

Document Title: Trial Master File Creation and Maintenance

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Summary of Amendments

Version:	Modification:
Version 7.0	Updated to bring in line with updated eTMF process
Version 8.0	Addition of references to GD019 and TPL054

Key related documents:	<p>Trust Research Policy</p> <p>SOP011: Archiving of Research Studies</p> <p>SOP009: Project Management of Royal Papworth Sponsored Studies</p> <p>SOP015: Site Recruitment and Initiation</p> <p>SOP041: File Notes</p> <p>SOP085 Monitoring Research studies – External monitors and remote monitoring</p> <p>GD019 TMF and eTMF Process</p> <p>FRM042: Project Management Delegation Log</p> <p>FRM021 Sponsor Green Light Index</p>
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	FRM068 Site File Index TPL054 eTMF External Sponsor Letter – Observational / non CTIMP studies only
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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 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 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, maintenance and storage.
- c. 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, maintenance and archiving 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. The TMF is a collection of essential documents that tell the story of your study, documented proof that it was conducted well and allow the conduct of the 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 (POXXXX/ CRFXXXX) and a brief study title.
- e. If the study is a CTIMP which is managed by PTUC or sponsored by Royal Papworth NHS Foundation Trust, the TMF must be set-up as a paper TMF (pTMF) with all essential documents maintained as paper file/s (i.e., Sponsor and/or Site File).
- f. 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).
- g. For single centre studies managed by PTUC or sponsored by Royal Papworth NHS Foundation Trust the Sponsor and Site Files can be merged.

- h. 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 External Sponsor Letter (TPL054) should be sent to the external Sponsor at the feasibility stage to request using an eTMF.
- i. Prior to the study getting the Sponsor Green Light to start recruitment, the Sponsor and Site File must undergo thorough checking to ensure completeness. This is performed by one of the research team and is documented on the Sponsor/Site File Index (See GD019 for how to complete and sign off the TMF Index check). Refer to 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. Refer to GD019 for further guidance on tailoring the Sponsor File Index. The Chief Investigator (or their delegated representative) 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. For single centre studies managed by PTUC or sponsored by Royal Papworth NHS Foundation Trust the Sponsor and Site Files can be merged.
- c. For multi-centre studies 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.

- d. 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. Refer to GD019 for further guidance on tailoring the Site File Index. Chief Investigator or delegate (as appropriate) should then approve the agreed Site File index and file it in the Site File for reference.
- e. Where the Site File is electronic, the electronic folder structure should be updated in line with the agreed Site File Index for the study.
- f. 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. GD019: Trial Master File and electronic Trial Master File Guidance Document should be referred to for detailed step-by-step guidance.
- b. Documents should be filed as they are generated, according to the stage of the study, in reverse chronological order (i.e. newest on top).
- c. 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.
- d. The Sponsor and Site Files should be reviewed for completeness at least three times during the life of the research project. These quality control checks (TMF Index Checks), should be documented on FRM021 and/or FRM068 to show who performed the review and the date.
- e. 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).
- f. 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.
- g. 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.
- h. Amendments should be maintained with superseded study document 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 then signed and dated by staff member before being filed in superseded section.

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 must 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: <i>Management/Clinical Group</i>	<i>Directorate</i>	Research and Development Directorate					
Approval date: <i>(this version)</i>	Current active version approval date						
Ratified by Board of Directors/ Committee of the Board of Directors:	STET						
Date:	N/A						
This document supports: <i>Standards and legislation</i>	Medicines for Human Use (Clinical Trials) Regulations 2004 and all associated amendments. UK Policy Framework for Health and Social Care Research (2023)						
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							
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