Document Title: Phase I Risk Assessment, Management, and Risk Mitigation

Document Number: HLRI CRF SOP090

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Directorate:	Research and Development
Department:	Research and Development
For use by:	NHS Staff Trust-Wide
Review due:	July 2027

Summary of Amendments

Version Number	Modification:
Version 1	Creation of new SOP

Key Points of this Document

- This document sets out the procedures to be followed by all staff using the VPD HLRI CRF and all the R&D Study teams conducting trials at the VPD HLRI CRF.
- It provides guidance on the managing and conduct of Early Phase trials to ensure compliance with the Trust's policies.

1 Purpose and Contents

This document provides a procedure for the setup and management of Phase I Clinical Trials of Investigational Medicinal Products (CTIMPS) or devices in the CRF.
The procedures outlined in this document aim to:

a. Provide a risk assessment process for Phase I trials.
b. Provide risk management plans for Phase I trials.
c. Enhance participant safety.
d. Aid compliance with MHRA guidelines and Good Clinical Practice (GCP)
e. Provide guidance for Principal Investigators (PI) CRF and R&D staff.

2 Roles & Responsibilities

a. This SOP should be read in conjunction with SOP055: Roles and Responsibilities for the Conduct of Research Studies and Clinical Trials including CTIMPs (Clinical Trials of Investigational Medicine Products), which defines the overall responsibilities of the Sponsor, The Chief Investigator and Principal investigators when conducting clinical research studies.

b. This Policy applies to all personnel conducting research at the Trust whether full or part-time employees of the Trust, those working at the Trust with employment contracts funded partially or wholly by third parties (including those within CUHP AHSC), those seconded to and providing consultancy to the Trust, and to students undertaking training at the Trust.

3 Definitions and Abbreviations

The headings below contain the definitions of terms and meaning of abbreviations used within this document.

3.1 Definitions

Term	Definition
First in Human trial	A Phase I clinical trial where an investigational medicinal product or medical device is tested in humans (patients or healthy volunteers) for the first time
Allocate Optima	An electronic staff rostering system used by Royal Papworth Hospital
Healthcare professional	A Registered Nurse, Medical Doctors, Associate Practitioners and Clinical Trial Coordinators, Team members with RPH substantive or honorary contracts
Pharmacology	Pharmacology is the science of drugs and their effect on living systems. The study of a drugs mode of action, toxicology and pharmacokinetics
Pharmacodynamics (PD)	Examines the drug's effect on the body
Phase I trial	A clinical trial to study the pharmacology of an investigational medicinal product (IMP) when administered to humans, usually the first time in humans, to determine safe dose range and potential side effects, how it is metabolized and whether it might work in patients. May also include medical devices tested for the first time in humans.
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

3.2 Abbreviations

Abbreviation	Meaning
BLS	Basic Life Support
CCRC	Cambridge Clinical Research Centre
CCA	Critical Care Unit
CTIMP	Clinical Trial Investigational Medicinal Product
EST	Emergency Simulation Training
FIH	First in Human
GCP	Good Clinical Practice
ILS	Immediate Life Support
IMP	Investigational Medicinal Product
MHRA	Medicines and Healthcare products Regulatory Agency
PI	Principle Investigator
SAB	Scientific Advisory Board

4 Items Required

FRM013 R&D	Risk Assessment Tool
FRM099 HLRI CRF	Intensive Care Notification Form
GD040 HLRI CRF	Operational Manual
SOP099 HLRI CRF	VPD HLRI CRF Medical Cover for Research Studies
SOP055 R&D	Roles and Responsibilities for the Conduct of Research Studies and Clinical Trials including CTIMPs (Clinical Trials of Investigational Medicine Products)
DN765 RPH	Inter Hospital Transfer Guideline for Patients between Cambridge University Hospitals & Royal Papworth Hospital

5 Policy

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

6 Procedure

6.1 Application, risk assessment and mitigation process

The CCRC Scientific Advisory Board (SAB) reviews and carefully appraises all research applications for the VPD HLRI CRF and the medical and staff resources required.

a. On receipt of an application for a Phase I trial the VPD HLRI CRF Operations Manager, Team Leader and PI will complete a Phase I Risk Assessment Matrix and Contingency Plans (LOW, MEDIUM or HIGH).

b. Trials assessed as HIGH RISK, will require the PI to complete CCRC/FRM041 Phase I Risk Assessment Form.

c. The VPD HLRI CRF Operations Manager and Team Leader will review all completed forms prior to CCRC SAB review.

d. CCRC SAB will allocate a voting member with Phase I trial experience to review and advise the study documents including risk assessment forms.

All CTIMP trials, including Phase I trials, conducted at the VPD HLRI CRF or RPH are submitted to RGPAS for review of capacity and capability. Risk Assessments will be completed and reviewed by Clinical Trials Pharmacy and R&D Governance. All risks involved and mitigation actions are discussed in RGPAS prior confirmation of Capacity and Capability of any Trial conducted at the Trust.

6.2 CCA and Emergency Team Notification Process

Phase I trials assessed by SAB and RGPAS as requiring ICU Notification, will notify CCA following the process below:

a. CRF Team Leader will complete and ask PI to review and email a **FRM099 HLRI CRF Intensive Care Notification** form prior to participant dosing to inform of the date of the trial and potential requirement of a critical care bed to:

- CCA Clinical Leads, ALERT team, Resuscitation Team, Intensive Care Consultants, Head of nursing for Surgical Transplant and Anaesthetic and Operations Directors for STA.

b. PI or CRF Team Leader will inform the following bleep holders of the dosing date:

- 500/501 ICU Registrar on call
- 432/512 ALERT
- 450/451 Resus Officer

Prior to the planned visit ensure that the following information is passed in the 09:00/22:00 Trust Safety Huddle attended by relevant team members:

- Participant ID and details
- Disease group
- Sponsor details
- Name of drug, dose and route of administration
- Dosing date
- Refer back to the email with details about the study

c. PI must copy correspondence to the CRF Ops Manager, Team Leader and relevant study team.

d. If availability of a critical care bed in ICU cannot be confirmed for the day, the participant visit should be rescheduled if possible. If the visit cannot be rescheduled the request will be escalated to the CRF Clinical Director and Investigator and RPH Medical Director. To include CRF Operations Manager, Research Nurse Team Leader and team email address hlri.crf@nhs.net in the correspondence.

6.3 VPD HLRI CRF Responsibilities

The CRF Team Leader, or delegate, must file a copy of the pre-dosing information sent to CCA in the R&D studies shared N: drive.

6.4 Medical Cover

Medical cover for Phase I trials will be guided by this SOP and SOP099 HLRI CRF Medical Cover for Research Studies.

PI should be required to be present in person on the unit on dosing days. Medical cover may be delegated to a named Medical Doctor on the delegation log with knowledge of the protocol, acceptable Phase I experience or pharmacology post-graduate qualification. This person must be on the delegation log.

PI is responsible for providing 24-hour medical cover, including contact details, either on site, on the unit or by phone as determined by RGPAS, before participants receive any study medication.

6.5 VPD HLRI CRF Staff Training

All CRF staff must hold appropriate qualifications and have completed relevant training in line with the responsibilities of their role.

Research nurses delivering Phase I trials must have completed and be in date with ILS and relevant EST.

6.6 Medical Emergencies and access

CRF staff will respond to medical emergencies in line with RPH standard practice.

In a medical emergency, CRF Registered Nurses must escalate to the identified medical cover and/or RPH emergency teams (including 2222 Responders, Alert Team and CCA).

RPH Emergency Response will access the VPD HLRI CRF via the VPD HLRI-RPH link corridor. To gain access the Emergency team will press the clearly labelled locking release button. This will open all doors and will unlock the lift.

There are additional Emergency locking release buttons at the nursing stations inside the CRF which the CRF staff can also release in an emergency situation.

The dedicated emergency corridor connecting the VPD HLRI building to RPH Basement allows timely transfers of participants to CCA (see DN765 Inter Hospital Transfer Guideline for Patients between Cambridge University Hospitals & Royal Papworth Hospital).

In a non-emergency situation, the ALERT and Resuscitation officers have access cards for the VPD HLRI corridor and CRF.

6.7 Minimum Staffing Levels for Phase I Trials

a. VPD HLRI CRF Operational Manager and CRF Team Leader will assess information

provided on FRM013 R&D Risk Assessment Tool form to determine safe staffing levels and skill mix for trial visits, this will be included in the staff planning in Allocate Optima (Health Roster).

b. A minimum of two Registered Nurses must be present on the unit for the duration of each study visit.

c. Nurse in Charge will record the names of staff allocated to Phase I trials on a day-to-day basis.

7 References

a. SOP055: Roles and Responsibilities for the Conduct of Research Studies and Clinical Trials including CTIMPs (Clinical Trials of Investigational Medicine Products),
b. Guidelines for Phase I clinical trials (2018), updated 2022, ABPI
c. MHRA Phase I Accreditation Scheme Guidance v4.1 12 August 2022
d. Good Clinical Practice Guide (2012), London: MHRA
e. The Institute of Clinical Research (2008), Abbreviations used in Clinical Trials

8 Risk Management / Liability / Monitoring & Audit

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

b. 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).

c. 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.

d. 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 (2023)
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:	July 2027