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How to Participate in a Clinical Trial

This white paper describes how clinical trials are conducted, and the many ways volunteers can participate in them. We will begin with a practical definition of clinical trials, move on to a review of the costs associated with clinical drug development, and continue with a breakdown of the types of trials conducted by pharmaceutical companies. The prominent factors to be weighed when considering participation in a clinical trial will be analyzed by explaining some of the key benefits and risks associated with serving as a participant. We will conclude with an explanation of the rights you have as a human subject in a clinical trial, and we will describe how you can enroll as a clinical research subject.

Opioids are essential for pain management, but they also are associated with potential risks for abuse, overdose, and diversion.

Definition

Clinical trials are research studies involving human subjects that serve to test new drugs under development. It is through clinical trials that doctors, pharmaceutical companies, and regulatory agencies like the United States Food and Drug Administration (FDA) bring new, better, and safer medicines to market. Clinical trials are needed for prescription medications of all kinds, and are the foundation of the clinical development process that brings life-saving treatments to the medicine cabinets of patients worldwide – having a beneficial impact on human health, well-being, and life expectancy. Clinical trials are needed to determine the effectiveness and safety of medications, first by testing them in normal, healthy people and later extending the testing to people with medical illness. There are many steps involved in bringing a new drug from the chemist's bench to the patient's bedside. The most important of these steps is not related to drug discovery, chemistry, or manufacturing. It is related to the focus of this paper, the conduct of clinical trials.

500,000 new cases of morphine addiction were reported at the end of the Civil War.

Costs of Drug Development

According to industry reports, the pharmaceutical industry spent over $44 billion on research and development in 2007, with clinical development costs representing a large share of those expenses, over 60% of total research and development (R&D) costs. An analysis conducted in 2007 and reported by the Tufts Center for the Study of Drug Development shows that the combined cost of pre- clinical and clinical trials required to bring a drug to the market is over $1.2 billion. This expense includes the cost of drugs that fail to progress through the development pipeline as well as the costs associated with the drug that is approved. For every 5,000 drugs that are identified in discovery, only about 250 make it into pre-clinical studies, five into clinical studies, and ultimately only one becomes approved as a therapeutic product. This is a result of the very careful scientific work that is done to bring a drug through development, as well as the efforts of regulatory authorities to ensure that the approval process is a well- defined and controlled.

Opioids continue to be the most prescribed medication in the US, accounting for 202 million prescriptions in 2009.

Classifications of Trials

The process of drug development begins with the identification of about 5,000 new drugs, some of which then move into pre- clinical testing, and then some of those move to clinical development. Clinical drug development is divided into for "phases" known as Phase 1, Phase 2, Phase 3 and Phase 4. Drugs that successfully meet their development objectives may be approved for marketing by the FDA or other regulatory authorities outside of the US. The four phases of clinical drug development are described below: Phase 1.

In 2010, there were 2 million new initiates to nonmedicinal use of prescription opioids in the U.S.

Phase 1

- Researchers test an investigational drug or device in a small group of people, normally about 20-100 subjects. Usually these are normal, healthy volunteers. These studies are designed to determine the basic characteristics of the drug, how a drug is absorbed by the human body, how it is broken down, and how the drug itself is distributed and eliminated.
- These studies follow extensive pre-clinical tests that give researchers an idea of the proper amounts of medication that should be tested.
- Following pre- clinical work (work done in animals), medicines are now brought forward into phase 1 human subject testing to understand the characteristics of the drug and its effects on human subjects. We primarily want to assess drug safety.
- Phase 1 studies offer us an opportunity to learn about the types of adverse experiences or side effects that might be associated with a new medication and allows researchers to determine if that medication is safe and appropriate for further development or testing.

Phase 2

- An investigational drug is given to a larger group of around 100-500 people to evaluate the effectiveness of the drug for a particular indication; patients with the disease or condition are given the drug. If a drug was being tested for arthritis, for example, phase 1 testing would provide information about the drug's safety and the doses to carry forward, and in phase 2, a small group of people with arthritis would be studied to determine whether the drug looks to be effective and if it is now safe in the clinical population.
- Phase 2 studies also aim to further document common, short- term side effects and risks associated with the drug or device under evaluation. It is common for phase 2 studies to also identify outcomes that will later be assessed in larger clinical trials, known as pivotal trials or phase 3 studies. For example, when testing a new drug under development for the treatment of cancer, scientists have to make a decision up front about the outcome that they will look for to determine if a drug is effective. Is it the number of cancer cells that will determine the effectiveness of the drug? Is it the size of the tumor? Or is it some other measure? These phase 2 studies give pharmaceutical scientists insight into what they should be looking for as they carry that drug forward into a pivotal trial.
- Phase 2 also offers drug manufacturers an opportunity to determine the drug doses, or the amount of medication that will carry forward into phase 3 studies. It also gives the drug manufacturers a chance to weigh the trade- offs between increasing the effectiveness of the drug by increasing the dose of the medication that will be used and the potential side effects that could result from using that medication.

The term "controlled substance" refers to a drug or other substance included in any of these schedules.

Phase 3

- In phase 3 studies, drug manufacturers have an opportunity to document the effectiveness and safety of their drug products by testing them in large groups of 1,000-5,000. Studies conducted during phase 3 are intended to gather critical information regarding the overall benefit/risk profile of the drug in pateints, as well as provide an adequate basis for labeling. The label, which is also known as the “package insert” is the small print insert that goes into your drug package or that your pharmacist hands to you. These are the instructions that doctors, pharmacists and patients get about the proper use of the medication.
- By the time the drug enters into this phase of testing, its basic characteristics are well known and it’s therapeutic effects have been identified. Manufacturers who initiate phase 3 trials generally are confident that their products will be shown to be safe and effective. Ultimately they hope to win regulatory approval so that they can bring their product to market. Even though the odds of success for drug products at this level are much greater than when entering the clinical evaluation, only one out of five drugs that enter into phase 1 testing will successfully complete phase 3.

Phase 4

- Phase IV studies are done after a drug has been approved by a regulatory authority like the FDA. They are conducted to further clarify a drug’s effectiveness or safety or may be done to expose new or special patient populations to a drug. For example, a drug might be tested in the elderly or a drug might be tested in children in phase 4, in order to determine the therapeutic benefits of the medication in these so called “special populations.” There also are occasions when phase 4 trials might be used to provide additional information that would be included in the package of a drug.

Pre-participation

What should people consider when they are contemplating participation in a clinical trial? One of the first things to consider is why you might like to participate.

- Program related benefits, such as physical exams, blood work, and heart monitoring performing by expert clinicians often are a benefit of participation. However, keep in mind that the procedures performed are study-related and are different from what might be done in a regular doctors’ office. Are you prepared to participate in study-related assessments?
- Most clinical trials today offer compensation for participation. The rates paid for participation usually depend on what is called ”the subject burden”. That is, if the subject is to be paid, the amount of payment is dependent on the amount of effort or time that is required on the part of the research participant in order to complete the trial. If the subject burden is low, a low payment can be expected, perhaps as low as $25 or $50 for a visit. However, if the subject burden is high, as it may be for many phase 1 studies, the payment can be high, as much as several hundred or even several thousand dollars in some cases. Is compensation of interest to you?
- Clinical trials have a highly structured treatment protocol. What is a protocol? A protocol is a study plan that describes exactly what will be done in a trial. It describes the type of people that can participate in a trial, the testing and assessments that will be done, the procedures that will be performed, the medications and dosages that will be used, the length of the study, the number of visits, and when those visits will take place. These are all rules related to the clinical trial. It is important that the investigators who are conducting the clinical trials follow the rules, but it is also important for the research participant to understand the requirements and adhere to them. Are you able to adhere to a study protocol?

- People should understand that a clinical trial does not always mean treatment. This has to do with the way these studies are designed. There are some studies called "open label" studies where everyone knows what medication and what dose is being administered. The drug company knows, the doctor who is running the clinical trial knows, and the research participant knows. They are very straightforward and simple in this regard. In some cases there are studies done called single blind studies where the drug company and doctor know what is being administered but the research participant does not. Finally, double blind studies are where both the doctor and the research participant does not know what treatment condition the research participant has been put in. These double blind trials are very important in testing the effectiveness and safety of drugs because we know that when people know what condition they are in, that that can influence the outcome of a study. Will you be participating in an open label, single blind, or double blind study?
- Another aspect to clinical trials is placebo control. You might be in a placebo condition for part or all of the clinical trial. A placebo is an inactive treatment, sometimes called a sugar pill, which has no know biological action. If a doctor is testing drug X, he or she wants to see if improvement occurs over time with the drug, but they have to compare it against something. The doctor could compare it to the beginning of treatment. However, it is better to compare it against the placebo treatment over time so that they can show there is no substantial improvement with inactive treatment in comparision to the active drug. Are you prepared to possibly receive placebo as part of your study participation?

These studies are conducted on individuals who are not interested in receiving treatment for their addictions.

Benefits of Participation

This list is not all inclusive but it offers some main benefits that can accrue to a clinical trial participant:

- Access to healthcare services that one might not have access to otherwise. Participants often get physical exams, blood work, electrocardiograms or EKGs, or other services that normally cost hundreds of dollars. These are provided at no cost to the participant as part of participation in aclinical study. These services typically are provided by highly trained people, many of them are among the top in their field, so the level of clinical care is relatively high. Participants can get copies of these reports to go over with their own doctors. This kind of information sharing is encouraged.
- Patients also participate to gain exposure to new treatments under development, treatments that are not yet available on the open market. Study participants often gain access to medications that they otherwise would not be able to obtain. This might be of interest, for example, if someone has tried several available medications for a particular disorder and has not found a good result and wants to try to enter a trial to get exposed to a new medication that is in development.

"Labeling is the cornerstone of risk minimizing efforts for most of the drugs approved by the FDA." (FDA, 2010)

- Self-satisfaction also is among the benefits of trial participation. Self-satisfaction is being satisfied by oneself for making contribution to science and for advancing medicine through participation in a clinical trial. Clinical trial participants often are motivated and rewarded by the sense of satisfaction they gain.

- Some people are motivated purely by altruism; specifically if they want to do something selfless to help their fellow man. One recent participant of a clinical trial conducted at Clinilabs reported that she was motivated to participate because her father suffered quite terribly and ultimately passed away as a result of diabetes. She wanted to participate in a diabetes trial to prevent other families from going through the same heartache that her family went through. Sometimes, simply the desire to help others is a motivation to participate in a trial.
- Finally, financial compensation, being paid to participate in a trial, is a benefit to participation. The compenstation offered should be fair and reasonably related to the subject burden, but should never be "coercive." High levels of compensation might compel someone to participate in a clinical trial without appropriately considering all of the other benefits and risks.

Risks of Participation

There are potential risks that could happen to a clinical trial participant. This list is not all inclusive but it should give a sense of some of the negative factors that you should consider.

- The most notable risks are called adverse events. An adverse event is any kind of untoward event that occurs as a consequence or in association with clinical trial participation. An example of an adverse event might be an abnormal lab test or a lab test that was normal when being evaluated at the outset of participation and after starting the clinical trial, the lab test is found to be abnormal. That would be considered an adverse event.
- Another aspect to clinical trials is placebo control. You might be in a placebo condition for part or all of the clinical trial. A placebo is an inactive treatment, sometimes called a sugar pill, which has no know biological action. If a doctor is testing drug X, he or she wants to see if improvement occurs over time with the drug, but they have to compare it against something. The doctor could compare it to the beginning of treatment. However, it is better to compare it against the placebo treatment over time so that they can show there is no substantial improvement with inactive treatment in comparision to the active drug. Are you prepared to possibly receive placebo as part of your study participation?
- There also are adverse events that are considered serious; serious adverse events. These occur rarely in trials, but because they do occur they have to be a consideration for every clinical trial participant. Serious adverse events include: hospitalization or prolongation of hospitalization, a life threatening event, death, significant disability or even a birth defect. These serious adverse events are well defined by regulatory authorities and well understood by the doctors and investigators who participate in clinical trials as well as participants in the trial themselves.
- You have to consider that you may have a chance of getting a placebo. If you are looking for treatment for a health condition, keep in mind that by participating in a clinical trial there is a chance that you may not be in an active treatment condition and that you will receive an inactive treatment.
- Some trials involve the discontinuation of existing treatment, and this could create the potential for relapse. For example, if you were considering participating in a clinical trial for the treatment of depression, and you were currently using an anti-depression medication, you might have to discontinue the use of that medication for a period of several weeks so that you could start the clinical trial.
- Some people may feel uncomfortable that they have to enclose personal information.
- A clinical trial may require a number of visits to the doctor's office that could impose on a person's schedule. The trial also might require the participant to undergo many procedures, which can be time-consuming or unpleasant.

Volunteer Rights

Every research subject should know their rights. This is important for all people who are considering participating in a clinical trial. Every clinical study that is done in the United States must be reviewed by an Institutional Review Board (IRB) or ethics committee. This is a committee that reviews clinical trial protocols to consider if the value of the clinical information being obtained is in balance with risks that the subject might be exposed to, and the committee makes sure that human rights are being protected. In 1947, at the Nuremberg trials in Germany, there were some very clear standards set forth regarding the use of human subjects in clinical research. These rules and regulations were the result of atrocities that were committed during World War II under the guise of "research" – leading people around the world to be concerned about the rights of human subjects in research studies. From the Nuremberg trial, those rules were refined into a document called the Declaration of Helsinki, which is still in use today. These rules form the basis of how we regulate clinical trials and ensure the rights of people who participate in them. Everyone that participates in a trial must provide written informed consent, which means that the doctor involved in a clinical trial must explain everything to you orally, and give you a written document that explains everything that will be done in the conduct of that trial. The informed consent document must tell you about all of the benefits and the risks associated with participating. You must have the opportunity to read the informed consent document and ask questions about the study. When you have all of the information that you need to make a decision about participation, you must sign the document, and the investigator must countersign it showing that informed consent was obtained. All of this has to be done before any clinical trial activity can take place. In some cases it could be the doctor that explains this to you, a nurse or a member of the clinical staff, but the investigator who is responsible for that trial should be available to answer any questions that you have as a research participant. In addition to knowing what you are getting into at the outset of a trial, you have the right to withdraw at any time. You do not have to give a reason or explanation. If you do not want to participate, you have the right to withdraw. If you have questions and you are considering participating in a clinical trial, talk to the investigator and learn what your rights are and about the trial that you are signing up for.

How to Participate

- The best way to become a participant in a clinical trial is to sign up; virtually every research site that is involved in the conduct of clinical studies has a patient database.
- In New York or New Jersey, you can register at Clinilabs. When we have a new trial we are able to reach out to people who have registered and ask them if they are interested in participating. To register, visit us at Clinilabs.com/survey.
- Go to credible websites to get information about the clinical trials going on in your geographic area such as clinicaltrials.gov and centerwatch.com. For trials in New York or New Jersey you can go to Clinilabs.com/currentstudies.
- Talk to your doctor. Many doctors know about the clinical trials being conducted in their area.
- Search the internet using sites such as Craiglist.com, Backpage.com or other internet locations to gain information about the clinical trials that are being advertised there.
- Join online communities like Facebook or Twitter, which have groups that will publish information about clinical trials. You can do that with Clinilabs by searching in Facebook and Twitter on the keyword "Clinilabs".

Participate at Clinilabs

There are several ways you can participate in clinical trials at Clinilabs:

Questionnaire Assessment: If you would like to enroll as a volunteer in one of Clinilabs' studies, complete our online questionnaire by visiting www.clinilabs.com/survey.

Confidential Telephone Interview: Contact us between 9 A.M. and 5 P.M. Eastern Standard Time (EST).

- NY: (212) 994-4567
- NJ: (732) 720-6393

Walk-In: Visit Clinilabs at either of our locations between the hours of 9 A.M. and 4 P.M. EST.

- NY: 423 W. 55th Street, 4th Floor, Manhattan (Between 9th and 10th Avenues)
- NJ: 4 Industrial Way West, Eatontown, NJ

About Clinilabs, Inc.

Clinilabs is a full-service contract research organization (CRO) that specializes in early- phase studies, from first-in-human to end-of-Phase-II. We work with normal, healthy volunteers and patient populations, as well as specialty ethnic populations (e.g., Japanese). The company manages multicenter studies worldwide, and owns and operates two Phase I units in the U.S. Our network of highly qualified investigator sites provides sponsors with top performance for early phase studies. Specialty projects, including pharmacodynamics, biomarker, CNS, cardiovascular, cardiac safety, sleep/wakefulness, metabolic, and Japanese bridging are among our strengths. Clinilabs is recognized globally as a leading specialty CRO, offering a true alternative to large CROs. For more information, please visit www.clinilabs.com.