Standard Operating Procedure (SOP)

Preparation and Maintenance of the Trial Master File (TMF)

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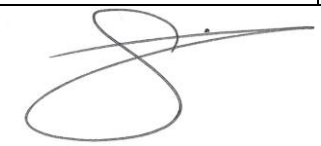
Signature of Authoriser			

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SOP Chronology

SOP Version Number:	Reason for Change:	Author:
V1.0	Original Version	Zuhur Balayah
V2.0	Review of Original Version	Ira Jakupovic
V3.0	Responsibility of TMF maintenance transferred to CI and study team. New SOP format.	Debbie Rolfe
v4.0	Correction of typos	Lucy Parker
V5.0	New Logo and Trust name Addition of Sponsored Device and International CTIMPs. Change of title to HORG	Debbie Rolfe

V6.0	Removal of Appendices- new format and minor corrections	Debs Rolfe
V7.0	Change of JREO to JRES. Insertion of Associated JRES documents table. Update to procedure and responsibilities to reflect current agreed practice, including removal of paper TMF held by JRES.	Georgia Bullock

Associated JRES documents

SOPs	WPDs	Docs	LOGs
JRESGOVSOP0016 Archiving	JRESWPD0023 General Research Definitions	JRESDOC0003 CTIMP TMF Index JRESDOC0004 CTIMP ISF Index JRESDOC0103 Non CTIMP ISF Index JRESDOC0076/76a International TMF Index	

Contents

1. Background

The requirement to set up and maintain a comprehensive set of essential study documents in a Trial Master File (TMF) is embedded in ICH GCP and the current Clinical Trials Regulations. The TMF allows the 'conduct of a clinical trial to be reconstructed and evaluated' (MHRA Inspectorate Blog).

The Chief Investigator (CI) of a Clinical Trial of an Investigational Medicinal Product (CTIMP) must set up and maintain a TMF as stipulated in the Clinical Trial Regulations. For multi-site trials, each participating site must also set up and maintain an Investigator Site File (ISF).

TMFs may be paper or electronic and the requirements are the same for both formats. A TMF may be comprised of both paper and electronic documents and different sections of the TMF may be stored in different locations. In such cases, it is important that the trial team/Sponsor is clear on where the documents are located:

'While we don't expect that the TMF is a single system that holds every document and we are happy to review a number of systems on inspection, it is expected that the organisation identifies all of these systems and has a clear understanding of the content of the TMF and where all of the essential documents are located' (MHRA Inspectorate Blog).

It is vital that TMFs are maintained throughout the study and that they are complete and accurate. Incomplete TMFs can result in a finding during a regulatory inspection.

2. Joint Research and Enterprise Services (JRES) Policy

All JRES SOPs will be produced and approved in accordance with the JRES SOP on SOPs and must be used in conjunction with local NHS Trust and University policies and procedures.

The JRES acts as the representative of both St George's University of London (SGUL) and St George's University Hospitals NHS Foundation Trust (SGFT). St George's will be the official name used on all SOPs to represent either institution acting as Sponsor.

3. Scope

The purpose of this SOP is to describe how to prepare and maintain a Trial Master File (TMF) throughout the lifetime of a trial, using the TMF Index supplied by the JRES which ensures that all documents are filed appropriately.

This SOP also covers the maintenance of trial-related documentation for non-CTIMPs sponsored by St George's.

4. Definitions

For general research-related acronyms used in this SOP, refer to General Research Definitions Working Practice Document (JRESWPD0023).

5. Responsibilities

5.1 Chief Investigator (CI)/Principal Investigator (PI)

The CI or PI at St George's is responsible for preparing and maintaining all the study files that form the TMF throughout the lifetime of the study.

For multi-centre trials that are sponsored by St George's, the PI at the respective sites will be responsible for the preparation and the subsequent maintenance of the Investigator Site File (ISF) in accordance with the requirements of St George's, the institution and any local requirements.

The CI will be ultimately responsible for the set-up and ongoing maintenance of the TMF. The CI may delegate this task to an appropriate member or members of their study team. This may be delegated to the assigned JRES Clinical Research Associate (CRA), for St George's sponsored CTIMPs, where the trial team is lacking administrative support and where the CRA is able to take on this responsibility. This must be agreed on a trial-by-trial basis, ensuring that the set-up of duplicate TMFs by both the JRES and the CI is avoided at all times. Responsibilities must be agreed and clearly defined at the start of the study and detailed on the Delegation of Duties log for the study.

The CI must ensure that the TMF is made available for the purposes of monitoring, audit or inspection and that it is stored in a secure location.

5.2 The JRES

The JRES will be responsible for the set-up and upkeep of an electronic Sponsor Site File (SSF) for each trial, using a standardised set of folders. The CI or their delegate must ensure that essential documents and important correspondence are provided to the JRES for their file.

Throughout the lifetime of the study, the Research Governance and Facilitation Officers (RGFO) and (for CTIMPs) the Clinical Research Associates (CRAs), will be responsible for the set-up and maintenance of the electronic SSF.

6. Procedure

6.1 JRES Procedure - Sponsored CTIMPs

- Upon notification of a CTIMP proposal, the JRES will provide the CI with a copy of the TMF Index for sponsored CTIMPs (JRESDOC0003).
- The JRES will set up and maintain an electronic SSF in the Investigators shared drive under the name of the CI.
- Trials must also be set up on the EDGE database system, following the template provided on the system.
- The JRES will provide any documents generated by the JRES (eg: monitoring reports, MHRA submissions) to the CI for the TMF.
- The JRES will ensure that any documentation and correspondence generated, or provided, by the trial team is filed in the electronic SSF. Documents not provided electronically will be scanned and saved and the paper copy destroyed as confidential waste.
- The CRAs will review the TMFs during monitoring visits and notify the trial team of any missing documents or incomplete sections.

6.2 Investigator Procedure – Sponsored CTIMPs

- The CI or delegated study team member will, throughout the lifetime of the study, ensure that all documents and correspondence are filed according to the TMF Index and that the TMF is stored in a secure location or locations.
- For multi-site trials, the Principal Investigator (PI) at each participating site will set up and maintain an Investigator Site File (ISF) using the ISF Index (JRESDOC0004).
- The CI or their delegate will ensure that the TMF contains all current and superseded documents. Superseded versions of documents (such as protocols, Patient Information Sheets) must be clearly marked as such (eg: by a strike through line, initialled and dated).
- Any important relevant communication, such as emails, should be printed and filed in the relevant section. Important correspondence which does not relate to any specific section must be filed under General Correspondence.
- Minutes for all trial-related meetings, such as meetings of the trial committees, must be present in the TMF.

- Where essential documentation is stored in a location other than in the paper TMF, a File Note should be placed in the relevant section of the TMF, detailing the location of the documentation.
- The CI or their delegate must respond to any monitoring findings relating to the TMF and ensure that the documentation is provided.
- The CI will ensure that the TMF is available for the purposes of monitoring, audit or inspection.
- At the end of the study and/or Close-out visit, and upon the resolution of any data queries, the complete TMF must be prepared for archiving by the CI or their delegate, following JRESGOVSOP0016.

6.3 JRES Procedure - Sponsored Non-CTIMP Studies and Hosted studies

- Upon notification of a study, the assigned RGFO will set up and maintain an electronic SSF in the Investigators shared drive under the name of the CI.
- Studies must also be set up on the EDGE database system, following the template provided on the system.
- The RGFO must provide copies of any documents throughout the lifetime of the study to the Investigator, eg: JRES Confirmation of Capacity and Capability, amendment approval emails, copies of financial contracts and insurance certificates.
- The RGFO will ensure that the SSF is kept up-to-date by filing all essential documentation when generated. Documents generated by the study team will need to be provided by the study team and filed by the RGFO.
- Upon receipt of the Final Study Report and confirmation from the RGFO, or where appropriate the Sponsor, that all outstanding queries are resolved following the Close-out visit, the study files will be archived following JRESGOVSOP0016.

6.4 Investigator Procedure - Non-CTIMP Studies and Hosted Studies

- The Investigator will ensure that any documentation generated in the lifetime of the study is filed according to the ISF Index.
- The Investigator will ensure that the ISF is available at all times for the purposes of monitoring, audit or inspection.
- The Investigator will ensure that any important correspondence received electronically is filed in the relevant section of the ISF.
- The Investigator will ensure that any protocol-related activity in respect of amendments or Annual Progress Reports are provided to the JRES in a timely fashion.
- The Investigator will ensure that the ISF contains all of the relevant study-related documentation and that where required, documentation is signed and checked.

- At the end of the study and/or Close-out visit and upon resolution of any outstanding queries, the ISF must remain intact and will be prepared for archiving following JRESGOVSOP0016 by the Investigator for studies sponsored by St George's or by following the instructions of the Sponsor where studies have been hosted by St George's.

6.5 Sponsored Device Studies and International CTIMPs

- TMFs and SSFs for these studies, when sponsored by St George's, will be set up and maintained as for sponsored CTIMPs. The JRES will provide the relevant International TMF Index (JRESDOC0076 or JRESDOC0076a) to the CI for the set up of the TMF.

7. References

ICH GCP.

http://www.ct-toolkit.ac.uk/routemap/trial-master-file/

https://mhrainspectorate.blog.gov.uk/2015/07/30/inspecting-clinical-trials-the-trial-master-file/

8. Appendices

None associated with this SOP.