EXHIBIT 19

ClinicalTrials.gov
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Comment Period Extended to 3/23/2015 for Notice of Proposed Rulemaking (NPRM) for FDAAA 801 and NIH Draft Reporting Policy for NIH-Funded Trials

Learn About Clinical Studies

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What Is a Clinical Study?

A clinical study involves research using human volunteers (also called participants) that is intended to add to medical knowledge. There are two main types of clinical studies: clinical trials (also called interventional studies) and observational studies. ClinicalTrials.gov includes both interventional and observational studies.

Clinical Trials

In a clinical trial, participants receive specific interventions according to the research plan or protocol created by the investigators. These interventions may be medical products, such as drugs or devices; procedures; or changes to participants' behavior, such as diet. Clinical trials may compare a new medical 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 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.

Clinical trials used in drug development are sometimes described by phase. These phases are defined by the Food and Drug Administration (FDA).

Some people who are not eligible to participate in a clinical trial may be able to get experimental drugs or devices outside of a clinical trial through an Expanded Access Program. See more information on expanded access from the National Library of Medicine.

Observational Studies

In an observational study, investigators assess health outcomes in groups of participants according to a research plan or protocol. Participants may receive interventions (which can include medical products such as drugs or devices) or procedures as part of their routine medical care, but participants are not assigned to specific interventions by the investigator (as in a clinical trial). For example, investigators may observe a group of older adults to learn more about the effects of different lifestyles on cardiac health.

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Who Conducts Clinical Studies?

Every clinical study is led by a principal investigator, who is often a medical doctor. Clinical studies also have a research team that may include doctors, nurses, social workers, and other health care professionals.

Clinical studies can be sponsored, or funded, by pharmaceutical companies, academic medical centers, voluntary groups, and other organizations, in addition to Federal agencies such as the National Institutes of Health, the U.S. Department of Defense, and the U.S. Department of Veterans Affairs. Physicians, health care providers, and other individuals can also sponsor clinical research.

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Where Are Clinical Studies Conducted?

Clinical studies can take place in many locations, including hospitals, universities, doctors' offices, and community clinics. The location depends on who is conducting the study.

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How Long Do Clinical Studies Last?

The length of a clinical study varies depending on what is being studied. Participants are told how long the study will last before enrolling.

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Reasons for Conducting Clinical Studies

In general, clinical studies are designed to add to medical knowledge related to the treatment, diagnosis, and prevention of diseases or conditions. Some common reasons for conducting clinical studies include:

- Evaluating one or more interventions (for example, drugs, medical devices, approaches to surgery or radiation therapy) for treating a disease, syndrome, or condition
- Finding ways to prevent the initial development or recurrence of a disease or condition. These can include medicines, vaccines, or lifestyle changes, among other approaches.
- Evaluating one or more interventions aimed at identifying or diagnosing a particular disease or condition
- Examining methods for identifying a condition or the risk factors for that condition
- Exploring and measuring ways to improve the comfort and quality of life through supportive care for people with a chronic illness

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Participating in Clinical Studies

A clinical study is conducted according to a research plan known as the protocol. The protocol is designed to answer specific research questions and to safeguard the health of participants. It contains the following information:

- The reason for conducting the study
- Who may participate in the study (the eligibility criteria)
- The number of participants needed
- The schedule of tests, procedures, or drugs and their dosages
- The length of the study
- What information will be gathered about the participants

Who Can Participate in a Clinical Study?

Clinical studies have standards outlining who can participate, called eligibility criteria, which are listed in the protocol. Some research studies seek participants who have the illnesses or conditions that will be studied, other studies are looking for healthy participants, and some studies are limited to a predetermined group of people who are asked by researchers to enroll.

Eligibility. The factors that allow someone to participate in a clinical study are called inclusion criteria, and the factors that disqualify someone from participating are called exclusion criteria. These are based on things such as age, gender, the type and stage of a disease, previous treatment history, and other medical conditions.

How Are Participants Protected?

Informed consent is a process in which researchers provide potential and enrolled participants with information about a clinical study. This information helps people decide whether they want to enroll or continue to participate in the study. The informed consent process is intended to protect participants and should provide enough information for a person to understand the risks of, potential benefits of, and alternatives to the study. In addition to the informed consent document, the process may involve recruitment materials, verbal instructions, question-and-answer sessions, and activities to measure participant understanding. In general, a person must sign an informed consent document before joining a study to show that he or she was given information on risks, potential benefits, and alternatives and understands it. Signing the document and providing consent is not a contract. Participants may withdraw from a study at any time, even if the study is not over. See the Questions to Ask section on this page for questions to ask a health care provider or researcher about participating in a clinical study.

Institutional review boards. Each federally supported or conducted clinical study and each study of a drug, biological product, or medical device regulated by the FDA must be reviewed, approved, and monitored by an institutional review board (IRB). An IRB is made up of physicians, researchers, and members of the community. Its role is to make sure that the study is ethical and that the rights and welfare of participants are protected. This includes making sure that research risks are minimized and are reasonable in relation to any potential

benefits, among other things. The IRB also reviews the informed consent document.

In addition to being monitored by an IRB, some clinical studies are also monitored by data monitoring committees (also called data safety and monitoring boards).

Various Federal agencies, including the Office of Human Subjects Research Protection and the FDA, have the authority to determine whether sponsors of certain clinical studies are adequately protecting research participants.

Relationship to Usual Health Care

Typically participants continue to see their usual health care providers while enrolled in a clinical study. While most clinical studies provide participants with medical products or interventions related to the illness or condition being studied, they do not provide extended or complete health care. By having his or her usual health care provider work with the research team, the participant can make sure that the study protocol will not conflict with other medications or treatments being received.

Considerations for Participation

Participating in a clinical study contributes to medical knowledge. The results of these studies can make a difference in the care of future patients by providing information about the benefits and risks of therapeutic, preventative, or diagnostic products or interventions.

Clinical trials provide the basis for the development and marketing of new drugs, biological products, and medical devices. Sometimes, the safety and the effectiveness of the experimental approach or use may not be fully known at the time of the trial. Some trials may provide participants with the prospect of receiving direct medical benefits, while others do not. Most trials involve some risk of harm or injury to the participant, although it may not be greater than the risks related to routine medical care or disease progression. (For trials approved by IRBs, the IRB has decided that the risks of participation have been minimized and are reasonable in relation to anticipated benefits.) Many trials require participants to undergo additional procedures, tests, and assessments based on the study protocol. These will be described in the informed consent document for a particular trial. A potential participant should also discuss these issues with members of the research team and with his or her usual health care provider.

Questions to Ask

Anyone interested in participating in a clinical study should know as much as possible about the study and feel comfortable asking the research team questions about the study, the related procedures, and any expenses. The following questions might be helpful during such a discussion. Answers to some of these questions are provided in the informed consent document. Many of these questions are specific to clinical trials, but some also apply to observational studies.

- What is being studied?
- Why do researchers believe the intervention being tested might be effective? Why might it not be effective? Has it been tested before?
- What are the possible interventions that I might receive during the trial?
- How will it be determined which interventions I receive (for example, by chance)?
- Who will know which intervention I receive during the trial? Will I know? Will members of the research team know?
- How do the possible risks, side effects, and benefits of this trial compare with those of my current treatment?
- What will I have to do?
- What tests and procedures are involved?
- How often will I have to visit the hospital or clinic?
- Will hospitalization be required?
- How long will the study last?
- Who will pay for my participation?
- Will I be reimbursed for other expenses?
- What type of long-term follow-up care is part of this trial?
- If I benefit from the intervention, will I be allowed to continue receiving it after the trial ends?
- Will results of the study be provided to me?
- Who will oversee my medical care while I am participating in the trial?
- What are my options if I am injured during the study?

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