Essential Documents Guidance

The purpose of this guidance is to aid study teams in determining what essential documents are required to be in the investigator site file (ISF) versus the trial master file (TMF). Every time a study is conducted, it is expected that the study team maintains an ISF that is audit ready. An ISF is required regardless of if it is an investigator-initiated, federally funded or industry-sponsored study. The ISF is composed of the regulatory binder and participant binders. The sponsor of the study will maintain the TMF. The TMF will include all applicable documents for the overall study and for each participating site. If the investigator is also the sponsor (considered the sponsor-investigator) for a multi-site or federally funded study that has other participating sites, it is expected that the sponsor-investigator will maintain both an ISF and TMF. This practice follows ICH GCP guidelines and aids the sponsor and the investigator in fulfilling FDA regulations.

The table within this guidance document lists the expected documents that are expected to be maintained during the course of the study and specifies whether the investigator or the sponsor is responsible for maintaining it.

Table 1: Essential documents

Type of Document	**Purpose**	**Location of Document: ISF (At the investigator site)**	**Location of Document: TMF (With the sponsor)**
Investigator's brochure (IB)/ package insert	Documents the current scientific information about the product that is being provided for the study. If there are multiple products being used, each product would have its own IB or package insert.	X	X
Protocol signature page	Documents the investigator's agreement to the protocol. This will be resigned when a protocol amendment occurs.	X (Original)	X (Copy)

Type of document	Purpose	Location of Document: ISF (At the investigator site)	Location of Document: TMF (With the sponsor)
Sample case report form (CRF)	This is a blank copy of the CRF(s) used for this study and includes what data is expected to be collected at each study visit.	X	X
Any written information given to participants in addition to consent	A sample of any additional written information given to participants (ex: drug diary, participant information sheet). This additional information needs to be IRB approved prior to being given to participants. A sample should be kept of each version if amendment(s) occur(s).	X	X
Subject recruitment advertisement	Samples of any recruitment materials used to enroll participants. Recruitment materials must be approved by the IRB prior to use.	X	
Financial aspects of trial	Documents the financial agreement between the investigator/institution and the sponsor.	X	X
Any signed agreements between sponsor/CRO and institution/investigator	Documents any agreements between the sponsor, their CRO and the institution/investigator.	X	X
Documented approval(s) and submission(s) of IRB for all protocol, amendments, continuing reviews, deviations, safety reports, etc.	Documents that all study materials have been submitted and approved by the IRB of record prior to being used in the study.	X	X
IRB composition/roster		X	X

Type of document	Purpose	Location of Document: ISF (At the investigator site)	Location of Document: TMF (With the sponsor)
Regulatory authority(ies) approval (Ex: FDA) (if applicable)	If the study has been submitted to the regulatory authority such as the FDA, a copy of the FDA submissions and the associated FDA correspondence (safe to proceed letter, requests for information).		X
MLs of all investigators	Documents the qualifications and eligibility to conduct the trial and/or provide medical supervision of subjects.	X	X
Training certificates of all staff on study	Ex: GCP, HSP, dangerous goods (IATA)	X	X
Normal lab ranges	Documents normal ranges of labs used for this study. The sponsor must have a record of all the normal ranges for each participating site.	X	X
Lab accreditations (ex: CAP/CLIA)	Documents lab credentials/accreditations of the lab(s) used for this study. The sponsor must have a record of all lab credentials/accreditations of the lab(s) used for each participating site.	X	X
Sample of label attached to investigational product(s) (IP)	Documents compliance with applicable labeling regulations and instructions provided to participants.		X
IP manual	Documents instructions needed to ensure proper storage, packaging, dispensing and disposition of IP if not included in protocol or IB.	X	X

Type of document	Purpose	Location of Document: ISF (At the investigator site)	Location of Document: TMF (With the sponsor)
Shipping records for IP	Documents shipment dates, batch numbers, method of shipment.	X	X
Certificate(s) of analysis of IP shipped	Documents identity, purity and strength of IP used.		X
Decoding procedures for blinded trials	Documents how in case of an emergency, identity of blinded IP can be revealed without breaking the blind for the remaining participants.	X	X
Monitoring reports	Documents the monitoring of the study conduct. This will occur multiple times throughout the course of the study.	X	X
Study communications	Communication between sponsor and site.	X	X
Signed ICFs	Documents that the ICF is obtained in accordance with GCP and the protocol and is dated prior to the participation of each participant.	X	
Source documents	Documents the existence of the participant and acts as the source of truth for where the study data was collected from.	X	
Signed, dated and completed CRFs	Documents that the investigator confirms that the data entered in the CRFs is accurate and complete.	X (copy)	X (original)

Type of document	Purpose	Location of Document: ISF (At the investigator site)	Location of Document: TMF (With the sponsor)
Documentation of CRF corrections	Documents all changes/additions or corrections made to CRFs after the initial data was recorded.	X (copy)	X (original)
Notification by investigator to sponsor of SAEs	This could include an email or other reporting method that follows the protocol.	X	X
Notification by sponsor and/or investigator to regulatory authority and IRB of unexpected SAEs	This could include a combination of submission documents and responses.	X	X
Notification by sponsor to investigators of safety information		X	X
Screening log	Documentation of the ID of potential participants who are screened	X	
Enrollment log	Documents the chronological enrollment of participants by participant ID.	X	
IP accountability at site		X	X
Signature sheet (if applicable)	Documents signatures and initials of all people on study	X	X
Record of retained body fluids/tissue samples (if applicable)	Documents location and ID of retained samples	X	X
Documentation of IP destruction (follow institutional policy as applicable)		X	X
Clinical study report	Documents results and interpretation of trials		X

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Document History

Version	Version Date	Brief Description of Change
1.0	12/11/2023	Initial