

Regulatory Binder

Home of Essential Documents

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Agenda

- Introduction and the **5Ws** of Regulatory Binder
- **Who** is responsible for maintaining a Regulatory Binder?
- **What** essential documents belong in a Regulatory Binder?
- **When** do studies require a Regulatory Binder?
- **Where** and how should regulatory files be maintained?
- **Why** are regulatory binders important?
- Action Steps and Key Takeaways
- Resources

Introduction to Regulatory Binder

- Organizing system (“home”) for essential documents for the conduct of a clinical study
- Houses “...documents that individually and collectively permit evaluation of the conduct of a trial [or study] and the quality of the data produced.” [ICH GCP E6\(R2\)](#)
- Provides easy reference by research team for study visits, and easy access by monitors, IRB and other regulatory authorities for study reviews or audits
- Other Terms: Site Study Binder, Trial Master File, Investigator Site File, Essential Documents Binder

Why are regulatory binders important?

- Assist in the successful management of a study by the investigator, sponsor, and monitor
- Confirm the validity of the study conduct and the integrity of data collected
- Demonstrate compliance with the standards of Good Clinical Practice (GCP) and with all applicable regulatory requirements

Who is responsible for maintaining a Regulatory Binder?

- Study Principal Investigator (PI) is ultimately responsible for the maintenance and accuracy of the regulatory binders
- PI may enlist other members of the research team to help maintain the binders (“housekeeping”)
 - Authorized by PI on Delegation of Authority (DOA) Log
 - Approved by IRB in RASCAL

When do studies require a Regulatory Binder?

- **All** clinical research studies
 - Interventional (e.g., drug, device, behavioral)
 - Observational
- Irrespective of funding source or regulatory oversight
- Throughout the life of the study
 - Retention as required by law and study sponsor

What essential documents belong in a Regulatory Binder?

Section	Purpose	Recommendations
Study Protocol	To establish a detailed plan of what the study will do, how it will be done, and why it is being done	All versions should be IRB-approved and filed in reverse chronological order
Study Product (Investigator's Brochure(s) (IB) or equivalent (package insert, drug label), device manual)	To document that relevant and current scientific information about the investigational product has been provided to the investigator	All relevant versions should be IRB-approved and filed in reverse chronological order

What essential documents belong in a Regulatory Binder?

Section	Purpose	Recommendations
Consent Documents (ICF, HIPAA, translated and other recruitment materials)	To document that subjects will be given appropriate information (content and wording) without coercion	Documents should be IRB approved/stamped and all versions filed in reverse chronological order
Qualification of investigator(s) and study team members	To demonstrate one is qualified by training, education, experience to conduct or serve as an engaged personnel in the study	Section should be up to date – covering the entire duration of study involvement for each personnel

What essential documents belong in a Regulatory Binder?

Section	Purpose	Recommendations
Laboratory Documents (CAP/CLIA certificates, lab ranges, CV lab director)	To document laboratories are certified or accredited to analyze study samples and deliver accurate test results	Section should be up to date – covering the entire duration of study involvement for each facility
Study Logs <ul style="list-style-type: none"> • Delegation of Authority • Screening-Enrollment • (Serious) Adverse Event • Protocol Deviation / Violation 	To provide a quick and comprehensive overview of the staff, enrollment progress and significant incidents or departures from protocol	Documents should be maintained and updated in real time

What essential documents belong in a Regulatory Binder?

Section	Purpose	Recommendations
IRB Documents (Initial approval, continuing review, modifications, closures)	To document IRB approval, demonstrating the protection of rights and welfare of participants	All IRB submissions should be filed in reverse chronological order, to include corresponding supporting documents
Study Monitoring (Site initiation, monitoring logs and letters, site close-out, data safety monitoring reports)	To document research is conducted in accordance with the protocol/regulations for the protection of participant welfare	Logs should be completed and signed at each visit; review and file initial and follow up monitoring letters

What essential documents belong in a Regulatory Binder?

Section	Purpose	Recommendations
Special Reporting (Protocol Deviation/Violation Unanticipated Problems, Adverse Events)	Notification by PI to sponsor and regulatory authorities of missed procedures and adverse reactions	Group relevant documents and reports per event from start to finish
FDA Documents (Initial Application, Approval, Annual Reports, Amendments, Withdrawals)	To document notification and approval by the FDA for (IND/IDE* studies) prior to initiation of research	Clearly label submission packets and file documentation submission confirmation and acknowledgement

*Investigational New Drug (IND); Investigational Device Exemption (IDE)

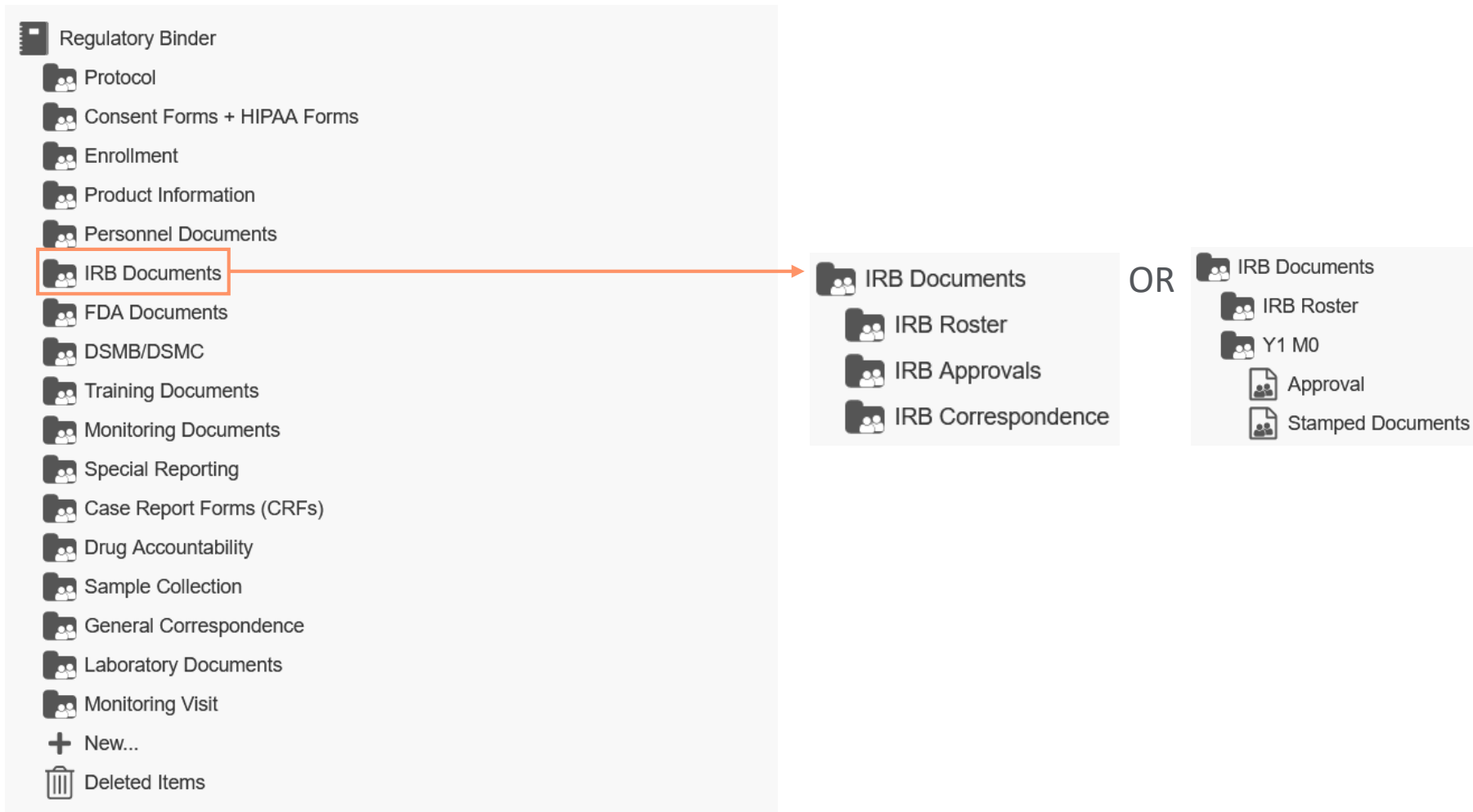
What essential documents belong in a Regulatory Binder?

Essential Document	Before	During	After
Delegation of Authority Log	X	X	X
Protocol	X	X	
Informed Consent Form/HIPAA	X	X	
Investigator's Brochure/Device Manual	X	X	
Initial IRB Approval Documents	X		
Initial FDA Application and Approval (IND/IDE studies)	X		
IRB Annual Renewal and Modification Approvals		X	
FDA Annual Reports/Amendments (IND/IDE Studies)		X	
Research Personnel Qualification and Training	X	X	
Laboratory Certificates and Lab Ranges	X	X	
Site Initiation Documentation	X		
Screening/Enrollment Logs		X	
Specimen Logs/Shipping Logs		X	
Protocol Deviation and Violation Logs		X	
Adverse Event Logs		X	
Monitoring Logs and Letters		X	
General Correspondence	X	X	
Sample Case Report Forms	X	X	
Drug/Device Accountability Logs		X	X
Documentation of Drug/Device Return or Destruction		X	X
Final Close-Out Monitoring Report			X
IRB Closure Approval			X
FDA Final Report (IND/IDE Studies)			X

Where and how should regulatory files be maintained?

- Physical binder (paper/printed copy): stored in a secure and locked location, accessed by key/code
- E-Binder (electronic files): stored on a secure application and server, accessed by username/password
- Hybrid format (paper/printed copy and electronic files)
- Essential documents are confidential

Sample e-Binder



Common Recordkeeping Issues

Example 1: Not having a set schedule to review and maintain the binder

Coordinator Greg was notified of an upcoming monitoring visit. He waited until one week before the visit to look through the regulatory binder. He discovered multiple versions of the drug brochures and safety reports in his emails that have not been filed. He spends the next several days printing and filing hundreds of pages and creating extra binders. Greg's PI also had to review and sign off on the large volume of safety reports in one sitting.

Action Step PI and Greg should set intervals (e.g., biweekly, no later than 1 week from the study change) to regularly review and upkeep the binders.

Common Recordkeeping Issues

Example 2: Using regulatory binder templates as is

Greg received a sample regulatory binder from a pharmaceutical company. He is using the binder as a model to set up the rest of the studies under his coordination, including a NIH-funded project and a patient registry. Greg finds a lot of the tabs are irrelevant and write notes-to-file to explain why these don't apply.

Action Step Greg should customize the organizing system according to each study's requirements by keeping only the necessary tabs while adding any missing sections.

Common Recordkeeping Issues

Example 3: Forgetting to update the DOA Log

Coordinator Sam joined the team in May 2019 and left the institution after one year. Greg later discovered that Sam's name was not added to the DOA Log.

Action Step Greg should add Sam to the DOA Log and complete the fields with any accurate and available information, such as Sam's name, start date, end date and assigned tasks. Greg should not sign in place of Sam but can explain the missing fields with a note to file or similar documentation. Greg should have the PI review and sign/date the new information in real time (i.e., not backdate to 2019). A protocol violation should be submitted to the IRB, as the protocol states only delegated staff will conduct study activities. The team should also develop a corrective action plan.

Common Recordkeeping Issues

Example 4: Failing to clearly label

Greg's PI has several *NewDrug-101* studies occurring concurrently. The regulatory binders for each are labeled "NewDrug-101." During a monitoring visit for one of the studies, the team could not locate several key documents. Documents were erroneously filed in a different regulatory binder investigating the same drug.

Action Step Clearly label each regulatory binder to include IRB number, PI name, distinctive "short title" and reorganize documents into the correct binders/sections.

Common Recordkeeping Issues

Example 5: Storing documents in an unrestricted shared drive

Greg's PI saves regulatory documents on the departmental shared drive. A staff member uninvolved in the research inadvertently deleted files.

Action Step If possible, retrieve the deleted files. The documents should then be moved to a secure, restricted location, preferably with audit trail capabilities.

Regulatory Binder: Key Takeaways

- Customize a system (“home”) that sparks joy... and success
- Do in real time
- Label, Label, Label
- Remember the 5Ws: Who, What, When, Where and Why
- Stay committed and be open to reorganizing

Resources

- Clinical Trials Office: [Regulatory Binder](#)
 - [Drug Study Checklist](#)
 - [Device Study Checklist](#)
 - [Behavioral Study Checklist](#)
- Electronic Regulatory Binder: [LabArchives](#)
- National Center for Complementary and Integrative Health (NCCIH): [Clinical Research Toolbox](#)
- [Maintaining IRB Approval](#)

Thank You

If you have any questions, please contact:

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