Applicable Clinical Trials

Applicable Clinical Trials

Definition of a Clinical Trial

The World Health Organization (WHO) defines a clinical trial as “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. Interventions include but are not restricted to drugs, cells and other biological products, surgical procedures, radiological procedures, devices, behavioural treatments, process-of-care changes, preventive care, etc.”

The U.S. National Institutes of Health (NIH) defines a clinical trial 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 those interventions on health-related biomedical or behavioral outcomes.”

Consistent with the definition developed by the WHO, The International Committee of Medical Journal Editors (ICMJE) defines a clinical trial as “any research project that prospectively assigns people or a group of people to an intervention, with or without concurrent comparison or control groups, to study the cause-and-effect relationship between a health-related intervention and a health outcome. Health-related interventions are those used to modify a biomedical or health-related outcome; examples include drugs, surgical procedures, devices, behavioural treatments, educational programs, dietary interventions, quality improvement interventions, and process-of-care changes. Health outcomes are any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events.”

The FDA defines an Applicable Clinical Trial (ACT) as follows:

- Trials of drugs and biologics: controlled clinical investigations, other than Phase 1 investigations, of a product subject to FDA regulation.
- Trials of biomedical devices: controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and pediatric post-market surveillance.

For complete statutory definitions and more information on the meaning of Applicable Clinical Trial, see Elaboration of Definitions of Responsible Party and Applicable Clinical Trial (PDF).Definition of a Clinical Trial

What is a Qualifying Trial

Under the National Coverage Decision (NCD), Medicare will cover those routine costs of qualifying clinical trials and the costs of items and services that are reasonable and necessary to diagnose and treat complications arising from participation in all clinical trials (Centers for Medicare and Medicaid Publication 100-3, Ch 1, Part 4, Section 310.1).

The trial may be “Qualifying” if it:

- Is funded/supported by NIH, CDC, AHRQ, CMS, DOD or VA

- Is supported by centers or cooperative groups that are funded by the NIH, CDC, AHRQ, CMS, DOD and VA
- Has an IND number
- Is conducted under an IND/IDE reviewed by the FDA
- Is exempt from having an IND/IDE
- Is conducted an abbreviated IDE

-OR-

Your trial (All three criteria must be "Yes"):

- Evaluates a Medicare benefit
- Has therapeutic intent
- Enrolls diagnosed beneficiaries

For additional information regarding “Qualifying Trials” please refer to Qualifying Clinical Trials on ResearchGO.

Do I need to register my “Qualifying Trial” even if it is not an “Applicable Clinical Trial” under FDAAA?

Yes, your trial must be registered in ClinicalTrials.gov if it is a “qualifying trial” even if it doesn’t meet the definition of an “Applicable Clinical Trial.” According to a recent CMS mandate, a clinical trial number must be reported on claims for items and services provided in clinical trials that are qualified for coverage as specified in the “Medicare National Coverage Determination (NCD) Manual, “ Section 310.1.

The clinical trials number to be reported is the number assigned by the National Library of Medicine (NLM) http://clinicaltrials.gov website (an 8-digit # preceded by “NCT”, a.k.a. “the NCT #”) when a study appears in the NLM Clinical Trials database.

When must my ‘Qualifying Trial” be registered in ClinicalTrials.gov?

Your “Qualifying Trial” must be registered in ClinicalTrials.gov prior to IRB approval

What are the penalties for failing to register?

According to the ICMJE:

Unregistered trials will not be considered for publication in journals that adhere to ICMJE standards. This penalty has not changed over time.

According to the FDA/NIH (Food and Drug Amendments Act of 2007):

Penalties may include civil monetary penalties up to $10,000 fine for failing to submit or for submitting fraudulent information to ClinicalTrials.gov. After notification of noncompliance, the fine may go up to $10,000 per day until resolved. For federally funded grants, penalties may include the withholding or recovery of grant funds.

What is an applicable clinical trial according to the Food and Drug Administration

Amendments Act (FDAAA) Section 801?

Applicable Clinical Trial (ACT) is the term used in Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (PL 110-85) to designate the scope of trials that may be subject to the registration and reporting requirements in FDAAA. FDAAA defines the term using two other terms defined in the Act, namely an “applicable drug clinical trial” or an “applicable device clinical trial.”

Detailed definitions can be found in the Elaboration of Definitions of Responsible Party and Applicable Clinical Trials document.

In general, a study is likely subject to the requirements of FDAAA if YES is answered to all five questions below:

1. Was the study initiated after September 27, 2007 (OR ongoing as of December 26, 2007)?
2. Is the study ‘interventional’ (i.e., participants are assigned to interventions by protocol)?
3. Does the study intervention include a ‘drug’, ‘biological product’, or ‘medical device’ (whether or not approved for marketing in the United States)?
4. Is the study not considered a phase I clinical investigation (e.g., a phase 2 study) OR not considered a ‘small feasibility’ device trial (e.g., a pivotal study)?
5. Does the study have at least one site located in the United States OR is the study conducted under an IND or IDE?

Are investigator-initiated trials applicable clinical trials?

Yes, investigator-initiated trials are applicable clinical trials if they meet the criteria outlined above.

Can non-randomized trials be considered ACTs?

Yes – non-randomized trials can be “Applicable Clinical Trials” if they meet the other criteria. In non-randomized trials, participants are expressly assigned to intervention groups through a non-random method, such as physician choice. Keep in mind, a single –arm study often uses a historical comparison. See below for details regarding ‘controlled’ studies.

What does ‘controlled’ mean when it comes to deciding if a study is an ACT or not?

A study where a control is not expressly outlined in the protocol may still be considered an applicable clinical trial if it meets the other criteria outlined above. A controlled clinical investigation is one that is designed to permit a comparison of a test intervention with a control to provide a quantitative assessment of the drug effect. The purpose of the control is to distinguish the effect of a drug from other influences. The control provides data about what happens to human subjects who have not received the test intervention or who have received a different intervention. Generally, the types of control that are used in clinical investigations are (1) placebo concurrent control; (2) dose-comparison control; (3) no intervention concurrent control; (4) active intervention concurrent control; and (5) historical control.

What clinical trials are specifically excluded from the definition applicable clinical trials according to FDAAA?

- Phase 0 and phase I drug trials (however, these trials may still require registration per FDAMA Section 113).

- Small feasibility device trials and larger clinical trials of prototype devices with a primary measure of feasibility rather than health outcomes.

- Trials that include only de-identified human specimens and do not include human subjects.

Additional information can be found in the Elaboration of Definitions of Responsible Party and Applicable Clinical Trials document.

Who is responsible for registering protocols and reporting results for applicable clinical trials?

The “Responsible Party” is the entity or individual responsible for meeting FDAAA requirements for registering protocols and reporting results of ACTs. The responsible party is generally either the regulatory sponsor or the principal investigator. Note that the regulatory sponsor and financial sponsor are sometimes the same entity (i.e., a pharmaceutical company).

Generally speaking, the regulatory sponsor of an ACT will register and report the results of the trial if they:

- Are the company/organization that initiates the trial (multicenter or otherwise) and its employees conduct the trial;
- Are an individual who initiates a trial, but has someone else conduct the investigation;
- Hold the IND or IDE.

Generally speaking, Principal Investigators of applicable clinical trials will register and report the results of the trial if:

- The obligation is delegated to the principal investigator by the regulatory sponsor;
- The principal investigator is responsible for conducting the trial, analyzing the data, has rights to publish results and has the ability to meet all of FDAAA’s requirements for the submission of clinical trial information.

Note: For investigator-initiated ACTs, where a UCLA PI holds the IND/IDE, the IND/IDE holder (sponsor-investigator) must serve as the responsible party. For investigator-initiated ACTs where there is no IND or IDE holder and UCLA is the regulatory sponsor, the PI will be the designated responsible party. [UCLA Policy Pending]

If there is more than one award supporting a non-IND/IDE ACT, who is the Responsible Party?

Investigators and institutional officials associated with the trial should work together to determine the Responsible Party and ensure that the other grantees are aware of the designation. For assistance in these situations, please contact the UCLA PRS Administrator.

If you have questions or need assistance, please contact the CTSI for non-cancer studies and JCCC for cancer studies.

Last updated: 26 Aug 2022

Source URL:https://www.researchgo.ucla.edu/applicable-clinical-trials

Drupal.jQueryUiFilter.globalOptions('accordion');