National Center for Complementary and Integrative Health

Essential Regulatory Documents
Guidance and Binder Tabs

Purpose: To provide an organizational framework and guidance for filing paper versions of essential study documents (or referencing location of an electronically stored file) and to provide a cover page with a description of the required contents for each binder section

Audience/User: Study coordinators or individuals responsible for establishing the essential document binder (synonyms: Regulatory Binder, Investigator Binder, Investigational Site File (ISF), and Study Binder)

Details:

- This document clarifies the standard content of the binder.
- It is the responsibility of the investigator to ensure compliance with good clinical practice (GCP), institutional review board (IRB), and applicable regulatory requirements.
- This document serves as a template and may be modified for study-specific needs/requirements.

Best Practice Recommendations:

- Store items in reverse chronological order, with the newest items within a section placed at the front of the section.
- Use the requirements note at the top of each binder tab to determine if that section is required for your study.
- Multisite studies: The lead site may choose to customize the binder tabs for the study and provide to all participating sites.
- Electronic documents: The recommendation is to store paper copies of documents in the binder. However, if you elect to use only electronic copies of particular documents, the following guidelines should be observed:
    - Either a) place a paper placeholder in the relevant location of the binder that directs an individual to the electronic location, or b) place a paper placeholder in one location in the binder that includes a list of all documents that are stored only in electronic format, along with the specific electronic path for each item.
    - Electronic-only documents should be limited to documents that a) are easily accessible by site staff; b) an inspector, auditor, or clinical monitor can be provided with easy access to the relevant electronic materials during a site visit; and c) the electronic location is controlled, regularly backed up, and is not in danger of disappearing or changing in the foreseeable future.
    - For e-mail correspondence, sites may want to include clarification in the binder that e-mail will be archived to a permanent storage medium on a particular schedule (specify in documentation) and the media will be stored in the binder or an easily accessible location.

References: Good Clinical Practice (E6) Section 8.1, 8.2, 8.3, 8.4

Tool Revision History:

Version		
Number	**Date**	**Summary of Revisions Made:**
1.0	29March2012	Approved version
2.0	24Apr2013	Additional tabs and example documents added

Regulatory Binder Tabs

Introduction:

The following tabs are recommended for use in the Regulatory Binder. This document serves as a template and may be modified for study-specific requirements. Documents should be filed in reverse chronological order. It is the responsibility of the investigator to ensure compliance with GCP and applicable regulatory requirements.

Please visit the NCCIH Clinical Toolbox Web site nccih.nih.gov/grants/toolbox to access the sample templates and tools included in the Regulatory Binder.

Required for both observational and interventional clinical research studies

Protocol and Amendments

This section should include:

- Log of Protocol Changes
- IRB-approved protocol
- Signed principal investigator (PI) protocol signature page
- IRB-approved protocol amendment(s)
- Signed PI protocol amendment signature page(s)
- If a protocol was not submitted or approved by the IRB, a note to the Study File needs to be generated to explain the surrounding circumstances, and the PI needs to sign and date the document.

Link to NCCIH Protocol Template Tools: nccih.nih.gov/grants/toolbox

Required for both observational and interventional clinical research studies

IRB-Approved Consent Documents

This section should include:

- Log of Informed Consent Versions
- All IRB-approved and stamped consent documents.

A version number and date should be on each consent document.

An expiration date of the consent document on the actual document is preferable, but cross-reference to the IRB approval letter of the protocol may be required.

Required for both observational and interventional clinical research studies

IRB Documentation

This section should include:

- Federalwide Assurance (FWA) number
- IRB registration (optional)
- Updated IRB Roster.

Link to the Office for Human Research Protections database (FWA and IRB registration): ohrp.cit.nih.gov/search/IrbDtl.aspx

Required for both observational and interventional clinical research studies

IRB Approvals and Correspondence

This section should include:

- Approval letters (e.g., protocol, protocol amendment(s), consent documents, continuing review)
- Correspondence related to contingent approvals or stipulations
- Original IRB application/submission
- IRB correspondence
- Progress reports.

If applicable, the section should also include:

- Approval letter/approved assent form for minors
- Approval letter/approved short form consent for speakers of non-English languages*
- Submission/acknowledgment of investigator's brochure
- Approval letter/approved advertisement or recruitment materials
- Approval letter/approved written educational or other materials provided to study subjects.

*The short form consent for speakers of non-English languages should be used for a single subject who may be illiterate, blind, or otherwise unable to read the consent document. This should be used when the full consent document has to be read or translated for subject.

Link to Informed Consent Checklist:
http://www.hhs.gov/ohrp/policy/consentckls.html

Required for both observational and interventional clinical research studies

Investigator Qualification Documentation

This section should include:

- Current curriculum vitae (CV) and/or other relevant dated documentation (e.g., biosketch) for all investigators (signed/dated within 2 years)
- A clinical (dental, medical, etc.) license for the principal investigator and each sub-investigator, if licensed.

CVs may be updated if an investigator's qualifications increase or change during the course of the study.

Do not remove expired CVs as they demonstrate qualification for the entire duration of the study.

Licenses should be filed behind the corresponding investigator's CV. Do not remove expired licenses.

The investigators must be actively licensed in the state in which the study is conducted.

The name on the license must correspond to the name on the investigator's CV and Form FDA 1572 Statement of Investigator, if applicable.

Required for both observational and interventional clinical research studies

Clinical Investigator's Brochure

(For any drug/product under investigation)

For studies that involve administration of investigational drugs, this section should include:

- Clinical investigator's brochure(s) (CIBs) or equivalent

  or

- Package insert; include labeling for approved medications.

The purpose of this document is to provide information on the mechanism of action, possible risks and adverse reactions, and the "expected" adverse reactions associated with the previous use of the drug or product.

If the package insert or the CIB is amended during the trial or is updated, it should be included here.

Required for clinical studies regulated by the FDA under investigational new drug (IND) and investigation device exemption (IDE) procedures

FDA Documents

For studies that involve administration of investigational drugs or devices that are conducted under and IND or IDE, this section should include:

- FDA Form 1572 for IND studies
- FDA Form 1571 for investigator-initiated INDs
- Instructions for Forms 1571 and 1572:

www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm071098.htm#form1571

Forms 1571 and 1572 can be downloaded from:

www.fda.gov/AboutFDA/ReportsManualsForms/Forms/default.htm

- FDA Document History Log: tracks all correspondence submitted to the FDA.
- Sample of Labels attached to investigational product containers
- Regulatory approval or authorization
- FDA Correspondence Log
- For additional information on significant risk device requirements see:

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm046706.htm

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

STATEMENT OF INVESTIGATOR

(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) PART 312)

(See instructions on reverse side.)

Form Approved: OMB No. 0910-0014
Expiration Date: August 31, 2011
See OMB Statement on Reverse.

NOTE: No investigator may participate in an investigation until he/she provides the sponsor with a completed, signed Statement of Investigator, Form FDA 1572 (21 CFR 312.53(c)).

1. NAME AND ADDRESS OF INVESTIGATOR

Name of Sponsor/Applicant/Submitter or Other

Address 1	Address 2	
City	State	ZIP or Postal Code

2. EDUCATION, TRAINING, AND EXPERIENCE THAT QUALIFY THE INVESTIGATOR AS AN EXPERT IN THE CLINICAL INVESTIGATION OF THE DRUG FOR THE USE UNDER INVESTIGATION. ONE OF THE FOLLOWING IS PROVIDED *(Select one of the following.)*

☐ Curriculum Vitae ☐ Other Statement of Qualifications

3. NAME AND ADDRESS OF ANY MEDICAL SCHOOL, HOSPITAL, OR OTHER RESEARCH FACILITY WHERE THE CLINICAL INVESTIGATION(S) WILL BE CONDUCTED — CONTINUATION PAGE for Item 3

Name of Medical School, Hospital, or Other Research Facility

Address 1	Address 2	
City	State	ZIP or Postal Code

4. NAME AND ADDRESS OF ANY CLINICAL LABORATORY FACILITIES TO BE USED IN THE STUDY — CONTINUATION PAGE for Item 4

Name of Clinical Laboratory Facility

Address 1	Address 2	
City	State	ZIP or Postal Code

5. NAME AND ADDRESS OF THE INSTITUTIONAL REVIEW BOARD (IRB) THAT IS RESPONSIBLE FOR REVIEW AND APPROVAL OF THE STUDY(IES) — CONTINUATION PAGE for Item 5

Name of IRB

Address 1	Address 2	
City	State	ZIP or Postal Code

6. NAMES OF SUBINVESTIGATORS *(If not applicable, enter "None")*

CONTINUATION PAGE – for Item 6

7. NAME AND CODE NUMBER, IF ANY, OF THE PROTOCOL(S) IN THE IND FOR THE STUDY(IES) TO BE CONDUCTED BY THE INVESTIGATOR

8. PROVIDE THE FOLLOWING CLINICAL PROTOCOL INFORMATION. *(Select one or both of the following.)*

☐ For Phase 1 investigations, a general outline of the planned investigation including the estimated duration of the study and the maximum number of subjects that will be involved.

☐ For Phase 2 or 3 investigations, an outline of the study protocol including an approximation of the number of subjects to be treated with the drug and the number to be employed as controls, if any; the clinical uses to be investigated; characteristics of subjects by age, sex, and condition; the kind of clinical observations and laboratory tests to be conducted; the estimated duration of the study; and copies or a description of case report forms to be used.

9. COMMITMENTS

I agree to conduct the study(ies) in accordance with the relevant, current protocol(s) and will only make changes in a protocol after notifying the sponsor, except when necessary to protect the safety, rights, or welfare of subjects.

I agree to personally conduct or supervise the described investigation(s).

I agree to inform any patients, or any persons used as controls, that the drugs are being used for investigational purposes and I will ensure that the requirements relating to obtaining informed consent in 21 CFR Part 50 and institutional review board (IRB) review and approval in 21 CFR Part 56 are met.

I agree to report to the sponsor adverse experiences that occur in the course of the investigation(s) in accordance with 21 CFR 312.64. I have read and understand the information in the investigator's brochure, including the potential risks and side effects of the drug.

I agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study(ies) are informed about their obligations in meeting the above commitments.

I agree to maintain adequate and accurate records in accordance with 21 CFR 312.62 and to make those records available for inspection in accordance with 21 CFR 312.68.

I will ensure that an IRB that complies with the requirements of 21 CFR Part 56 will be responsible for the initial and continuing review and approval of the clinical investigation. I also agree to promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to human subjects or others. Additionally, I will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

I agree to comply with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements in 21 CFR Part 312.

INSTRUCTIONS FOR COMPLETING FORM FDA 1572
STATEMENT OF INVESTIGATOR

1. Complete all sections. Provide a separate page if additional space is needed.
2. Provide curriculum vitae or other statement of qualifications as described in Section 2.
3. Provide protocol outline as described in Section 8.
4. Sign and date below.
5. FORWARD THE COMPLETED FORM AND OTHER DOCUMENTS BEING PROVIDED TO THE SPONSOR. The sponsor will incorporate this information along with other technical data into an Investigational New Drug Application (IND). INVESTIGATORS SHOULD NOT SEND THIS FORM DIRECTLY TO THE FOOD AND DRUG ADMINISTRATION.

10. DATE *(mm/dd/yyyy)*	11. SIGNATURE OF INVESTIGATOR Sign

(**WARNING**: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec. 1001.)

Public reporting burden for this collection of information is estimated to average 100 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Office of the Chief Information Officer
1350 Piccard Drive, Room 400
Rockville, MD 20850

Please DO NOT RETURN this application to this address.

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

FORM FDA 1572 (2/12) **PREVIOUS EDITION IS OBSOLETE.** **Page 2 of 2**

FDA Document History Log

Investigator Name:	Protocol:	IND Number:

List all documents submitted to the FDA.

Date of Correspondence	Type of Correspondence (i.e., submission, contact report, etc.)	Serial Number (If applicable)	Description

Version 3.0 – 2013-04-24

Page _____
Check if final page of log: □

Required for clinical studies regulated by FDA under investigational new drug (IND) or investigational device exemption (IDE) procedures

Financial Disclosure Forms

This section should include:

- Signed financial disclosure forms (FDF) for the principal investigator and sub-investigator(s) listed on Form 1572.

The names of the principal investigator and sub-investigator(s) should match the names listed on Form 1572. The protocol title and number should match the title and number listed on Form 1572.

If any of the five financial interest questions are checked Yes, a statement addressing the nature and amount of the interest, arrangement, or payment must be attached to the FDF. Appropriate identifiers (i.e., protocol number and investigator name) must be included on each document included in the submission.

This FDA form is required for any clinical study submitted in a marketing application in which the applicant or FDA relies on to establish that the product is effective and any study in which a single investigator makes a significant contribution to the demonstration of safety.

Link for additional information:

http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM341008.pdf

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Form Approved: OMB No. 0910-0396
Expiration Date: December 31, 2015

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable check box.

☐ (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		

☐ (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

☐ (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
FIRM/ORGANIZATION	
SIGNATURE	DATE *(mm/dd/yyyy)*

This section applies only to the requirements of the Paperwork Reduction Act of 1995.

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Do NOT send your completed form to the PRA Staff email address below.

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

FORM FDA 3454 (4/13)

PSC Publishing Services (301) 443-6740 EF

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Form Approved: OMB No. 0910-0396
Expiration Date: December 31, 2015

TO BE COMPLETED BY APPLICANT

The following information concerning _____ , who participated
Name of clinical investigator

as a clinical investigator in the submitted study _____
Name of

_____ is submitted in accordance with 21 CFR part 54. The
clinical study

named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable check boxes.

☐ any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;

☐ any significant payments of other sorts made on or after February 2, 1999, from the sponsor of the covered study, such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;

☐ any proprietary interest in the product tested in the covered study held by the clinical investigator;

☐ any significant equity interest, as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME	TITLE
FIRM/ORGANIZATION	
SIGNATURE	Date *(mm/dd/yyyy)*

This section applies only to the requirements of the Paperwork Reduction Act of 1995.

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 5 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Do NOT send your completed form to the PRA Staff email address below.

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

FORM FDA 3455 (4/13)

PSC Publishing Services (301) 443-6740 EF

Required for both observational and interventional clinical research studies

Study Communication

This section should include:

- A copy of all communication relative to the conduct of the protocol and agreements with other scientific collaborators, industry, and scientific directors, such as material transfer agreement, data sharing agreement (financial documents should not be included)
- Important decisions regarding study conduct, such as notes to the Study File.

All printed communication (e.g., e-mail) needs to be signed and dated by the individual printing and storing the document.

Communication about subject treatment/clinical care, protocol deviations, and study drug dosing should immediately be printed and stored in this tab.

E-mail correspondence may be saved to a compact disc (CD) for electronic storage and noted in this section.

Electronic media must be permanent media and must be appropriately secured and approved (e.g., password protected).

If saved to a CD or other electronic storage media, a note to the Study File needs to be generated describing the types of e-mail on the electronic media, the start and stop dates of the e-mail correspondence, and the signature and date of the individual creating the CD and writing the note to file.

If a study team member receives a new computer or if a newer version of the e-mail provider is used, it is highly recommended to create the CD and the note to file at the time of the transfer to prevent any important study communication from being lost in the transition.

Required for both observational and interventional clinical research studies

Delegation of Authority (DoA) Log

This section should include:

- An ongoing log that lists all study personnel and their specific responsibilities, signatures, initials, and obligation (start/stop) dates.

Any changes in site study personnel require an update to the DoA.

Delegation of Authority Log

STUDY NAME

Site Number: ____

The purpose of this form is to: a.) serve as the Delegation of Authority Log and b.) ensure that the individuals performing study related tasks/procedures are appropriately trained and authorized by the Investigator to perform the tasks/procedures. This form should be completed prior to the initiation of any study-related tasks/procedures. The original form should be maintained at your site in the study regulatory/study binder. This form should be updated during the course of the study as needed.

Please Print	Obtain Informed Consent	Source Document Completion	Case Report Form (CRF) Completion	Assess Inclusion and Exclusion Criteria	Physical Examination	Medical History	Medication History / Concomitant Medication	Collect Vital Signs	Review Vital Signs and Labs for Clinical Significance	Laboratory Specimen Collection/Shipping	AE Inquiry and Reporting	AE/SAE interpretation (severity/relationship to IP)	Administration of Investigational Product (IP)	IP Accountability	Regulatory Document Maintenance	Administrative	
NAME:	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	OTHER (specify):
STUDY ROLE:	SIGNATURE:														INITIALS:		DATES OF STUDY INVOLVEMENT:
NAME:	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	OTHER (specify):
STUDY ROLE:	SIGNATURE:														INITIALS:		DATES OF STUDY INVOLVEMENT:
NAME:	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	OTHER (specify):
STUDY ROLE:	SIGNATURE:														INITIALS:		DATES OF STUDY INVOLVEMENT:
NAME:	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	OTHER (specify):
STUDY ROLE:	SIGNATURE:														INITIALS:		DATES OF STUDY INVOLVEMENT:
NAME:	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	OTHER (specify):
STUDY ROLE:	SIGNATURE:														INITIALS:		DATES OF STUDY INVOLVEMENT:

I certify that the above individuals are appropriately trained, have read the Protocol and pertinent sections of 21CFR 50 and 56 and ICH GCPs, and are authorized to perform the above study-related tasks/procedures. Although I have delegated significant trial-related duties, as the principal investigator, I still maintain full responsibility for this trial.

Investigator Signature: ______________________________ **Date:** ______________________________

Site Signature Log/Delegation of Authority Log Version 2.0

Required for both observational and interventional clinical research studies

Clinical Research and Study Training

This section should include the following documents for all key (investigators, coordinators) personnel:

- Educational completion certificates for human subject protection training
- Documentation of study-related training.

All key personnel working on NIH grants and contracts involving human research participants are required to complete training in human subject protections. NIH has a free Web-based training that satisfies this requirement:

phrp.nihtraining.com/users/login.php.

Other free, optional Web-based trainings that are recommended include:

- Good clinical practices training for individuals involved in human subjects research: gcplearningcenter.niaid.nih.gov/
- www.nihtraining.com/crtpub_508/index.html.

If a certificate is not available at the end of each required training module, enter the appropriate documentation in the site training log.

Site-specific training: Consult your IRB or institution for training requirements.

Training Log

Investigator Name:	Protocol:	Site Number:

Printed Name	Signature	Title of Training	Date of Training

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Page _____

Check if final page of log: ☐

Required for both observational and interventional clinical research studies

Screening/Enrollment Log

This section should include:

- A log without identifying information that lists subjects who were screened (including screen failures) and enrolled in the study.
    - Note: Subjects may be tracked separately on logs, such as a coded list with a key.

Note: If screening and enrollment information is entered into an electronic data capture (EDC) system, please include a memo explaining this process.

Site Screening and Enrollment Log

Investigator Name:	Protocol:	Site Number:

Subject ID	Date of Consent	Version of Consent	Date Screened	Eligible for Enrollment?	Ineligibility Reason (if applicable)

Version 1.0 – 2013-04-23

Page _____

Check if final page of log: ☐

Required for both observational and interventional clinical research studies

Signed Consent Documents

This section should include:

- A copy of all signed consent documents
- Alternatively, consent documents may also be kept in a separate binder or in the subject's medical record.

If signed consent documents are kept in a separate binder, a note to the Study File explaining where they are stored and the reason needs to be generated, signed, and dated.

If a subject withdraws consent, this should be documented in the medical record, and specimen tracking should be addressed (if applicable). The signed consent document must be retained even if a subject withdraws consent.

Required for both observational and interventional clinical research studies

Study Product Records

This section should include:

- Documentation of study product (e.g., botanicals, probiotics, or other natural products disposition and accountability, or memo as to where records are located (e.g., research pharmacy) and who is maintaining accountability logs.

For blinded clinical studies, it is recommended that study product accountability records be filed in the research pharmacy to maintain the blind.

Investigational Product Accountability Log: Stock Record

Name of Institution:	**Product Name:**
Investigator Name:	**Manufacturer:**
Protocol No.:	**Dose Form and Strength:**
Protocol Title:	**Dispensing Area:**

Line No.	Date	Dispensed To / Received From	Dose	Quantity Dispensed and/or Received	Balance Forward / Balance	Lot No.	Recorder's Initials
Ex.	*15Feb2012*	*Manufacturer*	*10 mg*	*+ 100 tabs*	*500 / 600*	*98765*	*JAD*
1.							
2.							
3.							
4.							
5.							
6.							
7.							
8.							

Investigational Product Accountability Log: Subject Record

Name of Institution:	**Product Name:**
Investigator Name:	**Manufacturer:**
Protocol No.:	**Dose Form and Strength:**
Protocol Title:	**Dispensing Area:**

Line No.	Date	Subject ID Number	Subject's Initials	Dose	Quantity Dispensed and/or Received	Balance Forward / Balance	Lot No.	Recorder's Initials
Ex.	*15Feb2012*	*12345*	*ABC*	*10 mg*	*- 100 tabs*	*600* / *500*	*98765*	*JAD*
1.								
2.								
3.								
4.								
5.								
6.								
7.								
8.								

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Page _____

Check if final page of log: ☐

Required for both observational and interventional studies using clinical labs as a study procedure

Local Clinical Lab Certificates/Reference Ranges

For studies that use clinical laboratories for specimen testing, this section should include:

- Lab reference ranges if the reference range is not included on the lab form
- A copy of certifications or accreditations (College of American Pathologists [CAP], Clinical Laboratory Improvement Amendments [CLIA], or state certificate) or a memo indicating the laboratory maintains CLIA certification.

Required for both observational and interventional clinical studies collecting clinical samples

Specimen Tracking Log

This section should include:

- A log of research samples that includes type of specimen, purpose of storage, location of storage (e.g., freezer #, shelf #, location, box #), and link to subject ID number. If applicable, the log should be modified to track if consent for future use was obtained or withdrawn.

Specimen Tracking Log

Investigator Name:	Protocol:	Site Number:

Visit	Specimen Name/Type	Specimen ID (Accession #)	Date Collected	Date Shipped	Tracking #	Receiving Lab	Date Received	Comments

Required for both observational and interventional clinical research studies

Serious Adverse Events/Unanticipated Problems

This section should include copies of:

- Serious adverse event (SAE) form or memo
- Reports of unanticipated problems
- "Dear Doctor" letter and IND safety reports.

Unanticipated Problem (UP)

Protocol Name and Number:	Site Name:	Subject ID Number or List of Affected Subjects:
_____	_____	_____

1. Date UP Identified: __ __/ __ __ __/ __ __ __ __ (dd/mmm/yyyy)
2. Identify UP:
3. The Unanticipated Problem was unexpected in terms of nature, severity or frequency: ☐ Yes ☐ No
4. The Unanticipated Problem is possibly related to participation in the research: ☐ Yes ☐ No
5. The Unanticipated Problem suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized: ☐ Yes ☐ No

   If the answers to questions 3-5 are ALL "YES", report event as an Unanticipated Problem to NIDCR and IRB (if applicable).

6. Briefly Describe the UP (Attach additional pages or supplementary information as necessary. Include date of incident, date of discovery ,describe harm or potential harm that occurred to subject(s), whether the incident is resolved, whether the subject(s) remains on study):

7. What action was taken with the study as a result of the Unanticipated Problem? (Check all that apply.)

   ☐ No action
   ☐ Revise protocol to eliminate apparent immediate hazards to subjects
   ☐ Modification of inclusion or exclusion criteria to mitigate newly identified risks
   ☐ Implementation of additional procedures for monitoring subjects
   ☐ Suspension of enrollment of new subjects
   ☐ Notify currently enrolled subjects
   ☐ Suspension of research procedures in currently enrolled subjects
   ☐ Modification of consent documents to include a description of newly recognized risks (site and/or study wide)
   ☐ Provision of additional information about newly recognized risks to previously enrolled subjects
   ☐ Other:

8. Is the Unanticipated Problem a serious adverse event? ☐ Yes ☐ No

   If the Unanticipated Problem is a serious adverse event, submit this form and complete the Serious Adverse Event form.

Required for both observational and interventional clinical research studies

Protocol Deviations

This section should include copies of:

- Protocol deviation form or memo.

Requirements for reporting protocol deviations are specific to each local IRB; review the requirements to make sure that they are followed appropriately.

Protocol Deviation Tracking Log

Protocol ID/Number:		**Site Name/Number:**	
Protocol Title (Abbreviated):			
Principal Investigator:		**Page number [1]:**	

Ref No.	Subject ID	Date of Deviation	Date Identified	Deviation Description	Dev. Type [2]	Resulted in AE?	Did Subject Continue in Study?	Meets IRB Reporting Req. (Yes/No)	IRB Reporting Date
1									
2									
3									
4									
5									

Investigator Signature: _____ **Date:** _____

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Check if final page of log: ☐

Required for both observational and interventional clinical research studies

Clinical Site Monitoring Visits

This section should include copies of:

- A site visit log signed by the clinical site monitor(s) at each visit
- Visit reports
- Visit correspondence, such as a confirmation or followup letter.

Monitoring Visit Log

Investigator Name:	Protocol:	Site Number:

Name	Signature	Purpose of Visit	Date of Visit

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Page _____

Check if final page of log: ☐

Required for both observational and interventional clinical research studies

Sponsor Correspondence

This section should include:

- Records of correspondence with the sponsor, including approval of initial study documents, approval of protocol amendments, and approval to initiate the study.

NCCIH Document History Log

Investigator Name:	Protocol:	IND Number:

List all documents submitted to the FDA.

Date of Correspondence	Type of Correspondence (i.e., submission, contact report, etc.)	Serial Number (if applicable)	Description

Check if final page of log: ☐

Required for both observational and interventional clinical research studies

Data Safety and Monitoring Documents

This section should include copies of:

- The Data Safety and Monitoring Plan (if not included as part of the study protocol)
- Study reports generated for the independent safety monitor(s)
- Minutes from the independent safety monitor(s) meeting(s)
- Recommendations and correspondence from the independent safety monitor(s).

As needed for both observational and interventional clinical research studies

Other

This section should include:

- Other important study documents, such as certificates of confidentiality, literature or publications, etc.