| SOP number | **51.016** | Version | **5.0** |
|---|---|---|---|
| Title | **Preparation and maintenance of a Trial Master File** | | |

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| Prepared by<br>Signature | Pamela Sandu<br>Date |
| Approved by<br>Signature | Melissa Robert<br>Date |
| Released by<br>Signature | Julie Brittenden<br>Date |

| SOP category | NHS GG&C Sponsor R&I |
|---|---|
| Staff category | |

| Staff Category | R | A | C | I |
|---|---|---|---|---|
| Research & Development Systems Manager | | X | | |
| Research Governance | X | | | |
| Sponsor Research Co-ordinator | X | | | |
| Senior Research Administrators | X | | | |
| R&I Sponsor Pharmacy | X | | | |
| Project Management | X | | | |
| Contract Manager | X | | | |
| Industry Collaboration Project Manager | X | | | |
| University of Glasgow Head of Research Regulation and Compliance | | | X | |
| Data Management | | | | X |
| Chief Investigator | | | | X |
| Laboratories (Involved in Primary and Secondary End Points) | | | | X |

## 1. Scope

This procedure applies to Clinical Trial Investigational Medicinal Products (CTIMPs) and Clinical Investigations of Medical Devices (CIMDs) sponsored by NHS Greater Glasgow Health Board (NHSGGC), or co-sponsored with University of Glasgow (UoG). The conduct of a trial must be able to be reconstructed both during the trial and for some time after its completion from the documentation which is filed and retained within the trial master file (TMF).

## 2. Purpose

This procedure applies to NHSGGC R&I Department and details the process for preparation and maintenance of a TMF. A TMF is the collection of documentation that allows the evaluation of the conduct of the CTIMP/CIMD, the integrity of the trial data and the compliance of the trial with Good Clinical Practice (GCP).

## 3. Procedures

### 3.1. Abbreviations/Definitions

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| CIMD | Clinical Investigation of a Medical Device |
| CTIMP | Clinical Trial of an Investigational Medicinal Product |
| GCP | Good Clinical Practice |
| CI | Chief Investigator |
| PI | Principal Investigator |
| PM | Project Manager |
| R&I | Research & Innovation department |
| RC | Sponsor Research Co-ordinator |
| SRA | Senior Research Administrator |
| RCB | Robertson Centre for Biostatistics |
| TMF | Trial Master File - contains all trial essential documentation which should be sufficient to adequately reconstruct the trial activities undertaken, along with key decisions made concerning the trial |
| ISF | Investigator Site File |
| UoG | University of Glasgow |
| SIV | Site Initiation Visit |
| Essential documents | individually or collectively permit evaluation of the conduct of a trial and the quality of the data produced |

### 3.2. TMF preparation overview

The complete TMF includes the Sponsor/Co-sponsor TMF, Investigator Site File (ISF) as well as participants medical records.

R&I NHSGGC Sponsor/Co-Sponsor team includes a number of sub departments/teams and representatives from these teams form the overall Sponsor/Co-Sponsor team assigned for individual CTIMP/CIMD oversight.

All teams will follow this SOP and its designated part of the complete TMF index (Form 51.016A) to prepare their corresponding TMF Files independently after being notified that the CTIMP/CIMD funding application has been successful.

The Sponsor/Co-Sponsor TMF index is divided in sections and covers the following teams and third parties:

A. R&I Sponsor Research Co-ordinator (Sections 1-9)
B. Pharmacy (Section 10)
C. Pharmacovigilance (Section 11)
D. Monitor (Section 12)
E. Governance (Section 13)
F. Project Management (Section 14)
G. Data management (Section 15)
H. Vendors (i.e Laboratories) (Section 16)

All required documents, as per complete TMF indices (Form 51.016A), will be added to the file once these are available (or at routine intervals) and a copy of each document will be saved electronically in the common drive. All documents will be printed to comprise a paper TMF and stored in a locked cabinet in the corresponding team office. Only the printed and filed documents will comprise the TMF unless otherwise stated within the paper TMF.

The Sponsor Research Co-ordinator File will contain the cover sheet (Form 51.016J) indicating the storage locations, format and point of contact for all wider Sponsor/Co-Sponsor team files as well as third party vendor files.

Project Managers (PMs) (or their designees) working across Cancer Research UK Clinical Trials Unit (CRUK CTU, Glasgow) coordinating CTIMPs and CIMDs will maintain components of the TMF as per this SOP and CRUK CTU SOPs.

Project Management Unit (PMU), University of Glasgow (UoG) PMs, RCB PMs as well as external PMs coordinating CTIMPs and CIMDs will maintain components of the TMF following this SOP, as will Innovation PMs coordinating CIMDs.

ISF file is prepared by the PMs using Form 51.016C and send to each participating site as per SOP 56.001.

Participating sites and all third party contractors (i.e Laboratories (for sample processing and analysis), CRF, RCB (for Data management), other vendors, third party data processors, etc) will be responsible for preparing, maintaining and archiving their corresponding part of the TMF (in the form of the Investigator Site File - ISF) independently of one another according to their local processes and/or as per Sponsor/Co-sponsor instructions or agreed terms within this SOP.

The recommendation from the MHRA is that the Sponsor/Co-Sponsor should provide vendors with a TMF plan that cover the following points:

- Who holds the official TMF (or which parts each party holds when this is divided)
- The process of filing documentation in the TMF
- Documents that both parties must retain
- The structure of indexing of the TMF
- When eTMF is used - details of the system
- Access arrangements in place for both parties for oversight and trial management
- How TMF would be available if either party was inspected
- Arrangements for when the trial is completed - Archiving

The vendor TMF plan will be included in the contractual arrangement between the Sponsor/Co-Sponsors and the vendor involved in the trial and will be captured on Form 51.016L. This will be prepared by the Research Co-Ordinator liaising with the Vendor.

The source data plan (Form 56.002M) will cover information on the local flag system for medical records of the participants in the trial. This will also be discussed at the Site Initiation Visit in order to ensure that the participants' medical records will be retained for the duration of archiving period of the trial as well as according to the local policies.

### 3.3. Maintenance of Sponsor/co-Sponsor TMF

All study documents must be filed in sequential order as per notes provided in the index for each section with the most recent at top. Sections of the TMF will be maintained by the appropriate individuals of the Sponsor/Co-Sponsor team and updated regularly for the whole length of the trial. It is essential to maintain the site file with up to date information, anything not filed within the site file will be considered missing information, even if present on common drives or in personal folders, this must be an ongoing and regular practice throughout the life of the trial and not an activity to be

performed at the end of trial. The individual(s) responsible for the TMF section will assume responsibility for maintenance throughout the lifetime of the study (unless otherwise delegated). If other individuals wish to add/amend/remove a document from the TMF, they must make the responsible individual(s) aware.

If the CTIMP/CIMD involves the use of a vendor it will be expected that the vendor will maintain and store documents that they are responsible for and will make them available for audit/inspection as required. Storage and maintenance of trial documents will be clearly documented in the appropriate contracts.

Sponsor/Co-Sponsor wide team email correspondence detailing decision making will be stored electronically in the trial eFolder and will be filed in the appropriate sections of the TMF. A copy of all other relevant Sponsor/Co-Sponsor email correspondence, will also be stored electronically in the corresponding department/institution server.

### 3.4. File Notes

On occasion it may be required to add a note to the TMF to explain a particular course of action taken during the trial or clarify the information present for future observers. Form 51.016M may be used to document this information, other organisations involved in the running of the trial may have their own format for file notes which may be used, for activity relating to that which NHSGGC R&I are responsible for, Form 51.016M should be used and signed by R&I staff.

### 3.5. Quality Control (QC)

All sections of the TMF will be subject to QC review at least once in the lifetime of the of a trial: during set-up, conduct, close-out/reporting and before archiving. However, the contents of the TMF should be QC'd on an ongoing basis as the documents are filed. The QC review will involve the reviewer (the corresponding representative of each Sponsor/Co-Sponsor team) ascertaining that the TMF contents match the TMF index requirements and that the locations of documents is correct according to the index and any other directions provided. The review will be captured by each team in the corresponding cover page in Form 51.016K and any inconsistencies/errors/omissions will be actioned to correct the issue.

Once addressed, the person performing QC will add their name and the date in the "Signature/Date" part of the corresponding QC section. Actions must then be taken, where possible, to remove any issues identified within the TMF. Individual TMF Files may also be subject to QC review and audit by a designated member of the Research Governance team. When a review by the Governance Team has been completed, this will be documented by an audit and an audit report will be provided to the individual responsible and they will correct any inconstancies/errors/omissions in a timely fashion.

### 3.6. Archiving of TMF

The TMF will be archived according to SOP 51.024.

## 4. Referenced documents

- SOP 51.024 - Archiving Essential Documents from Clinical Research – Process for a Sponsored Clinical Trial of an Investigational Medicinal Product (CTIMP)
- SOP 56.001 - Site Set Up – Green for Go Process
- Form 51.016A - Complete R&I TMF Index
- Form 51.016C - Principal Investigator Site File: Essential clinical trial documentation for academic (non-commercial) trials
- From 51.016J - TMF Cover Sheet
- Form 51.016K - TMF index pages
- Form 51.016L - Vendor TMF Plan Template
- Form 51.016M - TMF/ISF File Note
- Form 56.002M - Source Data Plan
- GUI 51.016A - Quality Control of Trial Master File
- https://tmfrefmodel.com/ (CDISC – Trial Master File Reference Model)

## 5. Related documents

- None

## 6. Document history

| Version | Date | Description |
|---|---|---|
| 1.0 | 06/11/13 | Release of first version |
| 2.0 | 14/07/2016 | Updated to template v1.4 and to reflect inspection outcomes. |
| 3.0 | 17/12/2018 | Staff category, Author and Approver updated |
| 4.0 | 04/10/21 | Author updated. Reference to two of the associated forms updated (CI site file – form 51.016B now CI file and Sponsor file now TMF index – 51.016A). Admin updates (job titles and R&I office name change included). Section 6 updated to reflect current SOP numbering. Version updated. |
| 5.0 | 24/07/2023 | Author updated.<br>Significant text change to clarify the procedures covered<br>Creation of Forms K & L along with Removal of Forms B, D, E, F, G, H & I.<br>Creation of Guideline 51.016A. |