BU RDS SOP 006 V2

Title: File Management for Clinical Research	
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Document History

Version	Description of update	Date Effective
1.0	Clarification with regard to storing electronic study files under 'Procedure' and correction of typographical error.	25/11/2020

1. Scope

1.1 This Standard Operating Procedure (SOP) describes the procedure for good file management for clinical research purposes. The document applies to any member of staff involved in a research project sponsored by Bournemouth University (BU) involving the NHS.

1.2 As Sponsor, a Trial Master File (TMF) must be retained. This contains all the essential documents relating to the research project from the design and initiation, through to the completion of a given study. The TMF allows the conduct of the study, compliance with study requirements and integrity of data, telling the story of the study.

The TMF is comprised of the Sponsor's file and the individual site(s) Investigator Site Files (ISF). *If the study involves Pharmacy, there may also be a Pharmacy file.*

For the purposes of this SOP, the 'TMF' will refer to the Sponsor's file.

1.3 The Sponsor must maintain a record of the location of all essential documents and an index of those contained within the file.

2. Responsibilities

The *Sponsor* is responsible for ensuring investigators have control of and continuous access to the reported data. They are also responsible for ensuring that each site's Investigator Site File (ISF) is complete prior to archive by the completion of an ISF checklist or final monitoring visit.

The *Chief Investigator (CI)* may delegate the creation of the sponsor file but is responsible for data management, acting on behalf of the Sponsor. The CI or appropriate delegate is likewise responsible for study documentation from research design through to making amendments, to the analysis of data at the end of the project.

The *Clinical Governance Advisor (CGA)* is responsible for monitoring and auditing the contents of the TMF and for keeping an up-to-date electronic record of the correspondence and essential documents relating to the research project.

The *research team* is responsible for maintaining a complete ISF in accordance with Good Clinical Practice (GCP) guidelines, archiving the files alongside participant documents and records.

3. Procedure

3.2 A sponsor file and an ISF at each site must be compiled prior to participant recruitment taking place. A completed delegation log must be in place at each site, signed by the site Principal Investigator (PI). These files must be stored in a secure place or room with restricted access. The sponsor file and ISF may be created on the Edge system once confirmed with the CGA, in place of paper records.

The original copy of all informed consent forms must be filed in the ISF, with the only other copies being held in the medical record, and by the participant.

Maintaining a TMF/eTMF

3.3 An index for study TMFs can be found *in the appendix.* The TMF can be kept in paper form, electronically, or part paper-part electronic and it is the CI's/Researcher's responsibility to keep the TMF up to date. The participating site must also have the adequate facilities and security to maintain an electronic filing system. If the TMF is part paper-part electronic, then the paper TMF will either need to contain a file note signposting the location of electronic documents, or the CI/Researcher should clearly identify these on the paper TMF index.

3.4 All study documents must be version controlled and new protocols signed before use. Paper superseded documents should be retained and clearly marked (crossed out, initialled by the staff member, and identified with the date and version of the new document). Superseded electronic documents should be filed in a folder marked 'superseded'.

3.5 If the CI/Researcher chooses to keep an electronic TMF, the CI/Researcher should ensure that there is appropriate security and reliability, and that there will be no loss, alteration or corruption of the data and documents.

An e-TMF should have the following measures in place –

- User accounts;
- Secure passwords;
- Systems in place to lock/protect individual documents or the entire e-TMF (as required for archiving);
- Regular back up to a separate location;
- Audit trails that identify date/time/user details for creating, uploading, approving and deleting or changing documents;
- Role based permissions for restricted access activities (e.g. randomising and un-blinding).

'There should be a back-up of the e-TMF with the back-up stored in a separate location and/or media' (EMA, 2017).

The MHRA do not expect that the TMF will be a single system that holds every document, and are happy to be presented with any number of systems on inspection, ideally with a full list that identifies where each essential document is kept, for ease of access (MHRA, 2015).

3.6 Correspondence that will aid the reconstruction of key activities and decisions must be stored in the TMF and should be filed in chronological order.

3.7 Essential correspondence with the REC, HRA[1] (and MHRA) should be forwarded to the CGA by the CI/Researcher, and filed in the TMF. The CGA will keep these documents electronically for a governance audit trail. Similarly, all approved amendments should be forwarded to the CGA by the CI/Researcher.

3.8 The TMF must be made available to the CGA upon request.

3.9 The TMF must be archived in accordance with BU RDS SOP 001 – Archiving Clinical Research.

3.10 The NHS site will also keep an R&D folder which contains the approval and regulatory documentation pertaining to the study. These may be duplicates of documents already held in the TMF. The R&D folder will need to be archived with the ISF.

4. Abbreviations and definitions

CGA	Clinical Governance Advisor
CI	Chief Investigator
GDPR	General Data Protection Regulations
HRA	Health Research Authority
ISF	Investigator Site File
MHRA	Medicines and Healthcare Products Regulatory Agency
PI	Principal Investigator
REC	Research Ethics Committee
TMF	Trial Master File

5. Related documentation and references

BU RDS SOP 001 – Archiving Clinical Research

EU General Data Protection Regulation (GDPR) - https://www.eugdpr.org/

European Medicines Agency, Guideline on GCP Compliance in Relation to Trial Master File (Paper and/or Electronic) for Content, Management, Archiving, Audit and Inspection of Clinical Trials (2017) - http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2017/04/WC500225871.pdf

[1] Please note, as of June 2018, HRA approval is now HRA and Health and Care Research Wales (HCRW) approval

MHRA Inspectorate blog, (2015), *Inspecting clinical trials - The trial master file* - https://mhrainspectorate.blog.gov.uk/2015/07/30/inspecting-clinical-trials-the-trial-master-file/

RDS Suggested TMF (ISF and Sponsor File) template – see appendix

Appendix

Suggested Trial Master File Contents

SECTION	TITLE	CONTENT/COMMENTS	Sponsor File/ISF/Both
1	Protocol / amendments	Current protocol Protocol amendments Historical protocols	Both
2	**Sample** CRF/ QLQ Diary Cards		Both
3	Regulatory approval documentation[2] IRAS form submitted for approval	Separate section required for amendment approvals, notifications and site acceptance/non-acceptance of the amendment	Both
4	Site signature /responsibility log (of each participating site)	In addition to original being filed in site's investigator site file	Both
5	Curriculum Vitae and GCP certificates	CVs for all research personnel listed in the signature/responsibility log	Both
6	Patient Identification form Patient recruitment /screening form		ISF
7	Sample of current and all historical Patient Information / Informed Consent form and GP Letter Completed patient Information and Informed Consent Forms	 In ISF, not Sponsor file unless REC approved	Both ISF **only**
8	Correspondence inc. study set-up with regulatory bodies	File in chronological order all correspondence to/from the coordinating research body. File email communication Include a separate section here for newsletters	Both (set-up correspondence with REC/HRA/MHRA in Sponsor file only)
9	Minutes from Initiation meeting Monitoring logs Notes of telephone calls	If the study is not monitored state this in a file note in this section Document telephone call in relation to agreements or significant discussions regarding trial administration, trial conduct, adverse events or protocol violations	Both
10	Blank serious adverse event forms and guidelines for their completion Completed SAE forms from participating sites		Both Sponsor file
11	Notification of serious adverse events and/or safety reports	By Investigator to co-ordinating research body By co-ordinating research body to Investigator	Both

[2] The regulatory approvals received will depend on your study – in most cases, HRA approval will be provided. If your study involves patients or midwives, then REC approval will be given. If your study is an investigation using medicinal products or devices (including apps and software), then you will receive MHRA Clinical Trial Authorisation.

		By co-ordinating research body to regulatory authorities (if this will not be supplied place a file note stating this)	
12	Randomisation details	Instructions (if applicable)	Both
13	Instructions for handling trial medication and trial related materials Shipping records	This responsibility is normally that of the clinical trial pharmacist if this is the case place a file note in this section stating this	Both ISF
14	Clinical Laboratory	Laboratory normal reference ranges (including revisions) Laboratory certificate(s)	ISF
15	Contracts/Participating Site's Organisation Information Document R&D 'confirmation of capacity and capability'	Investigator Commitment Statement/Study Acknowledgement Indemnity Confidentiality Clinical Trial Agreement including financial details. Completed and signed FDA 1572 form (if applicable) Financial disclosure letter (if applicable)	Both Both
16	Investigator's Brochure Safety alert letters/Updates		Both
17	Completed Data Queries		Both
18	Study Training Materials		Both
19	Miscellaneous (specify)…….		Both

Commented [SW1]: Commercial projects only

AFTER THE COMPLETION OF THE TRIAL THE FOLLOWING MUST BE ALSO FILED IN THE TRIAL MASTER FILE

20	Investigational product(s) accountability at site	This will be with the clinical trials pharmacist	Pharmacy Site File
21	Documentation of Investigational product destruction	If destroyed at site this will be with the clinical trials pharmacist	Pharmacy Site File
22	Final report	From Investigator to REC	Both
23	Clinical study report	To document results and interpretation of trial	Both