Clinical Trial Requirements

Clinical trials must comply with additional requirements, beyond IRB review, that do not apply to other types of research that vary depending on funding source or regulatory body oversight. This includes registering clinical trials with ClinicalTrials.gov, posting of consent forms, good clinical practice training, and use of a single IRB. This guidance document provides information about clinical trial registration requirements set forth by the Food and Drug Administration (FDA), National Institutes of Health (NIH), and International Committee of Medical Journal Editors (ICMJE).

I. Registration & Reporting Requirements

ClinicalTrials.gov is a registry of federally funded, privately supported, and unfunded clinical trials involving human participants that is the result of a federal law requiring that clinical trials be registered to improve public access to information about clinical research, promote public trust in research, and inform future research. In some cases, registration is also required for journal publication.

Studies must be registered with ClinicalTrials.gov if:

- they involve drugs, devices, or biologics that are regulated by the FDA, **OR**
- they are funded by the NIH **AND** meet the NIH definition of a clinical trial, **OR**
- there is a plan to publish the results in a medical journal AND the study meets the ICMJE definition of a clinical trial

Responsibility for registration falls to the individual designated to be the **responsible party**. Normally the sponsor of the trial is the responsible party unless they have delegated this responsibility. The principal investigator (PI) is the responsible party in cases where there is no sponsor (investigator-initiated trials) or for NIH-funded clinical trials that do not involve FDA-regulated components. For research involving an IND, investigational new drug application, or IDE, investigational device exemption, with the FDA, the holder of the IND or IDE is the responsible party unless responsibility has been delegated to the PI. PIs who are the responsible party are ultimately responsible to ensure that registration occurs and the information provided is accurate and current.

To register your clinical trial go to: https://clinicaltrials.gov/

Registration of clinical trials must be timely. Please see the various agency requirements below for when trials should be registered and the various definitions of a clinical trial. Results from clinical trials must be reported to ClinicalTrials.gov no later than 12 months after the *primary completion date*. The *primary completion date* is defined as the date that the final subject was examined or received an intervention for the purposes of final collection of data for the primary outcome, whether the clinical trial concluded according to the pre-specified protocol or was

terminated. For clinical trials initiated on or after January 18, 2017, information submitted to ClinicalTrials.gov must be updated at least once every 12 months. See ClinicalTrials.gov for timelines for submitting study changes and information, most are to be reported within 30 days.

Research participants *must* be informed of the availability of clinical trial information on ClinicalTrials.gov. Federal regulations require the following language to be included verbatim in informed consent documents for *applicable clinical trials* initiated on or after March 7, 2012 and for all NIH-funded clinical trials subject to registration: *A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.*

Under federal law, penalties for failure to register, or for providing incomplete, false, or misleading registration information (including updates subsequent to initial registration) may include civil monetary penalties of up to $10,000 per incident and/or per day, non-compliance notices from the FDA, and, for federally-funded trials, the withholding or recovery of grant funds. Compliance with ClinicalTrials.gov registration requirements will be a term and condition of NIH awards. NIH grantees are required to certify their compliance with registration and reporting requirements in grant applications and progress reports. Failure to comply may lead to suspension or termination of funding and publicly identifying the clinical trial record as noncompliant in clinicaltrials.gov. NIH may consider compliance with these requirements in decisions about future funding. Additionally, unregistered or improperly registered trials risk not being accepted for consideration by ICMJE member or other journals.

In addition to the agency requirements below, a qualifying clinical trial for which reimbursement for items and services will be sought from the Center for Medicare and Medicaid Services must be registered.

A. FDA Registration Requirements

The FDA requires registration with ClinicalTrials.gov for all ***applicable clinical trials*** that were initiated after 9/27/2007 or were initiated before 9/27/2007, but were ongoing as of 12/26/2007. Applicable clinical trials must be registered no later than 21 days after enrollment of the first participant.

***Applicable Clinical Trials*:**

Drugs and Biologics: A controlled clinical investigation, other than a Phase 1 clinical investigation, of a drug or biologic product subject to FDA regulation.

Medical Devices: A prospective clinical study of health outcomes comparing an intervention with a medical device against a control, or pediatric post market surveillance required by the FDA.

Applicable clinical trials generally include interventional studies (with one or more arms) of FDA-regulated drugs, biological products, or devices that meet one of the following conditions:

- The trial has one or more sites in the United States
- The trial is conducted under an FDA IND or IDE
- The trial involves a drug, biologic, or device that is manufactured in the United States or its territories and is exported for research

Registration is *not* required for small trials to determine the feasibility of a device or to test prototype devices where the primary outcome measure relates to feasibility, and not to health outcomes.

In addition to the registration requirements, FDA approval of an Investigational Device Exemption (IDE) or Investigational New Drug Application (IND) must be obtained when applicable.

B. NIH Registration Requirements

NIH requires registration at ClinicalTrials.gov for all clinical trials funded wholly or partially by NIH. Clinical trials must be registered no later than 21 days after enrollment of the first participant.

Clinical Trial: 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. This includes Phase 1 clinical trials, and trials that do not involve any FDA-regulated products (such as trials involving only behavioral interventions).

Prospectively Assigned: 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.

Intervention: 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.

Health-related biomedical or behavioral outcomes: 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.

C. ICMJE Registration Requirements

As of 2005, most medical journals, including member publications of the ICMJE, require registration with ClinicalTrials.gov as a condition of publication. Thus, researchers who plan to publish in an ICMJE member journal must meet ICMJE guidelines for clinical trial registration. Clinical trials must be registered at or before the time of first participant enrollment.

Clinical Trial: Any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Health-related interventions include any intervention used to modify a biomedical or health-related outcome (for example, drugs, surgical procedures, devices, behavioral treatments, dietary interventions, and process-of-care changes). Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events.

II. Public Posting of Consent Form

Under the 2018 Common Rule that took effect on January 21, 2019, one IRB approved consent form that is used when enrolling participants must be posted on a publicly available federal website for each clinical trial funded by any federal agency or department that has adopted the Common Rule. See https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html for a complete list of federal agencies and departments that have adopted the Common Rule. The consent form must be posted after the clinical trial is closed to enrollment and no later than 60 days after the last study visit by any participant. Only one IRB approved version must be posted. Reposting revised or modified consent forms is NOT required.

To post your consent form go to: https://clinicaltrials.gov/ or https://www.regulations.gov/, Docket ID: HHS-OPHS-2018-0021. Consent forms may be posted to either website.

For the purposes of the consent form posting requirement, a **clinical trial** is defined as: 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 (45CFR46.102b). Social, behavioral, and educational research studies funded by a Common Rule department or agency that fit the definition of a clinical trial must also comply with the posting requirement.

III. Single IRB

Effective January 2020, all federally funded, cooperative projects (those that involve more than one institution) that are not exempt must rely on approval by a single IRB for research conducted in the United States. The reviewing IRB will be identified by the Federal sponsor or proposed by the lead institution and subject to approval by the federal sponsor. This is separate from the NIH single IRB mandate that went into effect in January 2018. Remember to allow ample time for setting up reliance and administrative review.

IV. Good Clinical Practice Training

Good Clinical Practice Training (GCP) is required for all NIH funded investigators and staff who are involved in the conduct, oversight, or management of clinical trials. GCP training is available for CCH researchers through the CITI Program for Research Ethics & Compliance Training. GCP training is also recommended for all researchers conducting FDA regulated clinical trials.

Link to the CITI Program: http://www.citiprogram.org/login

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