

## SOP-QA-7 V4

**Title: Trial Master File (TMF)**

**Effective Date: 9-8-23**

**Review Date: 9-8-26**

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### Document History

Version	Description of update	Date Effective
3	Change to Scope at 1.2 Research Governance Manager changed to RGT at 3.3 Abbreviations added at 4	1-8-20
4	Clarification on SOP relevance at 1.1 Reference to single site studies at Sponsor location at 1.5	9-8-23

### 1. Scope

- 1.1 This SOP applies to all researchers, Sponsor staff, Clinical Trial Pharmacy staff and laboratory staff involved in projects sponsored, or co-sponsored, by the University of Aberdeen (UoA) and/or NHS Grampian (NHSG). This procedure does not apply to commercially sponsored research or research sponsored by an external non-commercial organisation (in such cases the external Sponsor shall provide guidance).
- 1.2  For Clinical Trials of Investigational Medicinal Products (CTIMPs) and Medical Device Clinical Investigations (MDCIs), a Trial Master File (TMF), which contains all the essential documents relating to the clinical trial, must be established and maintained. The requirement is set down in both EU and UK legislation (2001/20/EC Article 15(5) and SI 2004/1031 [as amended] 31A).
- 1.3 The TMF forms the basis for an inspection to confirm compliance with regulatory requirements (Directive 2005/28/EC Chapter 4, Article 16). The TMF is normally composed of a **Sponsor TMF**, held by the sponsor organisation (or to whom this function is delegated), and a **Study TMF**, held by the Chief investigator or delegate.
- 1.4  In addition, there may also be a **Pharmacy file** (held by the Clinical Trial Pharmacy), **R&D file** (held by R&D), **Laboratory file** (in a laboratory providing analysis) and **Investigator Site file(s)**. These files together are regarded as comprising the entire TMF for the trial.
- 1.5  For single site studies where the sponsor and site are co-located a specific investigator site file should not usually be constructed because it is the expectation that the TMF also contains all of the documents that would usually be found in the ISF.
- 1.6 A record of the location of essential documents must be maintained by the Sponsor or Investigator (eg TMP-QA-3 – Trial Master File Index (CTIMP and High Risk), TMP-QA-32 – Sponsor File Index or TMP-QA-50 - ISF Index (non-CTIMP)).

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**Key to symbols**  = Important point to note  = Warning


## 2. Responsibilities

Chief Investigator (CI)	Setting up of Study TMF (CI may delegate this task; see 3.3)
Research Governance Team	Setting up of Sponsor TMF
Clinical Trial Pharmacist (CTP)	Setting up of Pharmacy file
R&D	Setting up of R&D file
Research Monitor	Monitoring of all components of TMF


## 3. Procedure

- 3.1 The study TMF, Sponsor TMF and pharmacy file shall be set up using a TMF index (eg TMP-QA-3) to create a file index. If a document is not considered applicable then this should be documented in the TMF index. Some TMFs may be totally, or partly electronic in format, and for these, the exact locations of documents shall be clearly stated on the TMF index, which itself may be filed electronically. For hard copy TMFs, the TMF index must be kept in the front of all files.
- 3.2 The CI, or delegate, shall establish the study TMF at the beginning of the trial and prior to patient recruitment. Delegated responsibilities must be clearly documented in a delegation log (TMP-QA-13). The Research Governance Team (RGT) and CTP, or delegate(s), shall also set up their respective files prior to patient recruitment.
- 3.4 For hard-copy TMFs, the CI, or delegate, shall keep the study TMF secure in a lockable cabinet or room with restricted access. The RGT shall keep the Sponsor file. The pharmacy file and laboratory file shall be kept securely in pharmacy or the laboratory, as appropriate. The TMF index shall clearly document the location of all documents which are retained at different locations. Electronic TMFs (study, Sponsor, pharmacy etc) shall be held on a secure network drive.

### Maintaining a TMF

- 3.5 The CI, Research Governance Manager (RGM) and CTP, or delegate(s), are responsible for updating the study TMF, Sponsor, laboratory and pharmacy files, as appropriate, with any relevant and applicable documents as the study progresses, in accordance with the TMF index. If a document is not located in the TMF, a note to file shall be completed to detail the location and/or reason for this.
- 3.6  All filing must be done in a timely manner. Documents must be filed chronologically.
- 3.7 Correspondence which is necessary to construct key activities and decisions must be retained. Key email correspondence must be saved and filed individually and not as conversations.
- 3.8 Version control must be applied to all trial documents and shall use whole numbers only (see SOP-QA-1 - Management of SOPs). Outdated documents must be retained and identified as superseded. New versions of the protocol shall be signed and dated prior to use.
- 3.9 All copies of essential correspondence with the Research Ethics Committee (REC) and for CTIMPs and MDCIs, with the Medicines and Healthcare products Regulatory Agency (MHRA), shall be forwarded to the Sponsor by the CI, or delegate, and filed in both the study TMF and the Sponsor file.

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- 3.10 All approved amendments shall be forwarded to Sponsor, pharmacy and laboratory (as appropriate) by the CI, or delegate.
- 3.11 The study TMF, Sponsor file, and any additional files (eg R&D, Pharmacy, Laboratory) associated with the trial must be made available to the Sponsor, Trial Monitors and representatives of the MHRA, upon request.

#### Archiving a TMF

- 3.12 Once the trial has finished, the Sponsor, or delegate, is responsible for reviewing the complete TMF to ensure that all the required documents (including file notes) are present. Closed minutes of the Data Monitoring Committee (DMC), where applicable, shall be added prior to archiving. Following dissemination of the trial results, the TMF must be archived in accordance with SOP-QA-32 – Archiving.

#### 4. Abbreviations and definitions

CI	Chief Investigator
CTIMP	Clinical Trial of an Investigational Medicinal Product
CTP	Clinical Trial Pharmacist
DMC	Data Monitoring Committee
ISF	Investigator Site File
MDCI	Medical Device Clinical Investigation
MHRA	Medicines and Healthcare products Regulatory Agency
R&D	Research and Development (NHSG)
REC	Research Ethics Committee
RGM	Research Governance Manager
RGT	Research Governance Team
TMF	Trial Master File

#### 5. Related documentation and references

SOP-QA-1	Management of SOPs
SOP-QA-8	Investigator Site File
SOP-QA-27	Good documentation practice
SOP-QA-31	Research project closure
SOP-QA-32	Archiving
TMP-QA-3	Trial Master File Index (CTIMP and High Risk)
TMP-QA-13	Site delegation log
TMP-QA-32	Sponsor File Index
TMP-QA-50	ISF Index (non-CTIMP)

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