Standard Operating Procedure for:			
Study Specific Essential File Documentation			
SOP Number:	**45**	Version Number:	**5.0**
Effective Date:	**24th March 2025**	Review Date:	**24th March 2028**

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Purpose and Scope :

This Standard Operating Procedure (SOP) describes the process for maintaining essential documentation throughout the life of a clinical research study, as required under Good Clinical Practice (GCP). The purpose is to ensure that all essential documentation is maintained to allow accurate and robust reconstruction of the study and ensure verification of the data quality.

This SOP applies to and is mandatory for all clinical research being sponsored by Barts Health NHS Trust (Barts Health) and Queen Mary, University of London (Queen Mary). For sponsored studies of Clinical Investigations and other MHRA-regulated Medical Devices, please see *SOP 9* for guidance

Abbreviations:

Barts Health	Barts Health NHS Trust
CI	Chief Investigator
CRF	Case Report Form
CTA	Clinical Trials Agreement
GCP	Good Clinical Practice
IMP	Investigational Medicinal Product
ISF	Investigator Site File
JRMO	Joint Research Management Office
Queen Mary	Queen Mary University of London
PI	Principal Investigator
PID	Participant Identifiable Data
PSF	Pharmacy Site File
SOP	Standard Operating Procedure
TMF	Trial Master File

SOP Text:		
	Responsibility	**Activity**
1.	Chief Investigator (CI)	**Ensure essential documentation is maintained for every study from set up to archiving** It is the responsibility of the CI to ensure that all essential documentation is retained, maintained, and updated as needed at all locations and central facilities. Every study must have a separate and clearly identifiable Trial Master File (TMF) and each location must have an Investigator Site File (ISF) for each study. In single-centre studies however where a single team is responsible for both study management and delivery the TMF and ISF may be combined in a single file. This must be approved by the Joint Research Management Office (JRMO). For guidance on eTMF's please see *JRMO position and guidance on eTMF*.
2.	CI	**Ensure that the TMF is set up and maintained according to the contents page associated with this SOP.** The TMF must be set up prior to confirmation of sponsorship, (see *SOP 11a Barts Health-Queen Mary sponsorship of MHRA-regulated studies: Process for researchers*, *SOP 12a Barts Health-Queen Mary Sponsorship interventional studies (Researchers)* and *SOP 13a Barts Health-Queen Mary Sponsorship of research studies (Researchers)*). The TMF must be set up according to: • *Associated document 1 Trial Master File Checklist Template for MHRA regulated studies (Single Site) template* • *Associated Document 2 Trial Master File Checklist Template for MHRA regulated studies (Multi Site) template* • *Associated Document 3 Trial Master File Checklist for Interventional and Research Studies (single site) template* • *Associated Document 4 Trial Master File Checklist for Interventional and Research Studies (Multi site) template* Not all documents *(Templates 1 to 10)* will be relevant to every study – the CI may agree the exact contents of the TMF with the GCP and Governance team during the set up process.
3.	CI (Sponsored studies)/Principal Investigator (PI) (Hosted Studies)	**Source Data Agreement** *Associated Document 5 Source Data Agreement* to be completed to describe the key source data/source documents that will be recorded over the conduct of the study, highlighting if paper or electronic, which electronic systems are being used (where applicable) and the storage location.
4.	CI or delegate	**Ensure that all locations receive and maintain an ISF, including pharmacy and laboratory file(s) where applicable, in accordance with the content's pages associated with this SOP.** Each location should be given an ISF, set up as per the ISF contents page, (*Associated document 5 ISF Checklist Template for MHRA Regulated Studies* and *Associated document 6 ISF Checklist Template for Interventional and Research Studies*) or be sent a copy of the contents page to set up their own file. Each location pharmacy should be given a Pharmacy Site File (PSF), set

		up as per the pharmacy file contents page (*Associated document 7 PSF Checklist Template)*, or be sent a copy of the contents page to set up their own file. Locations must not be activated until their ISF (and PSF/Laboratory Site File where applicable) are in place. Multi-location studies must have a TMF held centrally and location file at each location, pharmacy, laboratory, and central facility. The coordinating team/CI is responsible for ensuring all central facilities are appropriately set up with all essential documentation, logs, and manuals before activation (See *SOP 46 Site selection, site initiation and site activation*).
5.	Governance team member and JRMO Clinical Trial Monitor as applicable	**Maintain sponsor oversight file.** Refer to *SOP 27 Internal Filing Process*.
6.	CI	**Ensure staff are appropriately trained.** Ensure that all staff within the study co-ordination team are logged on Co-ordination Delegation Log and their training is logged on study specific training log. Ensure all locations maintain appropriate delegation and training logs. For further information please see *SOP 34a Researcher Training*.
7.	CI	**Give special consideration to study correspondence, the Investigational Medicinal Product (IMP) sections of the TMF, wet signatures, Participant Identifiable Data (PID), file notes, data, duplication, blinded studies, version control and storage.** **Correspondence** The conduct of clinical research studies generates large amounts of correspondence, such as emails, letters, meeting minutes and telephone call reports. All relevant correspondence that is necessary for the reconstruction of key activities and decisions must be retained. The JRMO GCP and Governance team can provide advice on the correspondence that should be retained. It is recommended by the Medicines and Healthcare products Regulatory Agency (MHRA) that correspondence is effectively organised; for example, by topic area and dates or in relevant sections. **Final documents with wet/e-signatures** Original wet/e signature documents should be filed in the most appropriate location for the document type, for example, the signed Clinical Trial Agreement (CTA) should be located in the sponsor study file, whilst copies should be kept in the TMF and ISF, while the wet/e signature of the PI on the protocol signature page should be in the ISF. Contact the JRMO GCP & Governance Managers if unsure.

PID
Unless specified in the approved protocol and Research Ethics Committee application, PID must only be stored at the study location, for example in the ISF of Pharmacy file. All other files (TMF, sponsor file, and other central facility files) must not contain any PID.

Use of file notes
The use of file notes must not be considered best practice and only used when other documentation cannot evidence the necessary process.

The JRMO file note template is recommended for use and should be distributed to locations and facilities. The TMF should be a stand-alone document set that requires no additional explanation from CI or research team members.

The CI and teams should carefully consider the need for every file note. They are not to be used as an excuse for missing documents or used when other correspondence fully explains an event or occurrence.

Data
Case Report Forms (CRFs) may be stored separately from the ISFs and TMF, but the ISF/TMF must define their location. At the end of the study, the original paper copies of the CRFs must be kept at the study location.

Where electronic CRFs are used, each location must be given a complete copy of their electronic CRFs at the end of the study.

Duplication
Duplication of documents within the TMF is to be avoided as this can hinder effective use of the TMF. Where possible, file only one copy of the document in the appropriate file. For example, where annual reports are submitted to numerous parties, one copy should be filed in the TMF with the cover letters to each party.

Blinded studies
Special attention should be given to studies involving any form of blinding. Delegation logs should clearly document who is blinded and unblinded. In some cases, a separate unblinded section of the TMF may need to be established.

Version control
The CI is responsible for ensuring strict version control of all essential documents and ensuring that all locations receive up to date versions. A version control log must be kept and maintained for all essential documents submitted for regulatory approval. It is recommended that the document version control logs are used. Any other version control logs used must be approved prior to or during the MHRA regulated study final meeting or prior to confirmation of sponsorship for other studies

It is recommended that documents are filed in a sequential order, with the most recent version of the document filed on top. N.B. All modifications need to be approved by the sponsor before sending to the regulators for approval and before implementation (see *SOPs 17a Amendments for sponsored studies (including halting studies) - Process for JRMO*, *17b Amendments for hosted studies*, and *17c Amendments for sponsored studies (including halting studies) - Process for researchers regarding amendments*).

Superseded documents

		When documents are superseded, one complete copy of the old document must be retained in the TMF and ISF and must be clearly marked as superseded to avoid confusion. This ensures that there is a comprehensive catalogue in each location, and evidence that the location received each up to date version. Where possible the superseded document should be marked with the date and initialled by the person maintaining the documents, along with the document version number of the document superseding it. The version control log must be updated accordingly by the person responsible for maintaining the documents. **Storage** All study files must be stored in a safe, secure and confidential location that is accessible only by authorised staff (including monitors, auditors and inspectors). As some of the documents within the files will contain confidential data, it is important that they are retained in a secure place with restricted access to the relevant trial staff only.
8.	CI	**Documents must be filed in a timely manner.** TMFs must be kept up to date in order to comply with the UK regulations. Documentation that is relied upon for subsequent activities should be filed within the TMF before these activities take place, for example emails documenting safety analysis prior to next cohort being started.
9.	CI	**Archive documents at the end of the study.** Once the clinical study report has been submitted and acknowledged (for end of trial procedures, the TMF and ISF can be archived (see *SOP 18a Study closure sponsored regulated studies*, *SOP 18b Study closure for sponsored interventional and research studies and all hosted studies* and *SOP 20 Archiving)*.

Change control

This section outlines changes from version **4.0** to version **5.0**

Section changed	Summary and description of changes
All	General administrative changes
Associated Documents	Additional guidance to file content
Guidance Document	Reference to JRMO positioned and guidance eTMF

List of appendices

There are no appendices for this SOP.

List of associated documents and templates

Document ref.	Document name
Associated Document 1	Trial Master File Checklist Template for MHRA regulated studies (Single Site) template
Associated Document 2	Trial Master File Checklist Template for MHRA regulated studies (Multi Site) template
Associated Document 3	Trial Master File Checklist for Interventional and Research Studies (single site) template
Associated Document 4	Trial Master File Checklist for Interventional and Research Studies (Multi site) template
Associated Document 5	ISF Checklist Template MHRA regulated studies
Associated Document 6	ISF Checklist Template Interventional and Research Studies
Associated Document 7	Pharmacy SF Checklist Template
Associated Document 8	Source Data Agreement
Guidance Document	JRMO position and guidance eTMF
Template 1	Enrolment log
Template 2	Location delegation log
Template 3	Coordinating team delegation log
Template 4	Protocol version control log
Template 5	PIS, ICF and GP letter version control log
Template 6	Modification log
Template 7	File note template
Template 8	File note log
Template 9	Deviation log
Template 10	Trial specific training log