**Trial Delivery 01:**

**Research Documentation and File Management**

**IT IS THE RESPONSIBILITY OF ALL USERS OF THIS SOP TO ENSURE THAT THE CORRECT VERSION IS BEING USED**

All staff should regularly check the Research & Development Webpage for information relating to the implementation of new or revised versions. Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded version are promptly withdrawn from use unless notified otherwise by the SOP Controller.

The definitive version of all Gloucestershire Hospitals NHS Foundation Trust SOPs appear online. If you are reading this in printed form, check that the version number and date below is the most recent one as shown on the R&D website:

<http://www.gloshospitals.nhs.uk/en/About-Us/Research--Development>/

|  |  |
| --- | --- |
| **SOP reference:** | R&D SOP TD 01 |
| **Version:** | 4.0 |
| **Author:** | Janet Forkes |  |
| **Reviewed by Head of R&D** | Chantal Sunter |  |
|  06 /05 /2021 |
| **Implementation date of current version:** |  06 / 05 /2021 |
| **Date of Review:** |  01 / 05 / 2023 |

The Gloucestershire Hospitals NHS Foundation Trust wishes to acknowledge York Hospitals NHS Foundation Trust and University Hospitals Bristol NHS Foundation Trust who gave permission to use their templates in the development of these SOPs.

© Gloucestershire Hospitals NHS Foundation Trust 2021

No part of this document may be reproduced or transmitted in any form or by any means without the prior permission of the Gloucestershire Hospitals NHS Foundation Trust

**Version History Log**

This area will be updated with details of all changes made to the SOP whether due for full review or not.

|  |  |  |
| --- | --- | --- |
| **Version** | **Details of Change** | **Date Implemented** |
| 1.0 | Review and update along with reorganisation into the Gloucestershire R&D Consortium suite of SOPs previously SOP 09 | 01/11/2014 |
| 2.0 | Update on HRA and electronic data  | 01/02/2017 |
| 3.0 | Rebranding to GHNHSFT and updating of contact details  | 31/03/2018 |
| 4.0 | Updating of Trust intranet linkUpdating of site file contents page to include: section on unblinding of treatment in a blinded trialGCP certificates within the CV sectionClarification of source data/ use of source data forms Addition of electronic investigator site files  | 06/05/2021 |
|  |  |  |
|  |  |  |
|  |  |  |

This SOP will be reviewed every two years unless changes to any relevant legislation require otherwise

**Contents**

 **Page No.**

1. **Introduction, Background and Purpose 4**
2. **Who should use this SOP? 4**
3. **When this SOP should be used 4**
4. **Trial Master File, Investigator Site file, Pharmacy File 5**
	1. **.1 Indexing TMF 5**

**4.1.2 Indexing ISF (paper and electronic) 6**

**4.1.3 Indexing R&D Study Files 6**

* 1. **Essential documents 6**
1. **Source data, CRF and e-CRF completion 8**

**5.1 Source data 8**

**5.2 CRFs and electronic CRFs 9**

1. **File management 9**
2. **Storage 10**
3. **Version Control 10**
4. **Storage 10**
5. **Other SOPs and documents 10**

**Appendix 1: GCP Guidelines E8 12**

**Appendix 2a: Suggested Investigator Site File Contents 16**

**Appendix 2b: Suggested electronic Investigator Site File Contents 18**

**Appendix 3: Site File Note Template 19**

**Appendix 4 Trial Specific Training Log 20**

**Appendix 5: Study Specific Tracking Log 21**

**Appendix 6: Treatment Allocation Log 22**

**Appendix 7: Appointment Checklist 23**

**Appendix 8: CRF completion guidelines 24**

**Appendix 9: R&D Governance Study File Guidelines 27**

**Appendix 10: Example of Trial Specific Source Data Form 29**

**Schematic view of types of research documentation storage 30**

1. **Introduction, Background and Purpose**

Maintenance of the correct and appropriate documentation in a manner suitable for managing the conduct of the trial and enabling evaluation by audit and inspection is essential for GCP compliance.

It must be possible to reconstruct the conduct of the trial at all stages from:

* set up (prior to patient recruitment),
* during patient recruitment and direct involvement
* for some time after its completion

from the documentation which is filed and retained within:

* the Trial Master File (TMF)
* Investigator Site File (ISF)
* Trial Pharmacy File (TPF)
* Research and Development Study File (R&DSF)

from the perspective of :

* Sponsor/ CI
* PI and local research team
* Trust Research and Development Department (local research governance).

Trust policies and procedures must be adhered to in conjunction with this SOP and any that the Sponsor has written specifically for their trial. Any variations between SOPs from various sources should be discussed and decided upon before any trial activity starts at site.

1. **Who should use this SOP?**

All staff working on a trial should be familiar with the lay out and requirements of the file that is relevant to their role:

* + Chief Investigators (CIs) and trial co‐ordinators of clinical trials sponsored or co‐sponsored by the Trust;
	+ Principal Investigators (PIs) and research staff at sites where multi‐site studies sponsored or co‐sponsored by the Trust are being run;
	+ R&D office personnel, who manage the sponsorship of trials on behalf the Trust and support Trust hosted trials;
	+ PIs and research staff for externally‐sponsored trials “hosted” by the Trust.

1. **When this SOP should be used**

This SOP must be referred to as soon as a trial is being considered for adding to the Trust trial portfolio. This will ensure that the necessary procedures to secure the quality of every aspect of the trial shall be complied with.

In accordance with Good Clinical Practice (GCP) the Sponsor should ensure appropriately qualified individuals are responsible for the overall conduct of the clinical trial, handling the data, verifying the data, conducting the statistical analyses, and preparing the trial reports.

The Sponsor should normally delegate data management within a clinical trial to the CI. Where the CI further delegates data management to another member of the research team this should be clearly outlined on the Clinical Trial Delegation Log.

For hosted trials, the PI or Local Collaborator (LC) is responsible for delegating roles and responsibilities at the participating site documented on the delegation log.

1. **Trial Master File, Investigator Site File and Trial Pharmacy File**

**4.1.1 Indexing TMF**

The MHRA advise typically organising Sponsor files as follows:

|  |  |
| --- | --- |
| Global level files | Documents in this file are relevant to the conduct of the trial at any site ie Investigator Brochure. |
| Country level files | Documents in this file are country – specific and are relevant to the conduct of the trial at any site in that country |
| Site level files | Documents in this file are specific to the conduct of the trial at a particular investigator site ie, protocol signed by PI and delegation log |

Potential document sources for the Sponsor TMF include:

* Trial pharmacovigilance documentation (SAE cases and reconciliation)
* Trial medication blinding/ unblinding process where applicable
* Trial specific IMP documentation ( QP certification, certificates of analysis, shipping records)
* Regulatory documentation
* Trial contracts
* Clinical operations documentation
* Data management documentation
* R&D office documentation
* Vendor selection/ oversight documents
* Data management documentation
* Trial specific training records
* Trial specific computer system validation documentation
* Statistics documentation
* GDPR considerations

**4.1.2 Indexing ISF ( paper and electronic)**

The Site File Index provided by the Sponsor/TU should be used. If, because of local requirements additional sections are needed to make essential documentation storage more practical, the Sponsor/TU will be informed of the proposed format and copies of the ISF or eISF provided with annotations.

If a Sponsor does not provide a Site File/ Site File Index then the Trust proforma template will be used (based on NIHR templates – Appendix 2a and 2b)

**4.1.3 Indexing R&D Study Files**

The Trust indexes for both paper files and electronic files should be used for all types of research (see Appendix 9)

**4.2 Essential Documents**

Essential documents are those records created from following trial procedures as well as those listed in guidance relating to the conduct of the trial and should be retained to demonstrate compliance with ICH GCP (see Appendix1).

Below are listed the minimum essential documents listed in E8 of GCP Guidelines:

* Investigator’s Brochure
* Signed protocol and amendments, if any, and sample case report form (CRF)
* Information given to trial subject
	+ Informed consent form (including all applicable translations)
	+ Any other written information
	+ Advertisement for subject recruitment (if used)
* Financial aspects of the trial
* Insurance statement (where required)
* Signed agreement between involved parties e.g.:
	+ investigator/institution and sponsor
	+ investigator/institution and CRO
	+ sponsor and CRO
	+ investigator/institution and authority(ies) (where required)
* Dated, documented approval/ favourable opinion of Trust R&D department (Institutional Review Board) and Independent Ethics Committee (REC) of the following:
	+ protocol and any amendments
	+ CRF (if applicable)
	+ Participant Information Sheet/ 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
* Trust R&D department (Institutional Review Board) and Independent Ethics Committee (REC) composition
* Regulatory authority (MHRA) Authorisation/ approvals
* HRA
* Notification of protocol (where required)
* Curriculum Vitae and/ or other relevant documents evidencing qualifications of investigator(s) and sub-investigator(s)(signed and dated, updated annually)
* GCP certificates
* Normal values/ range(s) for medical / laboratory/ technical procedure(s) and/ or test(s) included in the protocol, (signed and dated by Laboratory Manager)
* Medical / laboratory/ technical/ procedures/ tests
	+ certification or
	+ accreditation or
	+ established quality control and/or external quality assessment or
	+ other validation (where required)
* Sample of label(s) attached to investigator product container(s)
* Instructions for handling of investigational product(s) and trial – related materials (if not included in protocol or Investigator’s Brochure)
* Shipping records for investigational product(s) and trial related material(s)
* Certificate(s) of analysis of investigational product(s) shipped
* Decoding procedures for blinded trials
* Master randomisation list
* Pre-trial monitoring report
* Trial initiation monitoring report

The list on the previous page is not exhaustive and has some key omissions, below are some or all of which will be required to demonstrate GCP compliance :

* IMP handling
	+ Qualified Person (QP) certification,
	+ green-light document to release and ship IMP(s)
* electronic database documentation
* trial specific training given by PI to research staff
* centralised records relevant to a number of trials
	+ written procedures
	+ staff training records
	+ maintenance and calibration records of equipment used in a trial

Therefore an assessment of all activities carried out within a trial will be undertaken to determine whether they need to be documented to enable reconstruction of the trial conduct from the paperwork alone. Consideration will also be given to centrally stored electronic data, for example, Trust Mandatory Training/ other staff training records. These must be stored in accordance with Trust IT policies and guidelines and site file notes placed in the TMF, SIF and TPF to indicate how these may be accessed by appropriately authorised Trust staff.

1. **Source data, CRF and e-CRF**

**5.1 Source data**

Patient information where it is recorded for the first time is defined as source data. Trial participants’ notes, hospital / clinical records in any format (paper or electronic) are source documentation for source data. Any format used must permit the reconstruction of the clinical care given to the participant and describe participant-specific events that have occurred during the conduct of the trial. Where copies are provided, they must be certified by the provider.

Key events to be recorded in trial participants’ notes include:

* Eligibility decision and any required supporting information not available elsewhere within the notes (signed and dated by PI or Co-investigator)
* Provision of subject information sheet/ invitation to consider the trial (including version and date)
* Receiving informed consent(including version and date)
* Randomisation or trial entry
* Trial visits or follow up phone calls required by the protocol
* Treatment and dosing decisions, including changes to concomitant medication
* Reconfirmation of consent
* Any trial–related decisions relating to the clinical care of the subject
* Adverse events, their seriousness, causality and severity
* Withdrawal, termination or end-of trial involvement including any protocol defined follow up.

Where trial specific templates are provided by the Sponsor or devised by the research team to capture trial specific information, completed sheets should be retained within the hospital notes and blank versions filed in the site file. ( See appendix 10)

The definition of source data must be agreed with the Sponsor during trial set up and documented so that future Sponsor monitoring for Source Data Verification purposes can be facilitated with the minimum of additional work for the research team.

The recording of data will be:

* Completed contemporaneously
* Signed and dated by the person making the entry. This may be wet ink signature or an appropriately controlled electronic signature
* If retrospective entries or annotations are made then these should be obvious and will be signed and dated with the date the entries where added – electronic entries must have a clear audit trail
* All entries must include the details of the staff involved in the consultation and are countersigned where decisions have been made by staff other than the person making the entry. For example, a nurse is making the entry about dosing when the clinician decides to amend the dose – this then will need to be countersigned by the treating clinician.
* Where data is stored centrally on a trust computer system, the clinician must still be able to demonstrate that they have assessed these reports during the course of the trial.

**5.2 Case Report Forms (CRFs) and electronic - Case Report Forms (e-CRF)**

CRFs should be completed according to the specifications of each study by a delegated member of the research team, who has received training on the data collection requirements of the specific trial / study. CRFs should be completed in a timely fashion and, where possible within one month of the event taking place, unless another time frame is specified in the protocol (see Appendix 8 for Trust guidelines on completion CRFs). Access to eCRF systems must be in place for the PI as well as the research nurses/ co-ordinators and data officers.

1. **File management**

TMF, ISF, TPF and R&DSF should all be maintained contemporaneously. All documents must be filed in date order from most recent date to oldest date.

Copies of all correspondence between the site staff, Sponsors and trial participants must be retained. This includes printing off emails, faxes (including receipts), with highlighting of pertinent information or adding numbering to the documents so that it is easier to reconstruct the flow of information.

The research team must check whether a trial participant has more than one set of notes within the Trust, for example general hospital notes and departmental specific notes (maternity, haematology, oncology, ophthalmology). Notification that the patient is a participant in a trial must be included in all notes so that all health care teams are alerted to the patient’s involvement in a trial.

1. **Format**

The format of the documentation and its storage will be agreed with the Sponsor at trial set up. It therefor may be that the ISF is all paper based, or a combination of paper and electronic, or completely electronic.

Where a Sponsor provides an ISF format this should be used, but if one isn’t provided then the Trust proforma should be given to the Sponsor for sign off by them and used throughout the life of the trial. (See Appendix 2a and 2b)

1. **Version Control**

Systems should be in place for version control of documents. A chronology of amendments will be kept on file that records all the amendments submitted and the documents that they relate to. Old versions of documents should be retained on file alongside the new versions with the old versions, clearly marked as superseded.

1. **Storage**

Documents contained in the TMF, ISF and R&DSF may be original regulatory approvals and confidential information. The files should therefore be stored in a secure place with restricted access. A locked drawer, cupboard or dedicated room is recommended, depending on the size of the project.

Before, during and after the conduct of the research, it is useful to bear in mind the archiving of the documentation. Documentation may need to be retrieved at a future stage and so a catalogue or index of documents should be maintained to ensure this process is not burdensome. (Further details are given in the R&D SOP TD 04 End of Trial Procedures and Close Down and R&D SOP TD05 Trial Archiving.)

* 1. Where a study is not submitted electronically, digital versions of the documents should be requested from the sponsor and an Electronic Folder set up as above.
	2. If the documents are not available electronically at all the paper copies provided will be scanned and stored in the usual manner.
	3. The cover and spine of the physical R&D file should contain the same information as recorded on the R&D Number Allocation List
1. **Other SOPs and documents**

R&D SOP IR 01 Sponsorship

R&D SOP IR 02 Writing a protocol

R&D SOP RDVL 01 Scientific Review

R&D SOP RDVL 02 Application to the Trust for Sponsorship of a CTIMP

R&D SOP MR 01 Hosting CTIMPs and other Clinical Trials

R&D SOP MR 02 Confirmation of capacity and capability

R&D SOP TD 02 Training

R&D SOP TD 03 Informed Consent

R&D SOP TD 03 End of trial procedures – Close Down

R&D SOP Ph 01 Periodic reporting to Research Ethics Committee and MHRA

R&D SOP Ph 02 Adverse Event and Reaction Reporting

R&D SOP Ph 03 Research Misconduct and Fraud

R&D SOP Ph 04 Non-compliance and Serious Breaches

1. **Records management**

[**http://glnt313/sites/ghnhsft\_policy\_library/NonClinPolices/B0259.pdf**](http://glnt313/sites/ghnhsft_policy_library/NonClinPolices/B0259.pdf)

1. **Clinical and non clinical information systems management policy** [**http://glnt313/sites/ghnhsft\_policy\_library/NonClinPolices/B0676.pdf**](http://glnt313/sites/ghnhsft_policy_library/NonClinPolices/B0676.pdf)
2. **Health records** [**https://intranet.gloshospitals.nhs.uk/departments/corporate-division/health-records/**](https://intranet.gloshospitals.nhs.uk/departments/corporate-division/health-records/)
3. **Fax policy:** [**http://glnt313/sites/ghnhsft\_policy\_library/ActionCards/B0591%20ITS6.pdf**](http://glnt313/sites/ghnhsft_policy_library/ActionCards/B0591%20ITS6.pdf)
4. **Maternity Health records** [**http://glnt313/sites/ghnhsft\_policy\_library/NonClinPolices/B0556.pdf**](http://glnt313/sites/ghnhsft_policy_library/NonClinPolices/B0556.pdf)
5. **Information Governance Policy** [**http://glnt313/sites/ghnhsft\_policy\_library/NonClinPolices/B0413.pdf**](http://glnt313/sites/ghnhsft_policy_library/NonClinPolices/B0413.pdf)
6. **Data Quality** [**http://glnt313/sites/ghnhsft\_policy\_library/NonClinPolices/B0406.pdf**](http://glnt313/sites/ghnhsft_policy_library/NonClinPolices/B0406.pdf)
7. **Consent Policy** [**http://glnt313/sites/ghnhsft\_policy\_library/ClinPolices/A0297.pdf**](http://glnt313/sites/ghnhsft_policy_library/ClinPolices/A0297.pdf)
8. **IT Security** [**http://glnt313/sites/ghnhsft\_policy\_library/NonClinPolices/B0591.pdf**](http://glnt313/sites/ghnhsft_policy_library/NonClinPolices/B0591.pdf)
9. **E-Communications and Internet Use policy (including mobile phones and social networking)** [**http://glnt313/sites/ghnhsft\_policy\_library/NonClinPolices/B0590.pdf**](http://glnt313/sites/ghnhsft_policy_library/NonClinPolices/B0590.pdf)
10. **Quality Assurance and Quality Improvement Process** [**http://glnt313/sites/ghnhsft\_policy\_library/NonClinPolices/B0679.pdf**](http://glnt313/sites/ghnhsft_policy_library/NonClinPolices/B0679.pdf)
11. **EMA guidance to assist sponsors and investigators to comply with the requirements of the Clinical Trials Regulation (EU) No 536/2014.**[**https://www.ema.europa.eu/documents/scientific-guideline/draft-guideline-good-clinical-practice-compliance-relation-trial-master-file-paper/electronic-content-management-archiving-audit-inspection-clinical-trials\_en.pdf**](https://www.ema.europa.eu/documents/scientific-guideline/draft-guideline-good-clinical-practice-compliance-relation-trial-master-file-paper/electronic-content-management-archiving-audit-inspection-clinical-trials_en.pdf)
12. **EMA expectation on source data** [**https://www.ema.europa.eu/documents/regulatory-procedural-guideline/reflection-paper-expectations-electronic-source-data-data-transcribed-electronic-data-collection\_en.pdf**](https://www.ema.europa.eu/documents/regulatory-procedural-guideline/reflection-paper-expectations-electronic-source-data-data-transcribed-electronic-data-collection_en.pdf)
13. **MHRA position statement** [**https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\_data/file/470228/Electronic\_Health\_Records\_MHRA\_Position\_Statement.pdf**](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/470228/Electronic_Health_Records_MHRA_Position_Statement.pdf)

**Appendix 1: GCP Guidelines E8**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|   | Title of Document | Purpose | Located in Files of |   |
|   |  |   | Investigator/ | Sponsor |
|   |   |   | Institution |   |
| 8.2.1 | INVESTIGATOR’S BROCHURE | To document that relevant and current scientific information about the investigational product has been provided to the investigator | X | X |
| 8.2.2 | SIGNED PROTOCOL AND AMENDMENTS, IF ANY, AND SAMPLE CASE REPORT FORM (CRF) | To document investigator and sponsor agreement to the protocol/amendment(s) and CRF | X | X |
| 8.2.3 | INFORMATION GIVEN TO TRIAL SUBJECT | To document the informed consent | X | X |
|   | - INFORMED CONSENT FORM |  |  |
|   | (including all applicable translations) |  |  |
|   | - ANY OTHER WRITTEN INFORMATION | To document that subjects will be given appropriate written information (content and wording) to support their ability to give fully informed consent | X | X |
|   | - ADVERTISEMENT FOR SUBJECT RECRUITMENT (if used) | To document that recruitment measures are appropriate and not coercive | X |  |
| 8.2.4 | FINANCIAL ASPECTS OF THE TRIAL | To document the financial agreement between the investigator/institution and the sponsor for the trial | X | X |
| 8.2.5 | INSURANCE STATEMENT | To document that compensation to subject(s) for trial-related injury will be available | X | X |
|   | (where required) |   |   |   |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| 8.2.6 | SIGNED AGREEMENT BETWEEN INVOLVED PARTIES, e.g.: | To document agreements |  |  |
|   | - investigator/institution and sponsor |   | X | X |
|   | - investigator/institution and CRO |   | X | X |
|   | - sponsor and CRO |   |  | (where required) |
|   | - investigator/institution and authority(ies) (where required) |   | X | X |
| 8.2.7 | DATED, DOCUMENTED APPROVAL/FAVOURABLE OPINION OF INSTITUTIONAL REVIEW BOARD (IRB) /INDEPENDENT ETHICS COMMITTEE (IEC) OF THE FOLLOWING: | To document that the trial has been subject to IRB/IEC review and given approval/favourable opinion. To identify the version number and date of the document(s) | X | X |
|  | - 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 |   |   |   |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| 8.2.8 | INSTITUTIONAL REVIEW BOARD/INDEPENDENT ETHICS COMMITTEE COMPOSITION | To document that the IRB/IEC is constituted in agreement with GCP | X | X |
| 8.2.9 | REGULATORY AUTHORITY(IES) | To document appropriate authorisation/approval/notification by the regulatory authority(ies) has been obtained prior to initiation of the trial in compliance with the applicable regulatory requirement(s) | X | X |
|   | AUTHORISATION/APPROVAL/ |   | (where required) | (where required) |
|   | NOTIFICATION OF PROTOCOL |   |  |  |
|   | (where required) |   |  |  |
| 8.2.10 | CURRICULUM VITAE AND/OR OTHER RELEVANT DOCUMENTS EVIDENCING QUALIFICATIONS OF INVESTIGATOR(S) AND SUB-INVESTIGATOR(S) | To document qualifications and eligibility to conduct trial and/or provide medical supervision of subjects | X | X |
| 8.2.11 | NORMAL VALUE(S)/RANGE(S) FOR MEDICAL/ LABORATORY/TECHNICAL PROCEDURE(S) AND/OR TEST(S) INCLUDED IN THE PROTOCOL | To document normal values and/or ranges of the tests | X | X |
| 8.2.12 | MEDICAL/LABORATORY/TECHNICAL PROCEDURES /TESTS | To document competence of facility to perform required test(s) , and support reliability of results | X | X |
|   | - certification or |   | (where required) |  |
|   | - accreditation or |   |  |  |
|   | - established quality control and/or external quality assessment or |   |  |  |
|   | - other validation (where required) |   |  |  |
| 8.2.13 | SAMPLE OF LABEL(S) ATTACHED TO INVESTIGATIONAL PRODUCT CONTAINER(S) | To document compliance with applicable labelling regulations and appropriateness of instructions provided to the subjects |  | X |
| 8.2.14 | INSTRUCTIONS FOR HANDLING OF INVESTIGATIONAL PRODUCT(S) AND TRIAL-RELATED MATERIALS | To document instructions needed to ensure proper storage, packaging, dispensing and disposition of investigational products and trial-related materials | X | X |
|   | (if not included in protocol or Investigator’s Brochure) |   |  |  |
| 8.2.15 | SHIPPING RECORDS FOR INVESTIGATIONAL PRODUCT(S) AND TRIAL-RELATED MATERIALS | To document shipment dates, batch numbers and method of shipment of investigational product(s) and trial-related materials. Allows tracking of product batch, review of shipping conditions, and accountability | X | X |
| 8.2.16 | CERTIFICATE(S) OF ANALYSIS OF INVESTIGATIONAL PRODUCT(S) SHIPPED | To document identity, purity, and strength of investigational product(s) to be used in the trial |  | X |
| 8.2.17 | DECODING PROCEDURES FOR BLINDED TRIALS | To document how, in case of an emergency, identity of blinded investigational product can be revealed without breaking the blind for the remaining subjects’ treatment | X | X |
|  |   |   |  | (third party if applicable) |
| 8.2.18 | MASTER RANDOMISATION LIST | To document method for randomisation of trial population |  | X |
|  |   |   |  | (third party if applicable) |
| 8.2.19 | PRE-TRIAL MONITORING REPORT | To document that the site is suitable for the trial (may be combined with 8.2.20) |  | X |
| 8.2.20 | TRIAL INITIATION MONITORING REPORT | To document that trial procedures were reviewed with the investigator and the investigator’s trial staff ( may be combined with 8.2.19) | X | X |

**Appendix 2 Suggested Site File Contents (paper and electronic)**

**2a)**

**Investigator Site File Contents**

|  |  |  |  |
| --- | --- | --- | --- |
| **SECTION** | **TITLE** | **CONTENT/COMMENTS** | **SIGN & DATE WHEN COMPLETE** |
| 1 | Protocol / amendments | * Current protocol
* Protocol amendments
* Historical protocols
* Unblinding instructions and contact details (when applicable)
 |  |
| 2 | Sample CRF/QLQ Diary Cards | If too bulky to put in file place file note in this section stating where it can be found |  |
| 3 | Regulatory approvaldocumentation |  |  |
| 4 | Site signature /responsibility log |  |  |
| 5 | Curriculum VitaeGCP certificates | CVs for all research personnel listed in the signature/responsibility logGCP training specific to the level of freedom to act |  |
| 6 | Patient Identification formPatient recruitment /screening form  |  |  |
| 7 | Sample of current and all historical Patient Information / Informed Consent form and GP LetterCompleted patient Information and Informed Consent Forms |  |  |
| 8 | Correspondence  | File in chronological order all correspondence to/from the coordinating research body. File email communicationInclude a separate section here for newsletters |  |
| 9 | Minutes from Initiation meetingMonitoring logsNotes of telephone calls | If the study is not monitored state this in a file note in this sectionDocument telephone call in relation to agreements or significant discussions regarding trial administration, trial conduct, adverse events or protocol violations |  |
| 10 | Blank serious adverse event forms and guidelines for their completion |  |  |
| 11 | Notification of serious adverse events and/or safety reports | By Investigator to co-ordinating research bodyBy co-ordinating research body to InvestigatorBy 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) |  |
| 13 | Instructions for handling trial medication and trial related materialsShipping 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 |  |
| 14 | Clinical Laboratory | Laboratory normal reference ranges (including revisions)Laboratory certificate(s) |  |
| 15 | Contracts  | Investigator Commitment Statement/Study AcknowledgementIndemnityConfidentialityClinical Trial Agreement including financial details.Completed and signed FDA 1572 form (if applicable)Financial disclosure letter (if applicable) |  |
| 16 | Investigator’s Brochure Safety alert letters/Updates |  |  |
| 17 | Completed Data Queries |  |  |
| 18 | Study Training Materials |  |  |
| 19 | Miscellaneous (specify)……. |  |  |

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

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

**2b) Electronic Investigator Site File**



**Appendix 3 Site file note**

**File Note**

|  |  |
| --- | --- |
| **Study:**  | **Principal Investigator:** |
| **Date:**  | **Time:**  |

Print Name ...................................................................................................

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

Role ………………………………………................................................................

**Appendix 4 Trial Specific Training Log**

|  |  |  |  |
| --- | --- | --- | --- |
| **Topic** | **Date** | **Training given by** | **Training given to** |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |

**[Study Title] Training Log**

**Appendix 5 Study Specific Tracking Log**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **SIGNATURE** |  |  |  |  |  |  |
| **DATE RETURNED** |  |  |  |  |  |  |
| **SIGNATURE** |  |  |  |  |  |  |
| **LOCATION** |  |  |  |  |  |  |
| **DATE TAKEN** **FOR USE** |  |  |  |  |  |  |
| **VERSION** |  |  |  |  |  |  |
| **DOCUMENT** |  |  |  |  |  |  |

**Appendix 6 Trial Specific Treatment Allocation Log**

**Treatment Allocation Log**

|  |  |
| --- | --- |
| **Study:** | **Patient ID:** |

|  |  |  |  |
| --- | --- | --- | --- |
| **Date** | **Treatment** | **Dose** | **Comments** |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |

**Appendix 7: Appointment Checklist**

 **STUDY: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

***Patient Details***

**STUDY ID: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Appointment Date |  |  |  |  |  |  |
| Time |  |  |  |  |  |  |
| Visit No |  |  |  |  |  |  |
| Medical/Dr |  |  |  |  |  |  |
| Annual Review |  |  |  |  |  |  |
| Notes |  |  |  |  |  |  |
| Bloods |  |  |  |  |  |  |
| Meds |  |  |  |  |  |  |
| PFT |  |  |  |  |  |  |
| ECG |  |  |  |  |  |  |
| Echo / CIMT |  |  |  |  |  |  |
| Exam - Eye / E.Photos |  |  |  |  |  |  |
| Transport |  |  |  |  |  |  |
| Interpreter |  |  |  |  |  |  |
| GP letter |  |  |  |  |  |  |
| In Diaries |  |  |  |  |  |  |
| Comments |  |  |  |  |  |  |

**Appendix 8: CRF completion guidelines**

Case Report Forms should be completed as soon as possible and no more than a month after the trial participant’s visit or sooner if stipulated by the Sponsor.

**Paper CRF’S**

* Always check you are using the **correct version** number of the CRF.
* Always use a **black ink** ballpoint pen.
* Writing should be in **block capitals** wherever possible and only written in the designated box or lined area.
* If the CRFs are printed on carbonless duplication paper, always make sure that a suitable separator is inserted under the form being completed. In addition, it is important to ensure that the bottom copy is legible before sending the top copy to the Trials Office. If necessary, a copy of the top copy should be made and retained. If the CRFs are only written on standard paper then ensure photocopies are kept. However photocopies of Quality of Life questionnaires should not be made and retained at site unless stipulated in the protocol.
* Ensure all entries are **accurate, legible** and **verifiable** with the source data in the medical record and that data is entered in accordance with CRF completion guidelines for that particular trial.
* Where source data forms (SDF’s) are used to collect the information required for a CRF it is important not to rely on this data solely but also to check all other forms of information such as notes, correspondence, clinic sheets, OPMAS annotations, laboratory results, PAS (for information regarding inpatient and outpatient visits), or other relevant hospital system such as APEX or Oasis, pharmacy and radiotherapy prescriptions. Where protocol visits are widely spaced, for example three monthly, all the information for the time between visits should be reviewed. Any discrepancies between the source data form and other information should be discussed with the person responsible for completing the SDF.
* Any discrepancies with source data should be checked with a member of the medical team and an explanation of the significance should be noted in the CRF and/or patient’s medical records. For laboratory values outside the laboratory’s reference range or some other range agreed with the study Sponsor, or if a value shows significant variation from one assessment to the next, this should be commented on and the significance noted in the CRF and/or patients medical records.
* **Never over-write an entry**. Corrections should be made as instructed by the TU, below are listed some examples:
* Corrections should be made on the data query forms sent out by the Trials Unit (TU) and not on the retained copy of the CRF unless stipulated by the TU. If the retained copy is amended/updated this must be recopied and sent to the TU to ensure that they have the most up to date version. Ensure any amendments to the CRF’s are signed and dated.
* In some cases CRF’s are amended by the TU (some trials have an SOP in place to make self-evident correction) these amended CRFs are sent from the TU and should be attached to the relevant CRF.
* If it becomes apparent that data has been omitted or entered incorrectly in a manner which will not trigger the Trial Unit to issue a data query then the Trial Unit should be advised of the correct data in the format which they specify e.g. by email. Original CRFs should not be amended unless instructed to do so.
* Cross out the incorrect entry with a single line so that it is still readable. Never use correction fluid or obliterate entries made on the CRF. Enter the correct data and initial and date the correction.
* The procedure to be followed for the resolution of data queries should be agreed with the study sponsor / TU and these should be completed by site staff in a timely fashion.
* The CRF must be **signed** where indicated, by the Principal Investigator or designee (as appropriate) to assert that he/she believes they are complete and correct.
* CRFs should be kept in a **secure location** during the course of the study. When CRFs have been completed they should be filed in a secure location with a file note in the site file to say where they are stored. When the study is closed to both recruitment and data collection CRFs should be archived, or stored according to the protocol.

**Electronic CRFs**

* **Training** should be completed as designated by TU before entering any electronic data.
* The SOP provided by the TU for inputting data/answering discrepancies / amending data should be adhered to.
* Discrepancies should be answered in a timely fashion in accordance with trial SOP.
* All data must be **saved prior to logging out**, as unsaved data will be lost.
* Electronic CRF data should be verified by a nominated person/trained member of staff to certify that the completed data is correct and in accordance with the patients source data, as stipulated in trial SOP.

**In General**

* Ensure data entry is as complete as possible without omissions for both paper and electronic CRFs. **It is impossible for personnel doing the data entry to interpret blank spaces. If data is unavailable write, for example, ‘*unknown’, ‘missing’, ‘test not done’,*** etc as defined by CRF Completion Guidelines (if applicable). Avoid using the ambiguous phrase, *‘not available’*.
* Unless requested by the protocol, CRF or TU, laboratory values should be entered without conversion from printed reports even if in multi-centre study units of measurement differ from centre to centre, this applies to both paper and electronic CRFs. The units used should be specified where they differ from those shown on the CRF. If hard copies of laboratory values are required protocol, measures should be followed in terms of removing personal identifiable information such as the patient’s full name.
* The patient’s identity should remain as confidential as possible at all times, providing only data requested by the TU. A record must be kept by the Investigator of patients in the study consisting of the patient’s full name and study number; this is the Subject Identification Log.

**Appendix 9 R&D Governance Study File Guidelines**

1. **Allocation of unique identifiers**

Immediately upon receipt of a new application, the study details will be added to the R&D allocation list for the appropriate Trust(s) as stored on the RDSU Shared Network Drive

The R&D Reference is generated sequentially. For example YY\_XXX\_GHT, where YY denotes the year of submission and XXX is a sequential number starting from 001. The Trust acronyms are:

Gloucestershire Hospitals NHS Foundation Trust - GHT,

Research running across several or all the Gloucestershire NHS Trusts will be suffixed with MTS (Multi-Trust Study)

1. **Naming Electronic folders**

Each folder will use the following format:

R&D Reference\_BRIEF TITLE/ACRONYM

For example 15/001/GHT\_TEST

1. **Organising electronic folders on the shared IT drive GLNT199 (RDSU)**

The electronic folder for trials in feasibility/ set up and delivery stages will be filed as follows:

* PROJECTS
* folder for the year of submission
* TRUST acronym
1. **Sub folders within each electronic folder**

**R&D –** all governance documentation including:

* Trust Approval Letter
* Support Department approvals/agreements
* Local SSI Application form
* R&D Application form
* CVs/Good Clinical Practice certificates
* Sponsor Letters
* Indemnity Certificates
* Investigator Brochures
* Clinical Trial Agreements
* Original Ethics Favourable Opinions/Amendment prior to R&D Approval
* MHRA Clinical Trial Authorisations/Amendments prior to R&D Approval

**Current Study Documents –** One set of the current, approved protocol and patient documentation. Superseded documents will be moved to the SUPERSCEDED folder within this folder

**Finance** – all details of study funding will be stored here

For commercially sponsored trials the NIHR Costing Template **MUST** be included in this folder.

For academic trials details of any income or expenditure will be stored here.

**Amendments –** To be organised within subfolders named by the REC amendment reference number and date. It will include the Amendment Approval Notification (letter or email)

**Honorary Contracts/Letters of Access –** Copies of relevant Research Passport and associated documentation along with copies of Honorary Contracts and Letters of Access will be stored here.

**Correspondence –** any pertinent correspondence relating to the study.

**Serious Adverse Events/ Adverse Events –** Details of SAEs and any AEs that require reporting to the R&D Office.

**Governance Breaches –** Details of any governance breaches.

1. Where a study is not submitted electronically, electronic versions of the documents should be requested from the sponsor and an Electronic Folder set up as above.
2. If the documents are not available electronically then the paper copies provided will be scanned and stored as for all research submissions.

**Appendix 10 Example of Trial Specific Source Data Form**

****

**Schematic view of types of research documentation storage**

(these are examples not definitive for all types of research – refer to HRA clinical trials toolkit)

**Sponsor/CI Principal Investigator Trust Medical Records Trust Pharmacy**

Patient Notes

Paper : Electronic

Pharmacy Site File

Investigator Site File

Paper: Electronic

Trial Master File

Paper : Electronic

Key research specific documents:

* Patient Information Sheet
* Informed Consent Form
* GP Letter
* Source data forms
* Notes will be marked with and ALERT sticker on the outside and details of ‘Do not destroy – patient in clinical trial ,contact R&D’ on the inside
* Electronic notes will have a trial alert tab

All documentation as specified in the contents pages:

* Where sponsor uses a generic contents page and a section is not relevant, a site file note must be put in specifying the section is left empty intentionally
* Where a Sponsor does not provide an ISF then the generic Trust one (App 2a) should be used and sections not required have a Site File note completed
* Where a Sponsor has agreed for the site to use an eISF but not provided one the standard format should be used ( App 2b) and folders not required annotated as not applicable (n/a)

IMP specific information:

* Order/delivery receipts
* Accountability logs
* Temperature logs for refrigerators
* Unblinding information
* Specimen(s) of electronic prescription
* Pharmacy specific work sheets
* Pharmacy specific SOP(s)

All documentation as specified in the contents pages:

* + - * Documentary evidence of Trust Sponsorship/ co-sponsorship
			* Funding
			* Protocol development/ peer review
			* Regulatory submissions
			* Reporting schedules
			* Monitoring Schedules
			* IMP QP process
			* Unblinding processes
			* Independent data monitoring committee
			* Trial management committee
			* Trial supplies
			* Laboratory accreditations
			* Investigator Selection