Joint Research Management Office Standard Operating Procedure for:			
Study Specific Essential File Documentation			
SOP Number:	**45**	Version Number:	**4.0**
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Purpose:

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.

Regulation 31A (4) of SI 2004/1031 defines essential documents as:
"*The essential documents relating to a clinical trial are those which (a) enable both the conduct of the clinical trial and the quality of the data produced to be evaluated; and (b) show whether the trial is or has been conducted in accordance with the applicable requirements of the Directive*".

Scope:

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).

This SOP must be followed for all new sponsored studies set up after the effective date of this SOP. All studies active at the time of the SOP release should review their study files to ensure that all requested documentation is present. There is no requirement to migrate existing files to this format.

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
MHRA	Medicines and Healthcare products Regulatory Agency
Queen Mary	Queen Mary University of London
QP	Qualified Person (specially qualified pharmacist)
PI	Principal Investigator
PID	Participant Identifiable Data
PSF	Pharmacy Site File
REC	Research Ethics Committee
SOP	Standard Operating Procedure
TMF	Trial Master File
TSE	Transmissible Spongiform Encephalopathy

Relevant SOPs:

- SOP 11a Barts Health/Queen Mary sponsorship of MHRA-regulated studies: Process for researchers
- SOP 12a Barts Health/Queen Mary sponsorship of Sponsorship interventional studies (Researchers)
- SOP 13a Barts Health/Queen Mary sponsorship of Sponsorship research studies (Researchers)
- SOP 17a Amendments for sponsored studies (including halting studies) - Process for JRMO,
- SOP 17b Amendments for hosted studies
- SOP 17c Amendments for sponsored studies (including halting studies) - Process for researchers regarding amendments
- SOP 18a Study closure for MHRA-regulated studies
- SOP 18b Study closure for Interventional, Research and Hosted studies.
- SOP 20 Archiving
- SOP 46 Site selection, site initiation and site activation).

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 sites and central facilities. Every study must have a separate and clearly identifiable Trial Master File (TMF) and each site must have an Investigator Site File (ISF) for each study.
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. Certain documents such as the protocol and enrolment log are always required.
3.	CI (Sponsored studies)/ Principal Investigator (PI)(Hosted Studies)	**Source Data Agreement** *Associated document 5 Source Data Agreement* is 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	**Ensure that all sites 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 site should be given an ISF, set up as per the ISF contents page, (*Associated document 6 ISF Checklist Template for MHRA Regulated Studies* and *Associated document 7 ISF Checklist Template for Interventional and Research Studies*) or be sent a copy of the contents page to set up their own file. Each site pharmacy should be given a Pharmacy Site File (PSF), set up as per the pharmacy file contents page (*Associated document 8 PSF Checklist Template*), or be sent a copy of the contents page to set up their own file. Sites must not be activated until their ISF (and PSF where applicable) are in place.

		In single-centre studies 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). Multi-site studies must have a TMF held centrally and ISF at each site, pharmacy, laboratory, and central facility.
5.	CI	**Ensure all central facilities receive and maintain a TMF** Each central facility should be given a TMF file or provided with a copy of a contents page to set up their own file. 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).
6.	Governance team member and JRMO Clinical Trial Monitor as applicable	**Maintain sponsor oversight file** Refer to SOP 27 Internal Filing Process
7.	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 sites maintain appropriate delegation and training logs.
8.	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 (GCP Guide Ch. 10.3.2). 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. **IMP sections** The IMP section of the TMF must be reviewed by the Senior Trial Pharmacist who gives final Pharmacy approval on behalf of the sponsor, prior to confirmation of sponsorship being given. This will ensure that content page sections such as Qualified Person (QP) release, instructions for handling the IMP, sample labels for IMP, shipping record(s) for IMP, Certificate(s) of Analysis of IMP(s) shipped, IMP accountability at site, IMP(s) destruction records, Transmissible Spongiform Encephalopathy (TSE) certifications and

		temperature control logs (where applicable) are clearly marked as needed or not applicable. **Final documents with wet signatures** Original wet signature documents should be filed in the most appropriate location for the document type, for example, the wet signature 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 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 (REC) application, PID must only be stored at site, 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 JRMO file note template is recommended for use and should be distributed to sites 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 (CRF) 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 site and copies can be added to the TMF. Where electronic CRFs are used, each site 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 (MHRA GCP guide CH 10.10.3.3) 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 sites 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 amendments 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 site 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. It is considered best practice to store documents within a locked cupboard within a locked room. Consideration should be made to the location (e.g., protected from potential dampness and leaks).
9.	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.
10.	CI	**Archive documents at the end of the study** Once the clinical trial report has been submitted and acknowledged (for end of trial procedures see SOP 18a Study Closure for regulated studies and SOP 18b Study Closure for Interventional, Research and Hosted Studies) the TMF and ISF can be archived (see SOP 20 Archiving).

Change control

This section outlines changes from version **3.0** to version **4.0**

Section changed	Summary and description of changes
All	Essential documentation including TMF is now mandatory for all clinical research being sponsored by Barts Health and Queen Mary
All	Minor grammar, spelling and formatting corrections.
Associated Documents	Update to all associated documents
Templates	Update to all templates.

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	Source Data Agreement
Associated Document 6	ISF Checklist Template MHRA regulated studies
Associated Document 7	ISF Checklist Template Interventional and Research Studies
Associated Document 8	Pharmacy Site File Checklist Template
Template 1	Enrolment log
Template 2	Site delegation log
Template 3	Coordinating team delegation log
Template 4	Document version control log
Template 5	PIS, ICF and GP letter version control log
Template 6	Amendment log
Template 7	File note template
Template 8	File note log
Template 9	Deviation log
Template 10	Study specific training log