NIHR | Lancashire Clinical Research Facility

STANDARD OPERATING PROCEDURE

The Management and Conduct of Early Phase (First in Human; Phase I) Experimental Medicine Studies

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RESEARCH AND DEVELOPMENT

LCRF

BACKGROUND

The NIHR Lancashire Clinical Research Facility (LCRF) supports a variety of early phase clinical trials including first in human (FiH) and Phase I. The LCRF is not a MHRA Accredited site but seeks to ensure that all early phase clinical trials are conducted to a very high standard.

PURPOSE/OBJECTIVE

This SOP will provide a resource for members of the LCRF Senior Management Team, Clinical Teams, the Early Phase Review Committee (EPRC), Lancashire Teaching Hospitals Emergency Teams, support services and researchers and is designed to provide working instructions so that all early phase studies are managed and conducted in a consistent and uniform manner.

SCOPE

This SOP applies to all staff involved in the setup and conduct of all early phase clinical trials delivered in the LCRF.

PROCEDURE

1. WHO?

1.1. The Principal Investigator (PI) is responsible for the clinical safety of participants in their research study. The PI is also responsible for ensuring all relevant procedures and risk assessments, as outlined in this SOP, are completed and adhered to in order to ensure compliance with the standards set out in the MHRA Phase I Accreditation Scheme.

1.2. The EPRC is responsible for reviewing all documentation provided to them by the study PI, and/or research team, to authorise delivery of the trial within the LCRF. They are responsible for providing any recommendations prior to approving the trial to commence in the LCRF.

1.3. It is the responsibility of the LCRF Senior Management to monitor compliance with this SOP.

1.4. It is the responsibility of all staff to have read and understood this SOP.

2. WHEN?

This SOP describes the process of conducting and managing an early phase trial within the LCRF. This SOP must be followed when setting up and conducting an early phase trial within the LCRF. Many of the items described are fully expanded in associated SOP's. Anyone involved in early phase trials must read and adhere to all of these detailed documents.

3. HOW?

3.1. Application to conduct a FiH or Phase I trial within the LCRF

3.1.1. Researchers are encouraged to make early contact with the LCRF, preferably during protocol development or initial approach from a study Sponsor, to establish how best the research trial can be facilitated.

3.1.2. A LCRF study application form must be completed and submitted to the LCRF Lead as per LCRF-SOP- 08 and a date arranged for the initial trial meeting to be held.

3.1.3. All First in Human and phase I studies must be approved by the Early Phase Review Committee (EPRC) before LCRF Approval is granted. Following review by the EPRC the report will be fed back to the Principle Investigator (PI) and the LCRF Nurse Managers. All queries must be resolved prior to LCRF approval issued.

3.1.4. If the trial involves a Genetically Modified Organism (GMO) approval from the GMO Committee must be received before LCRF approval is given.

3.1.5. Each study must be registered and approved by the LCRF Manager before LTHTr Confirmation of Capacity and Capability is issued.

3.2. Study Risk Assessments

3.2.1. The LCRF early phase/complex study risk assessment must be completed for all FiH/phase I and complex phase 2 clinical trials. This must be completed by the PI/LCRF Medic/LCRF Lead/Lead Study Nurse before the trial is reviewed by the EPRC.

3.2.2. The study risk assessment must be submitted **two weeks** prior to the EPRC. This will ensure the EPRC have enough time to review the trial and study risk assessment before the committee meeting. The Chair of the Committee will be responsible for approving the risk assessment.

3.2.3. Documents used to complete the study risk assessment must be detailed within the risk assessment, including version numbers and dates.

3.2.4. Study risk assessments must be retained on EDGE and updated by the LCRF as required.

3.2.5. It is the responsibility of the PI to ensure the risk assessment is adhered to and updated as required to ensure it reflects the study documentation. The PI must review the Risk Assessment if there are any changes to the original documentation (for example, protocol amendments, new safety information, investigator changes). This review must be agreed and approved by the LCRF Medical Director and if deemed necessary by the medical director, further review by the EPRC. Risk assessment compliance will be assessed as part of the LCRF audit programme.

3.3. Communication of FiH/Phase I with the Emergency Teams

3.3.1. During set up the LCRF lead nurse must contact, preferably via email, the research lead for Lancashire Teaching Hospitals emergency theatres, critical care and the resus team and provide a synopsis of the trial, the latest version of the trial protocol and study timelines.

3.3.2. It is the responsibility of the LCRF lead nurse to follow the latest version of the 'Communication Procedure for all Early Phase Experimental Medicine Trials being delivered in the NIHR Lancashire Clinical Research Facility' document.

3.4. Management of Medical Emergencies

3.4.1. Please refer to LCRF-SOP-02 Management of Medical Emergencies

3.4.2. A full LTHTr trust standard resuscitation trolley is located in the clinical area of the LCRF which is checked daily and maintained in accordance with the trust's standard.

3.4.3. Each clinic room in the LCRF has emergency alarms that can be activated by staff and patients. When they are activated an audible alarm sounds throughout the LCRF (admin and clinical areas) and panels, located behind reception and in the agile room (admin area), indicate where the emergency is.

3.4.4. The alarms are checked on a daily basis by the LCRF clinical staff.

3.5. Emergency Scenario Training

3.5.1. It is a requirement that all LCRF staff have attended a planned scenario before conducting any early phase study work. A planned emergency scenario must be attended twice per year. This training is additional to the staff member's employer's mandatory training requirements.

3.5.2. Further details on the requirements of planned emergency scenarios is available in LCRF-SOP-20.

3.5.3. a trust emergency service scenario should be performed as required, to ensure the LTHTr outreach team, Hospital at Night team and the resuscitation team are aware of the location of the LCRF and that the resus procedures in place in the LCRF are fit for purpose. This will be managed by the LCRF Lead, Consultant Nurse for Critical Care and the Head of Resus at LTHTr.

3.6. Emergency Un-blinding

3.6.1. All blinded FiH or phase I trials in the LCRF must have a detailed and tested un-blinding plan. All staff must have a good knowledge of the un-blinding procedures as specified in the protocol.

3.6.2. If there are no defined un-blinding process in the protocol an agreed and detailed un-blinding plan must be created and signed off by the LCRF Medical Director and PI.

3.6.3. Un-blinding plans must be tested before recruitment commences by the LCRF Manager and/or trial lead nurse.

3.7. Management of the Investigational Medicinal Product (IMP)

3.7.1. The management of all IMPs within the LCRF is provided by LTHTr Pharmacy department.

3.7.2. Management procedures are developed by the LTHTr pharmacy clinical trials team following review of the trial protocol.

3.7.3. Trust pharmacy study specific SOP's must be approved internally within Pharmacy, shared with the relevant research team and PI before study commencement to give assurance of PI oversight.

3.8. Laboratory Monitoring

3.8.1. The LCRF Laboratory stores, processes, and packages samples for Phase 1 studies.

3.8.2. The LCRF Lead should be responsible for the Quality Processes in this area. This includes equipment calibration, staff training and auditing.

3.8.3. The fridges and freezers within this laboratory are monitored with Tutela probes which is the same monitoring system as the LCRF Drug Storage areas.

3.9. Subject Recruitment

3.9.1. For all LCRF FiH and phase I trials, participant medical histories must be verified to ensure they are eligible and medically safe to be involved.

3.9.2. For healthy volunteers this must be done by contacting their General Practitioner.

3.9.3. Patient verification must be confirmed by reviewing the participants' medical notes. If the participant is not a patient at LTHTr, then the either the participant's consultant or General Practitioner (GP) must be contacted for the information.

3.9.4. The participant must have been registered with their GP for 12 months to ensure they are eligible for the trial.

3.9.5. Eligibility verification must be performed by either the PI or the LCRF physician.

3.10. Out of Hours Medical Cover

3.10.1. All participants on FiH and phase I trials being delivered within the LCRF must be provided with a 24-hour emergency contact number which they can use when they are not present in the LCRF.

3.10.2. This emergency medical cover must be organised by the PI. If the PI is delegating the medical cover responsibilities, they must provide study related training to the medic. The PI must ensure all annual leave is covered by the co-investigator. The co-investigator and PI must not be on annual leave at the same time. The PI must inform the lead nurse of all pending annual leave in advance.

3.10.3. Every participant on a FiH or phase I trial will be given a contact card which details the out of hours details for the study team.

3.10.4. All contact numbers and the escalation plan must be documented on the LCRF Medical Cover Form and kept in trials study procedure manual.

3.10.5. Emergency out of hours contact procedures must be tested prior to commencing the trial. This testing must be documented in the study procedure manual. It is the responsibility of the lead nurse to test this procedure prior to the participant's first visit. These must be tested every three months or when there is a change of study personnel.

3.11. Training

3.11.1. LCRF staff working on FiH, or phase I trials are required to be trained appropriately and qualified to conduct their role and duties delegated by the PI.

3.11.2. LCRF staff must keep up to date training records and undertake Good Clinical Practice training every two years.

3.11.3. Training requirements for FiH/Phase I trials:

- Intermediate Life Support – Adult LCRF nurses
- Paediatric Life Support – Paediatric LCRF nurses
- Advanced Life Support – LCRF medic and PI's.
- Paediatric Advanced Life Support – LCRF medic/PI's (Paeds trials only)
- Good Clinical Practice – all staff
- Protocol training – all staff
- Emergency Scenario Training – LCRF nursing team, LCRF medics
- Venepuncture and cannulation – LCRF nursing and medical team
- AIMS course – LCRF nurses.
- Automatic external defibrillator online training – All staff
- Basic Life Support - All staff
- Anaphylaxis - All staff

3.12. Staffing Levels

3.12.1. Due to the location of the LCRF the guidelines stipulate that two trained staff members must be present when a participant is in the facility. For early phase trials this is reviewed on a study-by-study basis, unless stipulated in the protocol, and will be determined by the LCRF Lead and Senior Research Nurse following a risk assessment. Overnight admissions require two trained nurses and a practitioner.

3.12.2. The LCRF Senior Research Nurse will be responsible for ensuring the appropriate staffing levels are met.

3.12.3. The PI is responsible for ensuring the appropriate medical cover is organised. For inpatient studies the PI must ensure there is adequate medical cover. Depending on the risk assessment the medical cover will either be on call or physically in the facility overnight. This decision must be made in collaboration with the LCRF Medical Director.

3.13. LCRF Internal Audits

3.13.1. Early phase study audits will be conducted by the LCRF Lead and delegated quality lead and will relate to the MHRA phase I accreditation standards.

3.13.2. The planning, risk assessments, documentation and reports will use the UKCRF Network audit tools.

3.13.3. It is the responsibility of all staff to comply with and support the LCRF and Quality lead.

3.13.4. Reports and feedback from audits will be presented at the LCRF Operational Group meetings and discussed directly with the study team.

3.13.5. It is the responsibility of the LCRF Lead and the Quality Lead to ensure reports and findings are communicated to the study team in a timely manner and actions following the audit are met.

3.14. Study Documentation

3.14.1. Worksheets will be created by the lead nurse and Clinical Trials Support Officer (CTSO) and will be aligned with the current Health Research Authority (HRA) approval.

3.14.2. All worksheets should be approved by the Pland Sponsor.

3.15. Source Data Verification

3.15.1. Due to the nature of early phase trials, data collected must be verified for accuracy. This is called Source Data Verification (SDV). All data collected by the clinical team for early phase (FiH and phase I) trials must be checked by a second member of the team.

3.15.2. 100% data of all early phase trials must be verified as soon as practicable and before submission to the Sponsor.

3.15.3. Source data verification (SDV) must be documented on the relevant form and signed by the person completing SDV. The clinical team member must sign the form.

3.15.4. Actions/amendments made by the clinical team must be documented as per Good Clinical Practice (GCP).

4. OTHER RELATED PROCEDURES;

LCRF-SOP-20 LCRF Scenario Training

LTHTr Policy and Procedure for the Transfer of Patients, Common Core Document Including Adults, Women's, and Child Health

CONSULTATION WITH STAFF AND PATIENTS

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