

ClinicalTrials.gov Protocol Registration Quality Control Review Criteria

Introduction and Overview

This document provides an overview of the ClinicalTrials.gov Protocol Registration Quality Control (QC) review process, along with specific criteria intended to help responsible parties prepare study records with protocol registration information. ClinicalTrials.gov registration information includes 13 modules for describing the study protocol, including Study Identification, Study Status, Oversight, Study Design, Outcome Measures, Eligibility, and others. After a record is released by the responsible party in the Protocol Registration and Results System (also called the PRS), the record is reviewed by National Library of Medicine (NLM) reviewers before it is posted on ClinicalTrials.gov.

As part of the QC review process, the reviewer provides the responsible party with comments noting Major Issues and Advisory Issues. Each Major Issue must be corrected or addressed; Advisory Issues are suggestions for improving the clarity of the record. The QC review process ends when all Major Issues noted in PRS Review Comments have been corrected or addressed by the responsible party. However, NLM may notify responsible parties of issues with a record and request revisions after registration information has been posted publicly.

The responsible party is responsible for ensuring that the study follows all applicable laws and regulations and that the study record is consistent with these criteria. The posting of registration information following the QC review process does not necessarily mean that the information complies with Section 801 of the Food and Drug Administration Amendments Act (FDAAA 801) and the Final Rule for Clinical Trials Registration and Results Information Submission (42 CFR Part 11). The QC review process is intended to help identify apparent errors, deficiencies, and/or inconsistencies in the submitted information; however, it does not assess the appropriateness of the scientific design and analytic approach and cannot ensure that the information is “truthful and non-misleading” under the relevant regulatory standards. Additional information about FDAAA 801 and the Final Rule is available at <https://prsinfo.clinicaltrials.gov>.

General Preferred Formatting Overview

These instructions are intended as a style guide, and registration information should be provided in the format described below. However, the QC review focuses on substantive issues, so the review comments may not note every formatting issue within the registration information.

General Preferred Formatting Review Criteria

1. The study record is written in the third person.
2. The record does not have duplicate or redundant information provided for multiple data elements.
3. Free-text fields are blank if there is no information to report, and they do not contain text such as "TBD," "Pending," "N/A," "None," or similar.
4. Acronyms and abbreviations are spelled out, with the acronym or abbreviation provided in parentheses immediately after, at least the first time they are used (e.g., myocardial infarction (MI), major adverse cardiac events (MACE)).
5. There are no spelling or typographical errors.
6. Numerical values use a period for the decimal point and either a comma for the thousands separator or no separator (e.g., 1,234,567.89 or 1234567.89).
7. Symbols are spelled out (e.g., "percentage" for the % symbol, "number" for the # symbol).
8. A caret, (^) is used to indicate exponents (e.g., kg/m²).
9. "Participants" is the preferred term, rather than "subjects" or "patients."
10. Interventions are referred to by the same name throughout the study record.
11. If more than one name is used for the same drug (e.g., a generic name and a brand name), the study record clearly indicates that the drugs are the same.
12. Intervention names are the nonproprietary (i.e., generic) names instead of internal company serial numbers, if possible.
13. Outcome Measure Titles do not end with a period.

General Review Criteria

1. The record must be in English, with the possible exception of the Official Title; Name of the Sponsor; Collaborators; and Human Subjects Review Board Name, Board Affiliation, and Board Contact data elements.
2. The study involves one or more human subjects and evaluates biomedical and/or health-related outcomes.
3. Written results or conclusions are not presented in any free-text field.
4. Compensation, incentives, or rewards are not described unless they are part of the intervention itself.
5. The entries for each data element are consistent with the [Protocol Registration Data Element Definitions](#).

Study Identification Module Review Criteria

I. Unique Protocol Identification Number

1. Entries do not contain text such as “TBD,” “Pending,” “N/A,” “None,” or similar.

II. Brief Title and Official Title

1. The Brief Title is clear and informative, is written in language intended for the lay public, and includes information on the participants, condition being evaluated, and intervention or interventions being studied.
2. The Brief Title does not include technical study design terms (e.g., Phase 2, Single Group, Double Blind, Randomized, Pharmacokinetics).
3. Acronyms used to identify the study are provided in the Acronym data element.
4. **Overall Record Consistency:** The content of the titles is consistent with information provided in other parts of the study record. For example, if the titles identify the conditions and/or interventions, the respective data elements include the same information.
5. Formatting is as follows:
 - The Brief Title and Official Title do not end with periods.
 - The Brief Title and Official Title are written in title case, that is, the first letter of the first and last words and of each major word is capitalized.

III. Secondary IDs

1. Secondary IDs and Secondary ID Type are used appropriately, that is, the identifier is any other ID assigned to the study, and the type is consistent with the identifier provided.
 - For Secondary ID Type, “Other Identifier” is selected only when none of the pre-specified Secondary ID Type options applies.

Study Status Module Review Criteria

1. **Overall Record Consistency:** The Overall Recruitment Status is consistent with the study dates provided.
2. **Overall Record Consistency:** The study has approval from a human subjects protection review board (or is exempt, as appropriate) before the enrollment of the first participant. Please see the Oversight Review Criteria section for more information.
3. For Overall Recruitment Status, “Suspended,” “Terminated,” or “Withdrawn” is selected only if the study has been halted prematurely (i.e., these options are not used for studies that concluded normally or as expected).
4. The Why Study Stopped data element includes a descriptive and relevant reason for why the study was stopped prematurely.

Sponsor/Collaborators Module Review Criteria

I. Responsible Party, by Official Title

1. If the responsible party is the Principal Investigator or Sponsor-Investigator:
 - The investigator’s full name (first and last names) and professional title are provided.
 - The Investigator Affiliation includes the full name of the organization with which the investigator is affiliated (typically the PRS account’s organizational name or Sponsor Organization name) and does not include the names of individuals or departments.

II. Collaborators

1. For Collaborators, only the full name of any collaborating organizations is provided. Names of individuals, departments, or individual study sites are not included.

Oversight Module Review Criteria

I. Studies a U.S. FDA-regulated Drug Product and Studies a U.S. FDA-regulated Device Product

1. **Overall Record Consistency:** Studies a U.S. FDA-regulated Drug Product and Studies a U.S. FDA-regulated Device Product are consistent with the locations identified in the Facility Information, the information provided for Intervention Type, and all Investigational New Drug Application (IND)/Investigational Device Exemption (IDE)-related information. That is, it would be unusual to select “No” for Studies a U.S. FDA-regulated Drug Product or Studies a U.S. FDA-regulated Device Product if there is at least one U.S. location, and an Intervention Type of “Drug,” “Device,” “Biological/Vaccine,” “Radiation,” “Genetic,” “Combination Product,” or “Diagnostic Test” is selected.

II. U.S. Food and Drug Administration IND or IDE

1. **Overall Record Consistency:** If “Yes” is selected, the Study Type selected is typically “Interventional” or “Expanded Access.” It is unusual for “Observational” to be selected for Study Type for an IND/IDE study, but it can occur. If the Study Type is “Observational,” the specific drug, biologic, or device product is listed with the appropriate Intervention Type, Intervention Name(s), and Intervention Description. (**Note:** The intervention or exposure should not be described as “no drug” or “N/A.”)
2. The IND/IDE Number is in the correct format for each FDA Center.
3. Two or more IND/IDE Numbers are acceptable for studies that are investigating multiple drug or device products. The numbers must be separated by commas or semicolons.
4. The IND/IDE Number and IND Serial Number do not contain text such as “TBD,” “Pending,” “N/A,” “None,” or similar.
5. **Overall Record Consistency:** If “Yes” is selected for Availability of Expanded Access (for a Study Type of “Interventional” or “Observational” only), an investigational drug or biological product is listed for the Interventions data elements.

III. Human Subjects Review

1. **Overall Record Consistency:** If a study is enrolling participants (an Overall Recruitment Status of “Recruiting” or “Enrolling by invitation”) or has enrolled participants (an Overall Recruitment Status of “Active, not recruiting”; “Completed”; “Suspended”; or “Terminated”), the study has human subjects protection review board approval (i.e., Human Subjects Protection Review Board Status is “Submitted, approved” or the study is otherwise exempt, as appropriate).
2. The approval date (in mm/dd/yyyy format) may be used for the Board Approval Number if the human subjects protection review board does not assign approval numbers.

Study Description Module Review Criteria

1. **Overall Record Consistency:** The Brief Summary and Detailed Description do not unnecessarily duplicate information provided for other data elements, such as Outcome Measures or Eligibility.
2. The Brief Summary and Detailed Description are written in complete sentences and do not have formatting errors such as incorrect spacing or indentations, sentences that are missing periods, or similar.

3. The Brief Summary clearly states the study's hypothesis or the purpose of the study (for interventional and observational studies).
4. The Brief Summary clearly describes the availability of expanded access, including the procedure for requesting the investigational product (for expanded access).
5. The Brief Summary and Detailed Description do not include any bibliographic references or any references to external documents. **Note:** References are entered in the Citations data elements, and links to individual participant data (IPD) are provided in the Available IPD and Supporting Information data elements.

Conditions and Keywords Module Review Criteria

1. The Primary Disease or Condition Being Studied in the Trial, or the Focus of the Study data element provides the primary disease or condition being studied or the focus of the study.
2. Diseases or conditions are described using NLM's [Medical Subject Headings](#) (MeSH) controlled vocabulary or the Systematized Nomenclature of Medicine—Clinical Terms ([SNOMED CT](#)), when possible.
3. The Conditions and Keywords data elements do not include any verbs or extraneous information and are not provided in the form of sentences.
4. Each condition and keyword is listed individually, one per line.

Study Design Module Review Criteria

1. **Overall Record Consistency:** The Study Type (either "Interventional," "Observational," or "Expanded Access") and Study Design data elements are consistent with information provided in other parts of the study record.

The following applies to interventional and observational studies only:

2. For Enrollment, the actual enrollment (as opposed to the estimated enrollment) is specified for a study with an Overall Recruitment Status of "Completed" or "Terminated."

The following apply to interventional studies only:

3. **Overall Record Consistency:** The Study Phase is consistent with information provided for the Brief Title and Official Title and for the Brief Summary and Detailed Description (if provided).
4. **Overall Record Consistency:** For Study Phase, "N/A" is selected for trials that do not involve drug or biologic products.
5. If "Device Feasibility" is selected for Primary Purpose, the Enrollment is generally fewer than 10 participants, and the Primary Outcome Measure Information relates to the feasibility of the prototype device, not health outcomes.
6. The Interventional Study Model selected (either "Single Group," "Parallel," "Crossover," "Factorial," or "Sequential") is consistent with the Number of Arms, as follows:
 - If "Single Group" is selected, the study has one arm.
 - If "Parallel" or "Factorial" is selected, the study has two or more arms.
 - If "Crossover" or "Sequential" is selected, the study may have any number of arms.
7. The Interventional Study Model selected (either "Single Group," "Parallel," "Crossover," "Factorial," or "Sequential") is consistent with the Allocation, as follows:

- If “Single Group” is selected, the Allocation is “N/A (not applicable).”
 - If “Parallel,” “Crossover,” or “Factorial” is selected, the Allocation is either “Randomized” or “Nonrandomized.”
 - If “Sequential” is selected, the Allocation is either “N/A (not applicable)” or “Nonrandomized.”
8. For studies with two or more arms, the Allocation is either “Randomized” or “Nonrandomized.”

Arms, Groups, and Interventions Module Review Criteria

1. **Overall Record Consistency:** The Arms, Groups, and Interventions data elements are consistent with each other and with information provided in other parts of the study record.
2. The Arm Title or Group/Cohort Label is brief and informative. For example, “Aspirin” and “Placebo” are more informative than “Arm 1” and “Arm 2.”
3. The Arm Description or Group/Cohort Description include details about the intervention strategies administered (e.g., dosage, dosage form, frequency of administration, duration of administration) or groups evaluated.
4. The Intervention Type appears to be consistent with the information provided for the Intervention Name(s) and Intervention Description data elements.
5. **Overall Record Consistency:** All interventions that were pre-specified for administration as part of the study protocol are listed in the Interventions data elements, even those that are not the intervention of interest.
6. Each intervention is listed separately, unless the intervention is a combination drug product (i.e., multiple drugs combined in the same dosage form).
7. The Intervention Name(s) are specific, unless the study record clearly indicates that the study is not evaluating a specific intervention or exposure.
8. The Intervention Description includes sufficient details to distinguish the intervention being described from other, similar interventions.

Outcome Measures Module Review Criteria

1. **Overall Record Consistency:** The Outcome Measure Title, Description, and Time Frame are consistent with each other and with information provided in other parts of the study record.

The following apply to the Outcome Measure Title and Description:

2. The Outcome Measure Title describes the specific measurement that will be used (e.g., a descriptive name of the scale, physiological parameter, or questionnaire) and the metric for how the collected measurement data will be aggregated (e.g., mean change from baseline).

Examples of appropriate Outcome Measure Titles: “Number of Participants with Treatment-Related Adverse Events as Assessed by CTCAE v4.0,” “Mean Change from Baseline in Pain Scores on the Visual Analog Scale at 6 Weeks,” “Area under the Plasma Concentration versus Time Curve (AUC) of [drug name]”

Examples of inappropriate Outcome Measure Titles: “Safety,” “Tolerability,” “Efficacy,” “Feasibility,” “Pharmacokinetics,” “Bioequivalence,” “Toxicity,” “Pain,” “Quality of Life,” “Satisfaction”

3. The Outcome Measure Title is “outcome neutral,” when possible, especially when reporting a change in a continuous variable (e.g., “Change in Systolic Blood Pressure,” not “Decrease in Systolic Blood Pressure”).
4. The Outcome Measure Description includes information about the measurement or metric included in the Outcome Measure Title (e.g., a measure of “participants with response” should include a brief and informative description of the criteria for “response”).
5. The Outcome Measure Title and Description include a description of what will be measured, not the goal or objective of an assessment or of the study itself.

Example of an inappropriate Outcome Measure: “The aim of this project is to evaluate the efficacy and safety of subthalamic nucleus deep brain stimulation (STN DBS) in treating tics and behavioral features in patients with medically refractory Tourette’s syndrome (TS).”

6. The Outcome Measure Title and Description contain only information relevant to that outcome measure.
7. Each unique outcome measure is presented separately, even if some or all of the outcome measures share a common unit of measure.

Examples of unique outcome measures that must be entered as separate outcome measures: (1) “Blood Pressure” and “Heart Rate,” (2) “Visual Analog Score for Pain” and “Physicians Global Assessment to Measure Quality of Life,” (3) “SF-36 to measure quality of life” and “European Organization for Research and Treatment of Cancer 30-item core quality of life questionnaire (EORTC QLQ C-30)”

The following apply to the Outcome Measure Time Frame:

8. The Outcome Measure Time Frame indicates the specific time point or time points at which the outcome measure will be assessed and for which data will be presented. All time points are expressed from the participant’s perspective (e.g., use “from enrollment to end of treatment at 8 weeks” not “until end of study”). Specific Time Frames also include the cutoff point.

Examples of appropriate Outcome Measure Time Frames: “1 year”; “up to 24 weeks”; “through study completion, an average of 1 year”; “2 hours post-surgery”; “during hospitalization, approximately 5 days”; “post-intervention at Week 12.”

Examples of inappropriate Outcome Measure Time Frames: “postoperative,” “throughout the study,” “through study completion,” “from randomization to end of study,” “every 3 weeks”

9. Time Frames that relate to the particular time point when the intervention occurs (such as a procedure) are described based on the timing of the intervention or event.

Examples of appropriate Time Frames: “intraoperative,” “perioperative,” “preoperative,” “immediately before/after,” “pre-dose,” “during procedure”

10. Time-to-event Time Frames include the estimated period of time over which the event is assessed (e.g., “from the date of assignment until the date of first documented progression or date of death from any cause, whichever comes first, assessed up to 100 months”).

11. Each unique combination of measurement and time point is entered as a separate outcome measure (e.g., “Change from baseline in Hamilton Depression Rating Scale at 8 weeks” and “Change from baseline in Hamilton Depression Rating Scale at 12 weeks”).
12. Pharmacokinetic outcome measures (e.g., C_{max} , AUC) rely on multiple measurements over time, so these Time Frames may include multiple time points describing the intervals at which data are collected (e.g., “1, 2, 3, 4, 5, 6, 8, 12, 24, 48, 72, and 96 hours post-dose”).
13. Measures-of-change Time Frames specify two or more time points (e.g., “at baseline and in 6 months”).
14. A standard unit of time is specified.
15. One-letter abbreviations are spelled out for clarity.

Examples of appropriate Time Frames: “Day 0,” “Month 3”

Examples of inappropriate Time Frames: “D1,” “M3”

16. The overall time period for which each outcome measure is assessed is described, rather than the specific calendar dates at which the assessment occurs.

Eligibility Module Review Criteria

1. **Overall Record Consistency:** The Age Limits are consistent with the Eligibility Criteria and with information provided in other parts of the study record.
2. The Eligibility Criteria data element does not contain text such as “TBD,” “Pending,” “N/A,” “None,” or similar.
3. The Eligibility Criteria data element includes lists of inclusion and exclusion criteria in the format shown below:

Inclusion Criteria:

- Clinical diagnosis of Alzheimer’s disease
- Must be able to swallow tablets

Exclusion Criteria:

- Insulin-dependent diabetes
- Thyroid disease

Contacts, Locations, and Investigator Information Module Review Criteria

1. The Facility Name is the full name of the organization where the study is being conducted.
2. Each facility is listed in a separate field.

IPD Sharing Statement Module Review Criteria

1. The Plan to Share IPD selection is consistent with the IPD Sharing Plan Description.
2. The Plan to Share IPD and IPD Sharing Plan Description indicate and describe the plan to make de-identified IPD collected during the study available to other researchers. These data elements are not used to indicate that results have been, or will be, presented at conferences or published in medical journals.

References Module Review Criteria

I. Citations

1. Each citation is listed in a separate field.

II. Links

1. The links are to active Web pages related to the study. **Note:** Sites whose primary goal is to advertise or sell commercial products or services are not acceptable. Links to educational, research, government, and other nonprofit Web sites are acceptable.

III. Available IPD and Supporting Information

1. The Available IPD/Information Type, Available IPD/Information URL, Available IPD/Information Identifier, and Available IPD/Information Comments data elements are consistent with each other and with information provided in other parts of the study record.

ClinicalTrials.gov Quality Control Review Criteria: Document Upload Information

Document Upload Information Overview

This document provides the ClinicalTrials.gov Document Upload Information Quality Control (QC) Review Criteria to help responsible parties prepare study documents for upload. The full study protocol and statistical analysis plan (SAP) must be uploaded as part of results information submission for studies with a Primary Completion Date on or after January 18, 2017. The study protocol and statistical analysis plan may be uploaded before results information is submitted and then updated, as needed, by uploading new versions. Informed consent forms may optionally be uploaded at any time.

Uploaded study documents must be in Portable Document Format Archival (PDF/A) file format, and each document must include a cover page with the study's Official Title, its NCT Number (if available), and the date of the document. Each uploaded document should be the most recent version reviewed by the human subjects protection review board (if applicable). **Note:** Uploaded study documents will be posted on the ClinicalTrials.gov public website after a quality control review.

Document Upload Information Review Criteria

1. The Document must be in English.
2. The cover page includes the information needed to confirm that the Document is related to the study described in the study record, specifically, the study's Official Title, its NCT Number (if available), and the date of the Document.
3. The Document Date data element in the study record is consistent with the latest version date in the uploaded document.
4. The Document Type data element in the study record accurately reflects the content in the uploaded document (e.g., "Study Protocol with SAP" is selected for an uploaded study protocol that includes a statistical analysis plan).
5. The Document does not include any tracked changes or comments that do not appear to be part of a version that would be reviewed or approved by the human subjects protection review board.
6. The Document does not include the name, address, or other personally identifiable information (PII) of any study participant.
7. The Document does not include redactions of information that is required to be submitted and posted on ClinicalTrials.gov. Only PII, trade secret, or confidential commercial information may be redacted.