

Regulatory Binder: Set-up and Maintenance

Introduction

Federal and state regulations, institutional policy, and good clinical and research practices require investigators to maintain documents related to human subjects research. This tool was developed to assist researchers in organizing research-related documents. It details what documents may be stored in each section of a study-specific regulatory binder. Some of the sections or documents are not applicable to certain studies. Additionally, researchers may choose to store certain documents in places other than the regulatory binder. Finally, some sponsors or federal agencies may require that investigators keep documents that are not specifically referenced in this guidance.

Some general hints for maintaining a regulatory binder:

- If it's not documented, it never happened!
- Signed and dated notes-to-file can be utilized in all of the sections:
 - To note an error in record keeping
 - To note that certain documents are stored in places other than the regulatory binder (i.e. a note to file indicating where outdated versions of the protocol are kept, a note to file indicating that signed case report forms are kept in study subject files, etc.)
 - To record missing documentation or incomplete data
 - To explain how information was obtained
 - To detail who obtained information
 - To clarify any discrepancies
- All forms submitted to any federal agency pertaining to human subject research should be retained (even if not specified in any of the sections in this document).
- All authorizations, approvals, and/or notifications of protocols, protocol amendments, or other documents should be retained, even if not specified in this document. This includes the authorizations, approvals, and/or notifications of protocols, amendments or other documents from any regulatory authority (i.e. any governmental agency, authorities that review submitted clinical data and authorities that conduct inspections).
- All communications with regulatory authorities (i.e. any governmental agency, authorities that review submitted clinical data, and authorities that conduct inspections) regarding the study should be retained.
- All signed agreements should be retained, even if not specified in this document.

1. Protocol

- A copy of the final, IRB approved dated protocol
- Sponsor's protocol
- Copy of the signed protocol

- Amendments to the protocol
- All outdated versions of the protocol
- Documents showing dates and reasons for any deviation from the protocol.
- All versions of the protocol and amendments should be dated.

2. IRB

All submissions to the IRB, IRB approvals/acknowledgements, copies of IRB approved documents, and any revisions to the documents should be retained in the regulatory binder. Examples of documents requiring IRB approval and documents that must be retained include:

- Copy of the grant application
- Copy of the original human subjects research application submitted to the IRB;
- Initial IRB approval letter
- Written information provided to subjects (i.e., diaries, pain scales, questionnaires, educational booklets)
- Advertisements for recruiting purposes
- Retention materials
- Safety Reports
- Continuing Review reports
- Amendments
- Protocol deviations
- HIPAA applications
- All other documents submitted to the IRB
- All correspondences with the IRB.
 - The retained communications should include all required reports, e-mails, faxes, memoranda, and letters. In addition, logging phone conversations is encouraged to track when conversations take place and the substance of the communications.
- All other correspondences involving human research protections, including correspondences with other researchers
 - The retained communications should include all required reports, e-mails, faxes, memoranda, and letters. In addition, logging phone conversations is encouraged to track when conversations take place and the substance of the communications.

For more information on documents that must be submitted to the IRB, please refer to our website available at <http://www.uvm.edu/irb/>.

3. Consent Forms & HIPAA Authorization Forms

- All versions of the consent forms
- Original copies of the IRB approved consent forms, marked by the IRB approval stamp
- Documentation of where signed consent forms are kept

- Original copy of the approved HIPAA authorization form, marked with the approval stamp
- Documentation of where signed HIPAA authorizations are kept

4. Study staff information

- Curriculum vitae for all investigator(s) and key study staff
 - CVs should be signed, dated, and updated every 2 years
- Licenses
 - Valid licenses for all professional study staff
 - Current professional certification (may be indicated on CVs)
- Training records and certifications for investigators and key research office personnel
 - Human Subjects Research Training
 - HIPAA Training (if applicable)

5. FDA

- Copies of all versions of FDA Form 1572 for all involved investigators
- IND safety reports
- Investigational New Drug Application FDA Form 1571 if the PI is a Sponsor-Investigator
- FDA Financial Disclosure Form (FDA Form 3455)
- Investigational device exemption information
- Investigator-initiated IND or IDE application
- All forms submitted to FDA pertaining to human subjects research
- All correspondences with FDA
 - The retained communications should include all required reports, e-mails, faxes, memoranda, and letters. In addition, logging phone conversations is encouraged to track when conversations take place and the substance of the communications.

6. NIH

- Copy of the approved NIH grant application
- All Progress Reports submitted to NIH
- All forms submitted to NIH pertaining to human subjects research
- All correspondences with NIH
 - The retained communications should include all required reports, e-mails, faxes, memoranda, and letters. In addition, logging phone conversations is encouraged to track when conversations take place and the substance of the communications.

7. Sponsor

- Documentation of where the clinical trial agreement & study budget between the investigator/institution and the sponsor for the trial is kept. It is recommended that such financial information is maintained in a separate area.

- Safety information from sponsor
- Notification to the sponsor of adverse events and related reports
- All correspondences with the Sponsor and/or Contract Research Organization
 - The retained communications should include all required reports, e-mails, faxes, memoranda, and letters. In addition, logging phone conversations is encouraged to track when conversations take place and the substance of the communications.

8. Monitoring/DSMB

- Adverse Event Reports
- DSMB reports
- Copy of all audit reports
- All correspondences with the monitor
 - The retained communications should include all required reports, e-mails, faxes, memoranda, and letters. In addition, logging phone conversations is encouraged to track when conversations take place and the substance of the communications.
- Trial monitoring reports
 - Pre-trial visit
 - Initiation visit
 - Periodic monitoring
 - Closeout visit

9. Product Information

- Investigator brochure and updates
- Package insert
- Device manual
- Sample of product label
- Instructions for handling investigational product(s) and trial-related materials

10. Laboratory Documentation

- Laboratory certifications (e.g. CLIA) and updates of laboratory certifications
- Updates to normal value(s)/range(s) for medical lab technical procedure(s), test(s) included in the protocol
- Medical/laboratory/technical procedures/tests and updates including:
 - Certification
 - Accreditation
 - Established quality controls/external quality assessment
 - Other validations
- Copy of the laboratory director's CV

11. Drug/Device Accountability

- Shipment and receipt records for investigational products and study related supplies, including documented shipment dates, batch numbers, and methods of shipping the investigational product

- Dates, quantities received, batch/serial numbers, and expiration dates
- Inventory of the investigational product at the study site
- Documentation of investigational product return, disposal, or destruction as specified by the sponsor
- Certificates of analysis of investigational products shipped
- Documentation of investigational product accountability at study site
- Verification that dosing/device use was in accordance with the approved protocol including records regarding when the subjects received the drug/device and the specific dosage/device the subjects received
- Drug/Device Accountability Log
- Drug/Device Dispensing Log

12. Data Collection

- Master randomization list (instructions on how to randomize)
- Decoding procedures in blinded trials for emergency situations
- Sample of the Case Report Forms (CRF)

13. Study Logs

Examples of study logs include:

- Subject screening log
- Subject identification code list
- Subject enrollment log
- Signature sheet
- Delegation of Responsibility Log
- Monitoring Visit Log
- Record of retained body fluids/tissue samples
- Lab shipment Log