St George's University of London

St George's University Hospitals NHS
NHS Foundation Trust

Standard Operating Procedure (SOP)
Preparation and maintenance of the Trial Master File (TMF)

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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

Table of Contents	Page
1. Background	3
2. Joint Research and Enterprise Office (JREO) Policy	3
3. Scope	3
4. Definitions	3
5. Responsibilities	
1. Chief Investigator/Principal or Lead Investigator	4
2. Joint Research and Enterprise Office (JREO)	4
6. Procedures	
1 JREO procedure for sponsored CTIMPs	5
2 Investigator procedure for sponsored CTIMPs	5
3 JREO procedure for Non-CTIMP studies	6
4. Investigator procedure for Non-CTIMP studies	6
5. JREO procedure for Sponsored Device Investigations	7
6. Investigator procedure for Sponsored Device Investigations	7
7. JREO procedure for Sponsored International CTIMPs	7
8. Investigator procedure for Sponsored International CTIMPs	7
7. References	7
8. Appendices - none	7

1. Background

The requirement to maintain a set of essential documents within the Trial Master File (TMF) comes from ICH GCP guidelines. ICH GCP is an internationally recognised standard for the initiation, conduct, recording and reporting of clinical research involving human participants, particularly drug trials. The principles of GCP were adopted in UK law in the Medicine for Human Use (Clinical Trials) Regulations 2004, which implement the European Clinical Trials Directive 2001/20/EC that was established to achieve standardisation of research activity in Clinical Trials throughout the European community. As a consequence, it is a legal requirement to maintain a TMF for all Clinical Trials of Investigational Medicinal Products (CTIMPs) within the scope of the Regulations.

For the purposes of this SOP the maintenance of trial related documentation will be applied to both CTIMPs and non-CTIMPs studies sponsored by St Georges.

2. Joint Research and Enterprise Office (JREO) Policy

All JREO SOPs will be produced and approved in accordance with the JREO SOP on SOPs and must be used in conjunction with local NHS Trust and St George's policies and procedures.

The JREO acts as the representative of both St George's University of London (SGUL) and St George's University Hospital's NHS Foundation Trust (SGHFT). St George's will be the official name used on all SOPs to represent both institutions acting as clinical trials Sponsor.

3. Scope

The purpose of this SOP is to inform the Investigator and any nominated members of the research team on how to prepare and maintain a Trial Master file (TMF) throughout the lifetime of a study and to ensure that the filing system utilising the appropriate TMF index supplied by the JREO is used appropriately.

4. Definitions

For general research management related acronyms used in this SOP refer to "General Research Definitions" working practice document JREOWPD0020

5 Responsibilities

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

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

For multicentre trials that are sponsored by St Georges , 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 Georges, the institution and any local requirements.

The CI will be ultimately responsible for ensuring that updated documentation is provided to any participating sites, support departments and where necessary the JREO as guardians of the Sponsor Site File (SSF). The CI may of course delegate this task to the Study co-ordinator. Responsibilities must be agreed and clearly defined at study start.

Upon receipt of a TMF/SSF status report it will be the responsibility of the CI to collaborate with the JREO to provide highlighted missing essential documentation for filing.

The CI will ensure that the TMF will be made available for the purposes of monitoring, audit or inspection and will be held in a suitably secure location.

5.2 The Joint Research and Enterprise Office (JREO)

The JREO will be responsible for the set up and upkeep of the SSF. Where the JREO is responsible for the initiation of any trial related activity during the lifetime of the study, a copy of any essential documentation will be provided to the CI for filing in the trial TMF within 3 working days.

Throughout the lifetime of the study the lead Research Governance and Facilitation Officer (RGFO) and where appropriate for CTIMP studies the Regulatory Support Officer (RSO) will be responsible for the maintenance and upkeep of the SSF.

The TMF and SSF will be reviewed periodically to ensure presence of correct versions of essential documentation. The TMF/SSF review will be co-ordinated by the JREO and undertaken by the assigned RSO or where appropriate the lead RGFO. Any missing documentation will be noted on a TMF/SSF status report included within the routine monitoring

visit or SSF review. A copy of the report will be provided to the CI and where appropriate the lead RGFO/RSO.

6 Procedure

6.1 JREO Procedure Sponsored CTIMPs

a) Upon notification of a CTIMP proposal the JREO will provide the CI with a copy of the TMF index JREODOC0003 for sponsored CTIMPs.

b) The JREO will set up a paper CTIMP Sponsor Site File (SSF) using the JREO CTIMP file index JREODOC0066 and will also set up a full electronic SSF using the same filing reference locations.

c) The JREO will maintain the SSF and provide copies of any documentation generated via the JREO as required for the TMF to the Chief Investigator or delegated Study team member within 3 working days. Examples of such documentation generated by the JREO during the lifetime of a study include MHRA submission, Open to Recruitment Letter and monitoring reports.

d) Upon receipt of any study related documentation for the trial SSF generated by the Study team, the JREO will ensure it is filed both physically and electronically according to the JREO site file index. Documents not provided electronically will be scanned and saved in the e-SSF Examples of documents that may be generated via the Study team include Annual Progress reports and Patient Information Sheets.

e) Upon receipt of the Final study report and confirmation from the RSO that all outstanding queries are resolved following TMF review the SSF will be archived together with the TMF following JREOSOP0016.

6.2 Investigator Procedure – Sponsored CTIMPS

a) The Chief Investigator or delegated study team member will obtain a copy of the TMF index JREODOC0003 and throughout the lifetime of the study ensure all documents generated are stored according to the index provided in a secure location.

b) The Investigator will ensure the TMF is available at all times to the Joint Research & Enterprise Office for the purposes of monitoring, audit or inspection.

c) The Investigator will ensure that the TMF reflects all the most relevant study related information and that all superseded documents are stored and marked as such (clearly identifiable as superseded by a strike through line, initialled and dated). Any important relevant communications should be printed and stored within the correct indexed section to enable restructure of any important trial events at any given point in time.

d) The Investigator will provide documentation indicated as required by the sponsor or as requested following a TMF review, to the JREO team within 3 working days.

e) At the end of the study and/or close out visit and upon resolution of any outstanding queries the TMF must remain intact and will be prepared for archiving following JREOSOP0016 by the Investigator.

6.3 JREO Procedure for Sponsored NON-CTIMP studies or hosted studies

a) The assigned RGFO / (RSO if determined high risk) , upon notification of a proposed project will create an electronic folder to represent the study eSponsor File using the available e-folder template. Where appropriate any protocol related documents will be uploaded to the eSponsor File as they are received to facilitate the management, approval and the subsequent safe conduct of the study.

b) The RGFO will also provide email confirmation of capacity and capability, a copy of this must be filed/saved in the e-Site File.

c) The RGFO may also provide copies of any documents throughout the lifetime of the study to the Investigator e.g JREO Amendment approval email, copies of financial contracts, copy of insurance certificate where applicable and as required.

d) The RGFO will also ensure that the eTMF is kept current and up to date by efficient filing. Documents not provided electronically must be scanned and uploaded into the eTMF File. Examples of documents that may be generated via the Study team e.g. Annual Progress reports, Patient Information Sheets. Once scanned spare copies of paper documents will not be kept and must be disposed of according to local confidential waste management policies.

e) 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 JREO study file will be archived together with the ISF following JREOSOP0016.

6.4 Investigator Procedure Non CTIMP studies

a) The lead Investigator will ensure that any documentation generated in the lifetime of the study is filed according to the ISF index.

b) The lead Investigator will ensure that the ISF is available at all times for the purposes of monitoring, audit or inspection.

c) The lead investigator will ensure that any important correspondence received electronically is filed in the relevant section of the ISF.

d) The lead Investigator will ensure that any protocol related activity in respect of amendments or Annual Progress Reports are provided to the JREO in a timely fashion within 3 days of generation or upon request.

e) The investigator will ensure that the ISF reflects all of the most relevant study related documentation and that where required documentation is signed and checked where appropriate.

f) 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 JREOSOP0016 by the Investigator for sponsor studies or under the instruction of the sponsor where studies have been hosted by St George's.

6.5 JREO Procedure for Sponsored Devices

a) Upon notification of a Device proposal the JREO will provide the CI with a copy of the TMF index JREODOC0082 for Sponsored Device Investigations.

b) The JREO will set up a physical Sponsor Site File (SSF) using the JREO Device file index JREODOC0082 and will also set up a full electronic SSF using the same filing reference locations.

c) For Maintenance of the TMF and exchange of documentation refer to 6.1

6.6 Investigator Procedure for Sponsored Devices

a) Refer to 6.2

6.7 JREO Procedure for Sponsored International CTIMPs

a) Refer to 6.1 using JREODOC0076 International TMF index

6.8. Investigator Procedure for Sponsored International CTIMPs

a) Refer to 6.2

7 References

ICH GCP E6

The Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031) and as amended

EU Clinical Trials Directive 2001/20/EC

JREOSOP0016 Archiving of Clinical Trials at St Georges

8 Appendices

There are no appendices associated with this SOP