Clinical Trial Guidance

A clinical trial is a type of research study with human subjects. Clinical trials try to answer a research question about health related outcomes. Typically a clinical trial is a research study in which one or more human subjects are prospectively assigned to one or more interventions to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes. An intervention is the act of interfering with an outcome, course of action, treatment, condition, health related curriculum, or process in some way.

Clinical trials are the primary way that researchers find out if a new treatment, course of action, condition, process, or curriculum (like a new drug, diet, therapy, movement, or medical device is safe and effective in people). These studies are usually completed to add to knowledge (treatment, prevention, diagnosis, etc) of health related issues. Clinical trials involving drugs and devices have four phases (See Appendix B).

How do you know if your protocol is a clinical trial?

There are four requirements:

1. Your research involves living humans
2. You assign a participant to one of your protocol’s groups: control or intervention
   a. A control group does not get the intervention you’re researching.
   b. The intervention group does try the intervention being researched.
   c. Some researchers add more groups beyond the two (control and intervention) to see if variations in the interventional protocol might work, but this is not a requirement of qualifying as a clinical trial.
3. Your research is designed to evaluate the effects of the intervention on health outcomes
4. The intervention that you’re assessing must focus on health-related outcomes. Health outcomes can be physical or behavioral.
   a. For example, you are a therapist and you want to see if the curriculum you have created to help people newly diagnosed with a disease is effective in their coping with the diagnosis. This is a clinical trial because it is assessing a mental health related outcome.
   b. For example, you are trying to see if certain foods do or do not affect blood glucose and if intervening on the diet of a person will affect their blood glucose. This is a clinical trial because it is assessing the physical health related outcome.

If your study is a clinical trial, you must do the following:

1. Good Clinical Practice (GCP) training in research reports. Here at NC State, this means that all research team members must complete the appropriate CITI training for their area of research (either Social-Behavioral-Educational (SBE) or Biomedical) and the NC State IRB Training via Reporter.

2. Use of a Single IRB
   a. If your research team is made up of researchers from NC State University and other places, this study must be reviewed by one IRB called the IRB of record.
   b. This IRB of record is usually the IRB where the research staff are completing the most work with humans. Any co-collaborators from other institutions will need to be named on your eIRB application and either a reliance or individual investigator agreement will need to be filed.
   c. Requesting an agreement can be done through our website at: https://research.ncsu.edu/sparcs/compliance/irb/irb-for-researchers/

3. Registration & Reporting on ClinicalTrials.gov
   a. Once you receive IRB approval, you must register your study on ClinicalTrials.gov within 21 days of enrolling your first human subject.
   b. Your consent form must discuss being a clinical trial, include your ClinicalTrials.gov registration information, and be posted to ClinicalTrials.gov
   c. Your aggregated research results must be reported to ClinicalTrials.gov within 12 months of data collection completion.
   d. When your study is approved by the NC State University IRB office, you will receive an approval letter with information about your responsibilities regarding your clinical trial. This includes registration/login information to clinicaltrials.gov
## Clinical Trials Comparison Chart

What different agencies and regulations require

<table>
<thead>
<tr>
<th>Food and Drug Administration (FDA)</th>
<th>National Institutes of Health (NIH)</th>
<th>Health and Human Services (HHS)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition:</strong> An investigation or research that involves one or more human subjects, undertaken to assess/evaluate the safety or effectiveness of a medical device.</td>
<td><strong>Definition:</strong> A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.</td>
<td><strong>Definition:</strong> Clinical trial means a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.</td>
</tr>
<tr>
<td><strong>Clinical Research vs. Medical Treatment</strong></td>
<td><strong>FDA Definition vs. NIH Definition</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Valid CITI Good Clinical Practice (GCP) training by all research team members</strong></td>
<td><strong>Use of Single IRB for multisite protocols</strong></td>
<td><strong>Use of Single IRB for multisite protocols</strong></td>
</tr>
<tr>
<td><strong>Use of Single IRB for multisite protocols</strong></td>
<td><strong>If your research includes an investigational new drug (IND) or investigational device exemption (IDE) where there is significant risk, you must get FDA approval to use the device or drug in a clinical trial</strong></td>
<td><strong>If your research includes an investigational new drug (IND) or investigational device exemption (IDE) where there is significant risk, you must get FDA approval to use the device or drug in a clinical trial</strong></td>
</tr>
<tr>
<td><strong>Registering study on ClinicalTrials.gov within 21 days of enrolling first human subject</strong></td>
<td><strong>Registering study on ClinicalTrials.gov within 21 days of enrolling first human subject</strong></td>
<td><strong>Registering study 21 days after enrollment of first study participant. See Appendix A for details</strong></td>
</tr>
<tr>
<td><strong>Post your consent form(s) (with clinical trial information) to ClinicalTrials.gov</strong></td>
<td><strong>Post your consent form(s) (with clinical trial information) to ClinicalTrials.gov</strong></td>
<td><strong>Posting your consent form(s) on ClinicalTrials.gov</strong></td>
</tr>
<tr>
<td><strong>Update information in the clinical trial record at least once every 12 months to ClinicalTrials.gov</strong></td>
<td><strong>Update information in the clinical trial record at least once every 12 months to ClinicalTrials.gov</strong></td>
<td><strong>Update information in the clinical trial record every 12 months to ClinicalTrials.gov</strong></td>
</tr>
<tr>
<td><strong>Report summary results to ClinicalTrials.gov no more than a year after the clinical trial finishes</strong></td>
<td><strong>Report summary results to ClinicalTrials.gov no more than a year after the clinical trial finishes</strong></td>
<td><strong>Submit summary results to ClinicalTrials.gov no more than a year after the data collection is complete. Please see Appendix A of this document for details</strong></td>
</tr>
</tbody>
</table>

Updated 1/15/2020
Appendix A
ClinicalTrials.gov Registration and Posting of Research Results

Registering your study with clinicaltrials.gov
Once you have received formal email notification that your IRB protocol was approved by the NC State IRB Office, you have 21 days to register your study on ClinicalTrials.gov website’s PRS portal.

You must have a PRS account to register a study. This should be issued at approval from NC State University’s IRB Office. The NC State IRB office, as a PRS affiliated organization, will initiate an account application for you (creating your login access). If you did not receive information about your PRS account, please email the NC State IRB office to request a PRS log-in.

Once you have logged into the PRS portal, you will click on the “Records” button on the left hand, upper third of your screen. A menu of options will appear and you want to select “New Record.” You will need to complete all sections of the application, upload requested documents, and submit the application to PRS. It’s okay to copy and paste whatever you need from your eIRB application into the PRS portal, but the questions sometimes are very different from what NC State asks. Furthermore, PRS’ word allotment is far smaller than the word limit of the eIRB application’s narrative response sections.

Registration must include the following information:
- **Description** (title, design, primary outcome measure information)
- **Recruitment** information (eligibility criteria, recruitment study, why study stopped if applicable)
- **Location and contact information** (name of sponsor, facility/PI/research team contact information)
- **Administrative data** (secondary ID, IRB protocol status)

The PRS Administrators will review your application for completeness. When the application passes review by the PRS Administrators, your study will be posted to the ClinicalTrials.gov website.

Your application will be processed by the National Library of Medicine (NLM) at the National Institutes of Health (NIH), typically within 48 business hours. They will also manage your ongoing access and interface within the PRS system. Because NC State and the NC State IRB office does not administer the PRS system, you will need to direct most questions about the PRS system to the PRS Administrators.

Posting your results on clinicaltrials.gov
After your data collection is complete, you have 12 months to post your aggregated data to the PRS portal. You’ll use the same log-in that you did to register the study. If you lost or cannot remember your PRS log-in, please email the PRS Administrators. Unfortunately, NC State and the NC State IRB office has no administrative privileges to reset your PRS log-in.

As of 2019, the following information is requested by the PRS portal for reporting research results: participant flow, baselines, and outcomes within the scope of the research; what, if any, adverse events occurred, limits and caveats of the research results, and who to contact for more information about the study. Complete all application sections and submit for review by the PRS Administrators. Once approved, the research study will be posted to the ClinicalTrials.gov website.

Be prepared to include:
- Progress of participants in each treatment group, including number who started and completed the trial
- Participant demographics and baseline characteristics (age, sex, gender, race, ethnicity, and all other measures assessed at baseline and are used in the analyses of the primary outcome measures
- Outcomes and statistical analyses for each primary and secondary outcome measure by treatment group or comparison group, include results of scientifically appropriate statistical analyses performed on these outcomes, if any
- Table of all anticipated and unanticipated serious adverse events and other adverse events that exceed a 5% frequency threshold within any group, including time event occurred, a description of the event, collection approach (systematic or nonsystematic), and a table with the number and frequency of deaths due to any cause of treatment group or the comparison group
- Administrative information, included a point of contact to obtain more information about the posted summary results information

Updated 1/15/2020
Appendix B
Phases of a Clinical Trial Involving a Drug or Device
https://www.centerwatch.com/clinical-trials/overview

**Phase I** studies assess the safety of a drug or device. This initial phase of testing, which can take several months to complete, usually includes a small number of healthy volunteers (20 to 100), who are generally paid for participating in the study. The study is designed to determine the effects of the drug or device on humans including how it is absorbed, metabolized, and excreted. This phase also investigates the side effects that occur as dosage levels are increased. About 70% of experimental drugs pass this phase of testing.

**Phase II** studies test the efficacy of a drug or device. This second phase of testing can last from several months to two years, and involves up to several hundred patients. Most phase II studies are randomized trials where one group of patients receives the experimental drug, while a second "control" group receives a standard treatment or placebo. Often these studies are "blinded" which means that neither the patients nor the researchers know who has received the experimental drug. This allows investigators to provide the pharmaceutical company and the FDA with comparative information about the relative safety and effectiveness of the new drug. About one-third of experimental drugs successfully complete both Phase I and Phase II studies.

**Phase III** studies involve randomized and blind testing in several hundred to several thousand patients. This large-scale testing, which can last several years, provides the pharmaceutical company and the FDA with a more thorough understanding of the effectiveness of the drug or device, the benefits and the range of possible adverse reactions. 70% to 90% of drugs that enter Phase III studies successfully complete this phase of testing. Once Phase III is complete, a pharmaceutical company can request FDA approval for marketing the drug.

**Phase IV** studies, often called Post Marketing Surveillance Trials, are conducted after a drug or device has been approved for consumer sale. Pharmaceutical companies have several objectives at this stage: (1) to compare a drug with other drugs already in the market; (2) to monitor a drug's long-term effectiveness and impact on a patient's quality of life; and (3) to determine the cost-effectiveness of a drug therapy relative to other traditional and new therapies. Phase IV studies can result in a drug or device being taken off the market or restrictions of use could be placed on the product depending on the findings in the study.