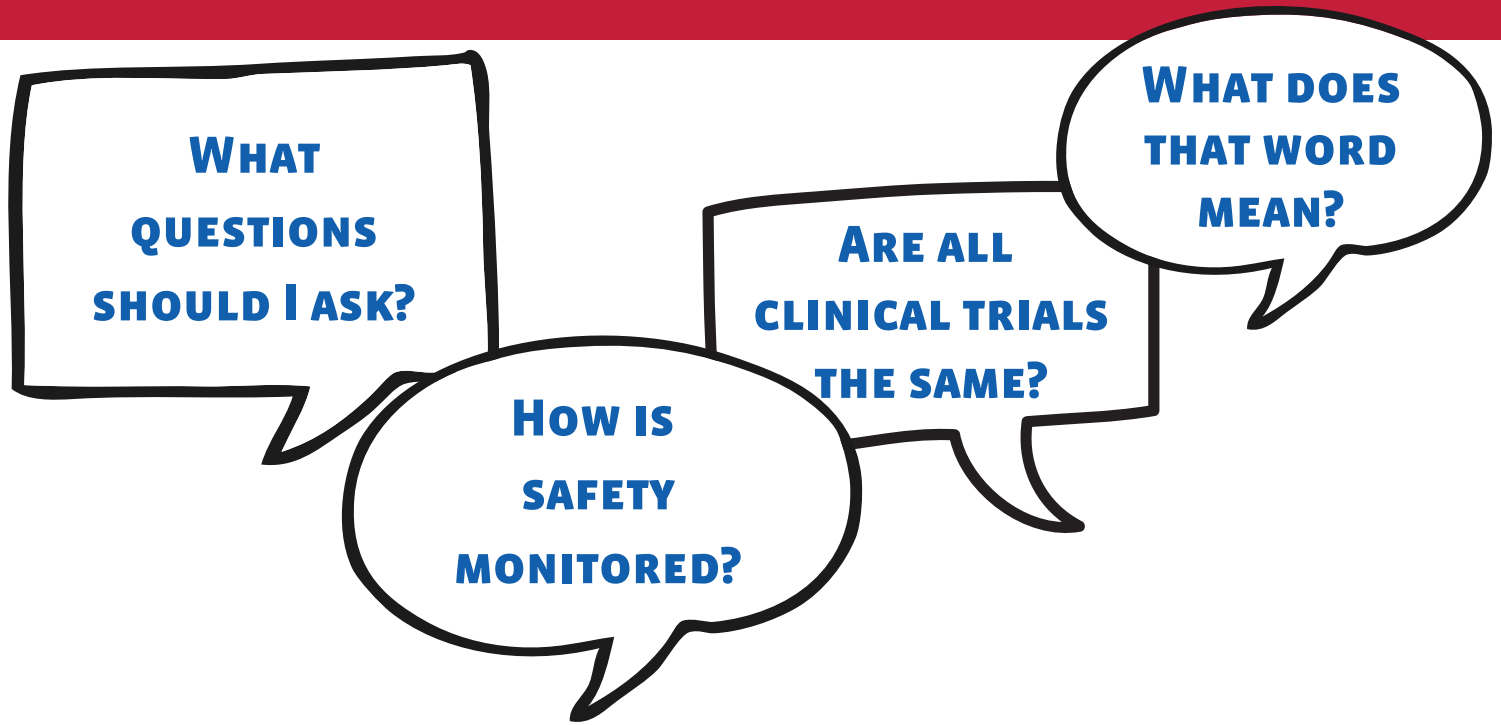
Clinical Trials 101:
A Guide for Participants



Are you considering enrolling in a

clinical trial for FA?

This guide will help!

FARA Friedreich's Ataxia Research Alliance

Clinical Trials : Introduction

Whether you are considering joining a clinical trial because you would like to play a more active role in your own health care, or to help researchers learn more about FA, or simply because there is no available treatment for FA yet, this guide will help you through this journey.

Who volunteers to take part in clinical trials?

- People of all ages can take part in clinical trials, including children.
- Each clinical trial will have specific criteria to define a suitable population for the questions being assessed in the trial.

Be informed!

- Understand what the trial is evaluating, your roles and responsibilities, how your safety is monitored, and know the terms.

Included Information:

- Drug Development Process
- Clinical Research: Explaining Trials vs. Studies
- Terms to Know
- Phases of Clinical Trials
- Safety Monitoring
- Etiquette: Do's & Don'ts for Clinical Trial Participants
- Informed Consent for Clinical Trials: A Companion's Guide for Participants & Parents

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What is the process for a drug to be approved?

TIMELINE

A drug or treatment only becomes available to the community after a long and complex process involving several steps.

On average, this process takes 12-15 years.

STOP

At any point, for any reason, the drug development program can be paused or cancelled.

A drug or a treatment is identified that might help people

Drug Development

For every 20,000 - 30,0000 compounds tested in this first step, only 1 is eventually approved

The drug or treatment is tested in laboratory and animal studies

Preclinical / Animal Studies

Regulatory agency reviews the preclinical studies and the proposed plan for human studies

Regulatory Evaluation

If the potential benefits appear to outweigh the risks, then clinical trials can be carried out on humans

(This packet focuses on clinical trials)

Clinical Trials

Only 10-20% of drugs that enter clinical trials get approved

If there is a clinical benefit, approval can be requested from the regulatory agency to market and sell the drug/treatment

Regulatory Approval

If approved, the focus is facilitating access to the drug. This is done through manufacturing, distribution, educating providers and working with health insurance/ payers

Access to Drug

This is an experimental process. The participants and the study team need to remain unbiased.
The outcome should remain objective and relevant to the intervention rather than to the perception of the parties.

EQUIPOISE

Each country has its own regulatory approval process. When a drug/ treatment is approved in one country, it does not mean that is will suddenly become available globally.

Global Access

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Sources: https://www.ema.europa.eu/en/from-lab-to-patient-timeline
https://pubmed.ncbi.nlm.nih.gov/3600702/
https://ascpt.onlinelibrary.wiley.com/doi/full/10.1111/cts.12980
https://www.fda.gov/drugs/information-consumers-and-patients-drugs/fda-drug-approval-process-infographic-horizontal

What does that word mean?

Clinical Research: Trial vs. Study

Clinical Trial

- Interventional
- Involves testing a drug / treatment / device
- Typically cannot participate in more than one clinical TRIAL at a time
- This packet is focused primarily on Clinical Trials

OR

Clinical Study

- Observational
- Includes:
  - Biomarker Studies
  - Natural History Studies
- Describing / measuring / observing the disease
- No intervention is being tested: no drugs, no treatments, no devices
- Informed Consent still applies
- Can evaluate a single point in time or over the course of time (longitudinal)

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Clinical Trials: Terms to Know

What does that word mean?

Trial Design Terms

Cohort
A group of people who participate in the study together. They may be in different study arms but the same cohort.

Crossover
Participants who receive placebo initially but have access to treatment later in the trial.

Delayed Start
Individuals either get randomized to treatment at the outset of the study or delayed to a specified time.

Double-Blind
All participants, investigators, health care providers, and sponsors are unaware of which study arm the participant is in. None of them know which treatment a participant is receiving.

Open Label
Participants, investigators, and health care providers are all aware of which treatment the participant is being given.

Placebo-Controlled
There are two (or more) groups (Study Arms). One group gets the active treatment, the other gets the placebo. Everything else is the same between the two groups. Any difference in outcome measures or safety is attributed to the active treatment.

Randomized
An experimental study in which people are allocated to study arms randomly. Reduces bias.

Study Arm
Each agent of treatment (or placebo) is a Study Arm. Examples of Study Arms: Placebo, Low-Dose, High-Dose.

Common Terms

Adverse Events
An unexpected medical problem that happens during a trial.
May be mild, moderate, or severe.
May be caused by something other than the drug or therapy being given.

Bio-markers
Characteristics that can be accurately and reproducibly measured. It can be an indicator of normal biological processes or it can be an indicator of disease status / progression.

Efficacy
Effectiveness. The ability of a drug or treatment to produce an effect.

Endpoint
The planned measure(s) that are important for evaluating the safety or the effect of a treatment. Primary and secondary endpoints are defined before the trial begins.

Placebo
Placebo is a harmless substance that has no therapeutic effect. It is used as a control in testing new drugs.

Termination
Discontinuing a trial before completion.
Can be at a site or the entire study.
Can be the decision of the sponsor, site IRB, or regulatory agency.

Tolerability
The degree to which the adverse effects from a drug or treatment can be tolerated by participants.

Washout
A period of time that participants need to stop an ongoing treatment before becoming eligible for the trial or for the next part of the trial.

Withdrawal
An individual discontinuing participation in a trial.
The participant may choose to withdraw or the investigators may require the participant to stop.

Types of Studies

Observational
Collects information about current health status.
No drugs, interventions, or treatments.

Interventional
An experiment that tests if a new drug, device, intervention, or treatment is safe and/or effective.

First in Human
A Phase 1 trial when a new drug is tested in people for the first time.
The treatment would have been tested in cells and animals...but not yet in humans.
The very first dose is called the Sentinel Dose. The aim is to find the safe dose range.

SAD
Single Ascending Dose.
Participants in a cohort receive a dose, one time. If there are minimal side effects, a new cohort receives a single higher dose.

MAD
Multiple Ascending Dose.
Participants in a cohort receive a dose multiple times. If there are minimal side effects, a new cohort receives a higher dose multiple times.

Efficacy Study
Phase 2 or Phase 3.
Goal: Determine whether the drug works in treating a specific symptom.

Investigator Initiated Study
Physician or academic researcher initiates and conducts the study.
No industry sponsor.

Registration Study
Clinical trial intended to provide sufficient data to support the filing of an Approval with a regulatory agency.

Safety Study
Establishes safety in either the short- or long-term. Or, if a drug is being repurposed, confirms safety in targeted disease.

Are all clinical trials the same?

Phases of Clinical Trials

* "...the phase concept is a description and not a requirement,...the phases of drug development may overlap or be combined."
-EMA Guideline

Purpose: What are we trying to learn?

	Number of People	What are the Side Effects?	How does the body process the drug?	How much and how often should it be taken?	How effective is the drug?	Does the benefit outweigh the risk?	Are there side effects from long-term use?	Cost effectiveness & comparison to other drugs?
	Varies by study. Fewer participants with rare diseases.							
Phase 1 "First in Human"	Small Group May be Healthy or FA Participants	✓	✓	✓				
Phase 2	Mid-Size	✓	✓	✓	✓			
Phase 3	Large	✓			✓	✓	✓	
Regulatory Approval FDA, EMA, etc.								
Phase 4 (Post-marketing)	Varies					✓	✓	✓

New drug application submitted → Application reviewed by agency → If approved, available to people with FA

Timeline:

From the first in human dose until a drug is available in pharmacies around the world, the process can take many years or even decades.

Sources: https://www.fda.gov/patients/clinical-trials-what-patients-need-know/what-are-different-types-clinical-research; https://www.fda.gov/patients/drug-development-process/step-3-clinical-research#phases
https://www.ema.europa.eu/en/documents/scientific-guideline/ich-e-8-general-considerations-clinical-trials-step-5_en.pdf

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Safety Monitoring in Clinical Trials: Roles & Responsibilities

How is my safety monitored?

Clinical trials are experiments. Each study and each site will approach these safeguards differently.
Before agreeing to participate, it is the duty of the participant to ask questions and understand how safety will be addressed.

Study Sponsor

Before Enrollment

- Takes responsibility for and initiates the trial
- Creates a protocol, including guidelines for monitoring safety
- Sponsors are pharmaceutical companies, academic institutions or non-profit organizations

During the Study

- Communicates regularly with the Site Study Team
- If an "adverse event" is reported Study Sponsor's medical experts:
  - Review it in real time
  - Report it to the DSMB and Regulatory Agencies

Regulatory Agencies (FDA, EMA, etc.)

Before Enrollment

- Provides guidelines and advice for trial design and supervision for how drugs or gene therapies are to be tested in humans
- Reviews pre-clinical data to assess safety

During the Study

- Receives ongoing notifications from the Study Sponsor about safety concerns in the study ("adverse events")
- Provides regulatory oversight, including the ability to recommend pausing the study for serious safety concerns

IRB: Institutional Review Board Ethics Committee

Before Enrollment

- Each Site Study Team conducts their own institutional or ethics review
- Assures informed consent document clearly explains the study protocol and possible risks / benefits

During the Study

- Provides general oversight and monitoring
- Approves any changes to the study protocol that might occur throughout the study time period

Data Safety Monitoring Board (DSMB)

Before Enrollment

- Set up by Study Sponsor
- Includes clinical experts in both:
  - Friedreich's Ataxia
  - Safety monitoring
- Can include members from the FA community

During the Study

- Monitors and reviews all study data throughout the trial
- Recommends action if a safety risk is found
- NOTE: Adverse events do not necessarily result in stoppage of the study because they can range in degree of severity (e.g., mild nausea or headache versus organ damage)

Site Study Team

Before Enrollment

- Assesses health records of potential Participants
- Clinicians determine whether potential Participants can safely participate in the trial

During the Study

- Monitors Participants' health during the study
- Evaluates all reported concerns ("adverse events") and communicates with the IRB and Study Sponsor
- Can withdraw Participants from the study if there are safety concerns
- It's important for the Site Study Team & Participant to openly communicate throughout the trial

Participant's Role

Before Enrollment

- Listens closely to the protocol and risks / benefits during Informed Consent
- Asks questions or clarifies any information you read or are told by the study team - this is critically important!
- Refers to FARA's Companion's Guide to Informed Consent

During the Study

- Follows the study protocol, including:
  - Instructions for taking drug
  - Attending clinic visits
  - Undergoing agreed upon procedures
- Alerts the Site Study Team if there are any health and safety concerns
- Participation is voluntary

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Clinical Trial Etiquette: Do's & Don'ts

Are there things I should or shouldn't do?

	Do	Don't
 **Clinic Visits**	Understand the difference between clinical RESEARCH visits and clinical CARE visits.	Don't ask the Site Study Team to provide clinical care (e.g. start the process for a new wheelchair, etc.) at a research visit.
 **Talking about the Trial**	Share with family and friends that you've enrolled in a clinical trial.	If the trial is blinded, don't share how you think the drug / treatment is making you feel - even with the Site Study Team. This can jeopardize the integrity of the research.
 **Compliance**	Follow the protocol. If you have a question, call the site.	Don't assume. Don't conduct your own study within the study. Don't change your vitamins, etc. without speaking to the coordinator.
 **Follow-Through**	Understand the number of visits, the tests that will be done, and any other requirements that you'll be asked to fulfill.	Don't lose interest in the study before you've completed it. Participation is voluntary. If you choose to enroll, it's important to fully participate through the end of the trial (assuming no adverse events, etc.).
 **Good Will**	Share your concerns. If something is not as you expected, ask. Be resilient and patient with the process.	Don't get discouraged by logistical bumps in the road. Keep in mind that this is research. It might be the first time this test is being conducted, etc. There will be a learning curve, and you can be a part of making it better.

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To view our Informed Consent PDF
Please click the link below

Informed Consent for Clinical Trials: A Companion's Guide for Participants

Or use this URL: www.curefa.org/consent

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