York and Scarborough Teaching Hospitals NHS Foundation Trust R&D Unit
Standard Operating Procedure
R&D/S28

Quality Assurance

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 Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded versions are promptly withdrawn from use unless notified otherwise by the SOP Controller.

The definitive versions of all R&D Unit 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 Unit website: https://www.research.yorkhospitals.nhs.uk/sops-and-guidance-/ or on Q-Pulse

SOP Reference:	R&D/S28
Version Number:	5.0
Author:	Jonathan Hawker
Implementation date of current version:	14th February 2023

Approved by:	Name/Position:	Monica Haritakis, Research QA Manager
	Date:	17th January 2023
	Name/Position:	Sarah Sheath, SOP Controller
	Date:	17th January 2023

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	Reviewers	Details of significant changes
1.0	1st February 2012		
2.0	10th November 2014		Removal of references to the North and East Yorkshire R&D Alliance. Change of Author. Updated information added to certain paragraphs.
3.0	15th June 2017		Change of author
4.0	22nd August 2017		Minor formatting changes
5.0	14th February 2023	Jonathan Hawker Monica Haritakis	Change of link to R&D Unit website. Change the Trusts name. Change of author. Added extra information regarding archiving, support departments and QA quarterly meetings. Formatting to existing sections

Contents

1 Introduction, Background and Purpose

Quality Assurance (QA) is an important component of every clinical research post, as all activities involved in delivering research contribute to the QA process. Every member of clinical research staff is responsible for the quality of their work.

All organisations involved in clinical research must have a Quality Management System (QMS) in place to support the clinical research activities they conduct. This ensures that the research studies are conducted in compliance with Good Clinical Practice (GCP) and other applicable regulatory requirements (such as the UK Medicines for Human Use Regulations). Compliance with these standards provides public assurance that the rights, safety and wellbeing of study subjects are protected consistent with the principles that have their origin in the Declaration of Helsinki, and that the study data are credible.

The York and Scarborough Teaching Hospitals NHS Foundation Trust R&D Unit has set up a Quality Management System that works alongside other quality systems within the Trust (e.g. within Laboratories, Pharmacy, Radiology). The QMS provides a framework for assuring quality of all clinical study activities conducted within the Trust. QA procedures, records and checks are maintained by the R&D Unit staff members, who are independent of the study teams, and have overarching QA oversight.

The purpose of this SOP is to detail the systems in place within the R&D Unit which make up the QMS.

2 Who Should Use This SOP

This SOP should be used by:

- R&D Unit staff engaged in setting up or managing all research studies: sponsored, co-sponsored or hosted by the Trust.
- Principal Investigators at Participating Sites conducting research studies sponsored or hosted by the Trust.
- All Trust staff working on research studies.
- Members of the R&D Group

3 When this SOP Should be Used

This SOP applies during the preparation of and throughout the conduct of a research study.

4 Procedure(s)

The QMS provides processes and procedures for planning and execution of all key research activities within the Trust. All processes supporting the management of clinical research are described in Policies, Standard Operating Procedures (SOPs), Guidance Documents and tools, such as templates, forms and checklists. These are to ensure that the activities are conducted in a uniform and consistent manner and

are compliant with GCP and regulatory requirements. The key elements of the R&D Unit Quality System include:

1) Documented procedures developed, implemented and kept up-to-date

The R&D SOP Controller (a member of R&D Unit staff) is responsible for coordinating the writing and reviewing of R&D SOPs relating to procedures for study approval and management, and is also responsible for ensuring that all R&D SOPs, forms and templates are version controlled and only the current versions of all SOPs are available to staff. Preparation, Review & Approval of SOPs for Research is detailed in SOP/S01 & S26.

The Q Pulse document management system is used to distribute new and updated SOPs. Team members are required to sign into Q Pulse, read the document and sign to say that they have read the required document before the implementation date. This allows individuals to easily create a record of their training within the Q Pulse platform.

2) A documentation system that allows for the retrieval of any records or documentation to show actions taken, decisions made and final outcomes

All SOPs (generic and study-specific) and study related documentation should be version controlled to ensure that it is accountable, traceable, and consistent and that all members of the study team are working to the most recent versions of each document. It is the responsibility of the Lead Research Team/Sponsor to version control all study related documents and adhere to the SOPs on creation and management of documentation (SOP/S01 & S26).

For Trust Sponsored studies the CI or designated member/s of the study team should draft all study-related documentation including protocol, case-report forms (CRFs), patient information sheets (PIS), study-specific SOPs and ensure that documentation complies with all regulations and guidelines. All documentation should be filed in TMF in accordance with R&D/F95 (Trial Master File contents list).

Every research project must have a written protocol detailing the methods and processes to be used. Where a study is sponsored or co-Sponsored by the Trust there should be an evidenced that the study protocol had gone through an appropriate review process before the research is undertaken. All documentation required to be submitted to Research Ethics Committees (REC) or the Medicines and Health Regulatory Authority (MHRA) must also be version controlled.

For Hosted Studies the PI or designated member/s of the study team should ensure that an Investigator Site File (ISF) is set up for the study using R&D/F11 (Investigator File contents list) ensuring that the latest versions of all study specific documentation and essential documents are stored in the paper ISF.

3) Defined organisational and accountability charts, roles and responsibilities

Organisational and accountability charts are maintained and kept up to date by the Head of R&D or delegated member of the R&D Unit. Lists of roles and responsibilities of R&D Unit staff are available via R&D unit website.

Dedicated Teams and procedures in the key support departments: Pharmacy, Labs, Radiology

The R&D department includes dedicated teams within the support departments who provide a research function. These departments are Labs, Pharmacy and Radiology.

There are research specific Labs and Pharmacy staff that are based within the Main Labs and Pharmacy department. They form part of the R&D department and have specific R&D functions and procedures. They have specialist knowledge on lab and pharmacy policy and procedures

Radiology, currently sits within the R&D Operations team.

All studies that involve processing of samples, use of medication or imaging must be sent to the relevant support department for review as part of the set-up process.

4) Appropriate documented training of personnel to meet the defined competencies of their role, including GCP training

The Clinical Trial Regulations require that each individual involved in conducting a clinical trial of an investigational medicinal product (CTIMP) should be qualified by education, training and experience to perform his/her respective task. This applies not only to the PI, but also to any members of the trial team to whom responsibilities are delegated.

A key requirement for anyone involved in the conduct of clinical research is Good Clinical Practice (GCP) training. GCP is the ethical and practical standard to which all clinical research is conducted. GCP training is mandatory for research staff involved with clinical trials using investigational medicinal products (CTIMPs).

It is recommended that research staff who are new to clinical research, or who have not been actively involved in clinical research for a period of time, undertake the face-to-face Introduction to GCP training course from the NIHR. GCP refresher training should be undertaken at least every three years. All staff working on CTIMPs are also advised to read the Clinical Trial Regulations.

It is expected that staff working on any research study conducted in the Trust, not just CTIMPs, are appropriately qualified to undertake the tasks they have been delegated. Staff are responsible for self-directed SOP training, and for setting up and maintaining individual research training folders.

Providing and documenting training for research staff is detailed is R&D/S25.

Self-directed training in The York and Scarborough Teaching Hospitals NHS Foundation Trust R&D Unit Standard Operating Procedures on Q-Pulse is detailed in SOPs in R&D/S22.

5) Documented evidence to demonstrate that computerised systems are fit for purpose (validation)

Computer system validation is essential to demonstrate that the system is fit for purpose. Validation applies to all systems that may impact on the integrity and quality of clinical research data.

Researchers are advised to use commercially produced and validated software wherever possible. Specialist software that has been produced ‘in-house’ or as a one-off application by a commercial company must be subjected to validation processes. Results of validation testing should be filed in the Trial master File (TMF).

Further details on validation requirement can be found in R&D/S29 (Data Management)

6) Use of equipment and materials that can be verified as suitably calibrated and fit for purpose

Any equipment needed for a research 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 be properly calibrated and maintained. The CI or Site PI is responsible for ensuring this is done and supporting information is kept in the TMF/ISF (see R&D/S09 Set-up and management of research studies).

Archiving

Archiving forms, the final part of the clinical trial process and therefore is covered by the same QA procedures as any other part of a study. The study sponsor must give the go ahead or 'green light' for a study to be archived. This status is usually given once the sponsor is satisfied that anything outstanding has been rectified. It is also entirely possible that the sponsor may send an archiving checklist to the research team as a part of the process for acquiring greenlight status. This is largely sponsor dependent and will require the delivery team to make sure key documents are located within the ISF before archiving takes place. It acts like a mini ISF audit to make sure everything is in place and up to date.

Archiving will also form a part of the CTA (Clinical Trial Agreement) which is issued between the sponsor and R&D department prior to a study opening. This acts as a contract and any archiving responsibilities will be included within these contractual obligations. This will include who has responsibility for the archiving of the study, the sponsor or the Trust.

7) R&D Group

The decision as to whether the Trust will sponsor a research study is made by the Trust's R&D Group. However, for low-risk research studies that would be exempt from Research Ethics Committee (REC) review, the R&D Group delegates authority for review and sponsorship to the R&D Unit and Clinical Lead for Research. Applications are managed by the R&D Group in accordance with applicable SOPs relating to different types of study.

The R&D Group will also consider amendments to sponsored studies when the R&D Unit considers that an amendment may impact on the Trust's previous decision to Sponsor a study. Further details are available in R&D/S74, Making Amendments to Trust Sponsored Research Studies.

The R&D Group will receive various routine or non-routine reports on the conduct of research studies in order to maintain Sponsor or Care Organisation oversight, including Quarterly Progress Reports, Serious Adverse Events and SUSARS, Adverse Incidents reported via the Trust's main incident reporting system and Serious Breaches. Additionally, the R&D Unit's Research QA Manager submits a report of monitoring activity to the Group at least once a year.

8) Data Monitoring Committees

Data Monitoring Committees will be established and function according to R&D/S72. For Trust Sponsored CTIMP studies a Data Monitoring Committee should usually be established. These are independent groups of experts external to a study that function to assess progress, safety and critical endpoints and provide the Sponsor with recommendations regarding study modifications, continuation or termination.

9) Quality Control (QC) activities, (review and checking). For example, monitoring of trial sites either on-site or through centralised or remote monitoring techniques

Monitoring is carried out according to R&D/S08 Monitoring of Trust Sponsored Research Studies. During the monitoring process a plan for the correction of any issues identified will be produced and where applicable suggestions for preventative action will be made. Persistent quality issues identified during monitoring visits will be brought to the attention of the Head of R&D who may refer this on to the R&D Group and/or initiate further necessary actions or staff training.

10) Quality Assurance (QA), including independent audit of R&D Unit processes and studies

Audits are designed to assess and assure the reliability and integrity of trials quality control systems and measure performance against recognised standards. It helps to demonstrate robust research processes to external sponsors/funders and can help prepare investigators for regulatory inspections. Auditing of research studies is carried out according to R&D/S71 Auditing of Research Studies and Processes.

11) A risk-based approach used to determine the extent of trial monitoring activities, processes and trials to audit, and computer validation activity

All Studies sponsored or co-sponsored by the Trust will be assessed for 'risk' during the research governance process (see R&D/S18 Risk Assessment). Each study sponsored by the Trust (excluding 'low risk' studies approved via proportionate review process) should have a study-specific Monitoring Plan based on the Monitoring Plan Template (R&D/T03) that will detail how the monitoring procedure (as set out in R&D SOP/08) will apply to the particular study.

For all Hosted studies, once confirmation of Capacity and Capability has been received, an Audit Prioritisation Tool will be completed by the Research Delivery Facilitators on the EDGE system. The prioritisation category assigned to the study will determine the likelihood of the study being audited (as set out in R&D/S71).

Key processes as outlined in the R&D Unit Standard Operating Procedures will be subject to regular audit. An annual audit schedule will be developed specifying the frequency of audits. In addition, specific triggered or "for cause" audits may be necessary, for example, where compliance issues have been identified by other means such as through monitoring, or concerns voiced by a study team.

12) Quarterly QA Meetings

The Research Quality Assurance Group which is made up of members of the R&D Unit and representatives of the support departments, meets quarterly to monitor and manage the quality in research across the Trust and outline ways to achieve consistent performance and service. The Group provides assurance that research activity in the Trust is managed and monitored according to applicable laws, policy and guidance. A report is produced after each meeting which is shared with the R&D Group.

13) Regulatory Inspection

In addition to monitoring and audit checks, CTIMPs may be inspected by the MHRA. Inspections will be managed in line with the SOP referenced R&D/S53 Managing MHRA Inspection (Clinical Trials of Investigational Medicinal Products).

14) Continuous improvement, including Corrective and Preventive Actions (CAPA)

The entire Quality System should be continually reviewed and improvements made where required. All R&D SOPs will be updated in line with any changes to the Clinical Trial Regulations or other governance requirements. Otherwise, all SOPs will be routinely reviewed every 3 years as a minimum**.**

5 Related SOPs and Documents

R&D/S01	Preparation, Review, Approval of SOPs for Research
R&D/S08	Monitoring of Trust sponsored Research Studies
R&D/S09	Set Up and Management of Research Studies
R&D/F11	Investigator Site File Contents
R&D/S18	Risk Assessment
SOP/S22	Self-directed training in York Foundation Trust R&D Unit SOPs
R&D/S26	Preparation, Review and Approval of Study Specific SOPs for Research
R&D/S25	Providing and Documenting Training for Researchers
R&D/S29	Data Management
R&D/S53	Managing MHRA Inspection (Clinical Trials of Investigational Medicinal Products)
R&D/F57	Audit Prioritisation Too
R&D/S71	Auditing of Research Studies and Processes
R&D/S72	Data Monitoring Committees for Clinical Trials
R&D/S74	Making Amendments to Trust Sponsored Research Studies.
R&D/F95	Trial Master File Contents
R&D/T03	Monitoring Plan Template