Document Title: HLRI-CRF Quality Management Plan

Document Number: R&D SOP125

Staff involved in development: *Job titles only*	HLRI CRF Operational Manager, HLRI CRF Team Leader,
Document author/owner:	HLRI CRF Operational Manager
Directorate:	Research and Development
Department:	Research and Development
For use by:	HLRI CRF
Review due:	February 2026

Summary of Amendments

Version Number	Modification:
1.0	

Key Points of this Document

Document to outline the quality management system of the HLRI CRF, providing an explanation of related procedures and structures of operation in the CRF.

1 Purpose and Contents

- This document provides a clear, high-level overview of the HLRI Clinical Research Facility (CRF) quality management system (QMS), including related procedures and governance structures that are in operation within this CRF.
- This QM demonstrates how the QMS of the HLRI CRF supports the delivery of research projects to the highest standards of research and clinical governance, thus ensuring that quality and safety considerations are embedded throughout the facility, promoting a culture of continual quality improvement.

2 Roles & Responsibilities

- This Quality Manual applies to all staff and investigators working within the HLRI CRF. It is every individual's responsibility to work within and adhere to current national legislation/ guidelines and local policies and procedures; these are referenced throughout the manual.
- All clinical research activity conducted in the HLRI CRF will be bound by the terms of this quality manual. 'HLRI CRF' includes both the physical HLRI CRF at Papworth Road, Cambridge. It also includes all HLRI CRF Core staff, HLRI CRF users and members of HLRI CRF Management team who must read this document.

3 Definitions and Abbreviations

3.1 Definitions

Term	Definition
Sponsor	An individual, or organization or two or more persons or organizations (joint/co-sponsorship) legally responsible for the conduct of clinical trials, pharmacovigilance, and the manufacture, importation and labelling of IMP.
Author	A subject matter expert and owner of the document responsible for its content and the lifecycle of the document. The individual is responsible for development of the draft document, submission as well as managing approval of the final draft, change requests and document review. The author may delegate aspects of these processes to other individuals.
QM	Quality Manual- A top level document that describes an organization's Quality Management System.
QMS	A Quality Management System (QMS) sets out the standards

	being worked to and how these are going to be met. The system should define what people, actions and documents are going to be employed to carry out the work in a consistent manner, leaving evidence of what has happened.
Review date	This is the date by which a scheduled review of the document content will be conducted by the author to assess the need for amendments.

3.2 Abbreviations

Abbreviation	Meaning
CAPA	Corrective Action Preventive Action
CCRC	Cambridge Clinical Research Centre
ICH GCP	International Conference on Harmonisation Good Clinical Practice
CTA	Clinical Trials Authorisation
CTIMP	Clinical Trial Investigational Medicinal Product
CSV	Computer Software Validation
Datix	The Trust incident reporting system
FRMS	Forms
HLRI CRF	The Clinical Research Facility (CRF) is a physical facility dedicated to early translational and experimental medicine clinical research.
HLRI	Heart and Lung Research Institute
IMP/ NIMP	Investigation Medicinal Product/non-IMP
MHRA	Medicines and Healthcare products Regulatory Authority
NIHR	National Institute for Health and Care Research
QA	Quality Assurance
QC	Quality Control
QM	Quality Manual QM - a top level document that describes an organization's Quality Management System
QP	Qualified Person
RPH	Royal Papworth Hospital
R&D	Research and Development Department
SAB	Scientific Advisory Board
SOP	Standard Operating Procedure

3.3 References

- ICH GCP Guideline (CPMP/ICH/135/95)
- Guideline for good clinical practice E6 (R2) - https://www.ema.europa.eu/en/ich-e6-r2-good-clinical-practice
- EU Directive 2001/20/EC
- EU Directive 2003/94/EC
- EU Directive 2005/28/EC
- The Medicines for Human Use (Clinical Trials) Regulations 2004, as amended.
- The Research Governance Framework for Health and Social Care, 2nd edition
- The Human Tissue Act 2004
- MHRAs guidelines: 'Guidance on the maintenance of regulatory compliance in laboratories that perform the analysis or evaluation of clinical trial samples.
- EudraLex volume 4, Annex 13: EU Guidelines to Good Manufacturing Practice Medicinal Products for Human and Veterinary Use.
- The clinical and research governance provisions of the Royal Papworth Hospital Trust/Governance.
- GDPR Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, as it forms part of the law of England and Wales, Scotland and Northern Ireland by virtue of section 3 of the European Union (Withdrawal) Act 2018 and as amended by the Data Protection, Privacy and Electronic Communications (Amendments etc) (EU Exit) Regulations 2019.

4 Policy

This SOP is mandatory and, as per the Trust's Information Governance and Records Management framework, non-compliance with it may result in disciplinary procedures.

5 Procedure

5.1 Introduction

The UK Policy Framework for Health and Social Care Research was published by the Department of Health and Social Care in 2017 and outlines key principles for the delivery of high-quality research in the NHS.

The delivery of high-quality clinical research is a key strategic priority of Royal Papworth Hospital NHS Trust and consistent with its aspiration to embed research in all aspects of its activity.

The HLRI CRF has been established to provide excellent, dedicated facilities and staffing resource to facilitate safe, high quality clinical research for cardiorespiratory patients
An effective Quality Management System (QMS) is an essential tool for ensuring consistent service quality and compliance with Good Clinical Practice (GCP) requirements and the Medicines for Human Use (Clinical Trials) Regulations.

The HLRI CRF QM sets out the standards to adhere to, how these will be met by all users of the HLRI CRF and how compliance is monitored. The system defines the people, actions and documents to be employed to carry out work in a consistent manner and generate evidence of what has happened.

5.2 Management responsibility

All core HLRI CRF team and users of HLRI CRF are responsible for:

- Adherence to Good Clinical Practice.
- Adherence to regulatory requirements related to their area of study and professional group where appropriate.
- Adherence to HLRI CRF quality processes and procedures.
- To complete HLRI CRF induction training and to supply evidence of appropriate training on request

GD040 HLRI CRF Operations Manual outlines the functional relationships between HLRI, RPH, CUH, UoC and HLRI CRF; the security, health and safety procedures; and the application and booking processes.

5.2.1 HLRI CRF Oversight groups

5.2.1.1 HLRI CRF Oversight groups

HLRI Operations Meetings

- To be accountable for all HLRI CRF activities.
- To act as the responsible individuals for all HLRI CRF policies and standard operating procedures.
- To encourage, support and embed a quality culture within the core HLRI CRF team and users.
- Review training of all core HLRI CRF staff and HLRI CRF users on quality processes as appropriate.
- Results of Internal Audits.
- Customer Feedback and Complaints.
- Recommendations for Improvement.
- Status of Deviation Reports and CAPA projects.

- Oversight the maintenance of the QMS and ensuring continued compliance with relevant legislation applicable to clinical research.

5.2.1.2 Management committee

This Committee is attended by RPH and UoC Senior Managers

- To encourage, support, embed and facilitate a good quality culture.
- To implement robust policies and procedures to deliver the quality policy as outlined in this document.
- Oversight of implementation of HLRI CRF QMS documents.
  - To receive updates from NIHR CRF Directors meeting and CCRC Scientific Advisory Board.
  - To receive updates on HLRI CRF activity.
  - To receive a monthly update from the CRF Operations Manager on the facility, staffing, quality management (new SOPs and incidents) and equipment.
  - To ensure all SOPs are reviewed as appropriate.
- To ensure the HLRI CRF functions within its financial means and retains robust information on income and expenditure.
- To receive a quarterly finance report.
- To ensure the educational and training needs of staff are met.
- To receive updates on regulatory approvals.
- To receive and undertake regular reviews of the HLRI CRF Risk Register to ensure consistency in the assessment of risk, to confirm appropriateness of action plans and monitor progress to reduce or control risk.
- To support the day-to-day operation of the facility under the leadership of the CRF Clinical Director and Operations Manager.
- Follow-up actions from Previous Management Reviews.
- Report on the progress of the HLRI CRF to HLRI Management Committee.
- Agree reports submitted to the CCRC as a part of the RPH contribution to the annual NIHR CRF Annual Report.

All CRF staff have a responsibility to report any areas of concern they have relating to the quality system to their line managers or HLRI CRF Operations Manager.

5.2.1.3 CCRC Scientific Advisory Board (SAB)

The Cambridge Clinical Research Centre (CCRC) includes all the clinical research facilities including CUH and HLRI CRF at RPH. The CCRC Scientific Advisory Board (SAB) reviews all research applications.

Overseen by the CCRC CRF Director and CCRC Director of Clinical operations, the Scientific Advisory Board (SAB) carefully appraises all research applications and the resources they will require.

The SAB members' collective expertise and experience is broad-based and is fully competent to assess study proposals in a range of diverse disciplines. If needed can undertake formal Peer Review.

The SAB meets monthly review new studies, study amendments and study renewals.

Process described in GD 034 Set up in the HLRI CRF.

5.2.1.4 RPH Research Governance Project Approval System

All proposed research studies to be conducted at RPH, including the delivery at HLRI CRF, are reviewed at Research Governance Project Approval System (RGPAS) meetings. These meetings are designed to assess feasibility and whether the Trust may have the capacity to conduct the study. The committee will conduct risk assessment of the study and review patient safety, operational and governance issues including contracts, indemnity, resources, and finances, where upon it will be agreed whether the study can proceed through to the next stage of our Governance process, and eventually through to study set up.

The PI (or their chosen representative) are required to attend to present their study and answer any queries that may arise during the meeting.

To note this process happens in parallel with CCRC Scientific Advisory Board (SAB) review. Approval by both the CCRC and RGPAS is required for a study to be undertaken at the HRLI CRF.

5.3 Premises

The HLRI CRF provides and maintains the infrastructure required to provide service to our users and conform to required regulations it includes:

- Buildings, workspace and associated utilities
- Consultation and examination rooms
- inpatient beds: 2 bays with 4 beds each, and 2 side rooms
- 2 clinical physiology room
- A dedicated clean utility room for the management of Investigational Medicinal Products
- 2 on-site sample processing rooms for rapid sample receipt preparation and short-term storage in –20 or –80 freezers.

GD035 House keeping in the HLRI CRF lay out the procedures that must be undertaken to ensure the day to day cleanliness and safety of the HLRI CRF clinical area.
GD034 HLRI CRF User guidelines are available to be shared with investigators, colleagues and users of the CRF.

A HLRI CRF Business Continuity Plan is in place to ensure the HLRI CRF is able to safely deliver clinical research studies in case of disruption or interruption. It include plans to ensure they can continue to exercise their functions in the event of a disruptive event and the HLRI CRF falls under this remit.

5.3.1 Process equipment (both hardware and software)

- The facility is supported by RPH digital team, RPH Clinical Engineering, RPH pharmacy, Communications Department
- The cleaning service is provided by external cleaning company OCS contracted with the University support services (i.e. communication etc.)
- The HLRI is also supported by Imaging, Physiotherapy and respiratory physiology.

5.4 Staff

The HLRI CRF employs a team of core staff who have been rigorously selected to ensure that they have the right qualifications, skills and competencies to carry out their roles. All staff have clearly defined job descriptions.

Staff are required to undertake annual Mandatory and Statutory training relevant to their role within the HLRI CRF. This is recorded and audited via annual appraisal and audit.

Staff are actively encouraged to undertake professional development courses and attend conferences and seminars to ensure that their skills are continuously developed and updated.

HLRI CRF Access and Induction for staff and visitors is described in GD 036 HLRI CRF Access and Induction.

5.5 Work environment

The HLRI CRF determines and manages the work environment ensuring that the workspace is suitable for all HLRI CRF staff and users.

5.6 Organisational Chart

An organisational chart providing generic details (i.e. job titles - not names) demonstrate reporting lines in the HLRI CRF (Appendix 1). The organisational chart is maintained by the HLRI CRF Clinical Director and Operations Manager and approved by HLRI CRF Management Committee. The chart is updated when required.

5.7 Document control

The quality management system has documented procedures to control and manage processes associated with the operational and administrative procedures within the HLRI CRF.

5.7.1 Documents

The quality management system includes the following:

- Documented standard operating procedures (SOPs) to ensure the effective planning, operation and control of the processes of the HLRI CRF.
- Guidance detail how specified work should be carried out to ensure a systematic approach.
- Document templates (FRMS).
- Any other records required to demonstrate conformity to the requirements listed in section 4.2.

5.7.2 Standard Operating procedures (SOPs) Production, Approval and Review:

RPH R&D Department SOP committee is responsible for co-ordinating the reviewing of RPH R&D SOPs which also includes those of the HLRI CRF. If any new SOPs, guidance documents or Forms are required, the HLRI CRF team will produce the SOP or necessary documents and the RPH R&D SOP committee will review, seek ratification and implementation. RPH R&D SOP committee is also responsible for ensuring that all, forms and templates are version controlled and only the current versions of all SOPs are available to staff, this will also include decisions on provision of any training required**.**

Relevant SOPs:

SOP001: Production, Approval and Review of SOPs
SOP060: Version Control of Study Documentation
SOP002: Training Records for Research Active Staff

5.7.3 Documents and records

Documentation control assists in the setting and maintenance of standards including written procedures. Written procedures and controlled templates and forms ensure consistency between HLRI CRF users and team, they provide structure, simplify how things are done and reduce variability in output.

A system is in place to ensure that the latest copies of all documents are available readily to ensure effective functioning of the HLRI CRF quality management system. All documents

that the HLRI CRF Team require access to are stored on the current contents spreadsheet of the HLRI CRF N Drive and access is granted on commencement of employment.

A vital part of document control is version control. This ensures that only the current version of a document is in use and that everyone is trained to use it. Version control applies to all controlled HLRI CRF master documents.

Changes to the content of master HLRI CRF controlled QMS documents occurs through a controlled approval process to ensure appropriate impact assessment and management of the change can take place.

Further guidance on documentation control is detailed in RPH R&D SOPs.

Relevant SOPs:
SOP001- Production, Approval and Review of SOPs;

SOP060 - Version Control of Study Documentation

5.7.4 Change Control

A system is in place to ensure that the latest copies of all documents are readily available to ensure effective functioning of the HLRI CRF quality management system. There is also a documented process used to ensure that changes to a system are introduced in a controlled and coordinated manner and to ensure that changes are appropriately controlled, documented and approved by designated functions.

Relevant SOPs:
SOP060 Version Control of Study Documentation
SOP002 Records for Research Active Staff

5.7.5 Retention of Records

Records are maintained to provide evidence of conformity to the requirements listed above, and to evidence the effective operation of the quality management system. SOP 011 archiving of research studies, details the storage, protection, retrieval, retention time and disposition of the HLRI CRFs quality records.

The termination of the end of a study is usually documented in the protocol. In most cases, this is the date of the last visit of the last participant or the completion of any follow-up monitoring and data collection described in the protocol. If a study is a CTIMP an end of study report must be sent to the regulatory body within 90 days. A non-CTIMP is less specific on time frame, but an end of study form should be filled in and sent to ethics. This would denote to ethics that the study is finished. The sponsor should also provide the site

with a final study closure letter. The protocol and/or IRAS form (see PART B) should outline plans for any samples at the end of the study e.g. being moved to a tissue bank, stored for a pending research study and transfer storage under HTA licence.

The HLRI CRF Team has a process for actively reviewing paper documentation held in the HLRI CRF and identifying that which can be archived off site. This has been arranged through the RPH RPH R&D department using the RPH R&D SOP S03 Archiving SOP to ensure that this is done in a planned and documented manner.

All HLRI CRF Team members are encouraged to use a Clear Desk policy at the end of every day. All documentation is stored when not in use in a locked cupboard in a locked room (R018 or R0 62).

The HLRI CRF Team conducts an annual review of documentation held and disposes of expired paper documentation that does not require archiving. All documentation that is awaiting archiving is stored in a locked cupboard (Medical records room R055).

Relevant SOPs:
SOP 11 Archiving of research studies

5.7.6 Deviation Reporting and CAPA

The HLRI CRF takes action to eliminate the cause of non-conformities and deviations to prevent recurrence, refer to RPH R&D SOP 50. HLRI CRF line managers and HLRI CRF Operations Manager are responsible for the quality of the work carried out within their team and for escalating any quality issues to the HLRI CRF senior management teams and, if applicable, RPH R&D quality representative.

Documenting deviations from agreed QMS processes is an essential way of assessing and evaluating the impact of the deviation, learning when things go wrong and identifying improvements.

Deviations from HLRI CRF QMS processes, either planned or unplanned, must be documented.

Relevant SOPs:
PTUC SOP 50- Handling of Protocol Non-Compliance
SOP 51 _Serious Breach of Protocol or GCP in CTIMPs and Non-CE Marked Devices

5.7.7 Incident Reporting

The HLRI CRF staff reports incidents via RPH Datix in accordance with RPH Trust policy. This may include any adverse events that are reportable for individual studies.

Incidents reported on RPH Datix will be investigated and followed through to timely completion in line with the Trust Incident Policy.

If the incident constitutes a deviation from the approved study protocol, appropriate action must be taken (refer to section 8.6).

Relevant incidents and near misses are also reported via the University of Cambridge reporting System (AssesNet- Online) when applicable

5.8 Risk Management

5.8.1 Risk assessment procedure

HLRI CRF processes are assessed to identify and manage risks that arise from HLRI CRF activities. Guidance must be provided as to the appropriate escalation process for risks identified. The HLRI CRF Management Committee maintains a HLRI CRF risk register.
Risk assessments and any mitigation activity are reviewed and updated on an ongoing basis by the monthly HLRI CRF Management Committee.
All studies conducted in the HLRI CRF undergo a risk assessment. The risk assessment is captured as part of RPH R&D set-up process.

Further details can be found in HLRI CRF Guidelines - Applying for use of HLRI CRF and SOP

5.8.2 Study approval process

Research activity conducted in the HLRI CRF requires prior approval from:

- A Research Ethics Committee | Health Research Authority
- The Medicines and Healthcare products Regulatory Agency MHRA for CIMP studies
- A competent authority, as appropriate
- RPH R&D department
- CCRC Scientific Advisory Board (SAB): The SAB meets monthly to assess new studies, study amendments and study renewals.

CCRC SAB approval is given initially for a period of one year, followed by an annual review and approval process.

These processes are happening in parallel, and approval is required from both.

Relevant SOPs:

- SOP034 Research Studies: Trust Confirmation of Capacity and Capability to Conduct Research Studies
- SOP005 Ethics Approval of Research Studies
- CCRC SOP2 Administration of new study applications

5.9 Equipment

The area and equipment used to conduct research can be critical to the quality of the data generated. Systems must be put in place to ensure necessary facility and equipment requirements are documented and processes put in place to ensure these are appropriately operated, monitored and maintained. Further guidance is detailed in GD 039 HLRI CRF Equipment management guidance.

All equipment is purchased and commissioned where appropriate, SOPs are implemented for the use of equipment. Only suitably trained personnel have access to equipment, and this training/competency assessment is documented.

HLRI CRF staff training on medical equipment, competences and lab training is in N drive – (Refer to current contents spreadsheet of the HLRI CRF N Drive) and reviewed during the annual appraisal. |Access to N drive is provided to the HLRI CRF employees on joining the team

All clinical equipment provided by sponsors are reviewed by the Clinical Engineering Department in compliance with NHS Resolution.

Study specific and specialist training involving equipment such as Centrifuges is managed by review of relevant SOPs and recording training activity in the Training folders.

5.9.1 Equipment Introduction

Where applicable the equipment is:

- Subject to risk assessment
- Given a unique identifier for traceability and record keeping.
- Validated
- Calibrated against traceable international or national standards.
- Maintained
- electrical safety tested.
- Safeguarded from adjustments that would invalidate results.
- Protected from damage and deterioration during handling, maintenance, and storage.
- Kept clean and fit for use.
- Decontaminated and decommissioned

5.9.2 Risk Assessment

Where applicable, equipment within the facility is subject to a risk assessment, as per Trust/local policy to assess impact on patients and trial data.
Potential safety issues are identified, and suitable procedures are implemented and documented to mitigate these risks.

5.9.3 Fridges and Freezers

Fridges and freezers within the facility are temperature monitored according to Guidance GD038 Temperature monitoring of fridges and freezers at the HLRI CRF

Fridges and freezers are lockable and access to keys are restricted to authorised personnel only. Keys are kept in the CRF A schedule for fridge and freezer defrosting is set according to RPH R&D SOP 029 Freezers: Management of Research and Development Freezers. Daily, weekly and monthly checks are undertaken and recorded as part of the housekeeping checklist. Paper records are stored in reception office.

Relevant SOPs:

- Guidance GD038 Temperature monitoring of fridges and freezers at the HLRI CRF
- RPH R&D SOP 029 Freezers: Management of Research and Development Freezers.

5.9.4 Calibration and Preventative Maintenance

- All equipment is subject to mandatory testing (for example PAT testing) according to RPH local policy. Clinical engineering is PAT tested and maintained by RPH Clinical Engineering department. The rest of the equipment, fridges, freezers, computers, and other equipment is PAT tested by the UoC.
- Where appropriate, equipment must be calibrated and regularly maintained to ensure it is fit for use. Ordinarily, the schedule for maintenance and calibration will be according to the manufacturer's instructions.
- Evidence of maintenance and calibration visits are being recorded in the RPH Equipment register.

5.9.5 Validation and CSV

- All equipment is allocated a unique identifier and is displayed on the equipment.

- A comprehensive log of all equipment in the facility is maintained, including details of the supplier, date received, serial numbers, as well as calibration and maintenance details. (Refer to current contents spreadsheet of the HLRI CRF N Drive).

5.9.6 Identification and Traceability

- All equipment is allocated a unique identifier and is displayed on the equipment.
- A comprehensive log of all equipment in the facility is maintained, including details of the supplier, date received, serial numbers, as well as calibration and maintenance details. (Refer to current contents spreadsheet of the HLRI CRF N Drive).

5.9.7 Decommissioning of Equipment

Any equipment that is no longer required or is faulty must be decommissioned as per RPH Policy.

5.9.8 Patient Safety Alers and Medical Devices

Patient safety includes Infection and Protection Control Committee and quality reports which includes headline summary on patient feedback, IPCC, Incident/datix and health and Safety mandatory training. This are provided to HRLICRF management committee and R&D.

5.10 Training

The HLRI CRF ensures that all staff working in the HLRI CRF are appropriately qualified and have received adequate training to enable them to carry out their duties and the duties delegated to them by the PI. Personnel folders are kept in a locked cabinet in the Staff room (R018).

Relevant SOPs:

SOP049- GCP Training for Research Staff

SOP 002 Training Records for Research Active Staff

5.10.1 Staff Induction

HLRI CRF staff are appropriately inducted following the guidelines and checklists included in RPH R&D induction programme. Staff will be provided with the list of SOPs s that they must be trained before they can start work on their duties and studies. GD 033 HLRI CRF Staff Induction Handbook.

5.10.2 Training File Maintenance

The HLRI CRF team f maintain an individual training file that includes their CV, job description, training certificates etc. This is in line with R&D SOP02. Training Records for Research Active Staff.

5.10.3 Training competency

The HLRI CRF Operations Manager and Research Nurse team leader are responsible for ensuring that training and resources are available to enable staff to be competent for their specified role. Staff training in some areas (e.g. cannulation) requires a competency assessment to provide evidence of competency. Competency assessments are completed in line with the SOPs describing the procedure being undertaken.

5.10.4 Quality System Training

All staff are required to read and record the fact that they have read and understand this manual and the associated SOP's that relate to the Quality System.

5.10.5 GCP Training

Certified GCP training is essential for all staff working on trials – this training must be refreshed according to RPH trust policy every 3 years. If a sponsor requests a more recent certification for GCP this will be undertaken if necessary. Staff are responsible for ensuring that details of GCP and other essential training are recorded on their CVs and the associated certificates kept in individual training files.

'Prior to leaving the HLRI CRF all staff review their Training folders and ensure that the folder is up to date as of the last day of service. The Training folder will be retained so that it is available for monitor review during the life course of the studies that the member of staff was involved in. Once the last study is closed and archived the Training record can be destroyed using the confidential waste route.

5.10.6 External personnel

Where relevant expertise is not available in-house the HLRI CRF employs out-sourced, external personnel to support its activities. The HLRI CRF also has external users. The HLRI CRF is responsible for ensuring that any external personnel working with/in the HLRI CRF comply with relevant regulations whilst working for the facility, refer to induction guidelines.

5.10.7 Emergency Scenarios

HLRI CRF manages the Emergency Scenario Training using the UKCRF Network Emergency Scenario Training Document. When the UKCRF documentation is reviewed and updated, the local Emergency Scenario training is reviewed in line with the new recommendations and amended accordingly.

HLRI CRF clinical staff will have their life support skills tested regularly with Emergency Scenarios which is provided in addition to their attendance at the Trust's Immediate Life Support training.

The training together with a yearly planned and if possible unplanned scenarios are delivered by Cambridge Clinical Research Centre Education team in collaboration with RPH Education team.

Ward-based Emergency Simulation Training is aimed at all patient-facing staff groups such as Nurses and Receptionists, Training includes 1-2 simulated clinical emergency scenarios that candidates have to manage in the actual ward environment.

During EST, candidates will actively participate in at least one scenario, which will expose them to a medical emergency. Examples may include anaphylaxis; acute coronary syndrome; life-threatening asthma; hypoglycaemia and syncope, as per recommendations by the MHRA (MHRA phase I accreditation scheme guidance document 2015) or topical scenario such as sepsis.

Each scenario is followed by a facilitated debriefing session using an advocacy-inquiry technique (learning conversation). The debriefing is led by a suitably qualified and experienced person.

All the simulated scenarios will be relevant to the candidate's workplace and to the studies that they are expected to facilitate in their respective units.

All EST events will have an accompanying lesson plan, A CAPA plan will be written by the EST Education Team in conjunction with Senior HLRI CRF Clinical Staff who will ensure the CAPA plan is implemented.

Relevant SOPs and documents:

SOP2: Training Records for Research Active Staff

UKCRF Network Emergency Scenario Training Guidance document version 5. June 201

5.11 Investigational Agents

The use of all IMPs in a clinical trial are covered by a CTA issued by the MHRA. All clinical trials will have full RPH R&D approval prior to IMPs being received from the Sponsor.

5.11.1 IMP Receipt

As per MHRA guidance, the receipt and storage of IMP is delegated to the Pharmacy Department. This is clearly stated in RPH SOP 072. RPH Pharmacy are responsible for ensuring that IMP have been manufactured, handled and stored according to GMP (EU Directive 2003/94/EC), that each batch has been certified by the Sponsor's QP and that labelling adheres to Eudralex, volume 4, annex 13. Refer to the Pharmacy SOPs for further details.

5.11.2 Temperature Mapping and Monitoring

All IMPs have instructions for storage with specified temperature ranges. All IMPs are stored in secure, temperature monitored locations to ensure that the temperature range specified is not breached. In the event of a temperature deviation, the following SOPs are in place and are followed: refer GD 38 HLRI CRF Temperature monitoring of fridges and freezers which details the actions required in the case of temperature deviations, and arrangements for out of hours action/ quarantine.

5.11.3 Accountability

Accountability of all IMP (and NIMP) is recorded at all times, ensuring that adequate reconstruction of IMP and NIMP movement is documented. This is achieved by following SOP 082 Returns of IMP to pharmacy.

5.11.4 Handling of non-conforming IMP

Any non-conforming IMP is quarantined or returned immediately to the Pharmacy Department, as per SOP 075 ensuring that no product is used. The Sponsor and research team is notified of the non-conformance and the non-conformance is logged and followed up by the relevant SOPs

Relevant SOPs:
SOP 072 - Supply of Clinical Trials Investigational Medicinal Products (IMP) Dispensing Returns and Accountability
SOP074- Handling of Drug Alerts and Recalls of Investigational Medicinal Products (IMPs) or other trial related drugs
SOP 076 - Transport, Storage and Environmental Monitoring of IMP's
SOP075 - Quarantine of IMP's (Investigational Medicinal Products)

SOP081- Destruction of Waste IMP (Investigational Medicinal Product) pdf
SOP082- Returns of IMP to Pharmacy

5.11.5 IMP storage at the HLRI CRF

Clinical trial and other drugs obtained for research purposes will also be stored in the the HLRI CRF treatment room (for CRF based studies only). They will be stored in either a fridge or freezer as required. The HLRI CRF treatment room is temperature regulated and monitored with the same system as the main pharmacy department. The Pharmacy team is responsible for all the activities related to the IMPs storage at the HLRI CRF. Eg. storage, dispensing, destruction, quarantine, including the delivery and documentation, temperature monitored of the fridges and freezers. Keys for the fridge/freezer with IMPs will be kept with the Pharmacy team. Pharmacy folders will also be stored at the CRF in locked cupboard.

Relevant SOPs and documents:

SOP 76 Transport, Storage and Environmental Monitoring of IMP's (Investigational Medicinal Products)

CT 15 Authorisation of IMP(Investigational Medicinal Product) storage areas outside of the Pharmacy Clinical Trials Department

DN223 Pharmacy Department Operational Procedure

5.12 Processes

Standard Operating Procedures (SOPs), templates, guidance and forms are being used to facilitate consistency and reproducibility of tasks.

5.12.1 Data integrity

The Trust understand the importance of GCP data generated in the conduct of research and that such data is fundamental to ensuring the quality and integrity of research outcomes and the safety and protection of research participants.

Data must at all times during its lifecycle be attributable, legible, contemporaneous, original and accurate (ALCOA) so that it is reliable and can accurately reconstruct activities as they occurred should it be required to do at any given time. Data governance measures

in place shall ensure that the data is complete, consistent, enduring, and available throughout the data lifecycle.

Compliance with data integrity principles is achieved through an environment of data integrity compliance culture which is strategically supported by:

- RPH Standard Operating Procedures
- Periodic review and monitoring
- Training
- Encouraging reporting of data integrity breaches
- All Core staff and HLRI CRF users must have read RPH SOP Source Data Documentation

The HLRI CRF is subject to official review by regulatory authorities e.g. The Medicines and Healthcare products Regulatory Agency (MHRA).

5.13 Audits

5.13.1.1 Quality control and assurance

- Quality Control (QC) is a pivotal part of the QMS. Clear permitted parameters should be defined during the development of quality processes.
- QC will be undertaken by those performing, managing, or supervising a process to ensure that the required standards have been met.
- QC checking, inspection and monitoring activities must be documented and will form part of the QMS.
- QC activities will be reviewed to indicate the degree of adequacy of performance and to monitor trends where there is improvement or deterioration.
- Quality Assurance (QA) is the independent assurance that the defined requirements for a process have been followed. QA may use similar techniques to QC, but the fundamental difference is that QA is independent of the activity being audited.
- An internal audit programme will be devised and implemented by the HLRI CRF Operations Manager.

5.13.2 Internal Audits

- Internal audits will be conducted to verify that each HLRI CRF quality system is compliant with the established HLRI CRF and regulatory requirements and to verify the effectiveness of each system.
- The HLRI CRF QA representative or CRF Operations Manager will compile and administer an agreed internal audit programme in the HLRI CRF. This will include implementing, scheduling, communicating, maintaining, and monitoring the programme.

- An internal audit programme will be planned and maintained with audits conducted periodically to monitor compliance with HLRI CRF policies and procedures and regulatory requirements.
- Audit activities will be selected according to the audit programme and HLRI CRF priorities and requirements and will be performed by persons who are not responsible for the area being audited. Each audit activity should be reported and acted upon as necessary.
- HLRI CRF will create a rolling programme of systems and process audit to be conducted using SOP063 Internal Good Clinical Practice (GCP) Audit. The primary purpose of the GCP audit is to provide assurances to the quality of all activities delivered in the HLRI CRF. The rolling program audit will serve to provide assurance that clinical trial activities are being performed in accordance with UK clinical legislation, applicable standard Operating Procedures (SOP's) and Good Clinical Practice (GCP)
- Additionally triggered audits may also be carried out if there are concerns with any aspect of a clinical trial. All reports generated from the rolling systems audit, or the triggered audits will be submitted to the HLR ICRF Management Committee in a quarterly based, this may initiate further necessary action or training.
- All Studies delivered at the HLRI CRF will be assessed for 'risk' during the SAB review process using the UKCRF risk assessment form and the research governance process (RGPAS) if applicable using SOP025 Assessment and Registration of Trust Risk Rating for Research Studies and FRM013 Risk Assessment tool. SOP065 should also be consulted for the Risk-adapted approach to the Management of Clinical Trials of Investigational Medicinal Products.
- In addition, specific triggered monitoring or 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.

Relevant SOPS:

SOP025 Assessment and Registration of Trust Risk Rating for Research Studies FRM013 Risk Assessment tool.
SOP065 should also be consulted for he Risk-adapted approach to the Management of Clinical Trials of Investigational Medicinal Products.

5.13.3 Internal Audit Report

- An internal audit report should be created to summarise audit findings.
- This audit report would document the observations and findings of the components audited, with a comment and recommendations where appropriate. This report should then be issued to the personnel responsible for the area audited for review and action and

for escalation to senior management as required**.** Findings and actions identified by audit should be documented and addressed in a timely manner with implementation of corrective and preventive actions verified and documented as per section 8.6.

- Non-compliance / deviations will be managed according to section 8.6 and /or RPH policy.
- Continual review of audit findings and the management of associated corrective and preventive actions are performed to ensure continuous quality improvement.

Audit programme for system and process such as archiving, contract management, delegation, deviation recording and reporting, cleaning, equipment registry, training and competency management, sample processing and management. To consider vendors and suppliers that are contracted if relevant. cupboard contents. Studies are being audit by RPH R&D process

5.13.4 Third Party Audits

- A system will be maintained to manage regulatory inspections and third-party audits and any associated responses and actions. Findings or observations identified during an inspection or audit must be responded to and resolved in a timely manner.
- If the HLRI CRF conduct external audits of vendors or service providers, such as suppliers or laboratories etc., then an external audit programme is required.
- In addition to Royal Papworth Hospital performing, monitoring and Health and Safety, Inspection, Clinical Environmental audit checks, studies might be audited by Sponsors, CRO, commercial partners, CTIMPs may be inspected by the MHRA (Medicines & Healthcare products Regulatory Agency).

5.13.5 Complaints and complain handling

It is important that feedback from stakeholders is taken into account as part of the process for evaluating and continually improving the quality of the service provided by the HLRI CRF The CRF will adhere to the Trust policy for managing complaints.

Complaints will be directed to the HLRI CRF Operations Manager or HLRI CRF Research Nurse Lead in the first instance, who will investigate the issue and attempt to resolve as quickly as possible.

If local resolution of a complaint is not possible, the issue may be escalated to the HLRI CRF Clinical Director or RPH R&D Director as appropriate.

If necessary, participants may be referred to the hospitals Patient Advice and Liaison Service (PALS) for RPH.

The University also have a service for complaints if required. University of Cambrige complaints and disclosures. - https://www.studentcomplaints.admin.cam.ac.uk/staff-support/handling-complaints-and disclosures#:~:text=If%20you%20wish%20to%20submit,ac.uk%20within%2028%20days.

Refer to local, RPH Complaints Policy, DN 195 for the pprocess for receiving, investigating, and responding to a complaint under the NHS complaints regulations.

Positive comments are reported back to staff and constructive feedback is used to improve our users' experiences. RPH uses Laudit platform a digital reporting portal to enable the recognition and celebration of the everyday extraordinary measures that staff perform in their roles.

5.13.6 Feedback and continuous improvement, including corrective and preventative actions (CAPA)

The HLRI CRF Operations Management Committee actively encourage and facilitate feedback from all service stakeholders to drive continuous improvement. The Quality Management Plan should be continually reviewed, and improvements made where required. All RPH R&D SOPs and guidance will be updated in line with any changes to the Clinical Trial Regulations or other governance requirements. Otherwise, all SOPs will be routinely reviewed as per RPH R&D, every 3 years as a minimum.

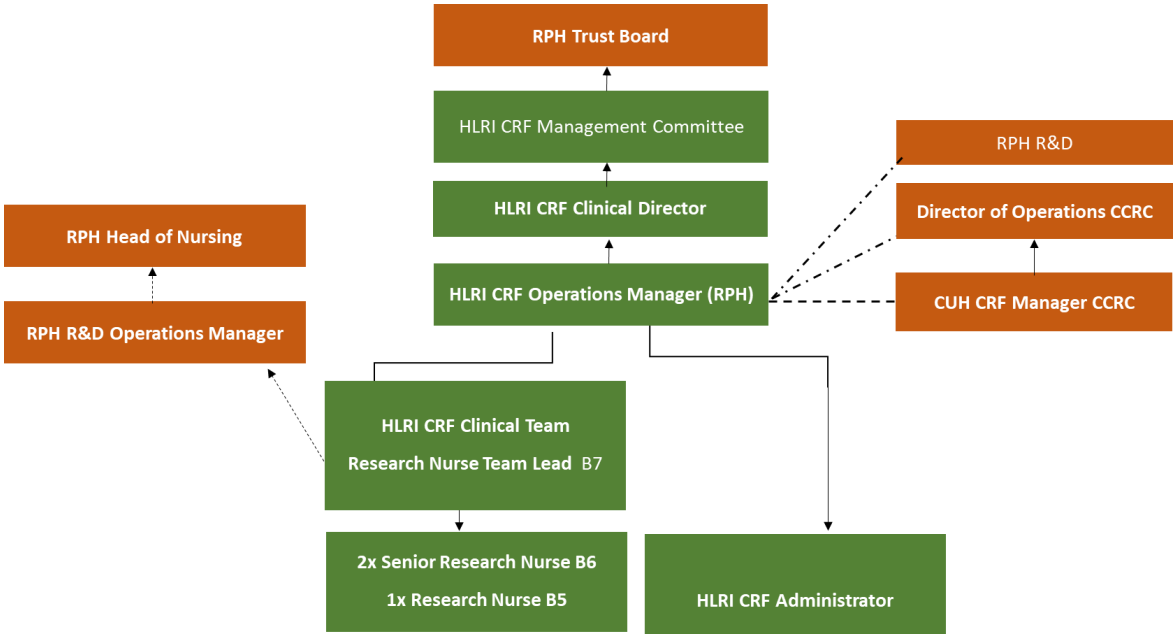
Identified Corrective and Preventative Action (CAPA) plans will be monitored to completion and trends reviewed to assess effectiveness of CAPA.

HLRI CRF QMS quality event trends will be monitored and reviewed for improvement opportunities.
Associated SOPs/Guidance Documents: CAPA Guidance Document GD02

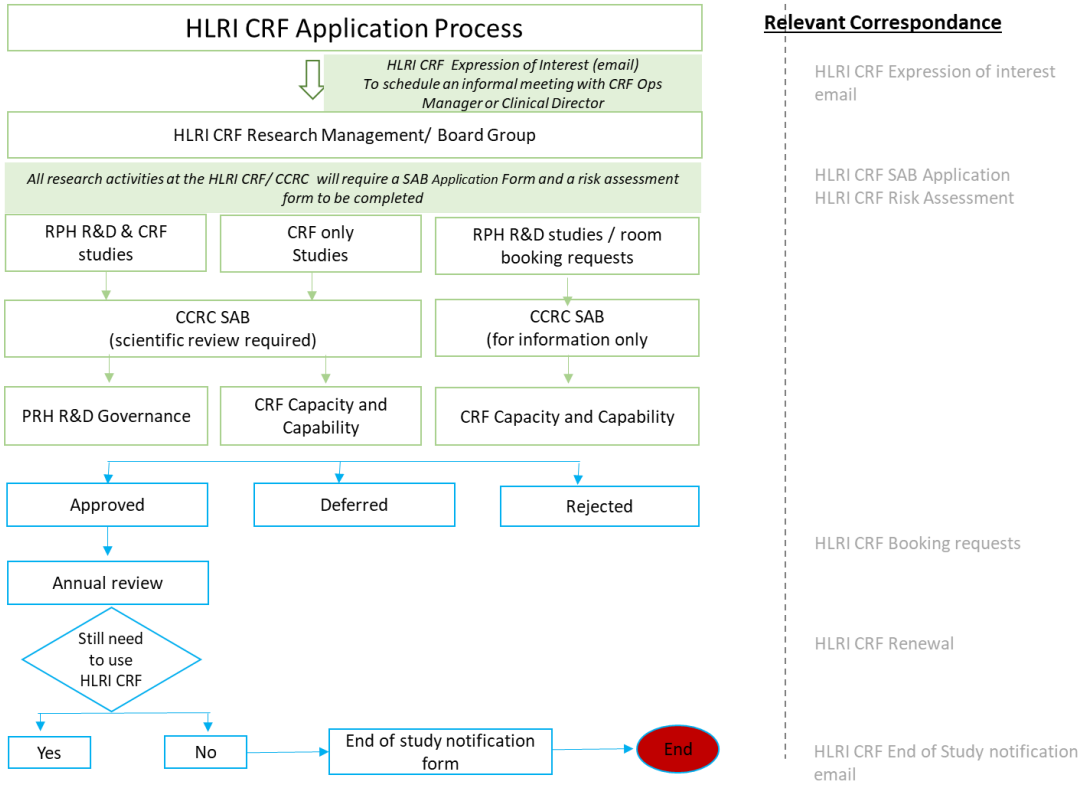
All SOPs and procedures can be found : Standard Operating Procedures :: Royal Papworth Hospital

5.14 Appendix

Appendix 1 HLRI CRF Structure and reporting lines



Appendix 2



6 Risk Management / Liability / Monitoring & Audit

1. The R&D SOP Committee will ensure that this SOP and any future changes to this document are adequately disseminated.

2. The R&D Department will monitor adherence to this SOP via the routine audit and monitoring of individual clinical trials and the Trust's auditors will monitor this SOP as part of their audit of Research Governance. From time to time, the SOP may also be inspected by external regulatory agencies (e.g. Care Quality Commission, Medicines and Healthcare Regulatory Agency).

3. In exceptional circumstances it might be necessary to deviate from this SOP for which written approval of the Senior R&D Manager should be gained before any action is taken. SOP deviations should be recorded including details of alternative procedures followed and filed in the Investigator and Sponsor Master File.

4. The Research and Development Directorate is responsible for the ratification of this procedure.

Further Document Information

Approved by: *Management/Clinical Directorate Group*	Research and Development Directorate
Approval date: *(this version)*	Current approved version date
Ratified by Board of Directors/ Committee of the Board of Directors:	STET
Date:	N/A
This document supports: *Standards and legislation*	Medicines for Human Use (Clinical Trials) Regulations 2004 and all associated amendments. UK Policy Framework for Health and Social Care Research (2018)
Key related documents:	Trust Research Policy Trust Policy DN1 Document Control Procedures

Equality Impact Assessment: Does this document impact on any of the following groups? If YES, state positive or negative, complete Equality Impact Assessment Form available in Disability Equality Scheme document DN192 and attach.

Groups	Disability	Race	Gender	Age	Sexual orientation	Religious & belief	Other
Yes/No	NO	NO	NO	NO	NO	NO	NO
Positive/Negative							

Review date:	DATE

I certify the contents of this SOP has been reviewed and ratified

Patrick Calvert 24-02-2024

....

Signed by Dr Patrick Calvert, Clinical Director of R&D Date

SOP Release Date: ……..