Lifespan

# General Guidance for Maintaining a Regulatory Binder

- ✓ Study documentation should be well organized, providing a complete and thorough history from protocol development to study completion. Maintaining a study binder allows the research team to easily reference information, and provides access to essential documents by trial monitor, auditor, IRB, or regulatory authorities (e.g. OHRP, FDA).

- ✓ Each section outlines regulatory documentation requirements, general guidance for organization and record keeping. Where applicable, references to federal regulations and good clinical practice guidelines have been provided. *Note: Participant identifiable documents such as signed consent form, lab results and completed case report forms should be maintained separately in a subject specific binder/file.*

- ✓ Label the binder with the following information
  - IRB study number
  - Study Title
  - PI
  - Sponsor
  - Institution and location
  - Binder number (if multiple binders; e.g. binder #1 of 3)

- ✓ Tailor the binder to meet the needs of the specific protocol. The binder is a template. Include only applicable sections and add any additional sections pertinent to your study

- ✓ Keep documents up-to-date. Ensure timely review of material to confirm most current documents are on file

- ✓ Identify a key personnel member responsible for maintaining the binder

- ✓ Store binder in a readily accessible, secure location

**For assistance in determining applicable sections or compiling documents,**
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# REGULATORY/IRB DOCUMENT BINDER
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## A. REGULATORY DOCUMENTS

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2. Key Personnel List
3. Training and Licensure (*as applicable to the study)*
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5. Enrollment/Screening Log
6. Sponsor Contact Information, Sponsor Agreement, and other formal correspondence *
7. Laboratory Documentation/Normal Lab Values/CLIA certificate*
8. Randomization Instructions*
9. Emergency un-blinding procedures*

**This section may not be applicable to your study*

## B. IRB DOCUMENTS

Note: paperwork should be filed in reverse chronological order (most recent documents in front, oldest in the back).

1. Protocol
2. Recruitment Materials (currently approved Ads, Flyers, Brochures, etc)
3. Consent/Assent Forms (every approved version)
4. IRB Documentation (Initial Application, Amendments and Continuing Reviews)
5. HIPAA Waiver of Authorization, Prep to Research*
6. Data Collection Tools
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9. Unanticipated Problems (UAPs)/ Adverse Events/Deviations
10. Standard Operating Procedures
11. Notes to File

**This section may not be applicable to your study*

## ADDITIONAL BINDER TABS APPLICABLE TO DRUG/DEVICE STUDIES

FDA 1571/1572

Financial Disclosure

IND (Drug Study)

IDE (Device Study)

Investigator Brochure/Package Insert/Device Manual

Drug/Device Accountability

# Curricula Vitae (CV)

## Requirements

- ☐ CV for the PI

Filing Tips:

- ✓ Unless otherwise requested by the sponsor, CVs should be signed, dated, and updated every 2 years to verify that the information is accurate and current
- ✓ If CVs are filed collectively or electronically for the department, write a signed and dated note-to-file indicating the location (include copy of note-to-file here)

References:
GCP: 4.1.1; 8.2.10; 8.3.5

# Key Personnel

## Requirements

- ☐ Key Personnel List
  - IRBNet, Research Application part 1

Filing Tips:

- ✓ List all personnel under the supervision of the P.I. who will interact with human subjects or their identifiable data
- ✓ Submit an updated personnel list for IRB review and approval whenever there is a change in personnel who will interact with or obtain informed consent from research subjects

# Training and Licensure

## Requirements

- ☐ Valid license/certification for all professional staff
- ☐ Copy of training certification for all personnel required to complete human subjects training
  - Information on training requirements can be found at: http://www.lifespan.org/research-and-clinical-trials/office-of-research-administration/research-administration-training
  - CITI course and exam: http://www.citiprogram.org
- ☐ Additional training records/certification for study staff
  - E.g. phlebotomy, vital signs, etc.

Filing Tips:

- ✓ Note expiration dates to ensure valid documents are requested and maintained
- ✓ If training documentation is filed collectively or electronically, write a signed and dated note-to-file indicating the location (include copy of note-to-file here)

References:
GCP: 4.1; 8.2.10

# Study Logs

## Recommended Study Logs

- ☐ Screening/Enrollment Log
  - Record all subjects were screened for study inclusion; note whether subject was found to be eligible or ineligible
- ☐ Staff Signature Log
  - Document the signature and initials of all IRB approved personnel collecting and recording study data
- ☐ Delegation of Responsibility Log
  - Document the role of key personnel on the study; may be combined with the staff signature log to facilitate record keeping
- ☐ Monitoring Log
  - Record dates of monitoring visits; industry-sponsored trials only
- ☐ Other protocol-specific study logs
  - E.g. temperature log; device calibration log

Filing Tips:

- ✓ Refer to the Investigator Toolbox located on the Research Protection Office Website website, found at http://www.lifespan.org/research-and-clinical-trials/office-of-research-administration/institutional-review-board for log templates and record keeping tools

- ✓ Update all study logs in a timely manner

- ✓ If logs are maintained electronically, write a note-to-file indicating the location (include copy of note-to-file here)

References:
GCP: 4.1.5; 8.3.20; 8.3.21, 8.3.22, 8.3.24

# Sponsor

## Requirements

- ☐ Sponsor contact information (e.g. name, phone number, address)
- ☐ Copy of all versions of Sponsor's protocol (include version dates)
- ☐ All correspondence to and from the sponsor
  - E.g. letters, emails, meeting notes, notes of telephone calls
  - Document correspondence in a manner that date, persons involved and study relevance is apparent
- ☐ Signed Agreements, including financial agreements

Filing Tips:

- ✓ If documents are filed collectively or electronically, write a signed and dated note-to-file indicating the location (include copy of note-to-file here)
- ✓ Confidential financial matters should be filed separately ~ write a signed and dated note-to-file indicating the location (include copy of note-to-file here)
- ✓ Fax confirmations and shipping receipts (if applicable) should be retained with corresponding documents as evidence of receipt/submission

**References:**
GCP: 8.3.11; 8.2.4; 8.2.6

# Laboratory Documents

## Requirements

- ☐ Current lab certification and updates
  - E.g. CLIA, CAP
- ☐ Copy of Lab Director's CV
- ☐ Copy of normal lab/reference values and updates

Filing Tips:

- ✓ Maintain updated certification to document the competency of all lab facilities being utilized, and to support the reliability of test results
- ✓ If lab documentation is filed electronically or in another location, write a note-to-file indicating the location (include copy of note-to-file here)

References:
GCP: 8.2.11; 8.2.12; 8.2.14; 8.3.6; 8.3.7

# Randomization and Emergency Unblinding

## Requirements

- ☐ Randomization Instructions
  - To ensure that the benefits of randomization are realized, well defined and carefully planned procedures should be in place prior to the start of a trial

- ☐ Procedure for Emergency Unblinding of Randomized Medication
  - Unblinding must be undertaken by a pre-determined process to ensure that participants are not unblinded unnecessarily and study results are not compromised.

Filing Tips:

- ✓ Develop SOPs to describe the randomization process and conditions under which unblinding occurs, including who is authorized to request/conduct procedures

References:

FDA: 314.126(i)

GCP: 4.7

# Protocol

## Requirements

- ☐ Original IRB approved protocol and all amended versions

Filing Tips:

- ✓ Each protocol should contain a version date and/or version number
- ✓ You must maintain all versions of the protocol, but outdated versions can be filed separate from the regulatory binder ~
  if previous versions are maintained electronically or in another location, write a note-to-file indicating the location (include copy of note-to-file here)


References:
GCP: 8.2.2; 8.3.2

# IRB Documentation

## Requirements

- ☐ Copies of all signed and dated submissions:
  - Initial Application for Human Research
  - Continuing Review(s)
  - Revisions to protocol
  - Deviation/Exceptions
- ☐ Original notification of IRB approval or IRB decisions
- ☐ Copy of investigator response to IRB notification (if applicable)
- ☐ Approved/validated recruitment materials
- ☐ Approved/validated study information distributed to participants
- ☐ Any additional correspondence related to the study (e.g. e-mails)

Filing Tips:

- ✓ Submissions should be signed and dated
- ✓ Approved/validated recruitment materials and additional study information distributed to participants should include version dates and/or version numbers; *a separate tab has been provided for filing copies of these materials for easy access during course of the study*
- ✓ File documents in reverse chronological order

**References:**

Federal Regs: 45 CFR 46; 21 CFR 50; 21 CFR 56

GCP: 3.1.4; 4.10; 5.17.3; 8.3.2; 8.3.19; 8.4.7

# Recruitment Documents and Study Materials

## Requirements

- ☐ Copy of most recently approved recruitment materials
- ☐ Copy of most recently approved study information to be distributed to subjects
    - E.g. study contacts, instruction sheets

Filing Tips:

- ✓ Approved/validated recruitment materials and additional study information distributed to participants should include version dates and/or version numbers

# Consent/Assent Forms

## Requirements

- ☐ Original IRB approved (stamped) copy and all amended versions
  - Copy this approved document for use when enrolling participants
  - Do not use expired/out-dated versions to consent subjects
  - Provide a copy of the signed consent form to each subject

- ☐ Consent Revision Log (optional)
  - Tracks the changes/amendments between consent/assent form versions, the date amendments were submitted for review and the final approval date

Filing Tips:

- ✓ You must maintain all versions of the consent form(s), but outdated versions can be filed separate from the regulatory binder ~ if previous versions are maintained electronically or in another location, write a note-to-file indicating the location (include copy of note-to-file here)

- ✓ Filing previous versions of the consent form with a line drawn across the front page will assist in ensuring only the most recent version is used to consent subjects

- ✓ After obtaining informed consent, generate and file (in each subject's folder) a Consent Process Note. Sample templates and guidance for generating this documentation has been provided.

References:
Federal Regs: 45 CFR 46
GCP: 8.2.3; 8.3.2; 8.3.12

# HIPAA

## Requirements

- ☐ Prep to Research Form
  - A new prep to research form should be submitted whenever there is a change in study personnel ~ new study staff must be added to the form if they will review records
- ☐ Waiver of Authorization
- ☐ Disclosures of PHI

Filing Tips:

- ✓ Information on HIPAA Policies, Information, Training and Forms can be found at: http://www.lifespan.org/research-and-clinical-trials/office-of-research-administration/institutional-review-board

References:

Federal Regs: 45 CFR Part 160; Subparts A and E of Part 164

# Data Collection

## Requirements

- ☐ Blank set of current case report forms (CRFs), data collection sheets, surveys, study questionnaires, subject diaries, etc…

Filing Tips:

- ✓ Study should include version dates and/or version numbers
- ✓ All outdated versions should also be on file (file behind current versions)
- ✓ If documents are filed electronically or in another location, write a note-to-file indicating the location (include copy of note-to-file here)

References:
GCP: 8.3.14; 8.3.15; 4.9.3

# NIH

## Requirements

- ☐ Copy of the NIH grant application and progress report
  - Submit a copy of the most recent progress report to the IRB at the time of continuing review

- ☐ Correspondence (e.g. e-mails) with the NIH and collaborators

Filing Tips:

- ✓ If documents are filed collectively or electronically, write a signed and dated note-to file indicating the location (include copy of note-to-file here)

# DSMB

## Requirements

- ☐ Copy of Data Safety Monitoring Plan (if applicable)
- ☐ Copy of all DSMB reports
  - Submit a copy of the most recent DSMB report to the IRB
- ☐ Any additional correspondence (e.g. e-mails, letters, meeting minutes) with the DSMB and its members
- ☐ Monitoring/Audit reports

Filing Tips:

- ✓ If documents are filed collectively or electronically, write a signed and dated note-to-file indicating the location (include copy of note-to-file here)

References:
GCP: 8.3.10; 5.19.3

# Unanticipated Problems Adverse Events, Deviations

## Requirements

- ☐ Copy of all Unanticipated Problems (UAPs) submitted to the IRB and supporting documentation
- ☐ Copy of each reportable Adverse Event (AE) sent to the IRB and sponsor
- ☐ IND Safety Reports sent to the sponsor/participating sites
- ☐ All pertinent correspondence regarding the event(s)

Filing Tips:

- ✓ Information on reporting events to the IRB and applicable forms can be found on IRBNet

References:
FDA: 21 CFR 312.32; 21 CFR 812.150 (b)(1)
GCP: 5.16.2; 8.3.18; 4.11: 5.17.1; 8.3.16; 8.3.17

# Standard Operation Procedures (SOPs)
# Manual of Operations (MOO)

## Requirements

- ☐ Current Manual of Operations
  - A reference document that details how to operationalize the scientific aspects of a protocol and all study related, IRB approved procedures

- ☐ Standard Operation Procedures
  - Written instructions (step-by-step outline) to ensure consistency of the performance of study related functions

Filing Tips:

- ✓ When developing SOPs and MOOs include a version number and date and signed approval page

- ✓ All out of date versions should be on file (behind current versions)

- ✓ If documents are filed electronically or in another location, write a note-to-file indicating the location (include copy of note-to-file here).

References:
FDA: 21 CFR 312.53
GCP: 2.13

# Note To File

## Requirements

- ☐ Any note or memo to file that:
  - Explains discrepancies or missing documents in the regulatory binder
  - Identifies the location of documents that are filed outside of the binder, i.e. collectively/central files or electronically

- ☐ Include the following information
  - Protocol number
  - Topic of memo/event (e.g. IRB communication)
  - Date of event or date note generated
  - Detailed description any follow-up as necessary
  - Signature/initial of person generating the note

Filing Tips:

- ✓ Notes to file are also valuable tools to document, explain or clarify any study discrepancies, deviations, questionable data or study procedures within subject files (to which it applies)

- ✓ When in doubt – Write a Note !!
  - Better to have an explanation now than questions later

- ✓ Post-its are not notes to file