

ClinicalTrials.gov: Definitions, Laws, and Regulations

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Who is responsible for ClinicalTrials.gov registration and results information submission?

- A. Sponsor
- B. Principal investigator of an investigator-initiated study
- C. Individual designated by a sponsor, grantee, contractor, or awardee

D. All of the above



Knowledge Check

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Key Definitions and Terms [42 CFR Part 11]



Applicable clinical trial (ACT)

- Applicable drug or device clinical trial
- Not all trials are applicable clinical trials (e.g., Observational studies, Expanded Access)
- Controlled drug clinical investigation
- Clinical trial of combination product with drug or device primary mode of action (PMOA) meeting all other requirements above

Responsible Party (RP)

- Sponsor of the clinical trial (as defined in 21 CFR 50.3); or
- Principal investigator (PI) of the clinical trial; if designated by the sponsor and has access and rights to all the data; or
- Pediatric postmarket surveillance of a device product that is not a clinical trial, RP is the entity who FDA orders to conduct the postmarket surveillance of the product





Control or controlled

- Data collected on human subjects in the clinical trial is compared to concurrently or non-concurrently collected data (e.g., historical controls, including a human subject's own baseline data) as reflected in the primary/secondary outcome measures
- One or more arms
- Pre-specified outcome measure(s)

Primary Completion Date (PCD) or Completion Date

- Date that the final subject was examined or received an intervention for purposes of final collection of data for the primary outcome measure
- For clinical trials with more than one primary outcome measure with different completion dates, it is the date on which data collection is completed for all primary outcomes



- Informed consent statement regarding ClinicalTrials.gov [21 CFR 50.25(c)]
- Certification of Compliance (Form FDA 3674)
- Clinical trial registration and results information submission requirements [42 CFR Part 11]
- Prohibited Acts under the FD&C Act



Informed Consent Requirement [21 CFR 50.25(c)]

• The following statement must be reproduced word-for-word in informed consent documents for **applicable clinical trials**:

"A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results information. You can search this Web site at any time."

 The statement is not required to appear in a particular section of informed consent documents



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- A certification must accompany certain applications and submissions to FDA
 - Include NCT numbers, if available
- Form FDA 3674 may be used to satisfy the certification requirement
- Examples of submission types where Form FDA 3674 would be expected:
 - Original IND, new protocol to IND
 - NDA/BLA, efficacy supplement to NDA/BLA
 - ANDA
 - Certain device submissions (e.g., PMA, HDE)

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Certification of Compliance

Form FDA 3674 - Certifications To Accompany Drug, Biological Product, and Device Applications/Submissions:

GUIDANCE FOR SPONSORS, INDUSTRY, RESEARCHERS, INVESTIGATORS, AND FOOD AND DRUG ADMINISTRATION STAFF

Additional copies are available from:

Office of Good Climical Practice, Office of Special Medical Programs
Food and Drug Administration

WO Bldg. 32, Room 5172
10903 New Hampshire Avenue
Saives Spring, MD, 20993-0002
301-796-8340
gcp questions@dda.hhs.gov

U.S. Department of Health and Human Services Food and Drug Administration Office of Good Clinical Practice, Office of Special Medical Programs Revised June 2017

OMB Control No. 0910-0616 See additional PRA statement in Section IV of this guidance.



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Clinical Trial Registration Requirements [42 CR Part 11]



- Required to register within 21 days of first human subject enrolled [42 CFR 11.24]
- Registration information[42 CFR 11.28]
 - Descriptive information e.g., title, summary, phase, intervention name(s), study design
 - Recruitment information e.g., eligibility criteria, sex/gender, age-limits, accepts health volunteers
 - Outcomes primary, secondary outcomes and timeframes
 - Location and contact information
 - Administrative data
- Subject to quality control [42 CFR 11.64(b)]
- Correct or address issues within 15 days of electronic notification [42 CFR 11.64(b)]

Clinical Trial Results Information Reporting Requirements [42 CFR Part 11.44]



- Responsible parties for ACTs subject to the final rule requirements are required to submit results information
- Standard submission deadline is 1 year after primary completion date
 - Partial results should be submitted, and remaining information submitted later, if applicable
- Exceptions to deadline:
 - Certification for delayed submission
 - Extension requests for "good cause"
 - Waiver of the requirements for submission of results information

Clinical Trial Results Reporting Requirements [42 CFR 11.48]



- Submission of data in tabular format:
 - Participant flow
 - Demographics and baseline characteristics
 - Primary and secondary outcomes
- Full protocol
- Statistical analysis plan
- Subject to NIH quality control review [42 CFR 11.64]

Clinical Trial Information Update Requirements [42 CFR 11.64]



- At least every 12 months
- Certain data elements within 30 days
 - Responsible Party (including any change in the sponsor/RP company name, e.g., resulting from a merger, acquisition or dissolution)
 - Expanded access information
 - Overall recruitment status
 - Study start date
 - Individual site status
 - Human Subjects Protection Review Board Status
 - Primary completion date
- Certain data elements within 15 days
 - Device product not approved or cleared by U.S. FDA



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Prohibited Acts under the FD&C Act

- Failing to submit a certification or knowingly submitting a false certification required by section 402(j)(5)(B) of the PHS Act
- Failing to submit clinical trial information required under section 402(j) of the PHS Act
- Submitting clinical trial information under section 402(j) of the PHS Act that is false or misleading in any particular

Key Messages



- Responsible Parties are responsible for submission of registration, results information, and updating the ClinicalTrials.gov registry
- A Certification of Compliance must accompany certain applications and submissions and Form FDA 3674 may be used to satisfy the certification requirement
- Contact the NIH/NLM for questions related to submission of registration, results information and/or updating the registry
- Informed consent forms for studies that are ACTs must include a statement regarding ClinicalTrials.gov [21 CFR 50.25(c)]