Resource Document for UMass Researchers/Staff to Comply with the NIH Revision to the Definition of a Clinical Trial

Office of Research Compliance

University of Massachusetts, Amherst
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A. Revised NIH Definition of Clinical Trial

Website: https://grants.nih.gov/policy/clinical-trials/definition.htm


A research study\(^1\) in which one or more human subjects\(^2\) are prospectively assigned\(^3\) to one or more interventions\(^4\) (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.\(^5\)

\(^1\)See Common Rule definition of research at 45 CFR 46.102(d).

\(^2\)See Common Rule definition of human subject at 45 CFR 46.102(f).

\(^3\)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.

\(^4\)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.

\(^5\)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.
B. Determination If Your Human Subject’s Research Study Meets the Revised NIH Definition of a Clinical Trial?

Please use resources below to make this determination or contact the Human Research Protection Office at 413-545-3428 or email at humansubjects@ora.umass.edu:


C. NIH Policies for Data and Safety Monitoring of Clinical Trials

Notice/Policy: [https://humansubjects.nih.gov/data_safety](https://humansubjects.nih.gov/data_safety)

**Note:** If your study involves a clinical trial you must include a Data and Safety Monitoring Plan (DSMP) commensurate with the risk of your study.

**Note:** This plan needs to be approved by the IRB prior to enrolment of any Human Subjects.


A DSMP should include a general description of a plan establishing the overall framework for the oversight and monitoring of a study. When formulating the DSMP, the PI, and the study team should consider the protocol, phase, intervention(s), target population, subject safety and privacy, risks and benefits involved in the study, data integrity and confidentiality, study coordination, and how the team will address each of these elements. When modifications to the DSMP are made before the trial begins (e.g., in response to the peer review or IRB review), a final IRB-approved monitoring plan must be submitted to the NIMH PO prior to the commencement of human subjects activities. The minimum required DSMP content should include the following elements.

**Note:** If these elements are noted elsewhere in the application or proposal, they need not be repeated but should be referenced in the DSMP section:

1. **Summary of the Protocol:**
   - A brief description of the study design (e.g., interventions, procedures, tests and scans, biospecimen collection, interviews and focus groups, study visits)
   - Primary and secondary outcome measures/endpoints
   - Sample size and target population
   - Inclusion/exclusion criteria and how the criteria will be evaluated
   - For multi-site trials, a list of proposed participating clinical sites and data coordinating centers and a description of each site’s role

2. **Roles and Responsibilities (Note this must be listed in DSMP section):**
   - Identification and description of individuals responsible for monitoring the trial (e.g., PI, ISM, DSMB), their roles, qualifications, and the frequency of the monitoring activities. If the monitoring entity is an ISM or a DSMB, provide the NIMH PO and Office of Clinical Research (OCR) review with a list of the proposed membership and assurances to ensure that there are no conflicts of interest with the study team or proposed institutions.

3. **Trial Safety:**
   - Description of any specific events that would preclude a participant from continuing the intervention
   - Description of any procedures in place for managing any medication related issues (e.g., medication washout, allergic reactions, drug interactions, discontinuation/stoppage of medication, use of rescue medications)
   - Description of the potential risks and the measures in place to protect participants against foreseeable risks
o Description of the consent/assent procedures (e.g., by whom, how and under what conditions will a subject be consented)

o Description of the mechanisms in place to protect subject privacy (e.g., interviews will take place in a private room, whether results of testing data will be shared with participant’s legally authorized representative, privacy for minors, secure means of communication between investigators and participant, e.g., telephone, web portal)

o Description of the trial stopping rules for the study, if any (e.g., increased suicidal ideation, greater than expected morbidity or mortality rate)

o Description of the plan for management of incidental findings (e.g., a brain tumor or potential structural abnormality discovered during a scan)

o Description of the process for the disclosure of any conflicts of interest that may potentially challenge participant safety or bias the data and how the conflict will be managed

o For multi-center studies, a description of the procedures for ensuring compliance with the monitoring plan including requirements for data reporting across study sites

o Description of the data security in place to protect the confidentiality of the data (e.g., password protected encrypted electronic records) and any limits to confidentiality (e.g., suicidal ideation, child abuse)

4. Reportable Events:

   o Description of the process and timelines (e.g., hours, days) for collecting and reporting Adverse Events (AEs), Serious Adverse Events (SAEs), and Unanticipated Problems Involving Risks to Subjects or Others to appropriate monitoring and regulatory entities (See NIMH Reportable Events Policy for definitions and timeframes)

   o Specific plan and timeframe for reporting IRB and/or ISM/DSMB actions to the NIMH (e.g., protocol violations, non-compliance, suspensions, terminations)

5. Data Management, Analysis, and Quality Assurance:

   o Identification of data sources (e.g., questionnaires, medical records, biospecimen collections, audio/video recordings)

   o Description of the security measures in place to protect data sources including how the data will be labeled and stored

   o Quality assurance measures for subject recruitment, enrollment, enrollment targets, and for the validity and integrity of the data. E6 Good Clinical Practice (R1): 1.46 defines quality assurance as “All those planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with Good Clinical Practice (GCP) and the applicable regulatory requirement(s)”

If your study involves an NIH-defined Phase III or multisite clinical trial your DSMP must include a Data and Safety Monitoring Board.


If you have any questions, please contact the Human Research Protection Office at 413-545-3428 or email at humansubjects@ora.umass.edu
D. Good Clinical Practice (GCP) Training

The principles of Good Clinical Practice (GCP) help assure the safety, integrity, and quality of clinical trials by addressing elements related to the design, conduct, and reporting of clinical trials. GCP training describes the responsibilities of investigators, sponsors, monitors, and IRBs in the conduct of clinical trials.

GCP training aims to ensure that:

- the rights, safety, and well-being of human subjects are protected
- clinical trials are conducted in accordance with approved plans with rigor and integrity
- data derived from clinical trials are reliable

The policy applies to NIH-funded clinical investigators and clinical trial staff who are responsible for the design, conduct, oversight, or management of clinical trials. The policy describes the investigator as the individual responsible for the design and conduct of the clinical trial at a trial site or, if a team of individuals at a trial site are involved, the investigator leading the team. The policy describes clinical trial staff as those who are responsible for study coordination, data collection, and data management.

Website: https://grants.nih.gov/policy/clinical-trials/good-clinical-training.htm


Note: The policy applies to all active grants and contracts, no matter what point they are in the life cycle of the trial. This policy is effective January 1, 2017
Course available through CITI (preferred) and through NIH

https://grants.nih.gov/grants/policy/faq_nih_good_clinical_practice.htm#5163

https://gcp.nidatraining.org/

Steps to Complete the GCP training through CITI

1. **Log into your CITI Account** ([https://about.citiprogram.org/en/homepage/](https://about.citiprogram.org/en/homepage/))

2. Click “Add a Course”

3. **You will see the page below.**

   ![CITI Program](image)

   **CITI Course Enrollment Procedure**

   CITI provides courses in Human Subjects Protection, Good Clinical Practice, Health Information Privacy, Lab Animal Welfare, and The Responsible Conduct of Research. Your organization likely has several requirements and perhaps some options to meet your institutional obligations.

   - You will be provided a series of enrollment questions below.
   - Your responses will determine the curriculum for the course(s) you are going to take.
   - Please read the questions and responses carefully to make the best choice.

   **Human Subjects Protection Course:**

   - If you have NOT completed a CITI course at this institution previously, you may be required to complete the BASC course at this time.
   - If you have completed the CITI Basic course since 5-1-2019, the software is programmed to show you the CITI refresher course now.
   - You may be able to fulfill your refresher obligation with the CITI Good Clinical Practice Course. Please consult your IRB office.

   For more detailed information review the instructor's page of your institution. This page is available as a link at the top of this page.

   **Laboratory Animal Welfare Course**

   If you are planning to use lab animals in your work, you may be required to complete the CITI Lab Animal Welfare course. You should:
4. Scroll down to answer the Human Subjects Questions:

Select “Group 3” for the Good Clinical Practice course.

5. Answer other Questions visible on the screen. (Question #2 will need to be answered for animal users).

6. You will be taken back to the main screen where the GCP course will now be visible and accessible.
E. NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information


Frequently Asked Questions: https://clinicaltrials.gov/ct2/manage-recs/faq#42CFRPart11

Note: This policy is effective January 18, 2017

The NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information sets the expectation that all NIH-funded awardees and investigators conducting clinical trials will register and report results of their trial in Clinicaltrials.gov.

Both the NIH policy and the federal regulation aim to increase the availability of information to the public about clinical trials – information that is not systematically available from other public sources. The regulation and NIH policy do not affect the design or conduct of clinical trials or define what type of data should be collected during a clinical trial. Rather, they aim to help ensure that information about clinical trials and their results are made publicly available, in a timely manner, via ClinicalTrials.gov, a publicly accessible database operated by the NIH’s National Library of Medicine (NLM).

Once the study has been approved by the IRB, please contact Iris Jenkins at ijenkins@ora.umass.edu or 413-577-0643 to obtain a log-in for the www.clinicaltrials.gov website.