Site Master File

SMF

Template v1.0 | 2019

TABLE OF CONTENTS

COMPONENTS:

SITE MASTER FILE | SMF
*Documents maintained **on-site***

TRIAL MASTER FILE | TMF
*Documents sent to the study **Sponsor***

DOCUMENT VERSION KEY
ORIGINAL COPY N/A

NOTE | *The following pages offer further reference and guidance, as well as space for Monitor/other auditor notes and verification of binder contents. Each page should be filed under the respective section tab in the site Regulatory Binder/SMF.*

The **Site Master File (SMF)** or Regulatory Binder contains essential documents. The requirement to maintain a set of essential documents within a Trial Master File (TMF) comes from International Conference on Harmonisation Good Clinical Practice (ICH GCP). GCP guidance defines essential documents as:

> *"…those documents which individually and collectively permit evaluation of the conduct of the clinical trial and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, sponsor, and monitor with the standards of Good Clinical Practice and with all applicable regulatory requirements."*

Master Files should be established at both the Sponsor/Coordinating Center and at each local site – prior to the commencement of any research activities – and be maintained throughout the study to ensure **inspection readiness**. These documents can be audited by the sponsor and regulatory authorities as part of the compliance process to confirm the validity and integrity of the data and to demonstrate the compliance of the investigator, sponsor and monitor with the standards of GCP and all applicable regulatory requirements. Final close-out of a trial can only be done when the monitor has reviewed the SMF and confirmed that all necessary documents are present and compliant to 1) reconstruct the conduct of the trial at the site (SMF) and 2) reconstruct the conduct of the trial as a whole (Sponsor TMF). If need be, the contents of this binder can be expanded to other binders in any manner that maintains orderly organization and assures ready access.

To be completed at the Close-Out visit

THIS SITE MASTER FILE MUST BE COMPLETE AND ACCURATE WHEN RECORDS ARE ARCHIVED[1] AT THE CLOSE OF THE TRIAL

As the Principal Investigator of record, I certify that this Site Master File has been reviewed and found to be complete and accurate.

PRINCIPAL INVESTIGATOR NAME (Printed)	CLINICAL MONITOR NAME (Printed)
INVESTIGATOR SIGNATURE	CLINICAL MONITOR SIGNATURE
DATE	DATE

[1] **Record Retention [21 CFR 312.621 & ICH GCP E6 §5.5.12]** *Research teams must abide by Federal regulations, GCP and local IRB requirements for record retention. Records should never be destroyed without written authorization from the sponsor or granting agency.*

Tool

Regulatory Binder | SMF | TMF Essential Document (ED) Directory

Purpose

To provide an organizational framework and guidance to site study teams and monitors for filing paper versions of essential study documents in the master files that will facilitate management of the clinical trial, audit and inspection

Details

- This document clarifies the standard content of EDs within the TMF.
- It is the responsibility of the Investigator to ensure compliance with local, State and Federal regulations and guidelines governing the conduct of clinical studies.
- The following pages outline the required documents according to ICH E6 Guidance for Industry: Good Clinical Practice (GCP).
- Please note that all human subject research should adhere to ICH GCPs regardless of the type of clinical study.

Best Practice Recommendations

- Store items in reverse chronological order, with the newest items within a section placed at the front of that section.
- Use the requirements, references and guidance noted at the front of each binder section to ensure compliance.
- **TIP**: It is good practice to keep a site master file of investigator CVs so they are available for all studies. This reduces reporting burden and works well for medical licenses as well as lab certifications. If you use this format, insert a note-to-file (NTF) in the relevant tab of the binder noting the location of the master file so that it is readily accessible for monitor review or audit.
- In addition and separate from this **Regulatory Binder**, the following should also be prepared at each local site:
    - **Financial Binder** containing (most financial information should <u>not</u> be in the Regulatory Binder): Clinical Trial Agreement (CTA) or Study Agreements, Confidentiality Agreements (CDA), Insurance Policies (where required), Budgets, Payments, Invoices
    - Individual **Subject Binders**
    - Other, as necessary (i.e. Master CV binder as noted above)
- **Electronic documents**: If you elect to use only electronic copies of particular documents as a part of your site regulatory file, the following guidelines should be observed:
    - Either a) place an NTF 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 are easily accessible by site staff so that an inspector, auditor or clinical monitor can be provided with easy access to the relevant electronic materials during a site visit; The electronic location should be secure, controlled, regularly backed-up and never be in danger of disappearing or changing in the foreseeable future
    - For email correspondence, sites may want to include clarification in the binder that email 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

CFR	Code of Federal Regulations
CLIA	Clinical Laboratory Improvement Amendments
CM	Clinical Monitor
COC	Certificate of Confidentiality
COI	Conflict of Interest
CRA	Clinical Research Associate
CRF | eCRF	Case Report Form | electronic-CRF
CTA	Clinical Trial Agreement
CTD	European Clinical Trials Directive
CV	Curriculum Vitae
DHHS	Department of Health & Human Services
DSMB	Data &Safety Monitoring Board
ED	Essential Documents
EDC	Electronic Data Capture
FDA	Food & Drug Administration
FDF	Financial Disclosure Form
FWA	Federal Wide Assurance
GCP	Good Clinical Practice
GINA	Genetic Information Nondiscrimination Act
GLP	Good Laboratory Practice
HIPAA	Health Insurance Portability and Accountability Act
HSTC | HSTE	Human Subjects Training Certification / Education
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
IDS	Investigation Drug Service (Pharmacy)
IMP	Investigational Medicinal Product (CTD)
IND	Investigational New Drug
IOR	Investigator of Record *(see also PI) – listed in Box 1 of FDA Form 1572*
IP	Investigational Product
IRB	Institutional Review Board
MF	Master File
MTA	Material Transfer Agreement
NIH	National Institutes of Health
NTF	Note-to-File
OHRP	Office for Human Research Protection
PI	Principal Investigator *(see also IOR) – listed in Box 1 of FDA Form 1572*
RA	Regulatory Affairs
RDRC	Radioactive Drug Research Committee
REB	Research Ethics Board
RSC	Radiation Safety Committee
SAE	Serious Adverse Event
SC	Study Coordinator
SD	Source Document
SMF	Site Master File
SS	Signature Sheet
SUSAR	Suspected Unexpected Serious Adverse Reactions
TMF	Trial Master File
UPIRTSO	Unanticipated Problem Involving Risks to Subjects or Others

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1 PROTOCOL & AMENDMENTS

SITE MASTER FILE ●
SPONSOR TMF ■

● ORIGINAL ● COPY ■ N/A

REQUIREMENT & PURPOSE

Contains the initial study protocol and any subsequent amendments (when applicable).

The protocol describes the objective(s), design, methodology, statistical considerations, and organization of a research study.

REFERENCE & GUIDANCE

- 21 CFR 312
- ICH E6 GCP §1.44, 1.45, 4.5, 5.23, 6, 8.2.2, 8.3.2
- When amendments are issued, they should be filed accordingly
- Outdated versions of the protocols should NOT be removed from this MF

Refer to the back of this page for Monitor Notes

1 PROTOCOL & AMENDMENTS

Monitor Notes	Date of Verification | Entry

2 INVESTIGATOR BROCHURE | IB

SITE MASTER FILE ●
SPONSOR TMF ■

● ORIGINAL ● COPY ■ N/A

REQUIREMENT & PURPOSE

This section contains the Investigator's Brochure or equivalent (package insert, "Information for Investigators") and amendments, when applicable.

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/product.

REFERENCE & GUIDANCE

- 21 CFR 312
- ICH GCP §1.36, 5.12, 7, 8.2.1
- When updated IBs are issued they should be filed accordingly
- Outdated IBs should NOT be removed from this MF

Refer to the back of this page for Monitor Notes

Monitor Notes	Date of Verification | Entry

3 SIGNATURE SHEETS | SS
STUDY PROTOCOL & IB

SITE MASTER FILE ●
SPONSOR TMF ●

● ORIGINAL ● COPY ■ N/A

REQUIREMENT & PURPOSE

Contains the initial study protocol SS, the IB SS and any subsequent amendments (*as applicable*).

PROTOCOL SS | *Completed signature sheets document PI receipt of the protocol (or amendments) and assures that the clinical trial will be conducted according to all requirements of the protocol, the Declaration of Helsinki, FDA/ICH Guidelines for Good Clinical Practice and all other applicable regulatory requirements.*

IB SS | *Signed signature sheets for the IB document that relevant and current scientific information regarding the investigational product has been received and reviewed by the PI.*

REFERENCE & GUIDANCE

- 21 CFR 312
- ICH GCP §1.36, 1.44, 1.45, 4.5, 5.12, 5.23, 6, 7, 8.2.1, 8.2.2, 8.3.2
- When amendments are issued, they should be signed and filed accordingly – Monitors should confirm that all applicable amendment/versions are completed per policy.

Refer to the back of this page for Monitor Notes

Monitor Notes	Date of Verification | Entry

4 STATEMENT OF INVESTIGATOR | FDA FORM 1572

SITE MASTER FILE ●
SPONSOR TMF ●

● ORIGINAL ● COPY ■ N/A

REQUIREMENT & PURPOSE

Contains all versions of the FDA Form 1572 that were signed over the course of the study.

The FDA Form 1572 is the Statement of Investigator. According to the CFR, the PI/IOR is responsible for ensuring that the research study is conducted according to the protocol and in compliance with applicable regulations, for assuring that human subjects' rights, safety and welfare are protected, for controlling any investigational product being used during the study and for providing any documentation requested by the Sponsor, IRB or any other regulatory authority.

By signing the FDA Form 1572, the PI/IOR agrees:

- To conduct the trial in accordance with the protocol
- To personally conduct or supervise the investigation
- To inform patients that the drugs are being used for investigational purposes and to adhere to the requirements for obtaining informed consent
- To report adverse events to the sponsor
- To ensure that all staff members assisting in the trial understand their obligations
- To maintain accurate records
- To report all unanticipated problems promptly to the IRB
- To ensure that the IRB provides continuing review of the clinical investigation
- To make no changes to the protocol without IRB approval except for the immediate protection of subjects

REFERENCE & GUIDANCE

- 21 CFR 312.53(c)
- ICH GCP §4.1, 4.3
- Only one PI/IOR should be listed in Box 1 of the 1572: There is no such thing as a co-investigator under FDA regulations; Form FDA-1572 must be signed by an individual.
- Outdated 1572's should NEVER be removed from this MF
- FDA Guidance: *Information Sheet Guidance for Sponsors, Clinical Investigators, and IRBs: Frequently Asked Questions – Statement of Investigator (Form FDA 1572)*
- Expiration Date: There is no need to prepare and sign a new 1572 when the OMB approval date (upper right corner of page 1) has expired. However, any time that you make changes or updates to the FDA Form 1572, be sure to use the most current version of the form.
- A double-sided 1572 is not required. However, the FDA recommends that multi-page documents be stapled so that there is no question about what form the investigator signed.
- **If there are any changes to the PI/IOR (Box 1) or sub-investigators (Box 6), a new FDA Form 1572 must be completed, signed and submitted to the Sponsor.**

Refer to the back of this page for Monitor Notes

Monitor Notes	Date of Verification | Entry

5 EXPERIENCE & TRAINING

SITE MASTER FILE ●
SPONSOR TMF ●

● ORIGINAL ● COPY ■ N/A

REQUIREMENT & PURPOSE

Includes CVs, medical licenses, HSTC/HSTE and any other training required to conduct the trial.

This section documents:

- *the qualifications and eligibility of key personnel to conduct the trial and / or provide medical supervision of study participants; and*
- *that study personnel have received adequate study-specific training in order to execute the protocol.*

Includes the following key personnel for IND studies:

- PI/IOR – Listed in Box 1 of the FDA Form 1572; and
- All other sub-investigators listed in Box 6 of the FDA Form 1572

For non-IND studies, includes all investigators / sub-investigators listed on an authorized pre-scriber list or delegation log. This will be protocol-specific and may include:

- Study coordinator
- Pharmacist of record
- Imaging Technicians or Imaging Facility Director

REFERENCE & GUIDANCE

- 21 CFR 312
- ICH GCP §4.1, 4.3, 5.6, 8.2.10, 8.3.5
- If you are utilizing central files for local staff personnel qualifications, experience or training please insert a NTF noting the location of such MFs.

CURRICULUM VITAS (CV)

- To verify affiliation to the study site, **the name on the CV must match the name and address listed on FDA Form 1572**, **medical licenses** (if applicable) and human subject research education certification.
- Must be signed and dated within two years of date submitted (Best practice - not an FDA mandate)
- Should include clinical trials experience
- Outdated CVs should NOT be removed from the file
- Should be updated to reflect significant changes such as affiliation, education, responsibilities, etc

MEDICAL LICENSURE:

- All licenses must be current
- Expired licenses should NOT be removed from the file

HUMAN SUBJECTS TRAINING CERTIFICATION / EDUCATION (HSTC/HSTE):

- Required for anyone listed on the FDA Form 1572. The NIH does not endorse any specific program to fulfill the requirement for Human Subjects Protections Training. Sites may utilize the CITI training (www.citiprogram.org) or training specific to your Institution
- Must be current

TRAINING:

- May include - but is not limited to - rater certifications, specimen collection/shipping, lab safety, phlebotomy certifications, etc
- Training can include a site initiation visit report and/or Investigator Meeting attendance record
- The training records should reflect appropriate training for all study personnel

Refer to the back of this page for Monitor Notes

5 EXPERIENCE & TRAINING

Monitor Notes	Date of Verification | Entry

6 DELEGATION & SIGNATURE LOGS

SITE MASTER FILE ●
SPONSOR TMF ●

● ORIGINAL ● COPY ■ N/A

REQUIREMENT & PURPOSE

The Delegation and Signature Log should be completed prior to beginning trial-related activities and updated as needed to reflect changes in staff, role assignments and/or the delegation of responsibilities.

Regulations require that the PI/IOR personally supervise the conduct of the clinical trial; however, the PI can delegate certain study-related tasks to co-investigators and other study staff. It is important to note that the PI is responsible for providing adequate supervision of those to whom tasks are delegated and ensuring that tasks are delegated only to individuals appropriately qualified by means of education, training, and experience.

The Delegation and Signature Log details study staff that significant study-related tasks have been delegated as well as each individual's dates of involvement in the trial. The log will also document that the PI is responsible for, accountable for, and has approved such delegation of duties. In addition, the full legal signature and initials of all study personnel authorized to make entries and corrections on CRFs and source documents will be captured.

REFERENCE & GUIDANCE

- ICH GCP §8.3.24
- Delegation & Signature Log Instructions

Refer to the back of this page for Monitor Notes

6 DELEGATION & SIGNATURE LOG

Monitor Notes	Date of Verification | Entry

7 FINANCIAL DISCLOSURE FORM | FDF

SITE MASTER FILE ●
SPONSOR TMF ●

● ORIGINAL ● COPY ■ N/A

REQUIREMENT & PURPOSE

This section contains completed FDFs for the PI and any sub-Investigators (anyone listed in Blocks 1 and 6 of the FDA Form 1572) as well as the spouses and children of all such key personnel to document the financial agreement between investigator/institution and the trial sponsor.

Financial disclosure promotes objectivity in research by establishing standards to ensure there is no reasonable expectation that the design, conduct, or reporting of research will be biased by any conflicting financial interest of an Investigator.

Certification or Disclosure | All key personnel must:

- Certify that there is no financial interest or
- Disclose specific financial interests
- Complete FDA form(s) 3454 or 3455, or equivalent forms

REFERENCE & GUIDANCE

- 21 CFR 54
- 42 CFR 50, Subpart F
- 21 CFR 312
- ICH GCP §8.2.4
- FDA Guidance: Financial Disclosure by Clinical Investigators
- NIH Notice OD-00-040
- A new FDF must be completed any time there is a change in the investigator's financial situation (i.e. stock purchases, etc.) OR if new personnel are being added at your site.
- Completed FDFs must NEVER be removed from this TMF
- If FDFs are not required for a given protocol, the Sponsor should provide you with a note-to-file to be inserted into this section in place of the FDFs
- The Institutional Form 700-U or 9510 (Statement of Economic Interests for Principal Investigators) differ from these FDFs and should be filed in your Financial Binder and/or submitted to the appropriate reviewing office at your site (Contracts & Grants, Clinical Trial Administration, etc); These records are not sent to the Sponsor.

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Monitor Notes	Date of Verification | Entry

8 LABORATORY ACCREDITATIONS, CERTIFICATION & NORMAL VALUES

SITE MASTER FILE ●
SPONSOR TMF ■

● ORIGINAL ● COPY ■ N/A

REQUIREMENT & PURPOSE

Contains lab certifications (CAP, CLIA, etc.), lab normal ranges and CV of the laboratory director (when appropriate).

Lab accreditations certify qualifications of local or central laboratories to perform required study tests and support reliability of results of medical, laboratory, standardized procedures and other tests. Documents lab normal values and/or ranges that are used to interpret clinical test results. When required, the CV of the laboratory director details qualifications and competence to conduct tests for clinical trials.

NOTE: *For research labs that test protocol specimens but do NOT report any subject-specific results for the diagnosis, treatment, prevention or assessment of the health of subjects, such certifications (CAP/CLIA) are not relevant. In this case, documentation that the lab director and/or personnel performing the tests have training and qualifications to assure ability to perform the tests as required by the protocol is required.*

REFERENCE & GUIDANCE

- 21 CFR 58
- 21 CFR 312
- 42 CFR 493.3
- ICH GCP §4.2, 8.2.11, 8.2.12, 8.3.6, 8.3.7
- Certifications must be current
- Expired certifications should NOT be removed from this MF

Refer to the back of this page for Monitor Notes

Monitor Notes	Date of Verification | Entry

9 INVESTIGATIONAL PRODUCT | IP

SITE MASTER FILE ●
SPONSOR TMF ●

● ORIGINAL ● COPY ■ N/A

REQUIREMENT & PURPOSE

Contains information/forms regarding IP shipment, handling, storage, use and destruction.

The documents included in this section demonstrate the site accountability for the investigational product provided, document that the investigational products have been used according to the protocol, document destruction of unused investigational products by the sponsor or at the site.

Depending on local regulations, the investigator may choose to assume control of the investigational drug or utilize the local Investigational Drug Service (IDS). If the investigator chooses to assume control of the IP, handling, dispensing and administration of the IP must be in accordance with all state and federal laws and local regulations.

This section may contain (but is not limited to):

- Arrangements with local Investigational Drug Services (IDS)
- Study Medications Accountability Log
- Sample of label attached to investigational product containers
- Dose Adjustment Log
- Medication Compliance Log
- Temperature Log
- Shipment Logs

REFERENCE & GUIDANCE

- 21 CFR 312
- ICH GCP §4.6, 5.13, 5.14, 8.2.15, 8.3.8, 8.3.23, 8.4.1

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Monitor Notes	Date of Verification | Entry

10 IRB MEMBERSHIP & FEDERAL WIDE ASSURANCE | FWA

SITE MASTER FILE ●
SPONSOR TMF ●

● ORIGINAL ● COPY ■ N/A

REQUIREMENT & PURPOSE

Documentation containing IRB membership, the FWA number and FWA expiration date.

The IRB roster documents that the IRB is constituted in agreement with GCP.

The FWA is a contract between the Institution and the federal government to assure the protection of human subjects. Through the FWA, an institution commits to the DHHS that it will comply with the requirements in the HHS Protection of Human Subjects regulations. The PI is responsible for ensuring that a current Assurance is in effect while conducting research on human subjects.

REFERENCE & GUIDANCE

- 45 CFR 46
- OHRP Procedures for Registering IRBs and Filing Federal Wide Assurances of Protection for Human Subjects
- If your site does not publish the IRB roster, then the FWA itself can be provided in lieu of a roster
- An Institution must update its FWA every 5 years, even if no changes have occurred, in order to maintain an active FWA
- A copy of the actual Assurance document must be on file with the Institution and/or IRB

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Monitor Notes	Date of Verification | Entry

11 IRB APPROVALS & CORRESPONDENCE

SITE MASTER FILE ●
SPONSOR TMF ●

● ORIGINAL ● COPY ■ N/A

REQUIREMENT & PURPOSE

Includes all IRB approvals, correspondence and related documents

This section documents proof of submission for study-related materials/information and that the clinical trial has been subject to IRB review and approval. This section also documents proof of submission to IRB regarding any amendments as well as the completion of the clinical trial.

Approval will be granted for multiple items, including but not limited to:

- Protocol / Amendments
- IBs / Amendments
- Informed consent forms (ICFs) / Amendments
- Other written information to be provided to the study participants
- Renewals
- End of study / Termination letter

REFERENCE & GUIDANCE

- 45 CFR 46
- 21 CFR 50
- 21 CFR 56
- 21 CFR 312
- ICH GCP §3, 4.4, 4.5, 4.10, 4.13, 5.11, 5.17.3, 8.2.3, 8.2.7, 8.3.2, 8.3.3, 8.3.19, 8.4.7
- This section should include all email correspondence

Refer to the back of this page for Monitor Notes

11 IRB APPROVALS & CORRESPONDENCE

Monitor Notes	Date of Verification | Entry

12 INFORMED CONSENT FORMS | ICF & HIPAA AUTHORIZATIONS

SITE MASTER FILE ●
SPONSOR TMF ●

● ORIGINAL ● COPY ■ N/A

REQUIREMENT & PURPOSE

Includes all versions of the IRB-approved ICFs with IRB stamp, version number and date.

This section documents proof of submission regarding ICFs and that the clinical trial has been subject to IRB review in accordance to the protection of human subjects. This section documents the informed consent process at the site and documents that the study participants and study partners will give their full informed consent to participate.

Informed consent is an ongoing process during which information is presented to an individual to enable them to voluntarily decide whether or not to participate in or continue participation in a study. As defined by the OHRP: "The informed consent process is the critical communication link between the prospective human subject and an investigator, beginning with the initial approach of an investigator to the potential subject (e.g., through a flyer, brochure, or any advertisement regarding the research study) and continuing until the completion of the research study."

The ICF describes the purpose of the study, procedures, risks, benefits, alternative treatments, statement regarding confidentiality of records, the subject's rights, etc. The informed consent document must be written in language that is understandable to the subject or their legally authorized representative. The ICF(s) must be approved by the local (IRB) and bear the IRB approval stamp before it can be used. Additionally, when changes to the ICFs are necessary, IRB approval must be obtained prior to use.

HIPAA Authorizations | *The HIPAA Privacy Rule imposes requirements to obtain authorization before using or disclosing PHI about an individual. Some States prefer that all ICFs include language that satisfies the HIPAA Privacy Rule. However, other State (including CA) or local laws require a separate "stand-alone" HIPAA authorization form that must be used in addition to the IRB-approved ICF.*

REFERENCE & GUIDANCE

- All ICFs must contain the "Required Elements of Informed Consent" in accordance with 21 CFR 50.25, 38 CFR 16.116 and 45 CFR 46.116
- 45 CFR 46, 21 CFR 50, 21 CFR 56, 21 CFR 312
- ICH GCP §1.28, 4.8, 8.3.12, 8.2.3, 8.3.2
- Stand-alone HIPAA authorizations should also be placed in this section
  - Clinical Monitors should note on their consent form tracking log whether or not the site uses a separate stand-alone HIPPA Authorization.
- Decision-making capacity assessments and surrogate consent (when applicable) should be included in this section.
- Non-English translations, IRB approval of translations and official translation Certifications (as applicable/required by local regulations) should be included in this section.
- Sponsor reviews and approval notifications to submit to your local IRB should be placed in this section.
- Legal /RA approvals for significant changes to the ICFs provided for the study should be included here.

Refer to the back of this page for Monitor Notes

Monitor Notes:	Date of Verification | Entry

13 RECRUITMENT & RETENTION MATERIALS

SITE MASTER FILE ●
SPONSOR TMF ■

● ORIGINAL ● COPY ■ N/A

REQUIREMENT & PURPOSE

Includes all IRB approvals for recruitment and retention materials.

This section documents proof of IRB submission of all recruitment and retention materials and that the materials have been subject to IRB review/approval in accordance with GCP/CFR to ensure the protection of the rights and welfare of human subjects.

R&R materials and their approvals reside only in the on-site MF.

REFERENCE & GUIDANCE

- 45 CFR 46
- 21 CFR 50
- 21 CFR 56
- 21 CFR 312
- ICH GCP §3, 4.4, 4.5, 4.10, 5.11, 5.17.3, 8.2.3, 8.2.7, 8.3.2, 8.3.3, 8.3.19

Refer to the back of this page for Monitor Notes

13 RECRUITMENT & RETENTION MATERIALS

Monitor Notes	Date of Verification | Entry

14 CORRESPONDENCE & MISCELLANEOUS DOCUMENTS

SITE MASTER FILE ●
SPONSOR TMF ■

● ORIGINAL ● COPY ■ N/A

REQUIREMENT & PURPOSE

Contains trial-related communications and miscellaneous documents.

This section documents that the site has received pertinent information regarding the protocol and investigational product. Memos from Sponsor may require additional communication or training with the study team or clinical monitor. The correspondence included in this section documents any agreements or significant discussions regarding trial administration and conduct. It may also detail appropriate approvals from other applicable authorities.

Miscellaneous Documentation may include, but is not limited to:

- Imaging Certifications
- Executed MTA with NCRAD
- Approved CoC
- Site activation letter
- Decoding procedures for blinded trials
- Imaging [MRI/PET] certifications/approvals required for site activation

REFERENCE & GUIDANCE

- ICH GCP §4.4, 4.9, 8.3.11
- This should include all email correspondence not specified to be filed elsewhere in the TMF
- When filing memos and reports from the Sponsors, be sure to note whether PI signature as proof of receipt/review is required
- The Site Approval / Activation Email that you receive to begin Screening and Enrollment should be printed and filed here

Refer to the back of this page for Monitor Notes

14 CORRESPONDENCE & MISCELLANEOUS DOCUMENTS

Monitor Notes	Date of Verification | Entry

15 MONITORING LOG & REPORTS

SITE MASTER FILE ●
SPONSOR TMF ■

● ORIGINAL ● COPY ■ N/A

REQUIREMENT & PURPOSE

Contains the monitoring log and all site visit reports.

The Monitoring Log details all site visits conducted, visit activities and findings of the clinical monitor.

Other reports in this sections may include, but are not limited to:

- Site Selection Visit (Pre-Trial Monitoring) Report
- Site Initiation Report
- Monitoring Visit Reports
- Consent Form tracking log
- Final / Close-out Visit Report: A close-out report by the monitor to document that all activities required for site close-out are completed and essential documents are in the appropriate files.

REFERENCE & GUIDANCE

- 21 CFR 312
- ICH GCP §4.13 & 8.4.7

Refer to the back of this page for Monitor Notes

15 MONITORING LOG & REPORTS

Monitor Notes	Date of Verification | Entry

16 SERIOUS ADVERSE EVENT | SAE & UNANTICIPATED PROBLEMS

SITE MASTER FILE ●
SPONSOR TMF ■

● ORIGINAL ● COPY ■ N/A

REQUIREMENT & PURPOSE

This section contains records of reports and reviews of unanticipated problems and adverse events occurring at the local site and other sites participating in the clinical trial. This includes correspondence/notifications sent to the PI and the IRB (when applicable).

Unanticipated problems can occur in any type of research (medical or non-medical) and may include occurrences such as adverse events, research participant complaints, protocol deviations, and other untoward events involving risk. This section documents that the principal investigator/site, the IRB and all other authorities have been properly notified of unanticipated problems, unexpected serious adverse events or other safety information (including DSMB summary reports and UPIRTSOs) pursuant to protocol requirements, federal regulation, applicable state and local law and local site/University policy. Outside of the US, Suspected Unexpected Serious Adverse Reactions (SUSAR) reporting requirements may vary.

REFERENCE & GUIDANCE

- 45 CFR 46.103(b)(5)(iii), 45 CFR 46.116(b)(5)
- 21 CFR 50.25(b)(5)
- 21 CFR 56.108(b)(1)
- 21 CFR 812.150(a)(1)
- 21 CFR 312.32 IND Safety Reports
- OHRP "Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events"
- ICH GCP §1.1, 1.2, 1.50, 1.60, 4.11, 5.16, 5.17, 8.3.16, 8.3.17, 8.3.18
- DIRECTIVE 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.

Refer to the back of this page for Monitor Notes

16 SAEs & UNANTICIPATED PROBLEMS

Monitor Notes	Date of Verification | Entry