York and Scarborough Teaching Hospitals NHS Foundation Trust R&D Unit
Standard Operating Procedure
R&D/S09

Set Up and Management of new Studies by Research Delivery Teams

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 R&D Unit's website and/or Q-Pulse 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 Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded versions are promptly withdrawn from use unless notified otherwise by the SOP Controller.

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Author:	Jonathan Hawker
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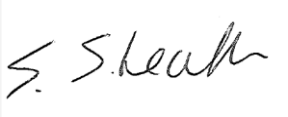
Approved by:	Name/Position:	Lydia Harris, Head of R&D
	Signature:	
	Date:	13th July 2022
	Name/Position:	Sarah Sheath, SOP Controller
	Signature:	
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This SOP will normally be reviewed every 3 years unless changes to the legislation require otherwise

Version History Log

This area should detail the version history for this document. It should detail the key elements of the changes to the versions.

Version	Date Implemented	Details of significant changes
1.0	12th July 2007	
2.0	21st October 2009	Version History log added. Front page box updated. SOP renumbered and renamed. Coverage extended – SOP no longer exclusively aimed at Alliance Trust sponsored CTIMPs; may now be used in externally sponsored CTIMPs where appropriate
3.0	14th November 2011	Broadened applicability to research studies of all types. Addition of Source Data Location List, File Note Template, File Note Log and Screening/Enrolment Log. Minor typographical changes and cross referencing of SOPs. Addition of University of York to Section 2; minor related modifications.
4.0	18th August 2017	Removal of references to the North and East Yorkshire R&D Alliance. Change of author.
5.0	15th August 2022	Included new section on Electronic Site files. Added hyperlinks to various documents mentioned in the SOP. Updated terminology and wording of several sections. Removed all sections detailing the set up of TMF's. Changed author.

Contents

		Page No
Version		**2**
1	**Introduction, Background and Purpose**	**1**
2	**Who Should Use This SOP**	**1**
3	**When this SOP Should be Used**	**1**
4	**Setting up a new clinical research study**	**1**
4.1	Organise the Investigator Site File (ISF)	1
4.2	Electronic Site Files	2
4.3	File Notes	2
4.4	Document Control	3
4.5	Personnel - Training	3
4.6	Delegation of Authority and Signature Log	3
4.7	Source Data Location List	3
4.8	Standard Operating Procedures	4
4.9	Equipment	4
4.10	Pharmacy and IMP supply	4
4.11	Other involved departments	4
5	**Running the Study**	**5**
6	**Related SOPs and Documents**	**7**

1 Introduction, Background and Purpose

This SOP establishes a procedure for setting up and managing research studies by the Trust's research delivery teams. In relation to studies of all kinds it supports compliance with the UK Policy Framework for Health and Social Care Research; in relation to clinical trials of investigational medicinal products (CTIMPs) it supports compliance with the UK Clinical Trial Regulations.

In general, the practices required for high quality conduct of research are similar, whatever type of study is involved. Where particular actions are required for some studies only, such as CTIMPs, this is stated in the SOP.

2 Who Should Use This SOP

This SOP should be used by all staff involved in the delivery of research studies sponsored, co-sponsored or hosted by the Trust.

3 When this SOP Should be Used

This SOP should be followed when setting up, initiating, running or providing services for a research study.

This SOP ends at the point where the Medicines and Healthcare Products Regulatory Agency (MHRA) and/or the Research Ethics Committee (REC) have to be informed that the study has terminated. Study Close-Out and procedure for notifying the regulatory authorities are the responsibility of the study Sponsor. Research delivery teams should follow the sponsor's instructions and deadlines for study close out procedures, including data clearing, Investigator Site File (ISF) checklists and document archiving instructions.
Where a study Sponsor has specific SOPs for their project, or issues Investigator Site File in a particular format, the Sponsor's arrangements take priority, provided they enable compliance with the UK Clinical Trial Regulations and / or UK Policy Framework for Health and Social Care Research as applicable. Applicability of SOPs should be established and documented when any study is initiated at the Trust Site.

4 Setting up a new clinical research study

4.1 Organise the Investigator Site File (ISF)

Some study Sponsors will provide the ISF ready for use,or give detailed instructions for how they wish the File to be assembled. In such cases the Sponsor's requirements must be followed, and the PI is responsible for ensuring this is done.

The task of organising/maintaining the ISF can be delegated to other appropriately trained members of the research team. This task can be delegated to the team of Clinical Trails Assistants for completion and it should be documented on the study Delegation Log. Please refer to

SOP/S107 outlining the role of a CTA and for delegation of tasks to a named person.

When appropriately delegated, the CTA Team takes responsibility for setting up the ISF which contains all the 'essential documents' (in accordance with ICH-GCP) relating to the study. These are documents that are generated before the study commences, during the study and after the study has finished. The CTA team must prepare the ISF, with the required contents page and numbered sections with dividers, before Site initiation. For the content and layout of the ISF see the R&D SOP/F11.

It is often required for some of the sections of the ISF to be kept by departments such as Pharmacy, Laboratory or Radiology. The essential requirement is that all the documents a particular Investigator Site should have are within that Site. They need not all be in the same lever-arch file or in the same location within the Site, but it must be possible to assemble the whole ISF immediately if required for monitoring/audit or inspection. If a section of the ISF is blank as it is being held in a different location on Site a file note must be produced. This should state clearly where the documentation can be located.

An important part of Site Initiation is verification that the ISF is in place and that there are satisfactory arrangements for secure storage of study documentation. Documents filed within the ISF contain confidential person identifiable information and must be handled and stored in compliance with the General Data Protection Regulations. Access to the ISF documents must be controlled and limited to the delegated staff members.

4.2 Electronic Site Files

The use of electronic documentation in research is becoming more commonplace. This includes the use of electronic ISF's (eISF). As such it is important that the same attention and diligence be given to an eISF as the physical version. Both files should mirror one another in content.

A standard template must be used when constructing an eISF, this template can be located here Q:\R&D Clinical Research Projects to ensure secure and controlled access. Where at all possible the eISF template should not be modified. The only time this step can be deviated from is if an external sponsor requires the use of a bespoke template they have provided. Having a standard template is important for efficiency and from a research governance perspective.

It is important that any trial correspondence is filed by the year and month it was received (a template for this is located in each of the relevant correspondence sections of the eISF). This will allow quick and efficient access to any correspondence.

4.3 File Notes

File Notes can be utilised for documenting events related to study delivery which are import for reconstruction of the study conduct. File Notes should however be used cautiously. A useful file note has the following parts: A problem is identified, corrective actions outlined, a procedural change is identified for preventing recurrence, and this procedure is then instituted. It is

important to remember that once a file note is written it becomes a study record and it cannot be retracted.

A file note template (see R&D T20) is available for download. All file notes should be signed and dated by the individual with knowledge of the event leading to the file note and authorised by the PI if required. Cross referencing file notes indicating the location of documents within the ISF, or related to other administrative procedures, do not require PI authorisation. File notes should be referenced in a file note log (see R&D SOP/F59) within the ISF both electronically and in the hard copy ISF.

4.4 Document Control

All study documents should be dated, and version controlled throughout study set-up and during the study. Any amendment to a document should generate a new version with an appropriate date. It is advised that version numbers, dates and a study identifier should be on each page of study documents (e.g. in the page header or footer). Amendments Checklist and Amendments Log should be used to manage amendment implementation process (see R&D SOP/F18 and F118). Document Version Control log R&D SOP/F101 should be maintained throughout the study locally. This log should frequently be verified against the study sponsor's version control log.

4.5 Personnel - Training

The PI is responsible for:

- appointing research personnel if necessary, or making arrangements for support from the R&D research delivery teams at the Site and arranging any study specific training they need, including compulsory GCP training for CTIMP studies. All appropriately trained personnel must be signed on the study Delegation Log at the start of the study and through the study conduct.
- attending and participating fully in training (including Site Initiation where applicable) to ensure self and all Site personnel are trained on the Protocol and relevant Standard Operating Procedures.
- seeking further training on the Protocol or any other aspect of study conduct if they identify gaps in their knowledge.

The ISF should contain documentary evidence that all personnel are qualified by education, training and experience to perform their delegated tasks on the study. CVs, SOP Training Logs and GCP training records must be filed up to date, as must all Site Initiation and Monitoring/Audit Reports. Please see R&D SOP/S25 for details.

4.6 Delegation of Authority and Signature Log

This must be kept up to date in the ISF. All significant tasks such as taking consent, establishing participant eligibility, prescribing or dispensing IMP, or carrying out particular medical procedures or laboratory tests should be specifically delegated by the PI to those who have the necessary education, training and experience. This includes familiarity with the Protocol and GCP.

4.7 Source Data Location List

To enable the Monitor/Auditor to verify the data collected for the study, the location of source data should be clearly identified. The study team should

seek clarification at Site Initiation and keep a list in the ISF. Where study participants are patients the source data will usually be the patients' paper and/ or electronic health records; however care should be taken at the outset to list any departures from this – for example, separate study-specific records kept for healthy volunteers, portable records held by maternity patients or patients with chronic conditions, electronic records of imaging or blood test results, participant diaries. An example source data location list form is available – see R&D SOP/F58.

4.8 Standard Operating Procedures

The ISF should include details of which Standard Operating Procedures are to be applied. It is the PI's responsibility to secure clear agreement about this with the Sponsor during Site Initiation. If the Sponsor wishes to apply its own, Clinical Trial Regulations / UK Policy Framework for Health and Social Care Research compliant SOPs, copies should be provided for the ISF. In default, R&D Unit Standard Operating Procedures will apply to all studies conducted in the Trust.

4.9 Equipment

Any equipment needed for the study should be clearly identified, sourced and regularly checked. This may include fridges or freezers used for storage of IMP or samples, scales used for weighing participants, equipment used for medical procedures. All such equipment should have an asset code from the EME department and be properly calibrated and maintained throughout the study, as per manufacturer's recommendations. The PI and the study team are responsible for ensuring this is done and supporting information is kept in the ISF.

4.10 Pharmacy and IMP supply

The details of Pharmacy arrangements will vary from study to study and these will have been agreed during contract negotiations leading to completion of the clinical trial agreement. During the study initiation phase the PI should discuss the study with the local Pharmacy and ensure that appropriate communication takes place between the local Pharmacy and the Sponsor or Sponsor's representative on IMP supply, dispensing, storage and related issues.

PIs should be aware that participant recruitment will not be allowed until all necessary Pharmacy arrangements are in place and the IMP supplies have been obtained, ready for dispensing. This situation will be clearly notified by the R&D Unit when Capacity and Capability is confirmed.

4.11 Other involved departments

As for the Pharmacy arrangements described in 4.9, PIs should have discussions with local service support departments and any local sub-contractors in conjunction with the R&D Unit to ensure contracts and arrangement are in place at the right time. Where possible all supporting departments should be represented at any SIV's or set up meetings with the sponsor.

PIs in the Trust should be aware that participant recruitment will not be allowed until all necessary departmental and sub-contractual arrangements are in place and till confirmation of Capacity and Capability is formally issued

5 Running the Study

The requirement for all staff involved in running any type of study is to work to the standard set by the UK Policy Framework for Health and Social Care Research and by the UK Clinical Trial Regulations for CTIMP studies. Each member of staff should undertake GCP training before commencing work on a CTIMP study, preferably face to face if this is possible. GCP training must be updated as deemed appropriate by the study Sponsor and/or York and Scarborough Teaching Hospitals NHS Foundation Trust, every 3 years at the very minimum. Please see R&D SOP/S25 for details.

R&D Unit SOPs are relevant to particular elements of any study duties, such as those on Informed Consent, or Safety Reporting. The PI and study team should be aware of the Standard Operating Procedures to which they are working and should carry out self directed training as outlined in R&D SOP/S22. Some general guidance points are pertinent here, and should be observed in all cases:

1. The CI has overall responsibility for the study (for all Investigator Sites involved) and Site responsibility for all work done at the Chief Investigator Site – delegation must not mean abdication;
2. A Site PI has responsibility for all work done at the participating Investigator Site – delegation must not mean abdication;
3. All other staff must only work within the delegation arrangements documented in the ISF Delegation of Authority and Signature Log;
4. The study must be carried out strictly in accordance with the current version of the protocol as approved by MHRA and / or the REC and / or HRA. All amendments to study procedures and documentations must be formally reviewed, approved and implemented. Working outside the approved study protocol and legal agreement with the sponsor– for example be recruiting a few extra participants or collecting additional data – can have serious consequences, including invalidating the study insurance.
5. For compliance with Data Protection legislation, the NHS Confidentiality Code, and the National Data Opt-Out Policy, potential participants in research studies should be identified by members of their immediate clinical team. When appropriately delegated, the Trust research delivery teams are considered as part of the relevant clinical team for the study. Depending on the mechanism used to identify potential research patients, data opt-out choice must be checked on the hospitals patient's data base (CPD) prior to approaching patients with research information. Please see R&D SOP/S77 for details.
6. For a CTIMP, the tasks of:
    - explaining the study to a potential participant so that they understand the risks and objectives; and
    - determining that a particular participant meets all eligibility criteria and is suitable for the study;

    should only be delegated to medically qualified personnel, whose signatures should confirm their involvement.
7. After screening and/or randomisation, the participant's code/ID number should be entered in a Screening and Enrolment Log. . The Enrolment Log must be retained at site and archived at the end of the study.

8. Patient recruitment into a study must be recorded on a central database: EDGE. Please see R&D SOP/S15.

9. Key events related to a study conduct must be recorded in the research participants' hospital notes. Please see R&D SOP/S24 for details. Any requests for monitoring visits from the study sponsor, requests for internal or external audits or regulatory inspections must be facilitated, and access to source data records provided.

10. There must be a complete audit trail of all activity undertaken for the study – sufficient to allow the study to be recreated from the paperwork; and the paperwork should be ready for monitoring/audit or inspection at any time. It follows that:
    - ISF maintenance must be meticulous;
    - Any events or decisions not otherwise provided for should be recorded in dated and signed File Notes.
    - Any corrections that need to be made to the documentation should be made so that the original entry is not obliterated – a correction entry should be made, with the date of the change and signature of the person making it.
    - Regular team meetings should be held involving staff working on the study at a particular Site; these should be minuted or notes should be made of all significant decisions and follow-up actions to ensure the study PI can demonstrate oversight of the study.

11. All staff should be aware of the responsibility to record and report Serious Adverse Events, safety incidents and protocol and/or GCP breaches, and should follow the study protocol and the relevant R&D SOPs for safety reporting and escalation procedures, including response to product recalls and urgent safety measures.

12. Close communication with the relevant support departments must be maintained throughout the study conduct. The PI and study team must make themselves familiar with the relevant SOP and requirements, for example IMP prescribing and handling, collection of research samples or requesting and obtaining Radiology imaging results.

13. If there is any doubt about any aspect of setting up or running a research study in the Trust, it is essential to seek advice from the R&D Unit. It is important to note that some Sponsor instructions may occasionally contravene or conflict with local processes or arrangements. In this eventuality, investigators and research teams must ensure they seek advice or guidance from the R&D Unit. Please email Research.QA@YORK.NHS.UK for any patient safety or quality related queries, or Research.Governance@York.NHS.UK for any governance related issues, including any problems with availability of the study PI.

6 Related SOPs and Documents

All York Foundation Trust R&D Unit SOPs and Guidance documents are related to Set Up and Management of Research Studies and the full list of them should be checked. The following are of direct relevance:

R&D/S03	Delegation of Duties and Signature Log for the Trial Management of Trust Sponsored Studies
R&D/S04	Breaches of GCP or the Study Protocol
R&D/S05	Research Related Adverse Event Reporting Procedure for CTIMP Studies (including reporting of a pregnancy)
R&D/S06	Reporting Requirements During Research Studies
R&D/S07	Implementing Amendments for Research Studies NOT Sponsored by the Trust
R&D/S08	Monitoring of Trust Sponsored Research Studies
R&D/S14	Issuing Confirmation of Capacity and Capability
R&D/S21	Study Close-Out
R&D/S25	Providing and Documenting Training for Researchers
R&D/S26	Preparation, Review and Approval of Study-Specific Standard Operating Procedures for Research
R&D/S28	Quality Assurance
R&D/S63	Sub-contracting Services for Research Activities
R&D/S64	Setting up Research Studies Involving Imaging (including studies using Ionising Radiation)
R&D/S71	Auditing of Research Studies and Processes
R&D/S74	Making Amendments to Trust Sponsored Research Studies
R&D/S81	Case Report Form (CRF) Design and Completion
R&D/F11	Investigator Site File Contents List
R&D/F16	Study Delegation and Signature Log
R&D/F18	Amendment Checklist (Research Teams)
R&D/F58	Source Data Location List
R&D/F59	File Note Log
R&D/F71	Screening Log
R&D/F110	Enrolment Log
R&D/F118	Amendment Log
R&D/T20	File Note Template