TRIAL MASTER FILE

Research & Development

Standard Operating Procedure for the Management of the Trial Master File for Trials Sponsored or Hosted by West Hertfordshire Hospitals NHS Trust

SOP Number : SOP-06-07	**Effective Date:** October 2021
Version Number: v07	**Review Date:** 2 - 3 years

1.0 BACKGROUND

This document sets out the procedures to be followed by all West Hertfordshire Hospitals Trust (WHHT) staff who are involved in the preparation, maintenance and archiving of Trial Master Files (TMFs) and/or Site Files for research projects managed, sponsored or hosted by WHHT.

It provides guidance on how the Sponsor File should be compiled and how these files should be stored to ensure compliance with the Trust's policies

2.0 PURPOSE

- To achieve standard best practice of clinical research documentation for clinical trials sponsored by WHHT
- To ensure WHHT meets all regulatory, research governance and Trust requirements in the management of TMFs and other related documentation
- To ensure all clinical trials documentation can be readily available for regulatory and/or other auditing activities
- To ensure new research staff are appropriately trained in the setup and management of the TMF

3.0 APPLICABLE TO

Any relevant Trust employee involved with Clinical Trials of an Investigational Medicinal Product (CTIMP) sponsored by WHHT including, but not limited to, Unit Heads, Chief Investigators (CI), Principal

Investigators (PI), Co-investigators, Consultants, Research Fellows, Clinical Trial Pharmacists, Research Managers, Statisticians, Research Nurses, Trial Coordinators, the Research & Development Steering Group (RDSG) & Data Managers.

4.0 RESPONSIBILITIES

The Medicines for Human Use (Clinical Trials) Regulations 2004:1031 (as amended) outlines requirements for Trial Master File and archiving, as follows:

- The Sponsor will keep a TMF for a clinical trial. Where WHHT is the Sponsor of the study, this is generally delegated to the CI or delegated individual (DI)

- Where this is the case and WHHT is also a participating centre in the study, the Site Investigator File (ISF) would be the same as the Trial Master File (TMF)

- Where responsibility for the trial is delegated to a trials unit or external organisation, particularly in the case of co-sponsorship arrangements, the TMF would not be expected to include the SIF

- The Sponsor will ensure that the TMF is readily available at all reasonable times for inspection by the licensing authority or any person appointed by the Sponsor to audit the arrangements for the trial

- The CI/DI will ensure access to the TMF and related documents are available upon request of the R&D Office to conduct routine Sponsor audits

- The CI/DI should ensure that the TMF contains the essential documents relating to that clinical trial, which enable both the conduct of the clinical trial and the quality of the data produced to be evaluated. It must also contain evidence of trial conduct in accordance with the applicable requirements

- The Sponsor should ensure that the essential documents contain information specific to each phase of the trial

- The Sponsor should ensure that any alteration to a document contained, or which has been contained, in the TMF should be traceable. The Sponsor and the CI should ensure that the documents contained, or which have been contained, in the TMF are retained for at least 5 years after the conclusion of the trial and that during that period are:

  (a) Readily available to the licensing authority on request and (b); complete and legible

- The Sponsor and CI should ensure that the medical files of trial subjects are retained for at least 5 years after the conclusion of the trial

- The Sponsor should appoint named individuals within the organisation to be responsible for archiving the documents which are, or have been, contained in the TMF and access to those documents should be restricted to those appointed individuals

- If there is transfer of ownership of data or documents connected with the clinical trial—
  - the Sponsor should record the transfer; and

- The new owner should be responsible for data retention and archiving

5.0 PROCEDURE

5.0.1 All clinical trials sponsored by WHHT must have a comprehensive and up-to-date TMF. Appendix 2.0 provides a sample template for the TMF contents. The International Conference on Harmonisation-Good Clinical Practice (ICH-GCP) Master File checklist is also provided as guidance in Appendix 3.0. For further guidance on Site File documentation see Appendix 4.0.

5.0.2 The TMF will be verified at the study initiation meeting. This should be used to maintain a current TMF by the Research Team. If units have existing systems for managing the contents of the TMF (e.g. local guidance documents), then the existing system can be used provided it is GCP-compliant.

5.0.3 Copies of all versions of the protocol should be stored in the TMF. If older versions of protocols are stored elsewhere, a file note must be added to the TMF. All protocols should be approved by the CI prior to implementation; an authorisation signature and date by the CI should be included in the protocol.

5.0.4 The TMF should contain copies of sample Patient Information Sheet (PIS), Consent Forms, GP letters and blank Case Report Forms (CRFs).

5.0.5 All completed original consent forms (see SOP-04) and CRFs should be maintained in the TMF and/or Site File or in a secure location within the designated location and a file note must be added in the TMF describing the location and other relevant information (e.g. contact).

5.0.6 All documentation arising from communication between the study team and the R&D Office should be maintained in the appropriate section of the TMF. Prior to study initiation, the CI/DI should ensure a final approval has been granted. This also applies to all substantial and non-substantial amendments.

5.0.7 All documentation relating to the study and the ethics committee should be maintained in the TMF. The CI must ensure all Health Research Authority (HRA) approvals are obtained prior to study start. This also applies to all substantial amendments.

5.0.8 All communication documentation relating to the study and the Medicines and Healthcare products Regulatory Agency (MHRA) should be maintained in the TMF, where applicable. The CI must ensure all necessary regulatory approvals are in place prior to study start. For studies involving an Investigational Medicinal Product (IMP), the CI should ensure that an MHRA Clinical Trial Authorisation (CTA) is obtained prior to study start.

5.0.9 All documentation relating to research governance arrangements should be maintained in the TMF. Examples of documents include sponsorship letters, Administration of Radioactive Substances Advisory Committee (ARSAC), Research Agreements and Indemnity Statement.

5.0.10 For trials involving unlicensed IMPs an Investigator's Brochure (IB) should be maintained in the TMF. The CI should ensure that updated IBs are in circulation**.** For marketed products, an approved version of the Summary of Product Characteristics (SPC) should be maintained in the TMF. If IBs/ SPCs are not held within the TMF, a File Note should be included in the TMF describing the location**.**

5.0.11 All documentation relating to pharmacy and the trial should be maintained in the TMF. If documents are held in Pharmacy Study File instead of the TMF, a file note should be added to the TMF. See Appendix 5 for sample file note.

5.0.12 All laboratory documentation related to the study should be maintained either within the TMF or held centrally within the units or designated centres. If held centrally, a file note must be added to the TMF. Examples of documentations include accreditations, normal reference ranges, investigational product handling, invoices etc.

5.0.13 The TMF should contain study site staff records including items such as responsibilities and signature log (delegation log), evidence of GCP training, SOP training, current CVs (recommended to be updated every 2-3 years) (see SOP-07). If training records are held centrally within units, a file note can be added in the TMF.

5.0.14 Study specific information, guidance notes and randomisation instructions should be maintained in the appropriate section(s) of the TMF.

5.0.15 All information regarding pharmacovigilance should be maintained in the TMF. Records of Adverse Events (AEs) and Serious Adverse Events (SAEs), including follow-up reports should be maintained in the TMF. Other items including safety information, sample SAE forms, SAE logs, correspondences, Safety Reports to the MHRA, HRA and annual progress reports should also be held in the TMF. (see SOP-02 and SOP-05)

5.0.16 If documents are held elsewhere, a file note should be added to the TMF (Appendix 5.0). If, as part of the sponsor agreement, pharmacovigilance was delegated to a co-sponsor that is not WHHT, then this section does not apply.

5.0.17 All substantial and non-substantial amendments must be submitted to the RDSG for review and approval. All correspondences, including copies of approvals for substantial amendments from the HRA and MHRA should be held in the TMF.

5.0.18 All evidence of monitoring activities such as study initiation meetings, progress reports, minutes of research/team meetings, meetings of Data Monitoring Committees and Trial Steering Groups and monitoring logs should be held in the TMF.

5.0.19 For trials that have been audited by a monitor/auditor, it is recommended that audit reports are held separately from the TMF. Copies of all audits are maintained by the R&D Office.

5.0.20 The TMF should contain evidence/rationale for the selection of external vendors including a copy of the vendor oversight programme.

5.0.21 Other miscellaneous documentations such as publications, end-of-trial notifications, archiving etc. should also be maintained in the TMF as appropriate.

5.0.22 The TMF should be archived following study conclusion in accordance with Trust, Sponsor and regulatory requirements (see SOP-17).

5.0.23 Where WHHT is sponsoring a multicentre trial, the WHHT coordinating trial team should ensure that a site-specific TMF (site level) is set up and maintained during the course of the study (see appendix 2.0,3.0 and 4.0).

6.0 RELATED DOCUMENTS

- Standard Operating Procedures Working Group Terms of Reference
- Membership of Standard Operating Procedures Working Group
- SOP-02- SAEs (Sponsored)
- SOP-04- Informed Consent
- SOP-05- SAEs (Hosted)
- SOP-07- Research Staff Training
- SOP-17- Archiving

7.0 APPENDICES

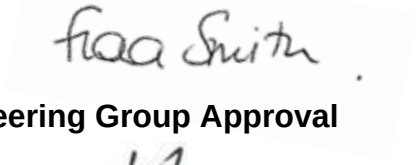
Appendix 1.0 - Definitions
Appendix 2.0 - Sample Trial Master File Contents
Appendix 3.0 - Masterfile Checklist
Appendix 4.0 - Guidance Note on Site File Documentation
Appendix 5.0 - File Note Template

8.0 VERSION HISTORY

Revision Chronology:		
Version Number	**Effective Date**	**Reason for Change**
SOP-06-07	**October 2021**	1. Change from general Standard Operating Procedures (gSOP) to SOP 2. Removal of the '10.0 Agreement' from the template - all agreement signatures will be collated on a new 'SOP Signature Sheet Document' 3. Other minor changes and clarifications of terms following review
gSOP-06-06	**October 2017**	Minor amendments following review
gSOP-06-05	**1/10/2015**	Minor amendments following dissolution of consortium
gSOP-06-04	**07/05/2014**	Minor amendments following review
gSOP-06-03		SOP amended for implementation at WHHT
gSOP-06-02 (MVCC)		SOP amended for implementation at MVCC
gSOP-06-02 (superceding gSOP-06-01)		Section 5.12 a section has been added stating that where RM/ICR is sponsoring a multi-centre study, the research team should maintain a site-file per site containing all essential documents.

9.0 AUTHORSHIP & APPROVAL

Author

Signature  **Date** 28/10/2021

R & D Steering Group Approval

Signature  **Date** 28/10/2021

Appendix 1: Definitions

Adverse Event (AE)
An unfavourable outcome that occurs during or after the use of a drug or other intervention, but is not necessarily caused by it.

Case Report Form (CRF)
A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject.

Chief Investigator (CI)
The investigator with overall responsibility for the research. In a multi-site study, the CI has co-ordinating responsibility for research at all sites. All applications for ethical review should be submitted by the CI. For Trust sponsored trials, the CI had been delegated the pharmacovigilance responsibility for identification, recording and reporting of safety events, including submission of Development Safety Update Reports (DSURs) to the MHRA and REC.

Clinical Trial
A clinical study in which participants are assigned to receive one or more interventions (or no intervention) so that researchers can evaluate the effects of the interventions on biomedical or health-related outcomes. The assignments are determined by the study protocol. Participants may receive diagnostic, therapeutic, or other types of interventions. A Study Type.

Clinical Trial of Investigational Medicinal Product (CTIMP)
A clinical trial that is within the scope of the UK Medicines for Human Use (Clinical Trials) Regulations 2004. An investigation in human subjects, other than a non-interventional trial, intended: a) to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more medicinal products, b) to identify any adverse reactions, or c) to study absorption, distribution, metabolism and excretion, with the object of ascertaining the safety and/or efficacy of those products.

Good Clinical Practice (GCP)
Good Clinical Practice is a set of internationally recognised ethical and scientific quality requirements which must be observed for designing, conducting, recording and reporting clinical trials that involve the participation of human subjects.

International Conference on Harmonisation (ICH)
International Conference for Harmonisation, a collaboration between regulators and the pharmaceutical industry in Europe, the United States and Japan to establish common standards for clinical trials. ICH GCP is a widely recognised standard for Good Clinical Practice in clinical trials.

Investigational Medicinal Products (IMP)
A pharmaceutical form of an active substance or placebo being tested, or to be tested, or used, or to be used, as a reference in a Clinical Trial, and includes a medicinal product which has a marketing authorisation but is, for the purposes of the trial - a) used or assembled (formulated or packaged) in a way different from the form of the product authorised under the authorisation, b) used for an indication not included in the summary of product characteristics under the authorisation for that product, or c) used to gain further information about the form of that product as authorised under the authorisation.

MHRA Clinical Trial Authorisation (CTA)
This is the authorisation from the Medicines and Healthcare products Regulatory Agency (MHRA) to conduct a Clinical trial of an investigational medicinal product (CTIMP). No CTIMP can commence in the

UK without both a CTA and a favourable ethical opinion. Applications to the MHRA and the Research Ethics Committee (REC) may be made in parallel.

Pharmacovigilance
The science relating to the detection, assessment, understanding and prevention of the adverse effects of medicines.

Principal Investigator (PI)
The investigator responsible for the research site. There should be one PI for each research site. In the case of a single-site study, the chief investigator and the PI will normally be the same person.

Serious Adverse Event (SAE) or Serious Adverse Reaction (SAR)
Any adverse event or adverse reaction that results in:

- death
- is life-threatening*
- requires hospitalisation or prolongation of existing hospitalisation
- results in persistent or significant disability or incapacity
- or is a congenital anomaly or birth defect

Comment: Medical judgement should be exercised in deciding whether an adverse event/reaction should be classified as serious in other situations. Important adverse events/reactions that are not immediately life-threatening or do not result in death or hospitalisation, but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed in the definition above, should also be considered serious.

* Life-threatening in the definition of a serious adverse event or serious adverse reaction refers to an event in which the subject was at risk of death at the time of the event. It does not refer to an event which hypothetically might have caused death if it were more severe.

Site File
Site Files are held by the PI at sites and contain copies of the essential documents, local approvals, signed consent forms and completed data forms.

Suspected Unexpected Serious Adverse Reaction (SUSAR)
An adverse reaction that is both unexpected (not consistent with the applicable product information) and also meets the definition of a Serious Adverse Event/Reaction.

The Medicines & Healthcare products Regulatory Agency (MHRA)
The MHRA is the competent authority for the UK in relation to the Directive 2001/20/EC and the Clinical Trials Regulations, and for Medical Devices, the competent authority in relation to the Medical Devices Regulations 2002.

The Regulations
Medicines for Human Use (Clinical Trial) Regulations 2004 transposed the EU Clinical Trials Directive into UK legislation, as Statutory Instrument 2004 no 1031. This became effective on the 1st May 2004. An

amendment to implement Directive 2005/28/EC was made to the Regulations as Statutory Instrument 2006 no 1928.

Trial Master File

The Trial Master File contains all essential documents held by the sponsor/Chief Investigator which individually and collectively permits the evaluation of the conduct of a trial and the quality of the data produced.

Appendix 2: Sample Trial Master File Contents

Essential documents required for Trial Master File	
1	**Trial Summary**
2	**Version control log**
3	**Contact details sheet**
Trial Specific Documentation	
6	Current approved protocol with signatures
7	Approved Patient Information Sheet (PIS), Informed Consent Form, GP Letter
8	Previous versions of protocol(s), PIS, Informed Consent Form, GP Letter
9	Study specific Standard Operating Procedures
Sponsorship and NHS Permission	
10	Trust Approval Letter
11	Letter of acceptance of sponsorship
12	Peer Review
13	Sponsorship delegation log
14	Project Management Delegation Log
15	Risk Assessment and superseded versions
Site Personnel	
16	Up-to-date, signed and dated CVs and GCP training records
17	Delegation Log

Finance	
18	Grant Application
19	Clinical Trial Agreement / Funding agreement letters
20	Finance correspondence: funder / contracts
21	Indemnity certificates / policy
22	Site Agreements
23	Research Account statements
24	Invoices
25	Finance correspondence with sites
26	Other finance correspondence other than contracts
MHRA and Ethics	
27	EUDRACT number
28	HRA correspondence
29	Adoption onto the NIHR portfolio
30	Ethics application including correspondence
31	Favourable Ethical Approval letter
32	MHRA application including correspondence
33	Clinical Trial Authorisation letter
34	Copy of the Annual Progress Report(s) to Ethics

35	Copy of the end of trial notification form and report sent to Ethics & MHRA
Amendments	
36	Amendments to ethical approval, a separate bundle of documents filed in chronological order for each amendment comprising copies of: 1) all the amended documentation 2) approval – Ethics, MHRA, HRA, R&D (as required)
37	Correspondence regarding the amendment
Pharmacovigilance	
38	Investigator's Brochure (IB) and/or Summary of Product Characteristics (SmPC) and updates
39	Pharmacovigilance SOP inc blank SAE forms
40	SAE reports
41	SUSAR reports
42	DSUR reports
43	Procedure for randomisation, unblinding and code break (if applicable)
44	Details of testing
45	Details of any code breaks
46	Details of any Protocol non-compliance or Serious Breach of protocol
47	Details of any Urgent Safety Measures
48	Notification of sponsors to Investigators of safety information
49	Copies of any adverse event reports made under the normal reporting procedures used by the Trust

Pharmacy	
50	Quality Agreement
51	Instructions for handling IMP (if not included in protocol)
52	Sample of label/ superseded versions of label (if applicable)
53	Shipping records, inc. ordering forms (if applicable)
54	IMP accountability
55	Termination: Documentation of IMP destruction
Data Collection, Analysis and Publication	
56	Data Management Plan
57	Database management
58	Sample case report forms (CRFs) + Copy of other approved data collection instruments (eg questionnaires)
59	Completed CRFs + data collection instruments
60	Data queries
61	Statistical Analysis Plan
62	Interim reports
63	Publication(s)
Monitoring	
64	Monitoring Plan

65	Audit Plan
66	Trial initiation Report
67	Monitoring Reports
68	Audit Reports
69	Close Down Report
70	Correspondence regarding monitoring and/or audit
Meeting	
71	Project team meetings
72	Project team correspondence
73	Trial Steering Committee meeting Terms of Reference
74	Trial Steering Committee meeting minutes
75	Trial Steering Committee correspondence
76	Data Monitoring Committee Charter / Terms of Reference
77	Data Monitoring Committee meeting
78	Data Monitoring Committee correspondence
Laboratory	
79	Lab accreditation certificates
80	Normal values/ ranges

81	Record of retained tissue/ body samples (if any)
82	Material Transfer Agreements
Participant Logs and Consent Forms	
83	Screening/enrolment log (including subject identification list)
84	Signed Consent Forms
Other	
85	Copies of all other correspondence relating to the trial (excluding REC, MHRA and R&D) records of all significant phone conversations relating to trial

Appendix 3: Masterfile Checklist

Ref: Section 8, ICH Guidelines for Good Clinical Practice)

Before the Clinical phase of the Trial Commences

ICH GCP Ref.	Topic	Located in Principal Investigator file (Site File)	Located in Chief Investigator file (Trial Master File)	Located in R&D Office file
8.2.1	Investigator's Brochure	X	X	X (Front Page)
8.2.2	Signed protocol and amendments, if any, and sample Case Report Form (CRF)	X	X	X (Protocol & Amendments)
8.2.3	Information given to trial subject nformed consent form	X	X	X
	-Any other written documentation (for example GP Letter)	X	X	X
	-Advertisement for subject recruitment	X	X	X
8.2.4	Financial aspects of the trial	X	X	X
8.2.5	Insurance statement (where required)	X	X	X
8.2.6	Signed agreement between involved parties, eg:	X	X	X
	-investigator/ institution and sponsor	X	X	X
	-investigator/ institution and authority(ies) where required	X	X	
8.2.7	Dated, documented approval of Independent Ethics Committee of the following: -protocol and any amendments -CRF (if applicable) - informed consent form(s) -any other written information to be provided to the subject(s) - advertisement for subject recruitment (if used) -subject compensation (if any) -any other documents given approval/ favourable opinion	X	X	X

8.2.8	Independent Ethics Committee composition	X	X (where required)	
8.2.9	Regulatory Authority Authorisation (where required)	X (where required)	X (where required)	X (where required)
8.2.10	Curriculum vitae and other documents evidencing qualifications of investigator(s) and sub-investigator(s)	X	X	X (CI/ PI only)
8.2.11	Normal values/ranges for medical/laboratory/technical procedures and/or tests included in the protocol.	X	X	
8.2.12	Medical/laboratory/technical procedures/tests - certification or - accreditation or - established quality control and/or external quality assessment or -other validation (where required)	X (where required)	X	
8.2.13	Sample of label(s) attached to investigational medicinal product container(s)		X	
8.2.14	Instructions for handling of investigational medicinal product(s) and trial-related materials (if not in protocol or Investigator Brochure)	X	X	
8.2.15	Shipping records for investigational medicinal product(s) and trial related materials	X	X	
8.2.16	Certificate(s) of analysis of investigational product shipped		X	
8.2.17	Decoding procedures for blinded trials	X	X (third party if applicable)	

8.2.18	Master Randomisation List		X (third party if applicable	
8.2.19	Pre-trial monitoring report		X	X
8.2.20	Trial initiation monitoring report	X	X	X

During the clinical conduct of the trial

In addition to having on file the above documents, the following should be added to the files during the trial as evidence that all new relevant information is documented as it becomes available.

ICH GCP Ref.	Topic	Located in Principal Investigator file (Site File)	Located in Chief Investigator file (Trial Master File)	Located in R&D Office file
8.3.1	Investigator's Brochure updates	X	X	X (Front Page only)
8.3.2	Any revision to: -protocol/amendment(s) and CRF -informed consent form -any other written information provided to subjects (Patient Information Sheets)	X	X	X (Protocol, Informed Consent, Patient Information Sheet))
8.3.3	Dated, documented approval of Independent Ethics Committee of the following: -protocol amendment(s) -revisions of: - informed consent form - any other written information to be provided to the subject (Patient Information Sheets) - any other documents given approval -continuing review of trial (where required)	X	X	X

8.3.4	Regulatory Authority Authorisation where required for -protocol amendment(s) and other documents	X (where required)	X	X
8.3.5	Curriculum vitae for new investigator(s) and sub-investigator(s)	X	X	X (New CI/ PI only)
8.3.6	Updates to normal values/ranges for medical/laboratory/technical procedures and/or tests included in the protocol.	X	X	
8.3.7	Updates of medical/laboratory/technical procedures/tests --certification or - accreditation or - established quality control and/or external quality assessment or -other validation (where required)	X (where required)	X	
8.3.8	Documentation of investigational medicinal product(s) and trial-related materials shipment	X	X	
8.3.9	Certificates of analysis for new batches of investigational product		X	
8.3.10	Monitoring visit reports		X	X
8.3.11	Relevant communication other than site visits -letters/ meeting notes/ notes of telephone calls/ printed emails	X	X	
8.3.12	Signed informed consent forms	X		
8.3.13	Source documents	X		
8.3.14	Signed, dated and completed case report forms (CRF)	X (copy)	X (original)	

8.3.15	Documentation of CRF corrections	X (copy)	X (original)	
8.3.16	Notification by originating investigator to sponsor of serious adverse events and related reports	X	X	
8.3.17	Notification by sponsor and/or investigator, where applicable, to Regulatory Authority and Independent Ethics Committee of unexpected serious adverse drug reactions and of other safety information	X (where required)	X	X
8.3.18	Notification by sponsor to investigators of safety information	X	X	
8.3.19	Interim or annual reports to independent ethics committees and Authority	X	X (where required)	X
8.3.20	Subject screening log	X	X (where required)	
8.3.21	Subject identification code list	X		
8.3.22	Subject enrolment log	X		
8.3.23	Investigational medicinal products accountability at site	X	X	
8.3.24	Signature sheet	X	X	
8.3.25	Record of retained body fluids/tissue samples (if any)	X	X	

After completion or termination of trial

After completion or termination of the trial, all of the documents identified in sections 8.2 and 8.3 should be in the file together with the following:

ICH GCP Ref.	Topic	Located in Principal Investigator file (Site File)	Located in Chief Investigator file (Trial Master File)	Located in R&D Office file
8.4.1	Investigational medicinal product(s) accountability at site	X	X	
8.4.2	Documentation of investigational medicinal product destruction	X (if destroyed at site)	X	
8.4.3	Completed subject identification code list	X		
8.4.4	Audit certificate (if available)		X	
8.4.5	Final trial close-out monitoring report		X	X
8.4.6	Treatment allocation and decoding documentation		X	
8.4.7	Final report by investigator to Independent Ethics Committee where required	X		
8.4.8	Clinical study report	X (if applicable)	X	

Appendix 4: Guidance Note on Site File Documentation

For WHHT sponsored multicentre studies, the following documents are also expected to be included.

1. Copies of all completed consent forms should be maintained in the file or a file note should be added if forms are held elsewhere. The original (unless protocol requires electronic completion) clinical trials consent forms should be stored in the Site File in accordance with the WHHT SOP on consenting (SOP-04).

2. The Site File should contain all patient related information such as subject screening / recruitment logs and a record of retained tissue samples (or a file note included if these logs are held electronically). This must be current.

3. The Site File should also contain a file note explaining the source documentation. Source documents are the original documents related to the trial, to medical treatment and the history of the subject e.g. medical record, laboratory reports, scans etc. Source documents must be traceable. If documents are stored separately from the patient medical notes, and they belong to the source data, then a note should be made in the file.

4. Other documents to include in the Site Investigator File as applicable:

    - Decoding procedures for blinded trials
    - Copy of signed, dated and completed case report forms (CRF)
    - Documentation of CRF corrections (copy)
    - Notification by sponsor and/or investigator, where applicable, to Regulatory Authority and Independent Ethics Committee of unexpected serious adverse drug reactions and of other safety information (where required)
    - Interim or annual reports to independent ethics committees and Authority
    - Subject screening log (original)
    - Subject identification code list (original)
    - Subject enrolment log (original)
    - Completed subject identification code list (original)
    - Final report by investigator to Independent Ethics Committee (where required)

Please contact the R&D office for any further clarification.

Appendix 5: File Note Template

File Note

Study:	**Principal Investigator:**
Date:	**Time:**

Note:

Print Name .....

Signature .....Date.....

Role ……..