ClinicalTrials.gov: Definitions, Laws, and Regulations

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U.S. Food and Drug Administration

Knowledge Check

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

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

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C. Individual designated by a sponsor, grantee, contractor, or awardee
D. All of the above

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

Key Definitions and Terms [42 CFR Part 11]

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

FDA's Role Related to ClinicalTrials.gov

- **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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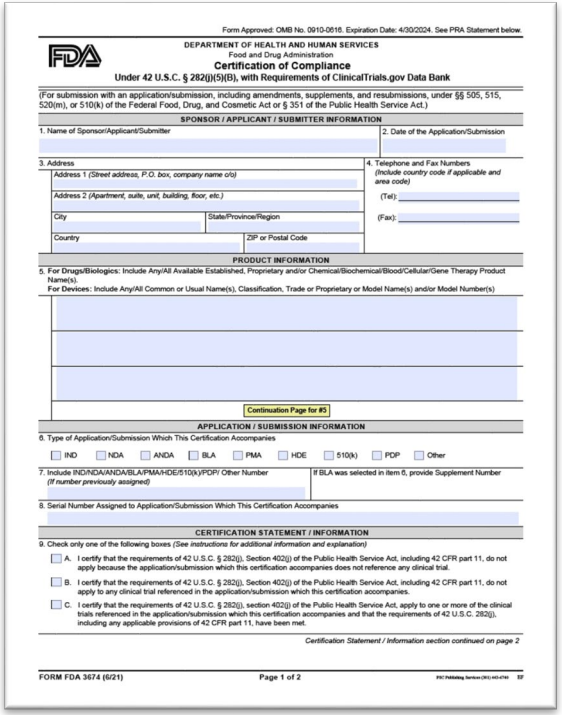
Certification of Compliance

- 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)



Form Approved: OMB No. 0910-0616. Expiration Date: 4/30/2024. See PRA Statement below.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Certification of Compliance

Under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank

(For submission with an application/submission, including amendments, supplements, and resubmissions, under §§ 505, 515, 520(m), or 510(k) of the Federal Food, Drug, and Cosmetic Act or § 351 of the Public Health Service Act.)

SPONSOR / APPLICANT / SUBMITTER INFORMATION

1. Name of Sponsor/Applicant/Submitter
2. Date of the Application/Submission
3. Address
   Address 1 *(Street address, P.O. box, company name c/o)*
   Address 2 *(Apartment, suite, unit, building, floor, etc.)*
   City | State/Province/Region
   Country | ZIP or Postal Code
4. Telephone and Fax Numbers *(Include country code if applicable and area code)*
   (Tel):
   (Fax):

PRODUCT INFORMATION

5. For Drugs/Biologics: Include Any/All Available Established, Proprietary and/or Chemical/Biochemical/Blood/Cellular/Gene Therapy Product Name(s).
   For Devices: Include Any/All Common or Usual Name(s), Classification, Trade or Proprietary or Model Name(s) and/or Model Number(s)

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APPLICATION / SUBMISSION INFORMATION

6. Type of Application/Submission Which This Certification Accompanies

☐ IND ☐ NDA ☐ ANDA ☐ BLA ☐ PMA ☐ HDE ☐ 510(k) ☐ PDP ☐ Other

7. Include IND/NDA/ANDA/BLA/PMA/HDE/510(k)/PDP/ Other Number *(If number previously assigned)* | If BLA was selected in item 6, provide Supplement Number

8. Serial Number Assigned to Application/Submission Which This Certification Accompanies

CERTIFICATION STATEMENT / INFORMATION

9. Check only one of the following boxes *(See instructions for additional information and explanation)*

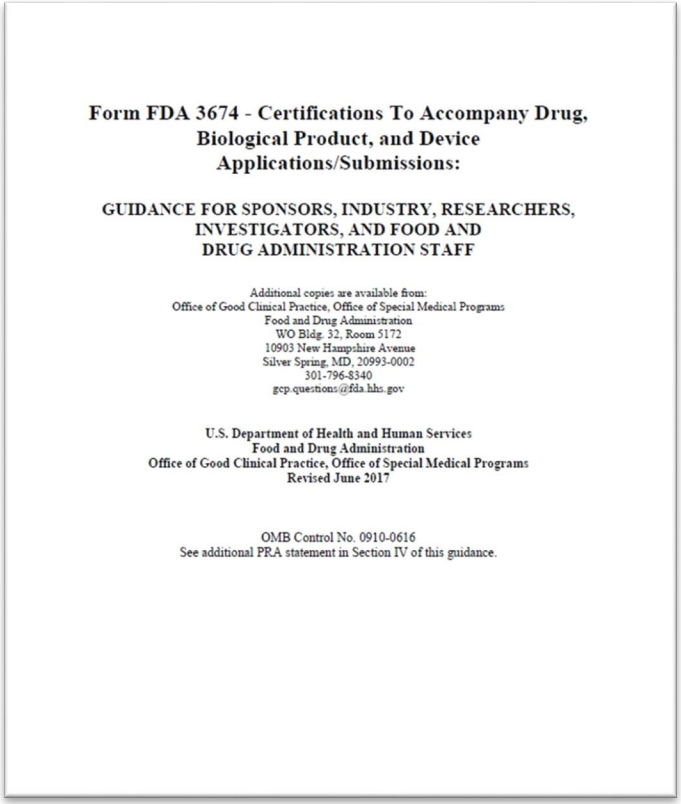
☐ A. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act, including 42 CFR part 11, do not apply because the application/submission which this certification accompanies does not reference any clinical trial.

☐ B. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act, including 42 CFR part 11, do not apply to any clinical trial referenced in the application/submission which this certification accompanies.

☐ C. I certify that the requirements of 42 U.S.C. § 282(j), section 402(j) of the Public Health Service Act, apply to one or more of the clinical trials referenced in the application/submission which this certification accompanies and that the requirements of 42 U.S.C. 282(j), including any applicable provisions of 42 CFR part 11, have been met.

Certification Statement / Information section continued on page 2

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 Clinical Practice, Office of Special Medical Programs
Food and Drug Administration
WO Bldg. 32, Room 5172
10903 New Hampshire Avenue
Silver Spring, MD, 20993-0002
301-796-8340
gcp.questions@fda.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.

FDA's Role Related to ClinicalTrials.gov

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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)]