1. Introduction and Who Policy Applies to

This Standard Operating Procedure (SOP) details the steps required when conducting clinical research with healthy volunteers at the University Hospitals of Leicester NHS Trust (UHL).

For the purposes of this SOP, a healthy volunteer is defined as an individual who has no known significant health problems or who does not have the condition studied within the particular research project they have volunteered to participate in.

Healthy volunteers help researchers to better understand health conditions by providing information that can be used as a comparator. They also play an important role in studies looking to prevent certain illnesses or health conditions, either using medicines or other methods (e.g. vaccine trials). Research requiring healthy volunteers can range from complex Phase I Clinical Trials of Investigational Medicinal Products (CTIMPs) or trials of Advanced Therapy Investigational Medicinal Products (ATIMPS) to non-interventional, observational and population studies.

Research with healthy volunteers is designed to develop new knowledge and may not provide direct benefit to the research participant.

The purpose of this SOP is to ensure that healthy volunteers are adequately protected during their participation in UHL research and that adequate records of their participation are maintained.

This SOP applies to all staff associated with research activity involving healthy volunteers in UHL sponsored and hosted research, including where UHL is a research location.

2. Policy Standards and Procedures

2.1. Eligibility and Consent

It is the responsibility of the Principal Investigator (PI) or delegate to identify potentially eligible healthy volunteers in accordance with the procedure agreed within the approved study protocol.

Healthy volunteers can be members of the public, students, or members of UHL staff. There must be no differentiation in the treatment of volunteers from these groups – they are all considered 'healthy volunteers'.

Research staff may not volunteer for any research where they are listed on the Delegation of Authority log. This is to avoid conflicts of interest and to ensure participation is free from any perceived or actual pressure.

When approaching healthy volunteers, only approved marketing materials and study related information must be used (e.g. leaflets, posters, Participant Information Sheets (PIS)). Volunteers must be given adequate time to read these and be given the opportunity to ask questions. If a healthy volunteer expresses willingness to participate, consent should be taken in accordance with the study protocol and relevant R&I SOPs.

For studies requiring registration in The Over-Volunteering Prevention System (TOPS), additional participant information and consent requirements apply (see section 2.5).

2.2. Medical History

As part of the consent procedure, a healthy volunteer may be required to formally declare they have no outstanding health conditions which could influence participation in the research. It is expected that the research sponsor will have appropriate mechanisms within the protocol for confirming participant medical history. Where possible, this must be confirmed against existing UHL medical records.

Where no records exist, it will not always be necessary to contact the volunteer's General Practitioner (GP), and there may be no research funding allocated to do so. However, as a minimum, a declaration must be obtained from the volunteer confirming that the information they have provided is accurate. If the research sponsor does not provide an appropriate declaration, one must be produced by the local delivery team.

For trials involving the administration of an investigational medicinal product (IMP) or device, the PI or delegate must consider whether the participants GP should be consulted over their planned inclusion.

Volunteer inclusion in a clinical trial of an investigational medicinal product (CTIMP) or clinical investigation of a medical device would usually require GP notification, as per study protocol.

If the PI or delegate deems the volunteer unable to take part in the research, a full explanation must be given to the volunteer and the reasons for exclusion documented in the Investigator Site File (ISF). Where a healthy volunteer is excluded due to new medical reasons discovered through the screening process, the PI must inform the GP or relevant medical team.

2.3. Confirmation of Volunteer Identity

It is expected that the trial sponsor will have appropriate mechanisms within the protocol for verifying participant identity. For low-risk trials, the use of a simple ID check such as name and date of birth, or trial-specific passcodes, is acceptable.

Research participants attending for high-risk interventions or overnight stays must be issued with a UHL patient identification band immediately on arrival at the hospital or research facility. No research intervention should take place without one, in case emergency treatment is required.

For more information, please see the UHL Patient Identification Band Policy (B43/200)

2.4. Volunteer Records

Once an individual has given formal consent to participate in the research, and their inclusion has been confirmed, a volunteer record should be created. This may be paper, electronic or a combination of both.

The PI, or delegated member of the research team, is responsible for ensuring all healthy volunteers have a suitable record of participation. It is expected that the procedure for recording volunteer participation will be detailed in the approved protocol, and an appropriate Case Report Form (CRF) provided by the Sponsor. As a minimum, the volunteer record should contain the following information:

- Full contact details of the healthy volunteer (including emergency contact information)
- Full study details (including study title, local reference number, IRAS ID and participant identifier)
- Copies of the PIS and signed ICF
- Source data for any outcomes recorded as per study protocol (such as clinical observations, test results, adverse events, etc.)

Where a Healthy Volunteer does not already have a UHL patient record, the PI or delegate should consider whether creation of a new clinical record is necessary to support participant safety, delivery of study procedures, clinical documentation requirements or emergency care. Where new clinical research

record is required, this should be created within the existing UHL Electronic Patient Record (EPR) wherever possible.

When the research ends, volunteer records must be archived alongside other essential research records.

2.5. The Over-Volunteering Prevention System (TOPS) - PHASE I AND HIGH RISK CLINICAL TRIALS ONLY

There are scientific, safety, and ethical reasons why healthy volunteers should not participate too frequently in trials of potential new medicines:

- The participant might be exposed to interacting substances in consecutive trials
- Research results might be influenced by a volunteers' participation in a previous trial
- An excessive volume of blood might be removed from the participant
- It is unethical for research participants to be exposed too frequently to pharmaceutical products from which they can derive no benefit
- The length of time between administration of Investigational Medicinal Products (IMPs) can vary (i.e. radioactive drugs may need a longer gap), which should be considered

As part of the application for regulatory and Research Ethics Committee (REC) approval, researchers must demonstrate how they will confirm that healthy volunteers are not currently taking part in other clinical trials or have not recently done so. In addition to requiring a full medical history, it is expected that sponsors of high-risk clinical trials will facilitate access to the Over-Volunteering Prevention System (TOPS) - a UK-wide database operated by the HRA for registering participants in healthy volunteer trials.

For UHL-hosted CTIMPs: requirements for using TOPS will be outlined in the research protocol; training and TOPS access is the responsibility of the sponsor organisation.

For UHL-sponsored CTIMPs: trials involving healthy volunteers must be highlighted during the study feasibility and sponsor review process. Where it is deemed appropriate to implement TOPS, this must be documented in the feasibility documentation, Sponsor Risk Assessment and Sponsor review documentation report.

Where TOPS is being used, the PIS must include an explanation about the requirement for volunteers to be registered on TOPS, and the additional personal information that will be required to facilitate this. For suggested wording, see R&I Template T-1108: TOPS Wording for PIS. A separate Informed Consent Form (ICF) must also be used alongside the study ICF, to record the volunteers' permission to be registered on the TOPS database. For suggested wording, see R&I Template T-1037: *Tops Consent Form*.

For UHL-sponsored research, access to the TOPS database will be administrated by the Research & Innovation (R&I) central office. The Head of Research Operations, or their delegate, will be responsible for:

- ensuring that appropriate wording is present in the PIS and TOPS ICF (reviewed as part of the Sponsor Review Process)
- registering studies requiring TOPS access onto the TOPS database
- supplying TOPS usernames and passwords to the Investigator (CI/PI) or delegate

2.5.1. Registering Volunteers in TOPS

The individual responsible for recruiting a healthy volunteer (e.g. Investigator, research nurse, clinical research practitioner) must make the volunteer aware that their national insurance number or passport number will be required to take part in a study that is using the TOPS scheme.

A separate consent form must be used and signed / dated by the volunteer to indicate their permission to have their details entered into the TOPS database. If not provided by the research sponsor, R&I Template T-1037 should be used.

The first time a volunteer presents themselves for a relevant study, the responsible individual must ensure that the volunteer has given consent for their details to be added to the TOPS database. If consent has been withheld, the volunteer must not be allowed to continue in the trial.

Once consent to be included in the TOPS database has been confirmed, the participants' unique identifier (NI number or passport number) must be entered into the TOPS database **before** the first dose of IMP is administered.

The PI must ensure all study personnel delegated to take consent are suitably trained to consent for TOPS registration.

2.5.2. Identification of an Existing Volunteer on TOPS

Where a volunteer is already registered on the TOPS system, a review of the existing record must be undertaken and a decision made and documented about whether the volunteer may continue with the research at UHL.

Where the TOPS database shows that a volunteer has received drugs and/or had more than 100mls of blood taken in the previous 12 weeks, their participation should be halted to enable a discussion and decision to be made.

Information about the volunteer must be passed to the PI and the PI must discuss continuation of the volunteer with the CI (if different to the PI). Where necessary, the CI may contact the previous study location for details of the procedures the volunteer has undergone.

Where the CI decides that it is appropriate for the volunteer to continue in the study, the PI must ensure their discussion and the rationale for the decision are clearly documented in the volunteer notes or participant CRF.

Where the CI considers that it is not appropriate for the volunteer to continue in the study, the PI must notify the volunteer and explain the reasons; these must also be clearly documented in the volunteer notes or participant CRF.

The PI or their delegate is responsible for ensuring adequate documentation is maintained of the volunteer's medical record, and their continued agreement to be registered on TOPS.

2.5.3. Co-operation with other TOPS locations

It is possible that other research locations registered on TOPS will make contact to request information about a volunteers' involvement in a study. Every effort must be made to assist them and the appropriate investigator contacted.

2.6. Notification Cards and Emergency Information

For Phase I or high-risk healthy volunteer trials, participants should be provided with a notification card containing key study and emergency contact information. Volunteers are encouraged to carry this card during participation in the study in case of medical emergencies.

3. Education and Training

Individuals working on UHL research projects must be appropriately trained and competent to perform their delegated duties. This may include training in GCP, study-specific procedures, relevant R&I processes

and training in the use of specific systems, such as TOPS. Training and competency must be appropriate to the individual's role and documented where required. For further information, see R&I SOP J-5013: Training for Staff Engaged in Research at UHL.

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Use of approved consent documentation for Healthy Volunteers in UHL Sponsored trials	Review of study files and monitoring reports	R&I Deputy Head of Research Operations	As per R&I monitoring and audit schedule, or as triggered	Reported via R&I Governance meeting
Compliance with TOPS requirements, where applicable	Review of sponsor documentation and study files	R&I Deputy Head of Research Operations	As per R&I monitoring and audit schedule, or as triggered	Reported via R&I Governance meeting

5. Equality Analysis Assessment

The Trust recognises the diversity of the staff and local community it serves. Our aim therefore is to provide a safe environment free from discrimination, harassment and victimisation and treat all individuals fairly with dignity and respect and, as far as is reasonably possible, according to their needs.

As part of its development, an Equality Analysis on this policy has been undertaken and its impact on equality has been reviewed and no detriment was identified.

6. EDI Statement

We are fully committed to being an inclusive employer and oppose all forms of unlawful or unfair discrimination, bullying, harassment and victimisation.

It is our legal and moral duty to provide equity in employment and service delivery to all and to prevent and act upon any forms of discrimination to all people of protected characteristic: Age, Disability (physical, mental and long-term health conditions), Sex, Gender reassignment, Marriage and Civil Partnership, Sexual orientation, Pregnancy and Maternity, Race (including nationality, ethnicity and colour), Religion or Belief, and beyond.

We are also committed to the principles in respect of social deprivation and health inequalities.

Our aim is to create an environment where all staff are able to contribute, develop and progress based on their ability, competence and performance. We recognise that some staff may require specific initiatives and/or assistance to progress and develop within the organisation.

We are also committed to delivering services that ensure our patients are cared for, comfortable and as far as possible meet their individual needs.

7. Supporting References

UHL Patient Identification Band Policy (B43/200)
R&I SOP S-1006: UHL Informed Consent for Research
R&I SOP C-2001: UHL Consent for Hosted Studies
R&I SOP J-5013: Training for Staff Engaged in Research at UHL
R&I Template T-1037: TOPS Consent Form Template
R&I Template T-1108: TOPS Wording for Participant Information Sheets

8. Key Words

Research, Innovation, Healthy Volunteers, Participants, Clinical Trial, Study, Early Phase, CTIMP, IMP, TOPS, Pharmacokinetics, Pharmacodynamics, ATIMP, CRF, Study

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CONTACT AND REVIEW DETAILS	
Guideline Lead (Name and Title): Jen Boston R&I Deputy Head of Research Operations	**Executive Lead:** Professor Nigel Brunskill Director of Research & Innovation
Details of Changes made during review: Merged existing R&I SOPs (S-1037 and C-2030); moved to new UHL template; content and terminology updated in line with current guidance and local practice; added guidance for identification bands and medical records; updated training requirements.	