WORK INSTRUCTION

WI43 - Establishing and Maintaining Trial Master Files and Investigator Site Files for RD&E Sponsored studies

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Controlled document

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DISCLAIMER

This generic R&D Work Instruction (WI) must be followed unless a study specific SOP/WI exists.

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Full History			
Version	**Date**	**Author**	**Reason**
1	14 June 2021	Quality Assurance Coordinator	Detailed instructions for process as referred to in accompanying S43.

Associated Trust Policies/ Procedural documents:	R&D SOP S43 Establishing and Maintaining Trial Master Files and Investigator Site Files for RD&E Sponsored studies
Key Words:	TMF ISF
In consultation with: QA Group (June 2021)	

Contents

1 INTRODUCTION

It is a legal requirement for Sponsors to keep a Trial Master File (TMF) for all clinical trials (Regulation 31a). The TMF should at all times contain the essential documents relating to a research study. The essential documents and data records stored in the TMF enable operational staff as well as monitors, auditors and inspectors to evaluate compliance with the protocol, the research study's safe conduct and the quality of the data obtained.

2. PURPOSE

This Work Instruction is designed to accompany the Standard Operating Procedure on Establishing and Maintaining Trial Master Files and Investigator Site Files for RD&E Sponsored studies (S43) to provide more detailed instruction where necessary.

3. SCOPE

This SOP is applicable to Chief Investigators, Principal Investigators and any personnel delegated with responsibility for the TMF and ISF, as well as by the relevant parties in R&D who are involved in its make-up e.g. the R&D Delivery Team and R&D Professional Services.

4. DEFINITIONS

CI	Chief Investigator
CTIMP	Clinical Trial of an Investigational Medicinal Product
EDGE	Online Clinical Research Management System
GCP	Good Clinical Practice
GOG	Governance Oversight Group
HRA	Health Research Authority
MHRA	Medicines and Healthcare products Regulatory Agency
ISF	Investigator Site File
PI	Principal Investigator
R&D	Research & Development
REC	Research Ethics Committee
SOP	Standard Operating Procedure
Sponsor	An individual, company, institution or organisation which takes responsibility for the initiation, management and financing of a clinical trial. Sponsorship activities may be delegated to the Investigator, CTU and/ or other organisations as appropriate
TMF	Trial Master File

5. DUTIES AND RESPONSIBILITIES OF STAFF

The **Chief Investigator (CI)** is responsible for establishing and maintaining a TMF/ISF. The CI may delegate this to a Clinical Trials Unit (CTU) or a member of the CI's research team. Any delegation will be clearly documented.

The **R&D Professional Services Team** is responsible for providing a template TMF/ISF Index and ensuring this is accessible.

Clinical Research Delivery Team personnel can be delegated by the CI to be responsible for maintaining the TMF/ISF.

6. PROCEDURES

6.1 Establishing a Trial Master File (TMF) and/or Investigator Site File (ISF)

The CI (or suitably delegated personnel) will ensure that a TMF is established as soon as possible after an outline protocol becomes available. The CI will also ensure that ISFs are established at all participating sites for multi-centre research studies. R&D will make available a template TMF or ISF Index/Table of Contents for CTIMP and non-CTIMP studies on the RDEResearch Website.

This requirement should be discussed with the CI by the R&D Professional Services Team during the study set up phase.

6.2 Maintenance and Storage of the TMF/ISF

6.2.1 All superseded versions of documents must be retained in the TMF/ISF alongside the new amended version(s), but marked as superseded by striking through the front cover with a single line and marking as superseded by the later version, signed and dated.

6.2.2 A Version Control Tracker should be utilised, a template 'Document Amendment Log' is available on the RDEResearch Website.

6.2.3 A file note (signed and dated by the CI/PI or delegate) must be placed in the relevant section of the file giving details of any missing or unavailable documents.

6.2.4 For electronic TMFs/ISFs there should be a standardised labelling convention for the storage of documents so that files are stored in chronological order and easily located e.g. standard date format, file name, version: *210615 Protocol V1*. For documents subject to version control, the use of files names should not replace version details being visible on displays and printouts.

7. DISSEMINATION AND TRAINING

7.1 This WI and associated templates and forms will be uploaded to the RDE Research website shortly after having been released.

7.2 All staff whose activities are subject to this WI should ensure that they take time to read and understand the content of this WI.

8. MONITORING COMPLIANCE AND EFFECTIVENESS OF THIS WI

8.1 In order to monitor compliance with this WI, the auditable standards will be monitored as follows:

No	Minimum Requirements	Evidenced by
1.	The CI will also ensure that ISFs are established at all participating sites for multi-centre research studies	Multi-centre checks with study coordinator.
2.	Previous version documents must be contained in the TMF/ISF and superseded.	TMF/ISF check
3.	For electronic TMFs/ISFs there should be a standardised labelling convention for the storage of documents.	Electronic TMF/ISF

8.2 Outcomes from audit will be presented to the R&D Governance Oversight Group (GOG) which will monitor any resulting action plans until all issues have been addressed to satisfaction.

8.3 Issues identified via the audit process which require escalation will be referred to GOG.

9. ARCHIVING ARRANGEMENTS

9.1 The original of this document will remain with the R&D Quality Assurance Coordinator. An electronic copy will be maintained on the R&D section of the Q-Pulse document management system and a pdf copy on the RDE Research website

9.2 Archive copies must be maintained for any documents which have been superseded. Archive copies in electronic format should be retained indefinitely.

10. REFERENCES

R&D SOP S43 Establishing and Maintaining Trial Master Files and Investigator Site Files for RD&E Sponsored studies