**PREFACE**

This clinical trial protocol template is a suggested format for Phase 2 and 3 clinical trials funded by the National Institutes of Health (NIH) that are being conducted under a Food and Drug Administration (FDA) Investigational New Drug (IND) or Investigational Device Exemption (IDE) Application. Investigators for such trials are encouraged to use this template when developing protocols for NIH-funded clinical trial(s). This template may also be useful to others developing phase 2 and 3 IND/IDE clinical trials.

The goal of this template is to assist investigators to write a comprehensive clinical trial protocol that meets the standard outlined in the *International* *Conference on Harmonisation (ICH) Guidance for Industry, E6 Good Clinical Practice: Consolidated Guidance (ICH-E6)*. Its use will also help investigators think through the scientific basis of their assumptions, minimize uncertainty in the interpretation of outcomes, and prevent loss of data. A common protocol structure and organization will facilitate protocol review by oversight entities.

It is important to note that the clinical trial protocol template is just one piece of information required for an IND or IDE submission. For complete details on IND or IDE submissions see 21 CFR Part 312: Investigational New Drug Application or 21 CFR Part 812: Investigational Device Exemptions, respectively.

**How To Use This Template**

It is important to incorporate all sections of the template into your protocol and to do so in the same order. If a particular section is not applicable to your trial, include it, but indicate that it is not applicable.

This template contains two types of text: instruction/explanatory and example.

**Instruction/explanatory text** are indicated by *italics* and should deleted. Footnotes to instructional text should also be deleted. This text provides information on the content that should be included. It also notes if a section should be left blank. For example, many headings include the instruction, “*No text is to be entered in this section; rather it should be included under the relevant subheadings below.*”

**Example text** is included to further aid in protocol writing and should either be modified to suit the drug, biologic or device (study intervention), design, and conduct of the planned clinical trial or deleted. Example text is indicated in [regular font]. Within example text, a need for insertion of specific information is notated by <angle brackets>.

Instruction/explanatory text should be deleted. Example text can be incorporated as written or tailored to a particular protocol. If it is not appropriate to the protocol, however, it too should be deleted. The section headers include formatting to generate a table of contents.

Version control is important to track protocol development, revisions, and amendments. It is also necessary to ensure that the correct version of a protocol is used by all staff conducting the study. With each revision, the version number and date located in the footer of each page should be updated. When making changes to an approved and “final” protocol, the protocol amendment history should be maintained (see Section 10.4).

**RESOURCES**

Center for Medicare & Medicaid Services (CMS)

* [Clinical Laboratory Improvement Amendments](https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/index.html?redirect=/clia/)

Code of Federal Regulations (CFR)

* [21 CFR Part 11: Electronic Records, Electronic Signatures](https://www.ecfr.gov/cgi-bin/text-idx?SID=007006046b07c9fc5244ec13ef4a77bb&mc=true&node=pt21.1.11&rgn=div5)
* [21 CFR Part 50: Protection of Human Subjects](https://www.ecfr.gov/cgi-bin/text-idx?SID=6d82202a67ba5bd44148d99f4aaf7198&mc=true&node=pt21.1.50&rgn=div5)
* [21 CFR Part 54: Financial Disclosure by Clinical Investigators](https://www.ecfr.gov/cgi-bin/text-idx?SID=bae2d66180fd49cb11f40a935cd760a7&mc=true&node=pt21.1.54&rgn=div5)
* [21 CFR Part 56: Institutional Review Boards](https://www.ecfr.gov/cgi-bin/text-idx?SID=64724709940d94a34270c77fdb8d307f&mc=true&node=pt21.1.56&rgn=div5)
* [21 CFR Part 58: Good Laboratory Practice for Nonclinical Laboratory Studies](http://www.ecfr.gov/cgi-bin/text-idx?SID=90f8b344173d4c43e0c515d0a0cbc4de&mc=true&node=pt21.1.58&rgn=div5)
* [21 CFR Part 210: Current Good Manufacturing Practice In Manufacturing, Processing, Packing, Or Holding Of Drugs; General](http://www.ecfr.gov/cgi-bin/text-idx?SID=90f8b344173d4c43e0c515d0a0cbc4de&mc=true&node=pt21.4.210&rgn=div5)
* [21 CFR Part 211: Current Good Manufacturing Practice For Finished Pharmaceuticals](http://www.ecfr.gov/cgi-bin/text-idx?SID=90f8b344173d4c43e0c515d0a0cbc4de&mc=true&node=pt21.4.211&rgn=div5)
* [21 CFR Part 312: Investigational New Drug Application](https://www.ecfr.gov/cgi-bin/text-idx?SID=27a0c0825d11663283856731fb14c8d2&mc=true&node=pt21.5.312&rgn=div5)
* [21 CFR Part 812: Investigational Device Exemptions](https://www.ecfr.gov/cgi-bin/text-idx?SID=0f8fa3b740966b3d21d5501233e2b493&mc=true&node=pt21.8.812&rgn=div5)
* [42 CFR Part 11: Clinical Trial Registration and Results Information Submission](https://www.gpo.gov/fdsys/pkg/CFR-2016-title42-vol1/pdf/CFR-2016-title42-vol1-part11.pdf)
* [45 CFR Part 46: Protection of Human Subjects Research](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html)

Food and Drug Administration (FDA)

* [Compliance Actions and Activities](http://www.fda.gov/ICECI/EnforcementActions/default.htm)
* [FDA Regulations Relating to Good Clinical Practice and Clinical Trials](http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ucm155713.htm)
* [Guidance for Clinical Investigators, Sponsors, and IRBs Adverse Event Reporting to IRBs – Improving Human Subject Protection](http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126572.pdf)
* [Guidance for Clinical Trial Sponsors: Establishment and Operation of Clinical Trial Data Monitoring Committees](http://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm127073.pdf)
* [Guidance for Industry: E6 Good Clinical Practice: Consolidated Guidance](https://www.fda.gov/downloads/Drugs/.../Guidances/ucm073122.pdf)
* [Guidance for Industry: Electronic Source Data in Clinical Investigations](http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm328691.pdf)
* [Guidance for Industry: Multiple Endpoints in Clinical Trials](https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM536750.pdf)
* [Guidance for Industry: Oversight of Clinical Investigations – A Risk-Based Approach to Monitoring](http://www.fda.gov/downloads/Drugs/Guidances/UCM269919.pdf)
* [Guidance for Industry: Providing Regulatory Submissions in Electronic Format - Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications](http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM333969.pdf)
* [Guidance for Industry: Providing Regulatory Submissions in Electronic Format — Standardized Study Data](http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM292334.pdf)
* [Guidance for Industry: Safety Assessment for IND Safety Reporting](http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm477584.pdf)

Department of Health and Human Services (HHS)

* [The HIPAA Privacy Rule](http://www.hhs.gov/hipaa/for-professionals/privacy/)
* [HIPAA Privacy Rule: Information for Researchers](https://www.hhs.gov/hipaa/for-professionals/special-topics/research/index.html)

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)

* [Guidance for Industry, E6 (R2) Good Clinical Practice: Consolidated Guidance](http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM464506.pdf)
* [Guidance for Industry, M3(R2) Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals](http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm073246.pdf)
* [Guideline for Industry, E3 Structure and Content of Clinical Reports](http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm073113.pdf)
* [Guidance for Industry, E9 Statistical Principles for Clinical Trials](http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm073137.pdf)
* [Final Concept Paper E9(R1): Addendum to Statistical Principles for Clinical Trials on Choosing Appropriate Estimands and Defining Sensitivity Analyses in Clinical Trials](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E9/E9__R1__Final_Concept_Paper_October_23_2014.pdf)

International Organization for Standardization (ISO)

* [Clinical Investigation of Medical Devices for Human Subjects -- Good Clinical Practice (ISO 14155:2011)](https://www.iso.org/obp/ui/%20-%20iso%3Astd%3Aiso%3A14155%3Aed-2%3Av1%3Aen)

National Institutes of Health (NIH)

* [Certificates of Confidentiality (CoC) Kiosk](http://grants.nih.gov/grants/policy/coc/index.htm)
* [Clinical Trials Registration and Results Information Submission](https://www.federalregister.gov/documents/2016/09/21/2016-22129/clinical-trials-registration-and-results-information-submission)
* [Financial Conflict of Interest](http://grants.nih.gov/grants/policy/coi/)
* [Inclusion of Children- Policy Implementation](https://grants.nih.gov/grants/funding/children/children.htm)
* [Inclusion Of Women And Minorities As Participants In Research Involving Human Subjects- Policy Implementation Page](http://grants.nih.gov/grants/funding/women_min/women_min.htm)
* [NIH Data Sharing Policies and Related Guidance on NIH-Funded Research Resources](http://grants.nih.gov/policy/sharing.htm)
* [NIH Data Sharing Policy and Implementation Guidance](http://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm)
* [NIH Genomic Data Sharing Policy](https://gds.nih.gov/03policy2.html)
* [NIH Grants Policy Statement, Section 8.2 Availability of Research Results: Publications, Intellectual Property Rights, and Sharing Research Resources](http://grants.nih.gov/grants/policy/nihgps/HTML5/section_8/8.2_availability_of_research_results_publications__intellectual_property_rights__and_sharing_research_resources.htm)
* [NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information](https://www.gpo.gov/fdsys/pkg/FR-2016-09-21/pdf/2016-22379.pdf)
* [NIH Public Access Policy Details](http://publicaccess.nih.gov/policy.htm)
* [Policy on Good Clinical Practice Training for NIH Awardees Involved in NIH-funded Clinical Trials](https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-148.html)
* [Required Education in the Protection of Human Research Participants](http://grants.nih.gov/grants/guide/notice-files/NOT-OD-01-061.html)

Office for Human Research Protections (OHRP)

* [Human Subject Regulations Decision Charts](http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html)
* [Informed Consent Checklist](http://www.hhs.gov/ohrp/policy/consentckls.html)
* [Informed Consent Tips](http://www.hhs.gov/ohrp/policy/ictips.html)
* [IRBs and Assurances](http://www.hhs.gov/ohrp/assurances/)
* [Regulations & Policy Index](http://www.hhs.gov/ohrp/regulations-and-policy/index.html)
* [Unanticipated Problems Involving Risks and Adverse Events Guidance](http://www.hhs.gov/ohrp/regulations-and-policy/guidance/reviewing-unanticipated-problems/index.html)
* [Vulnerable Populations](http://www.hhs.gov/ohrp/regulations-and-policy/guidance/vulnerable-populations/)

Other

* [Citing Medicine, 2nd edition: The NLM Style Guide for Authors, Editors, and Publishers](http://www.ncbi.nlm.nih.gov/books/NBK7256/)
* [CONSORT statement](http://www.consort-statement.org/)
* [International Committee of Medical Journal Editors (ICMJE): Recommendations](http://www.icmje.org/recommendations/)
* [Practical Aspects of Signal Detection in Pharmacovigilance: Report of CIOMS Working Group VIII](http://cioms.ch/shop/product/practical-aspects-of-signal-detection-in-pharmacovigilance-report-of-cioms-working-group-viii/)