1. Introduction

All investigational medicinal products (IMPs) must go through a series of trials before they can be licensed for use. This ensures that new treatments are safe and effective, and that we have as much information as possible on how the human body will respond to a new treatment.

First-in-human (FIH) studies are clinical trials that test new drugs, procedures, or treatments in humans for the first time. They usually take place as phase I clinical trials after the IMP has been tested in animal and laboratory studies. Novel devices may also be used in a FIH trial with the same enhanced standards for safety monitoring and reporting required.

Phase I trials aim to determine the dose and schedule of IMP, the safety and tolerability of the IMP, the pharmacokinetic (PK) and pharmacodynamic (PD) properties of the IMP and potentially look at early signs of efficacy.

Given the early stage in development of an IMP or device used in a Phase I trial, research staff and facilities must meet the standards for enhanced safety monitoring and reporting that are required in a Phase I protocol. Phase I trials are usually performed in a group of healthy volunteers and/or patients.

Any speciality within University Hospitals Leicester may undertake a Phase I trial, but only once arrangements for setup and conduct have been individually assessed as per the requirements of this Standard Operating Procedure.

2. Scope

This SOP applies to all UHL contracted staff working on Phase I trials at UHL and defines roles, responsibilities and requirements for setting up and managing a Phase I trial.

3. Procedure

3.I Requirements of a PI for a Phase I trial

In addition to the usual requirements of acting as a Principal Investigator (PI) for a Clinical Trial of an investigational medicinal products (CTIMP) and Clinical Investigation of a Medical Device, the following must also apply:

- The PI must be suitably qualified, with clinical experience and expertise in the relevant patient population and previous research experience in the delivery of early-phase CTIMPs and/or device trials as applicable.

- The PI should hold a permanent or honorary consultant position within UHL.
- The PI has responsibility for the conduct of the study. Roles and tasks may also be delegated according to skills, qualifications, and knowledge to other members of the research team and must be documented on the delegation log.
- The PI should delegate and support a sub-Investigator or sub-investigators (SI), including speciality trainees with previous trials experience following detailed training from the PI and study team. The SI will support the PI and take on the role of the PI when the PI is absent.
- The PI or SI is responsible for obtaining informed consent from participants enrolled in Phase I/FIH trials.
- The PI and SI(s) should be trained in the initial management and leading, of clinical emergencies as per UHL policy for clinical staff. It is expected that in the event of a cardiac arrest, the resuscitation team, on arrival would take over leadership with ongoing input from the PI or SI(s).
- The PI should be contactable both within and out of normal working hours or should delegate this, (in the case of annual leave or absence), to a SI. This may be a speciality trainee familiar with the trial but consultant cover should be available and provided if needed and must be in place.
- The PI or SI must be available overnight for trials involving overnight stay for patient review if required.
- The PI, in conjunction with the applicable study team, should ensure processes are in place to inform ICU of planned date of admission if indicated prior to admission, and at time of admission of the following: patient details, study details and patient location in the event of an emergency requiring rapid review and/or resus team attendance.
- The PI should ensure that the sponsor has provided adequate emergency medical telephone support which should be available at all times.
- The PI is responsible for communicating pertinent drug/trial updates to key staff including from safety/dose review meetings or urgent safety measures/communications.
- The PI or delegated staff must use the dosing day checklist (T1034) prior to dosing patients in a phase I trial.
- The PI must ensure the study risk assessment is complete and approved by Director of the research area/space and Director of Operations of the research area/space or other defined responsible persons within that speciality. The PI must ensure compliance to any requirements detailed in the study risk assessment.
- The PI must ensure that all staff are trained on all trial delegated procedures and that this is documented in the Investigator Site File (ISF).

3.2 Requirements of the unit/area where the Phase I trial is taking place

The unit/area must be suitable for hosting a Phase I trial;

- The unit must be easily accessible to the resuscitation team in emergency situations.
- The unit should have a resuscitation trolley stocked and checked as per current UHL and National Resuscitation guidance. All staff conducting the Phase I trial should be aware of its location.
- The unit should always have at least two nursing staff present at all times (including overnight if required) and more depending on the number of participants, and the schedule, risk and intensity of the study investigations.
- Staff must be competent to perform the observations and clinical requirements that are within the protocol in order to maintain patient safety.
- All nursing staff must be ILS trained and have anaphylaxis kits available to use if required. Oxygen and suction must also be available and functioning.
- Equipment required for the study must be available and in good working order, such as vital signs monitors, ECG machines, thermometers and pulse oximeters. These should be maintained, calibrated and checked as per current UHL guidance.
- All study equipment, including that provided by external study sponsors should be checked and approved by the UHL clinical engineering team prior to use.
- The unit should have emergency and nurse call buzzers in all areas where participant care will be undertaken.
- The unit must have door locks for toilets that can be opened from the outside in case of emergencies.
- The unit should have height and tilt adjustable beds available. In some cases, fully reclining chairs are acceptable, but this is dependent on the study requirements.
- Within the unit there should be areas to which there is restricted access (staff access only). This includes areas for IMP and equipment storage, sample handling and storage, and any other relevant functions.

3.3 Additional requirements for confirmation of Capacity & Capability of Phase I trials

- Sponsor and PI responsibilities must be clearly defined in the contract for the study, and where applicable in the protocol or supporting documentation.
- There must be a described process to detail how the sponsor will notify the PI immediately of safety information/toxicology data in the protocol and/or contract.
- The study risk assessment (T1033) should be completed in conjunction with the PI and local study set up team. It is the PI's responsibility to ensure that trial activity is conducted in accordance with the Phase I risk stratification matrix.

- T1033 must utilise all applicable study documentation such as the protocol, investigator brochure, available safety data for example. This study documentation should be listed in the risk assessment with all corresponding versions and dates detailed.
- The study risk assessment must be up to date and stored in the Investigator Site File or identified shared area accessible to the PI and study team. Site of storage may be area/space dependent. This may require update based on emerging safety information. The reason for updating must be documented.
- If the study is an ATIMP (Advanced Therapy Investigational Medicinal Product), the UHL ATIMP policy must be adhered to along with approval from the Genetic Modification Safety Committee.

3.4 Amendments or changes to the study

- If there is a study amendment or any changes to the safety information, there must be consideration by the PI whether the study risk assessment should be reviewed and updated. The study risk assessment should be versioned and dated.

4. Supporting Documents and Key References

ABPI Guidelines for Phase I Clinical Trials (20I2 Edition)

T1033 – Phase I Study Risk Assessment

T1034 – Phase I Dosing Day Checklist

6. Key Words

Phase I, First in Human (FIH), Research & Innovation.

7. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Sponsor Audit	Randomly chosen for audit	Carolyn Maloney	As and when	A report will be produced

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This table is used to track the development and approval and dissemination of the document and any changes made on revised / reviewed versions

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