

CRA TRAINING

ADVANCED II

SITE REGULATORY

REGULATORY BINDER / INVESTIGATOR SITE FILE BINDER

DAN SFERA

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INVESTIGATOR SITE FILE BINDER / REGULATORY BINDER

- ISF- Investigator Site File

- The National Institute for Health Research defines the **ISF as a file that contains all essential documents held by the Principal Investigator (PI) and/or sub-investigators conducting a trial which individually and collectively permit the evaluation of the conduct of a trial and the quality of the data produced.** The documents found in the ISF serve to demonstrate that the study is being conducted as per the standards of Good Clinical Practice and in accordance with all other applicable regulatory requirements.
- Other Names of the ISF: Regulatory Binder (very popular), Study Files, or Investigator Binder.
- This week we will be taking a look at the documents/files/binders that make up the ISF

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ISF DOCUMENTS

- **Site Visit (Monitoring) Log:** All monitors must sign in on the visit log. It is a documented proof at the study site to show that the visit was performed. It also documents the frequency of monitoring. The monitor and the designated staff both sign off.
- **Site Signature Log/Delegation of Authority Log:** This log documents responsibilities assigned to research team members and their dates of involvement in the project.
- **Site Personnel Signature Log:** This documents the names and provides handwriting samples of all personnel involved in the conduct of the study.

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ISF DOCUMENTS

- **Training Log:** This is a record of training provided, e.g. protocol training or other study-specific training of staff. This should include a site initiation visit (SIV) attendance log.
- **CVs/Financial Disclosures/Investigator Statements:** CVs, MLs, GCP certificates, IATA certificates, FDF, FDA Form 1572, Protocol Signature Page, Investigator Brochure Signature page, etc. Your study team will let you know which other documents to collect.
- **Screening and Enrollment Log:** This section should include a log of subjects who were screened (and reason for screen failure) and enrolled. Some studies allow for re-screening of subjects.

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ISF DOCUMENTS

- **Subject Visit Tracking Log:** This log tracks all enrolled subjects' visits, reason for early termination and keeps visits scheduled as per protocol.
- **Subject identification Code List:** This is a confidential list of the names of all the subjects that provides a link between their identity and their study code to allow the Investigator to reveal the identity of any subject, if necessary.
- **Informed Consent Forms:** This section of the binder should include consent form documents (IRB approved and stamped versions) **stored in reverse chronological order with the current approved version first.**

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ISF DOCUMENTS

- **Protocol:** This section should include the protocol (and protocol signature page) and all amendments (and amendment signature page or pages), **stored in reverse chronological order with the current approved version first.**
- **IRB Study Information including Approvals:** This section should include copies of the original IRB application/submission, IRB approval letters (contingent and final approval), and all correspondence with the IRB (including emails).
- **IRB Federal Wide Assurance Letter:** This section should contain the most current IRB assurance letter.

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ISF DOCUMENTS

- **Investigator Brochure/Investigational Product Information:** This section should include all version of the Investigator Brochure, Receipt Form and Package Insert.
- **Correspondence:** This section is for documenting all and maintaining all relevant, significant communication from the sponsor, CRO, or monitor. Study related newsletters may also be placed in this section.
- **IND Safety Reports:** Should include correspondence (including IRB acknowledgement- the IRB has to acknowledge the safety report and it has to be submitted by the PI or Sponsor) and copies of the Safety Reports.

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ISF DOCUMENTS

- **Advertising/Educational Materials:** Any IRB approved advertisements, recruitment flyers, written educational, or other materials provided to study participants, **stored in reverse chronological order with the most current documents first.**
- **Sample Tracking and Shipping:** This section should include a master log that allows tracking of research specimen sample collection, shipment (or transport), and storage, and packing and shipping training certification. Shippers of receipts can be placed in this section or in individual subject files
- **Investigational/Test Article:** This section includes- Shipment Records, Site Accountability Records, Subject Drug Accountability Records/Device Log, Blind Break Instructions and Interactive Voice Response System Instructions

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ISF DOCUMENTS

- **Local Lab Certificates/Central Laboratory Tab including Lab Manuals and Reference Ranges:** For every lab listed on FDA Form 1572, place a copy of (maintain current certifications for duration of study) Lab certificate(s) and reference ranges (for the duration of study) and Lab director's CV
- **Blank Set of Case Report Forms**
- **Notes to File (NTF)**
- **HIPAA Forms:** This section includes all IRB approved and stamped versions of any of the HIPAA forms (as applicable)- HIPAA Health Insurance Portability and Accountability Act.

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ISF DOCUMENTS

- **Protocol Deviations/Protocol Exceptions:** This section should include correspondence relevant to the issue and copies of the documents stored in reverse chronological order with the most current documents first. Please note that some Sponsor approved waivers may need to be approved by the IRB prior to implementation.
- **Adverse Events and Unanticipated Problems:** This section should include correspondence, copies and acknowledgements of reports for internal AEs and unanticipated problems reported to the IRB and Sponsor and regulatory authorities as applicable.
- **Temperature Logs for Refrigerator/Freezer:** Temperature logs document compliance with Protocol /Study Procedures requirements and GCP.

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ESSENTIAL DOCUMENTS FOR REGULATORY BINDER

- During the Clinical Conduct of a Trial, the following essential documents must be located in the regulatory binder-
- Documents are filed in reverse chronological order
 1. Investigator Brochure and Updates
 2. Any Revision or new approvals to protocol/amendment(s) and CRF, Informed Consent Form, any written information provided to subject and advertisements for recruitment
 3. CVs for investigators and sub-investigators
 4. Updates to Normal lab values
 5. Documentation of IP
 6. Certificates of Analysis for IP

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ESSENTIAL DOCUMENTS FOR REGULATORY BINDER

7. Monitoring Visit Follow Up Letters
8. Relevant Communications other than site visits
9. Signed Informed Consents
10. Source Documents
11. Case Report Forms
12. Financial Disclosures
13. Form FDA 1572
14. IRB Approval
15. Signed Confidentiality Agreement and Clinical Trial Agreement
16. Site Initiation Visit Report

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ESSENTIAL DOCUMENTS FOR REGULATORY BINDER

- Renewal Date for Certificates and licenses
 - Curriculum Vitae must be signed and dated every **two years**
 - International Air Transportation Association certificates must be renewed every **two years**
 - Good Clinical Practices certificates must be renewed every **two years**
 - Medical Licenses, Drug Enforcement Agency licenses, Registered Nurses licenses and physician assistance licenses must be renewed as needed

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CRA Training:

- ☐ Basic I: GCP for Site Monitors
- ☐ Basic II: Site Selection
- ☐ Basic III: Site Initiation
- ☐ Basic IV: Site Monitoring
- ☐ Basic V: Site Close-out
- ☐ Advanced: I: Source Documents
- ☐ Advanced II: Site Regulatory
- ☐ Advanced III: Protocol Deviations, IP Accountability, Miscellaneous

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