

Document Title: 054

Document Number: Preparation and Maintenance of the TMF

Version:	1.1
Ratified by:	R&D Committee
Date ratified:	19/11/2018
Name of originator/author:	Neil Hubbard
Directorate:	Corporate Services
Department:	Research and Development
Name of responsible individual:	Rachel Fay, R&D Manager
Date issued:	01/12/2018
Review date:	04/12/2020
Target audience:	All research staff
Intranet:	NA
Key related documents:	SOP019 Investigator Site File SOP044 Archiving RFLRDDOC0013 TMF Index RFLRDDOC0014 TMF Index Review Tool RFLRDWPD004 Sponsor Files
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 (2017)
Date equality analysis completed.	30/11/2017
<u>This is a controlled document</u>	
Whilst this document may be printed, the electronic version maintained on the RF website is the controlled copy. Any printed copies of this document are not controlled.	

Version Control

Version	Date	Author	Status	Comment
1	19 SEPT 2017	Lucy Parker	Final	New document
1.1	19 Oct 2018	Neil Hubbard	Final	Update from ReDA to EDGE Database. Removal or references to SOP Working group and replacing with QMS Working Group. Deletion of Reading log.

Contents

Section		Page
1	Introduction	4
2	Objective	4
3	Definitions	4
4	Scope	5
5	Equality statement	5
6	Duties	5
7	Details of procedure	6
8	Policy	7
9	Risk management/liability/monitoring & audit	7
10	Forms/templates to be used	7
11	Flowcharts	7
Appendices		
Appendix (1)	SOP reading log	8
Appendix (2)	Equality analysis guide and tool	9

1. INTRODUCTION

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.

2. OBJECTIVE

For the purposes of this SOP the preparation and maintenance of trial related documentation will be applied to all studies Sponsored by Royal Free.

3. DEFINITIONS

RF Royal Free London NHS Foundation Trust

Trial Master File (TMF) . A file which contains all the essential documents that demonstrate that the trial has been conducted in accordance with regulatory requirements and ICH GCP. The TMF is set up at the start of a study and is archived at the end of the study for a set period of time which will be defined either in the protocol or Clinical Trials Agreement The TMF will contain essential documents which enable both the conduct and quality of the trial to be evaluated. The Case Report Forms (CRFs), Laboratory Manuals, where applicable, are all part of the TMF.

However, during the active phase of the study they may be held separately within the appropriate departments. Responsibilities for the maintenance of each of these files may be delegated to appropriately placed/qualified study team members although the ultimate responsibility for their maintenance and upkeep will lie with the Chief Investigator (CI). The TMF and any of the subsections, e.g. Laboratory Manuals must be made available for monitoring and audit purposes throughout the lifetime of the study. The TMF may also exist electronically and will be referred to in this SOP as 'eTMF'.

Investigator Site File (ISF). This file is provided to each participating site at the Site Initiation Visit. It contains all the information site staff will need to conduct the clinical trial at the site. The ISF forms part of the TMF, and will be made available for monitoring and audit purposes throughout the study. For Studies Sponsored by RF, investigators should follow SOP019 Investigator Site File.

Sponsor File (SF) The SF is the file held in the RF R&D Office. Documents generated throughout the project development phase prior to study start will be retained in the SSF and e-TMF. The SSF will contain documentation to facilitate Sponsor oversight of all aspects of the study e.g. regulatory submissions, pharmacovigilance and financial arrangements. This is an electronic file. RF R&D Office staff will follow RFLRDWPD004 when setting up the Sponsor File.

4. 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) of a RF Sponsored study throughout the lifetime of a study and to ensure that the filing system utilising the appropriate TMF index supplied by the RF R&D Office is used appropriately.

5. EQUALITY STATEMENT

The Royal Free London NHS Foundation Trust is committed to creating a positive culture of respect for all individuals, including job applicants, employees, patients, their families and carers as well as community partners. The intention is, as required by the Equality Act 2010, to identify, remove or minimise discriminatory practice in the nine named protected characteristics of age, disability (including HIV status), gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, sex or sexual orientation. It is also intended to use the Human Rights Act 1998 to treat fairly and value equality of opportunity regardless of socio-economic status, domestic circumstances, employment status, political affiliation or trade union membership, and to promote positive practice and value the diversity of all individuals and communities.

This document forms part of the trust's commitment. You are responsible for ensuring that the trust's policies, procedures and obligation in respect of promoting equality and diversity are adhered to in relation to both staff and service delivery.

The equality analysis for this SOP is attached at Appendix (2).

6. DUTIES

The Trust is committed to the delivery of world class care and expertise to both staff and patients, and our values of positively welcoming, actively respectful, visibly reassuring and clearly communicating are fundamental to the delivery of this. This policy has been developed with our values in mind, and is intended to be implemented within the spirit of these values.

The CI or PI at RF 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 RF, the PI at the respective sites will be responsible for the preparation and the subsequent maintenance of the ISF in accordance with the requirements of RF, the institution and any other 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 RF R&D Office as guardians of the SF. The CI may of course delegate this task to the Study coordinator. Responsibilities must be agreed and clearly defined at study start

Periodically, the CI or a delegated member of their team should review the TMF using the TMF Review Tool (RFLRDDOC0014). If documents are found to be missing, it will be the responsibility of the CI to collaborate with the RF R&D Office 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.

7. PROCEDURE

Person Responsible	Task
CI	<p>The CI will ensure that any documentation generated in the lifetime of the study is filed according to the Study file index (RFLRDDOC0013)</p> <p>Ensure that the TMF is available at all times for the purposes of monitoring, audit or inspection.</p> <p>Ensure that any important correspondence received electronically is filed in the relevant section of the TMF and ensure that any protocol related activity in respect of amendments or Annual Progress Reports are provided to the RFL R&D Office in a timely fashion within 3 days of generation or upon request.</p> <p>The investigator will ensure that the TMF reflects all of the most relevant study related documentation and that where required documentation is signed and checked where appropriate.</p> <p>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 SOP0044 by the Investigator.</p>
Research Portfolio Manager	<p>The Research Portfolio Manager upon notification of a proposed project will create a EDGE record for the study. This will then auto-generate the agreed e-folders for the study.</p> <p>Where appropriate any protocol related documents will be uploaded as they are received to facilitate the management, approval and the subsequent safe conduct of the study.</p> <p>The Research Portfolio Manager will remind the CI of the location where they can download a copy of the index RFLRDDOC0013 TMF index.</p> <p>The Research Portfolio Manager will also provide copies of any documents throughout the lifetime of the study to the Investigator e.g. R&D Office Amendment approval email, copies of financial contracts where applicable and as required.</p> <p>The Research Portfolio Manager must also ensure that the</p>

	<p>eTMF is also kept current and up to date by efficient filing. For documents not provided electronically – then scan as compressed pdf. file and upload into the eTMF File.</p> <p>Examples of documents that may be generated via the Study team e.g. Annual Progress reports, Patient Information Sheets.</p> <p>Upon receipt of the Final study report and confirmation from the CI that all outstanding queries are resolved following the close out visit ensure that the RF R&D Office Sponsor File will be archived following SOP0044</p> <p>Follow RFLRDWPD0004 Sponsor File when creating the record.</p>
--	--

8. POLICY

This SOP is mandatory and non-compliance with it may result in disciplinary procedures.

9. RISK MANAGEMENT/ LIABILITY/MONITORING & AUDIT

- The QMS Group will ensure that this SOP and any future changes to this document are adequately disseminated.
- The R&D Office 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).
- In exceptional circumstances it might be necessary to deviate from this SOP for which written approval of the R&D Manager/Deputy R&D Director should be gained before any action is taken.
- SOP deviations should be recorded including details of alternative procedures followed and filed in the Investigator and Sponsor Master File.
- The R&D Office is responsible for the ratification of this procedure.

10. FORMS/TEMPLATES TO BE USED

RFLRDDOC0013 TMF Index
RFLRDDOC0014 TMF Index Review Tool

11. FLOWCHART

None applicable

APPENDIX 2

Royal Free London NHS Foundation Trust Equality Analysis guide and Tool

An equality analysis is a review of a policy, practice, function, business case, project or service change which establishes whether there is a negative effect or impact on particular social groups. This In turn enables the organisation to demonstrate it does not discriminate and, where possible, it promotes equality to meet the needs of the diverse patients and communities we serve.

This check list is a way to help you think carefully about the likely impact on equality groups and take action to improve services. This is also an opportunity to evidence positive practices in our services and demonstrate strategic integrity to ensure that our services and employment practices are fair, accessible and appropriate for all patients, visitors and carers, as well as our talented and diverse workforce.

Name of the policy / function / service development being assessed	Preparation and maintenance of the TMF
Briefly describe its aims and objectives:	For the purposes of this SOP the preparation and maintenance of trial related documentation will be applied to all studies Sponsored by Royal Free.
Directorate and Lead:	Rachel Fay, R&D Manager
Evidence sources: DH, legislation. JSNA, audits, patient and staff feedback	Medicines for Human Use (Clinical Trials) Regulations 2004 and all associated amendments. UK Policy Framework for Health and Social Care (2017)
Is the Trust Equality Statement present?	Yes X No if no do not proceed with Equality Analysis (EA)

If you are conducting an EA on a procedural document please identify evidence sources and references, who has been involved in the development of the document, process or strategy, and identify positive or negative impacts. It is the discussion regarding the equality impact of the document that is important.

SOP054: Preparation and Maintenance of the TMF

V1.1 19 OCT 2018

Uncontrolled document when printed or downloaded. Current SOP versions available <https://www.royalfree.nhs.uk/research/for-investigators/standard-operating-procedures-sops/>

Equality Analysis Checklist

Go through each protected characteristic below and consider whether the policy, practice, function, business case, project or service change could have any impact on groups from the identified protected characteristic, involve service users where possible and get their opinion, use demographic / census data (available from public health and other sources), surveys (past or maybe carry one out), talk to staff in PALS and Complaints and Patient Experience.

Please ensure any remedial actions are Specific, Measureable, Achievable, Realistic, and Timely (SMART).

Equality Group	Identify negative impacts	What evidence, engagement or audit has been used?	How will you address the issues identified?	Identifies who will lead the work for the changes required and when?	Please list positive impacts and existing support structures
Age	None identified	R&D administrative document	N/A	N/A	This SOP on the preparation and maintenance of the TMF introduces a requirement to include the Trust Equality Statement in all SOPs that describe the standard activities used in Research Studies and Clinical Trials at the Royal Free London Hospital NHS Foundation Trust.
Disability	None identified	R&D administrative document	N/A	N/A	
Gender Reassignment	None identified	R&D administrative document	N/A	N/A	
Marriage and Civil Partnership	None identified	R&D administrative document	N/A	N/A	
Pregnancy and maternity	None identified	R&D administrative document	N/A	N/A	
Race	None identified	R&D administrative document	N/A	N/A	

SOP054: Preparation and Maintenance of the TMF

V1.1 19 OCT 2018

Uncontrolled document when printed or downloaded. Current SOP versions available <https://www.royalfree.nhs.uk/research/for-investigators/standard-operating-procedures-sops/>

SOP 054: Preparation and Maintenance of the TMF

Equality Group	Identify negative impacts	What evidence, engagement or audit has been used?	How will you address the issues identified?	Identifies who will lead the work for the changes required and when?	Please list positive impacts and existing support structures
Religion or Belief	None identified	R&D administrative document	N/A	N/A	It also introduces a new Equality Analysis Template for the SOPs, that requires the presence of the Equality statement. These actions are designed to embed the equality agenda and promote equality compliance within the Trust.
Sex	None identified	R&D administrative document	N/A	N/A	
Sexual Orientation	None identified	R&D administrative document	N/A	N/A	
Carers	None identified	R&D administrative document	N/A	N/A	

It is important to record the names of everyone who has contributed to the policy, practice, function, business case, project or service change.

Equality Analysis completed by: (please include every person who has read or commented and approval committee(s). Add more lines if necessary)	Organisation	Date
QMS Group	Royal Free London NHS Foundation Trust	20/10/2017
R&D Committee	Royal Free London NHS Foundation Trust	30/11/2017

SOP054: Preparation and Maintenance of the TMF

V1.1 19 OCT 2018

Uncontrolled document when printed or downloaded. Current SOP versions available <https://www.royalfree.nhs.uk/research/for-investigators/standard-operating-procedures-sops/>