Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)

Clinical Research Policy
Guidance Document

Overview of Responsibilities for ClinicalTrials.gov: Compliance with Public Law 110-85 The Food and Drug Administration Amendments Act Title VIII Clinical Trial Databases

Version 1.0

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Change History

Date	Version	Change
September 22, 2009	1.0	Initial Draft
October 26, 2009		Revisions
September 19, 2010		Reformatting and update references
October 25, 2010		Copyedit

1.0 Introduction

The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) maintains an extensive clinical research portfolio conducting and supporting research on all stages of human development, from preconception to adulthood, to better understand the health of children, adults, families, and communities. Research may take place both in and outside the United States with some research primarily occurring in developing countries.

As a result of Public Law 105-115, known as the Food and Drug Administration (FDA) Modernization of 1997, the National Library of Medicine (NLM) within the National Institutes of Health (NIH) developed an Internet-based registry, http://ClinicalTrials.gov, to offer the general public up-to-date information for clinical trials for particular diseases and conditions that were considered life threatening. Compliance was voluntary, but clinical trials to be published in many medical journals had to be listed in a registry on the basis of a policy established by the International Committee of Medical Journal Editors (ICMJE) and published in multiple journals concurrently in 2004. On September 27, 2007, Public Law 110-85, known as the FDA Amendments Act of 2007 or FDAAA, in Title VIII broadened the scope of the ClinicalTrials.gov registry to all diseases and conditions and added several new features and responsibilities, including reporting results in summary form to include adverse event data within one year after a listed trial closed. The FDAAA Title VIII classifies certain clinical trials, termed "applicable clinical trials," as obligatory to be listed in the registry. An "applicable drug clinical trial" studies an FDA-regulated product to evaluate potential clinical effect. The NIH encourages listing of all clinical trials, whether required under the law or not.[1]

Currently, in a reaffirmation of policy regarding the obligation to register clinical trials, the ICMJE does not consider posting of clinical trial results in the same registry as the one initially listing the trial as a prior publication, but posting results in a different registry is considered prior publication.[2]

Definitions of Clinical Trial

Several definitions of the term "clinical trial" could apply to FDAA.

The FDA definition of a clinical trial is in the Code of Federal Regulations Title 21 Part 50 – Protection of Human Subjects, where a clinical investigation or trial is defined as "any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration (FDA) under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the FDA under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit."[3]

The NIH defines clinical research as:

[1] http://grants.nih.gov/ClinicalTrials_fdaaa/faq.htm#a4
[2] http://www.icmje.org/publishing_10register.html
[3] http://ecfr.gpoaccess.gov

1. Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are *in vitro* studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes:
    a. Mechanisms of human disease
    b. Therapeutic interventions
    c. Clinical trials
    d. Development of new technologies
2. Epidemiologic and behavioral studies
3. Outcomes research and health services research[4]

The NIH defines a clinical trial as a "biomedical or behavioral research study of human subjects designed to answer specific questions about biomedical or behavioral interventions (drugs, treatments, devices, or new ways of using known drugs, treatments, or devices). Clinical trials are used to determine whether new biomedical or behavioral interventions are safe, efficacious, and effective." [5]

On the Clinicaltrials.gov Web site, the NLM defines a clinical trial and clinical research as "a research study in human volunteers to answer specific health questions. Interventional trials determine whether experimental treatments or new ways of using known therapies are safe and effective under controlled environments. Observational trials address health issues in large groups of people or populations in natural settings."[6]

Defining "Applicable Drug Clinical Trial"

The FDAAA amends the Public Health Service Act to mandate registration and results reporting of "applicable clinical trials" in ClinicalTrials.gov. The FDAAA defines "applicable drug clinical trial" as a "controlled clinical investigation, other than a phase I clinical investigation, of a drug subject to section 505 of the Federal Food, Drug, and Cosmetic Act or to section 351 of this Act." [7]

Under the statute, the "applicable clinical trials" trials generally include:

(1) Trials of Drugs and Biologics: Controlled, clinical investigations, other than phase 1 investigations, of a product subject to FDA regulation; and

(2) Trials of Devices: Controlled trials with health outcomes, other than small feasibility studies, and pediatric post-market surveillance.

The FDAAA also includes a requirement that if an "applicable clinical trial" is funded in whole or in part by a grant from any agency of the Department of Health and Human Services, any

[4] http://grants.nih.gov/grants/glossary.htm
[5] http://grants.nih.gov/grants/glossary.htm#C14
[6] http://clinicaltrials.gov/ct2/info/about
[7] http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_public_laws&docid=f:publ085.110.pdf

grant or progress report shall include a certification that the responsible party has made all required submissions for the applicable trial to ClinicalTrials.gov.

Trials initiated after September 27, 2007, or trials initiated before that date and ongoing beyond on December 26, 2007, that involve a "serious or life-threatening disease or condition," must be registered in full 21 days after the first patient is enrolled. "Ongoing" in this context means a trial had one or more patients enrolled, but had not reached its "completion date," meaning study researchers had not examined the final subject or provided the final subject an intervention for the purposes of final collection of data for the primary outcome.[5] However, a clinical trial that was ongoing on the date of enactment of the FDAAA but was completed before December 26, 2007, is not subject to the requirements for listing results as noted in section 402(j) of the Public Health Service Act.

Summary of NIH Policy

NIH Policy with respect to FDAAA is to reinforce that NIH-funded research must comply with the law, clarification, and guidance on determining which clinical trials are considered "applicable" and must comply with the law and a statement that NIH funded-clinical trials that do not require compliance with the law are encouraged to be listed.[8]

Further guidance is provided on determination of the responsible party for "applicable" clinical trials with a graphic flow chart to assist. [9]An NIH Notification listed as NOT-OD-09-147 states that "Mechanisms previously established by NIH Institutes and Centers (ICs) to directly assist funding recipients in registering and reporting results for applicable clinical trials with ClinicalTrials.gov, such as NIH-funded contractor support for ClinicalTrials.gov registration and the inclusion of NIH-funded extramural applicable clinical trials in IC-controlled organization accounts when the NIH is not the Responsible Party for the trial (as defined in FDAAA), are no longer being supported. It is expected that the Responsible Party will undertake all activities associated with registration and reporting of results. In general, Responsible Parties are required to affiliate their applicable clinical trials with their Institution's organization account or their own individual account, as appropriate. They will no longer be registered in an IC organization account. While some IC staff may provide technical assistance as a public service during the process of transition from IC organization accounts and for registration, Responsible Parties are solely responsible for the content, quality and timeliness of registration and results reporting in accord with FDAAA. Responsible Parties are encouraged to consult with appropriate local officials, including counsel, to ensure compliance with their obligations under FDAAA. NIH ICs cannot in any way substitute for the Responsible Party in fulfilling its statutory duties."[10]

2.0 NICHD Policy on ClinicalTrials.gov

Purpose of NICHD Policy

The extensive clinical research portfolio and support of multiple consortia and networks places specific obligations upon NICHD to fully comply with the FDAAA and to clarify the recommended

[8] http://grants.nih.gov/ClinicalTrials_fdaaa/faq.htm#b1
[9] http://grants.nih.gov/ClinicalTrials_fdaaa/docs/registration_flow_chart.pdf
[10] http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-147.html

process. The NICHD developed this Guidance document to highlight appropriate measures and responsibilities for listing applicable and other clinical trial data on the ClinicalTrials.gov registry.

The reasons for listing NICHD-funded clinical trials on ClinicalTrials.gov are to improve accrual, maintain an accurate listing of clinical research activity, provide transparency, support publication in high-impact journals, and display in a credible public setting the high quality and exciting work the Institute supports.

Process of NICHD Policy Development

In an effort to address the FDAAA, the NICHD has completed the following activities to support the development of this guidance document:

- Conducted briefing at the NICHD Director's Staff meeting in late 2007
- Released an all hands e-mail to NICHD extramural staff on February 14, 2008
- Presented to NICHD extramural staff on March 6, 2008
- Attended briefing at the NIH Institute Directors' Meeting on July 10, 2008
- Discussed at NICHD Director's Staff meeting in July 21, 2008
- Released all hands e-mail reminder and update to NICHD extramural staff on December 15, 2008
- Conducted briefing at NICHD Director's Staff meeting in January 2009
- Discussed at NICHD Branch Chiefs' and Center Directors' Staff meeting in January 13, 2009, at which clarification was made that all awardees would be contacted by Grants Management Branch regarding memorandum from NIH Director's Office
- Conducted briefing to NICHD extramural staff on January 16, 2009.
- Communicated NIH policy on compliance with Public Law 110-85 pertaining to reporting requirements for ClinicalTrials.gov to all grant awardees on February 9, 2009 (NICHD Grants Management Branch)
- Presented an update of ClinicalTrials.gov to NICHD extramural staff on May 21, 2009
- Published NOT-OD-09-147 on September 4, 2009, to clarify the role of the NIH in providing assistance for the registration of, and reporting of results for, applicable drug clinical trials; specifically, the notice states that: "it is expected that the clinical trial Responsible Party will undertake all activities associated with registration and reporting of results. NIH ICs cannot in any way substitute for the Responsible Party in fulfilling its statutory duties."

Additionally, the NICHD developed this policy and guidance document through review of past standards and the existing NIH Policy.

The NICHD policy is consistent with NIH policy in that all applicable clinical trials are required to be registered and all other clinical research studies consistent with the NLM definition are encouraged to be listed in ClinicalTrials.gov.

General FDAAA Responsibilities

All "applicable" clinical trials must:

1. Be approved by a human subject review board and must conform to the regulations of the appropriate national health authorities, in order to be registered.
2. For trials initiated after September 27, 2007, be registered in full not later than 21 days after the first participant is enrolled.
3. Have registry records kept current and in compliance with the law.
4. Report summary results within one year following the completion of the clinical trial. Note that the completion date is determined by the clinical trial sponsor and reported to ClinicalTrials.gov. The summary results along with adverse events are due one year after the reported completion date.

Failure to comply can result in civil penalties.

Through the implementation of the FDAAA on Clinical Trials Registries, the NICHD will proceed in accord with NIH recommendations for funded *applicable* trials in the ClinicalTrials.gov registry by assigning or delegating the responsibility to the awardee or principal investigator, as appropriate.

Identifying the Responsible Party for "Applicable" Clinical Trials

"Responsible Party" is the term used in the FDAAA to refer to the entity or individual who is responsible for registering a clinical investigation and submitting and maintaining clinical trial information to the Clinical Trial Registry Data Bank on ClinicalTrials.gov. The statute defines the Responsible Party as:

> "(1) the sponsor of the clinical trial (as defined in section 50.3 of title 21, Code of Federal Regulations (or any successor regulation); or
>
> (2) The principal investigator of such clinical trial if so designated by a sponsor, grantee, contractor, or awardee, so long as the principal investigator is responsible for conducting the trial, has access to and control over the data from the clinical trial, has the right to publish the results of the trial, and has the ability to meet all of the requirements under this subsection for the submission of clinical trial information."

There are several ways to identify the Responsible Party. Per NIH guidance, investigators are encouraged to consult with their sponsored research office, institutional counsel, or other institution officials to determine if they are the Responsible Party for registering a trial. It is the applicant or grantee's responsibility to determine if they are obligated to register their clinical trials under the FDAAA.

The FDA's Investigational New Drug (IND) Program is the means by which an experimental drug or biologic product may be legally shipped across state lines. FDA reviews the IND application for safety to assure that research subjects involved in clinical research with the experimental drug or biologic product will not be subjected to unreasonable risk. An analogous mechanism for devices is termed an Investigational Device Exemption (IDE).

For NIH-funded clinical trials with an IND or IDE holder, consistent with FDA regulations, the IND or IDE holder is the sponsor and will be considered the Responsible Party unless this obligation is delegated to the principal investigator. This delegation should be done by a written agreement or memorandum of understanding signed by all parties, and the principal investigator or delegated party must have his or her own individual ClinicalTrials.gov account (a sample template for delegating responsibility is included in an Appendix to this document).

For NIH-funded clinical trials with no IND or IDE holder, the funding recipient will be considered the Responsible Party. For NIH-funded clinical trials in which NICHD is the IND or IDE holder, the NICHD will plan to formally delegate responsibility to the principal investigator. Per NIH Guidance NOT-OD-08-014[11], "responsible parties are solely responsible for the quality, and timeliness of registration and results reporting in accord with Public Law 110-85 Title VIII."

The NICHD is not responsible for listing, maintaining, or updating any applicable drug clinical trial on ClinicalTrials.gov for which NICHD is not the Responsible Party.

Responsible Parties for applicable drug clinical trials that are not compliant receive a letter citing the legal requirements. A civil monetary penalty of not more than $10,000 a day may be enforced for non-compliance. If violation is not corrected within the 30-day period after receipt of a citation letter, the Responsible Party may be subject to a civil monetary penalty of not more than $10,000 for each day of the violation until the violation is corrected.

Listing of Clinical Trials that Are Not Considered "Applicable"

Recipients of funding for any other clinical investigation that is not an applicable clinical trial are strongly encouraged by NIH and NICHD policies, but not required by FDAAA, to register clinical trial information on ClinicalTrials.gov. For non-applicable clinical trials, there are no FDAA requirements and therefore no civil monetary penalties for non-compliance. However, compliance with NIH and NICHD policies and expectations will be tracked and noted. In addition, records should be kept current and the data fields must be in compliance with ClinicalTrials.gov specifications.

Account Transfer

To obtain an account with ClinicalTrials.gov for either an organization or an individual, apply to the Protocol Registration System (PRS) at http://prsinfo.clinicaltrials.gov/. There is no charge for establishing or maintaining an account.

To transfer ClinicalTrials.gov accounts from one party, such as the NICHD, to another, the procedure is to provide to either the NICHD (through the Project Officer) or directly to *register@clinicaltrials.gov*, the following:

- The National Clinical Trial (NCT) number of the record (or the Unique Protocol ID if no NCT number has been issued yet);

[11] http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-014.html

- Name of the organization (or the PRS organizational account) to receive the trial;
- Account owner's name (username; *note: this user name must already exist in the recipient PRS organization account*); and
- Any and all NIH grant numbers applicable to the protocol.

NICHD Specific Responsibilities

To minimize questions about whether a given trial is an "applicable" clinical trial, the NICHD recommends that a portfolio or general initiative containing at least one potential "applicable clinical trial," for example a series of studies under an IND or IDE, be handled administratively as if every individual study *could* be an "applicable clinical trial." Consequently, for programs that hold one or more IND or IDE, the NICHD or its agent (relevant vendors or contractors such as a data coordinating center that is under contract) would not become the Responsible Party and would not provide support for registry listings and maintenance, but that responsibility would either be delegated or assigned to a qualified Responsible Party such as a principal investigator consistent with the NIH Policy. For further details refer to NIH Policy listings for FDAAA. [12]

For clinical trials that are not considered "applicable" but that are consistent with the NLM definition of clinical trial (see definitions earlier in this document), the NICHD will expect compliance with listing and reporting of results by the recipient (or designee) of an award. Plausible parties for entering and maintaining registry listings for clinical trials that are not considered "applicable" include principal investigators, data coordinating centers, or other designated staff. The NICHD expects to be informed of the name and contact information for the point of contact for maintaining ClinicalTrials.gov listings.

NICHD Support

NICHD will not maintain listings for clinical trials on ClinicalTrials.gov unless the NICHD is the Responsible Party. The NICHD can provide support in the form of technical advice with the goal of encouraging listing of all NICHD funded clinical investigations to improve accrual, maintain an accurate listing of clinical research activity, provide transparency, and display in a consistent setting the high quality and exciting work the Institute funds. Technical advice may be obtained through NICHD Program Officers. The NICHD will monitor compliance with the FDAAA for all "applicable" clinical trials funded by the NICHD.

As a convenience, appendices to this document review the following information:

1. NIH procedures for determining the responsible party for an "applicable" study
2. Data fields with definitions to be entered into protocol records for the ClinicalTrials.gov database
3. A Sample Document for Delegating Responsibility

Further questions regarding NICHD implementation of FDAAA and ClinicalTrials.gov policy may be directed to:

Steven Hirschfeld, M.D., Ph.D.
Associate Director for Clinical Research

[12] http://grants.nih.gov/grants/guide/notice-files/NOT-OD-10-007.html

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Bethesda, MD 20814
E-mail: hirschfs@mail.nih.gov

Appendix A: Determination of Responsible Party[13]

- This flowchart presents basic guidance on determining whether or not you would be considered to be the "responsible party" under FDAAA. **It may not address every situation.**
- The flowchart begins once you have determined that your NIH grant or cooperative agreement funds (in whole or in part) an "applicable clinical trial" that must be registered under FDAAA.
- Consult with your institution's sponsored research office, general counsel, or other similar official when determining whether or not you are the responsible party for an applicable clinical trial.

Step	Question	Answer
1.	Does the "applicable clinical trial" involve an IND/IDE?	If yes, go to Step 2. If no, go to Step 3.
2.	Are you the IND/IDE holder?	If yes, you would generally be considered the sponsor under FDAAA. Go to Step 4. If no, you would not generally be considered the sponsor under FDAAA, and not considered the Responsible Party unless you answer "Yes" to the question in Step 5. Go to Step5.
3.	Would you be considered the "initiator" of the trial? For example: (A) Grants: are you the recipient of a research assistance funding agreement such as a grant or sponsored research agreement? (B) Contracts: are you obtaining the goods or services for direct benefit or use under a procurement funding agreement such as a contract?	If yes, you would generally be considered the sponsor under FDAAA. Go to Step 4 to determine if you are the responsible party. If no, you would not generally be considered the sponsor under FDAAA, and not considered the Responsible Party unless you answer "Yes" to the question in Step 5. Go to Step 5.
4.	As sponsor, did you designate a principal investigator as the "Responsible Party"?	If yes, you would not generally be considered the Responsible Party under FDAAA. If no, you would generally be considered the Responsible Party under FDAAA.
5.	Are you a principal investigator designated as "Responsible Party" by the sponsor?	If yes, you would generally be considered the Responsible Party under FDAAA. If no, you would not generally be considered the Responsible Party under FDAAA.

[13] http://grants.nih.gov/ClinicalTrials_fdaaa/docs/registration_flow_chart_narrative.doc

Appendix B: ClinicalTrials.gov Data Entry Fields

Term	Definition
Titles and Background Information	
Organization's Unique Protocol ID	Unique identification assigned to the protocol by the sponsoring organization, usually an accession number or a variation of a grant number. Multiple studies conducted under the same grant must each have a unique number.
Secondary IDs	Other identification numbers assigned to the protocol, including unique identifiers from other registries and NIH grant numbers, if applicable. Provide up to 5 Secondary ID Numbers, one per line.
Brief Title	Protocol title intended for the lay public
Acronym	Acronym or initials used to identify this study, if applicable. Enter only the acronym. If supplied, the acronym is automatically displayed in parentheses following the brief title.
Official Title	Official name of the protocol provided by the study principal investigator or sponsor
Study Type	Nature of the investigation. Select one.
U.S. Food and Drug Administration (FDA) Information	Federal agency responsible for regulating and supervising the safety of foods, tobacco products, dietary supplements, Medication drugs, vaccines, Biopharmaceutical, blood transfusion, medical devices, Electromagnetic radiation emitting devices, veterinary products, and cosmetics. The FDA also enforces section 361 of the Public Health Service Act and the associated regulations, including sanitation requirements on interstate travel as well as specific rules for control of disease on products ranging from pet turtles to semen donations for assisted reproductive medicine techniques.
FDA Regulated Intervention	Indicate whether this trial includes an intervention subject to FDA regulation under section 351 of the Public Health Service Act or any of the following sections of the Federal Food, Drug and Cosmetic Act: 505, 510(k), 515, 520(m), and 522
Section 801 Clinical Trial?	If this trial includes an FDA regulated intervention, indicate whether this is an "applicable clinical trial" as defined in U.S. Public Law 110-85, Title VIII, Section 801. Briefly, applicable drug trials include controlled clinical investigations, other than phase I investigations, of a drug or biologic subject to FDA regulation. Applicable device clinical trials are controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and pediatric post-market surveillance.
Delayed Posting	If this is a Section 801 “applicable clinical trial”, indicate whether this trial includes a device NOT previously approved or cleared by the FDA for any use, as specified in US Public Law 110-85, Title VIII, Section 801. Select Yes/No. If "Yes" is selected, full posting of the trial information on ClinicalTrials.gov will be delayed until after the device has been approved or cleared.
IND/IDE Protocol?	Indicate if the protocol involves an Investigational New Drug Application (IND) or Investigational Device Exemption (IDE) under FDA regulations (Will not be made public - for administrative purposes only.)
IND/IDE Grantor	FDA center to which the IND or IDE was submitted, i.e., Center for Drug Evaluation and Research (CDER) or Center for Biologics Evaluation and Research (CBER) for INDs; Center for Devices and Radiological Health (CDRH) for IDEs. Select one. (Will not be made public - for administrative purposes only.)
IND/IDE Number	Number assigned to an Investigational New Drug Application (IND) or Investigational Device Exemption (IDE). (Will not be made public - for administrative purposes only.)
IND/IDE Serial Number	Use the serial number from the first submission of the protocol to the IND or IDE. (Will not be made public - for administrative purposes only.)
Has Expanded Access?	Indicate whether any non-protocol access is to be provided for the investigational drug or device. If so, an Expanded Access record should also be created for this IND/IDE.
Human Subjects Review	
Board Approval Status	Human subjects review board approval status. Select one.
Board Approval Number	Number assigned by the human subjects review board upon approval of the protocol. May be omitted if status is anything other than approved. If the human subjects review board do not assign numbers please enter the date of approval in mm/dd/yyyy format.
Board Name	Full name of the approving human subjects review board.
Board Affiliation	Official name of organizational affiliation of the approving human subjects review board
Board Contact	Contact information for the human subjects review board.
Data Monitoring Committee	Indicate whether a data monitoring committee has been appointed for this study. The data monitoring committee (board) is a group of independent scientists who are appointed to monitor the safety and scientific integrity of a human research intervention, and to make recommendations to the sponsor regarding the stopping of the trial for efficacy, for harms or for futility. The composition of the committee is dependent upon the scientific skills and knowledge required for monitoring the particular study.
Oversight Authorities	The name of each national or international health organization with authority over the protocol.
Sponsors	

Sponsor	Name of primary organization that oversees implementation of study and is responsible for data analysis. For "applicable clinical trials," sponsor is defined in 21 CFR 50.3.
Collaborators	Other organizations (if any) providing support, including funding, design, implementation, data analysis and reporting. The data provider is responsible for confirming all collaborators before listing them. Provide up to 10 full names of collaborating organizations.
Responsible Party	As defined in U.S. Public Law 110-85, Title VIII, Section 801, the term "Responsible Party," with respect to a clinical trial, means: 1. The sponsor of the clinical trial (as defined in 21 CFR 50.3) or 2. The principal investigator of such clinical trial if so designated by a sponsor, grantee, contractor, or awardee, so long as the principal investigator is responsible for conducting the trial, has access to and control over the data from the clinical trial, has the right to publish the results of the trial, and has the ability to meet all of the requirements for the submission of clinical trial information.
Study Description	
Brief Summary	Short description of the protocol intended for the lay public. Include a brief statement of the study hypothesis.
Detailed Description	Extended description of the protocol, including more technical information (as compared to the Brief Summary) if desired. Do not include the entire protocol; do not duplicate information recorded in other data elements, such as eligibility criteria or outcome measures.
Status	
Record Verification Date	Date the protocol information was last verified. Verification date is shown along with organization name on ClinicalTrials.gov to indicate to the public whether the information is being kept current, particularly recruiting status and contact information
Overall Recruitment Status	Overall accrual activity for the protocol
Why Study Stopped?	For suspended, terminated or withdrawn studies, provide a *brief* explanation of why the study has been halted or terminated. If desired, use brief summary or detailed description to provide additional information.
Study Start Date	Date that enrollment to the protocol begins.
Primary Completion Date	As specified in U.S. Public Law 110-85, Title VIII, Section 801, with respect to an applicable clinical trial, the date that the final subject was examined or received an intervention for the purposes of final collection of data for the primary outcome, whether the clinical trial concluded according to the prespecified protocol or was terminated. A "Type" menu is also included, with options Anticipated and Actual. For active studies, set Type to Anticipated and specify the expected completion date, updating the date as needed over the course of the study. Upon study completion, change Type to Actual and update the date if necessary.
Study Completion Date	Final date on which data was (or is expected to be) collected. Use the Type menu (Anticipated/Actual) as described above
Expanded Access Status	Status indicating availability of an experimental drug or device outside any clinical trial protocol. This data element is only applicable for Expanded Access records (see Expanded Access under Study Type).
Study Design	
Interventional Study Design	Primary investigative techniques used in the protocol. Select the most appropriate term describing the protocol from each of the following data elements.
Primary Purpose	Reason for the protocol (treatment, prevention, diagnostic, etc.)
Study Phase	Phase of investigation, as defined by the FDA for trials involving investigational new drugs.
Intervention Model	Single Group, Parallel, Cross Over, Factorial
Number of Arms	Number of intervention groups (enter 1 for single-arm study)
Masking	Open, Single Blind, Double Blind
Allocation	N/A, Randomized, Non-randomized
Study Classification	type of primary outcome or endpoint that the protocol is designed to evaluate
Enrollment	Number of subjects in the trial. A "Type" menu is also included, with options Anticipated and Actual. For active studies, set Type to Anticipated and specify the expected enrollment, updating the number as needed over the course of the study. Upon study completion, change Type to Actual and update the enrollment if necessary
Observational Study Model	Primary strategy for subject identification and follow-up.
Time Perspective	temporal relationship of observation period to time of subject enrollment
Biospecimen Retention	None, Samples With DNA, Samples Without DNA
Number of Groups/Cohorts	Number of study groups/cohorts. Enter 1 for a single-group study. Many observational studies have one group/cohort; case control studies typically have two
Primary Outcome	Specific key measurement(s) or observation(s) used to measure the effect of experimental variables in a

Measure	study, or for observational studies, to describe patterns of diseases or traits or associations with exposures, risk factors or treatment.
Arm Label	The short name used to identify the arm.
Arm Type	Experimental, Active Comparator, Placebo Comparator, Sham Comparator, No intervention, Other
Arm Description	brief description of the arm
Group/Cohort Label	the short name used to identify the group
Group/Cohort Description	Explanation of the nature of the study group (e.g., those with a condition and those without a condition; those with an exposure and those without an exposure). Note that the overall study population should be described under Eligibility.
Intervention Type	Drug (including placebo); Device (including sham); Biological/Vaccine; Procedure/Surgery; Radiation; Behavioral (e.g., Psychotherapy, Lifestyle Counseling); Genetic (including gene transfer, stem cell and recombinant DNA); Dietary Supplement (e.g., vitamins, minerals); Other
Intervention Name	For drugs use generic name; for other types of interventions provide a brief descriptive name.
Intervention Description	Cover key details of the intervention. Must be sufficiently detailed to distinguish between arms of a study (e.g., comparison of different dosages of drug) and/or among similar interventions (e.g., comparison of multiple implantable cardiac defibrillators). For example, interventions involving drugs may include dosage form, dosage, frequency and duration.
Conditions and Keywords	
Conditions or Focus of Study	Primary disease or condition being studied, or focus of the study. Diseases or conditions should use the NLM's Medical Subject Headings (MeSH) controlled vocabulary when possible.
Keywords	Words or phrases that best describe the protocol. Keywords help users find studies in the database. Use NLM's Medical Subject Heading (MeSH) controlled vocabulary terms where appropriate. Be as specific and precise as possible. Avoid acronyms and abbreviations.
Eligibility	
Study Population Description	For observational studies only, a description of the population from which the groups or cohorts will be selected (e.g., primary care clinic, community sample, residents of a certain town).
Sampling Method	Probability Sample, Non-Probability Sample
Eligibility Criteria	Summary criteria for participant selection. The preferred format includes lists of inclusion and exclusion criteria
Gender	Physical gender of individuals who may participate in the protocol.
Age Limits	Minimum and Maximum Age
Accepts Healthy Volunteers	Indicate if persons who have not had the condition(s) being studied or otherwise related conditions or symptoms, as specified in the eligibility requirements, may participate in the study.
Protocol Location, Contact and Investigator Information	
Facility	Full name of the organization where the protocol is being conducted; Include City, State Province, Postal Code, Country
Recruitment Status	protocol accrual activity at a facility
Facility Contact	Name and Contact Information
Facility Contact Backup	Name and Contact Information
Investigators	Name and Contact Information
Central Contact	Name and Contact Information
Central Contact Backup	Name and Contact Information
Overall Study Officials	Name and Contact Information
Related Information	
References	Citations to publications related to the protocol: background and/or results. Provide either the unique PubMed Identifier (PMID) of an article or enter the full bibliographic citation.
MEDLINE Identifier	Unique PubMed Identifier (PMID) for the citation in MEDLINE
Citation	Bibliographic reference in NLM's MEDLINE format
Results Reference?	Indicate if the reference provided reports on results from this clinical research study.
Links	Web site directly relevant to the protocol may be entered, if desired. Do not include sites whose primary goal is to advertise or sell commercial products or services.
URL	Complete URL, including http://
Description	Brief description of the linked page. If the page being linked is the protocol's home page on the sponsor's Web site, include the words "Click here for more information about this study:" and provide the name of the protocol.

Appendix C: Sample Template for Delegating *ClinicalTrials.Gov* Responsibility

[DATE]

To Whom It May Concern:

By means of this letter, I,_____ (Delegating Official), delegate the authority herein described to_____(the Delegate) on the following terms and conditions:

1. The effective date of this delegation is_____(specific date) and shall run until _____(specific date) or until revoked by the delegating official.

2. The authority is not subject to sub-delegation without the Delegating Official's prior and express written consent.

3. The Delegate is hereby responsible to address all legal responsibilities and expectations that are outlined in Public Law 110-85 and/or ClinicalTrials.gov.

4. The Delegate understands that non-compliance with legal responsibilities and expectations pertaining to Public Law-110-85 and/or ClinicalTrials.gov may lead to a monetary penalty.

_____
Signature (Delegating Official)

_____
Name and Title
Date:_____

Acknowledged and agreed: _____
Signature [Delegate]

_____
Name and Title
Date:_____