**What Studies Fall Under ClinicalTrials.Gov Registration and NIH GCP Training Requirements?**

1. **Non-NIH Funded Studies Requiring Registration on ClinicalTrials.Gov per DHHS Final Rule/FDAAA**

“Applicable clinical trials” initiated on or after September 27, 2007 or ongoing as of December 26, 2007 must be registered. This includes 1) controlled clinical investigations of drugs or biologics subject to FDA regulation, *other than phase 1 trials*, 2) controlled trials with health outcomes of devices subject to FDA regulation, *other than small feasibility studies*, and 3) pediatric postmarket surveillance required by the FDA.

Applicable clinical trials general include:

*Interventional studies* (with one or more arms) of FDA-regulated drugs, biological products, or devices that meet one of the following conditions:

* Conducted in one or more US sites
* Conducted under an FDA IND/IDE (Note: IND/IDE holder must register)
* Involves a drug, biologic, or device that is manufactured in the US/ territories and is exported for research
* \*\*Does not generally apply to phase 1 trials, behavioral interventions, small feasibility device trials, or cohort/case-control studies\*\*

*Observational study:* Pediatric post-marketing surveillance of a device product mandated by the FDA (as required under Section 522 of the Federal Food, Drug and Cosmetic Act).

See ClinicalTrials.Gov website for more information <https://clinicaltrials.gov/ct2/manage-recs/fdaaa> and <https://clinicaltrials.gov/ct2/manage-recs/resources#FDAAA2007> for a checklist and enhanced definitions.

1. **NIH-Funded “Clinical Trials” Requiring GCP Training & ClinicalTrials.Gov Registration**

“A research study in which one or more human subjects are prospectively assigned[[1]](#footnote-1) to one or more interventions,[[2]](#footnote-2) (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes[[3]](#footnote-3).”

Study must involve:

* Human subjects research, **AND**
* Prospective pre-determined assignment to one or more interventions, **AND**
* A health-related biomedical or behavioral outcome.

**See** [**NIH Decision Tree**](https://grants.nih.gov/policy/clinical-trials/CT-decision-tree.pdf)

**Examples that ARE Considered NIH Clinical Trials (**[**from NIH**](http://osp.od.nih.gov/sites/default/files/Case_Studies.pdf)**):**

1. A study is planned to randomly assign individuals to an experimental intervention to promote weight loss or to a control intervention. After a year, participants’ behaviors will be assessed to measure their adherence to exercise regimens. (Studies adherence to exercise regimens)
2. A large-scale study is designed to evaluate the effectiveness of community-based interventions in influencing smoking behavior. Thirty-four communities across the U.S. are randomly assigned to receive the experimental intervention or to receive one of two control interventions. Each community has a population between 100,000 and 500,000 individuals. The experimental intervention includes public awareness campaigns and educational pamphlets. (Investigates smoking behavior)
3. An investigator plans to administer a new experimental product to patients suffering from advanced stage Wilms tumors (rare and malignant kidney tumors). Due to the rarity of the disease, only five patients will be enrolled in the study. All patients will receive the new experimental product. Tumor size and the incidence of metastatic disease will be evaluated. (Study may have just a single arm)
4. A dose-escalation study is designed to determine the maximum tolerated dose of a new drug in healthy volunteers. The study will also measure the drug concentration in the blood (pharmacokinetics (pK)). (Determines maximum tolerated dose)
5. A new study will evaluate the performance of diagnostic tools used for the detection of breast cancer. The study will assign women between the ages of 40 and 50 to receive one film-screen mammography every two years for eight years. Another group of women, also between the ages of 40 and 50 will receive one digital mammogram every two years for eight years. Incidence and progression of breast cancers will be compared. (Studies cancer outcomes)
6. The primary objective of a study is to assess the dose-response relationships between testosterone and bone turnover, body composition, and other functions in normal young men. To achieve this objective, healthy men, age 20-50, will be treated with a Gonadotropin Releasing Hormone agonist to lower testosterone and estradiol for 16 weeks and then with placebo or 1 of 4 gradually increasing doses of testosterone gel (1.25, 2.5, 5.0 or 10 gm/day). The 6th group will receive placebo only. (Involves health-related outcome and prospective assignment)

**Examples that ARE NOT Considered NIH Clinical Trials (**[**from NIH**](http://osp.od.nih.gov/sites/default/files/Case_Studies.pdf)**):**

1. A study is designed to evaluate different types of printed public health announcements to identify the best designs for ensuring comprehension and retention of information in adults. Two printed announcements will be designed with identical information. Visitors to public libraries will be selected at random and asked to read one of the announcements and then to take a short survey assessing their comprehension and information retention. (Investigates understanding/remembering announcement rather than affecting health of readers)
2. Participants are randomly assigned to different processes for informed consent in order to assess the impact of interactive and multimedia components. The study measures participant preferences. (Study does not identify a health related outcome)
3. A study is designed to evaluate the efficacy of an in-vitro diagnostic device to detect circulating antibodies. Banked blood samples from identifiable, patients diagnosed with lupus and from patients who do not have lupus will be used to evaluate the device’s ability to detect circulating antibodies. (Study does not involve prospective assignment to an intervention nor identify a health related outcome; rather, it tests effectiveness of a medical device. NOTE: if the study was using the detection of circulating antibodies by the device to inform the use of therapy or assess disease state, it *would* be a clinical trial).
4. A study is designed to examine the effectiveness of maximal surgical resection vs. radiation in the treatment of multiform glioblastoma (both are approved as standard therapies for multiform glioblastoma). Participating in the study will not dictate the course of therapy. The 6-month survival of 6 Updated September 16, 2016 glioblastoma patients who decide to undergo maximal surgical resection will be compared to the 6-month survival of patients who opt to get radiotherapy. (Subjects are not prospectively assigned to interventions - patients and their healthcare providers select the therapy and investigators observe outcomes. NOTE: if the study prospectively assigned patients to receive surgery or radiation, it *would* be a clinical trial)

See NIH Website: <https://grants.nih.gov/policy/clinical-trials/definition.htm>

1. The term “prospectively assigned” refers to a pre-defined process (e.g., randomization) specified in an approved protocol that stipulates the assignment of research subjects (individually or in clusters) to one or more arms (e.g., intervention, placebo, or other control) of a clinical trial. [↑](#footnote-ref-1)
2. An “intervention” is defined as a manipulation of the subject or subject’s environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints. Examples include: drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and, diagnostic strategies. [↑](#footnote-ref-2)
3. A “health-related biomedical or behavioral outcome” is defined as the pre-specified goal(s) or condition(s) that reflect the effect of one or more interventions on human subjects’ biomedical or behavioral status or quality of life. Examples include: positive or negative changes to physiological or biological parameters (e.g., improvement of lung capacity, gene expression); positive or negative changes to psychological or neurodevelopmental parameters (e.g., mood management intervention for smokers; reading comprehension and /or information retention); positive or negative changes to disease processes; positive or negative changes to health-related behaviors; and, positive or negative changes to quality of life. [↑](#footnote-ref-3)