Royal Papworth Hospital
NHS Foundation Trust

Document Title: Trial Master File Creation and Maintenance

Document Number: PTUC SOP013

Staff involved in development: *Job titles only*	Senior R&D Manager, R&D Operational Manager, Clinical Project Managers
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For use by:	NHS Staff Trust-Wide
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Summary of Amendments

Version:	Modification:
Version 7.0	Updated to bring in line with updated eTMF process

Key Points of this Document

- This document sets out the procedures to be followed by all staff who are involved in the preparation, maintenance and archiving of paper and electronic Trial Master Files (i.e., Sponsor and Site Files) for research projects managed by Royal Papworth Trials Unit

Collaboration (PTUC), sponsored by Royal Papworth NHS Foundation Trust or hosted by Royal Papworth NHS Foundation Trust.

- It provides guidance on how the Sponsor and Site Files should be compiled and how these files should be stored to ensure compliance with the Trust's policies.

1 Purpose and Contents

a. A Trial Master File consists of essential documents to enable the efficient management, conduct, audit and inspection of a clinical trial. The Trial Master File is normally composed of a Sponsor File, held by the Sponsor organisation and Site File/s held by each Investigator site. These files together are regarded as comprising the entire TMF.

b. This document defines the procedures for the preparation, maintenance and storage of the Trial Master File (i.e. Sponsor and Site Files) for research projects managed by Royal Papworth Trials Unit Collaboration (PTUC), sponsored by Royal Papworth NHS Foundation Trust or hosted by Royal Papworth NHS Foundation Trust. This includes the timing of the compilation of the Trial Master File, who is responsible for its preparation and maintenance and storage.

c. This document details the requirements for the content of the Trial Master File as described in Good Clinical Practice (GCP: 'a standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected').

d. The subsequent archiving of research study Trial Master Files is outside the scope of this SOP and is described in SOP011: Archiving of Research Studies.

2 Roles & Responsibilities

a. This Policy applies to all personnel that are conducting research at the Trust.

b. The Sponsor is responsible for the set-up and updating of the Sponsor File although these tasks may be delegated to a member of the study team.

c. The Principal Investigator at each Investigator site is responsible for the set-up of a Site File although this task may be delegated to a member of the study team. This should be documented on the study delegation log.

d. It is the responsibility of all research personnel to read and follow the procedures prior to any research study commencing within the Trust. All research personnel should be aware of the requirements for the Sponsor File and Site File contents, maintenance and storage.

3 Policy

a. This SOP is mandatory and, as per the Trust's Information Governance and Records Management framework, non-compliance with may result in disciplinary procedures.

4 Procedure

4.1 Trial Master File (TMF)

a. Per GCP, a TMF is required to allow the conduct of a clinical trial to be reconstructed.

b. The Chief Investigator has overall responsibility for the maintenance of the TMF although this may be delegated. The TMF should be maintained in a timely manner and available for inspection at all times.

c. The TMF must be set-up for the start of the study prior to the recruitment of the first patient. The Chief Investigator, or a designated member of the study team, will take responsibility for setting up the file (i.e., Sponsor and Site Files) and responsibilities will be identified on FRM042: Project Management Delegation Log.

d. The TMF will be identified by the R&D code (P0XXXX) and a brief study title.

e. If the study is managed by PTUC or sponsored by Royal Papworth NHS Foundation Trust and is a non-CTIMP study, the TMF should be set-up as an electronic TMF (eTMF) (i.e., Sponsor File and Site File). Sponsor and Site Files cannot be merged; they must be maintained as separate files.

f. If the study is externally sponsored, the TMF (i.e., Site File only if externally sponsored), should ideally be set-up as an electronic TMF (eTMF). The use of an electronic Site File should be negotiated and agreed with the Sponsor at the feasibility stage.

g. If the study is a CTIMP, the TMF should be set-up as a paper TMF (pTMF) with all essential documents maintained as paper file/s (i.e., Sponsor and/or Site File).

h. Prior to the study getting the Sponsor Green Light to start recruitment, the Sponsor and Site File must undergo a Quality Assurance check to ensure completeness. See PTUC SOP009: Project Management of Royal Papworth Sponsored Studies and SOP015: Site Recruitment and Initiation for further details of the Sponsor Green Light procedure.

4.1.2 Sponsor File

a. The master Sponsor File Index (FRM021) should be used as a template to prepare the Sponsor File. The study team should agree which sections of the index are applicable to the study and amend the master index accordingly. The CPM/RN/CTC or CRA (as appropriate) should then approve the agreed index and file it in the Sponsor File for reference.

b. Where the Sponsor File is electronic, the electronic folder structure should be updated in line with the agreed Sponsor File Index for the study.

c. Where the Sponsor File is paper and consists of more than one volume, the contents of all volumes should be listed in Volume 1 and the files should be labelled File X of Y (e.g. File 1 of 2).

4.1.3 Site File

a. If the study is externally sponsored, the Sponsor may provide a Site File. If this is not the case a Site File should be prepared in accordance with the instructions below.

b. If the study is managed by PTUC or sponsored by Royal Papworth NHS Foundation Trust, the Trial Manager (or their delegated representative) will work with each Principal Investigator to ensure a Site File is set-up at each of the participating centres. Sites will be provided with the master Site File Index (FRM068). As the Principal Investigator at each Investigator site is responsible for the Site File, they may request to use their local Site File index and this will be assessed on a case-by-case basis.

c. The master Site File Index (FRM068) should be used as a template to prepare the Site File. The study team should agree which sections of the index are applicable to the study and amend the master index accordingly. The CPM/RN/CTC or CRA (as appropriate) should then approve the agreed Site File index and file it in the Site File for reference.

d. Where the Site File is electronic, the electronic folder structure should be updated in line with the agreed Site File Index for the study.

e. Where the Site File is paper and consists of more than one volume, the contents of all volumes should be listed in Volume 1 and the files should be labelled File X of Y (e.g. File 1 of 2).

4.2 Maintenance of Sponsor and Site Files

a. Documents should be filed as they are generated, according to the stage of the study.

b. Documents should be original where possible. Where the Sponsor and/or Site File is electronic, original documents that are paper (e.g., wet ink signed contracts), that need to be made electronic should be scanned using the departmental eTMF scanner (see GD019: Trial Master File and electronic Trial Master File Guidance Document).

c. The Sponsor and Site Files should be regularly reviewed for completeness. These quality control checks (TMF QC), should be documented on FRM021 and/or FRM068 to show who performed the TMF review and the date.

d. All correspondence relating to the conduct of the study should be filed in the file (i.e., Sponsor or Site File) and the section to which it pertains in chronological order.

e. Any documentation missing from the Sponsor or Site Files should be addressed by the inclusion of a file-note as described in SOP041: File Notes.

f. If any documents are filed separately from the Sponsor or Site File then a comment should be added to the Sponsor/Site File Index to signpost to this. For a study with a pTMF, a file note should be added to the relevant section of the Sponsor or Site File (as applicable) detailing where the document is stored.

g. Amendments should be maintained chronologically with superseded versions retained by filling in the relevant 'Superseded' section of the Sponsor or Site File (as applicable). Paper documents need to be scored through and marked as superseded.

4.3 Location and Access of Sponsor / Site File

a. Paper Sponsor Files should be held by the Trial Manager and located in a secure place with restricted access. The location should have environmental controls with adequate protection from physical damage.

b. Paper Site Files should be held by the Research Team and located in a secure place with restricted access. The location should have environmental controls with adequate protection from physical damage.

c. Electronic Sponsor and/or Site Files should be held on the secure R&D N:drive, which has restricted access.

d. Any or all of the documents in the Sponsor or Site Files may be subject to, and therefore should be available for, audit by an independent auditor and inspection by the regulatory authorities. Auditors and Inspectors should be given direct access to the paper or electronic files.

e. The TMF (Sponsor or Site File) should be made available for internal monitoring purposes, external monitors should only be provided with a copy of the eTMF. The guidelines for

this are covered in SOP085 Monitoring Research studies – External monitors and remote monitoring.

4.4 Archiving

a. At the end of the study all Sponsor and Site files should be prepared and submitted for archiving to PTUC / R&D.

b. The archived Sponsor and Site Files will continue to be available for audit / inspection by independent auditors or regulatory authorities in line with SOP011: Archiving of Research Studies.

5 Risk Management / Liability / Monitoring & Audit

a. The R&D SOP Committee will ensure that this SOP and any future changes to this document are adequately disseminated.

b. The R&D Department will monitor adherence to this SOP via the routine audit and monitoring of individual clinical trials and the Trust's auditors will monitor this SOP as part of their audit of Research Governance. From time to time, the SOP may also be inspected by external regulatory agencies (e.g. Care Quality Commission, Medicines and Healthcare Regulatory Agency).

c. In exceptional circumstances it might be necessary to deviate from this SOP for which written approval of the Senior R&D Manager should be gained before any action is taken. SOP deviations should be recorded including details of alternative procedures followed and filed in the Sponsor and/or Site File.

d. The Research and Development Directorate is responsible for the ratification of this procedure.

Further Document Information

Approved by: *Management/Clinical Directorate Group*	Research and Development Directorate
Approval date: *(this version)*	Current active version approval date
Ratified by Board of Directors/ Committee of the Board of Directors:	STET
Date:	N/A
This document supports: *Standards and legislation*	Medicines for Human Use (Clinical Trials) Regulations 2004 and all associated amendments. UK Policy Framework for Health and Social Care Research (2018)
Key related documents:	Trust Research Policy

Equality Impact Assessment: Does this document impact on any of the following groups? If YES, state positive or negative, complete Equality Impact Assessment Form available in Disability Equality Scheme document DN192 and attach.

Groups	Disability	Race	Gender	Age	Sexual orientation	Religious & belief	Other
Yes/No	NO	NO	NO	NO	NO	NO	NO
Positive/Negative							

Review date:	November 2023

I certify the contents of this SOP has been reviewed and ratified

..... 3rd December 2020

Signed by Dr Ian Smith, Clinical Director of R&D — Date

Release Date: 16th December 2020