

1. Introduction

This Standard Operating Procedure (SOP) details the steps required to conduct Clinical Trials of Investigational Medicinal Products (CTiMPs) with Healthy Volunteers; when research activity investigates any or all of the following:

- Absorption
- Distribution
- Metabolism
- Excretion

Commonly known as 'ADME' studies.

It is important to remember that Healthy Volunteers can be members of the general public, students, or members of staff from the University Hospitals of Leicester NHS Trust (UHL). There must be no differentiation in the treatment of volunteers from these groups – they are all Healthy Volunteers.

2. Scope

This SOP applies to all staff, and any external individual who are associated with any research activity where the UHL are acting as the Sponsor organisation.

3. Procedure

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

- The subject might be exposed to interacting substances in consecutive studies
- The results of a study might be influenced by the subject's participation in a previous study
- An excessive volume of blood might be removed from the subject
- It is unethical for subjects to be exposed too frequently to pharmaceutical products from which they can derive no benefit
- The length of time between administration of IMPs can vary i.e. radioactive drugs may need a longer gap and this should be taken into account

The UK Clinical Trials Regulations state that applications to the HRA/ REC should include information about how to check volunteers aren't taking part or have recently taken part in other trials. In addition to asking the volunteer to confirm their medical history, TOPS must also be used.

CTiMP studies involving healthy volunteers will be highlighted during the feasibility and Sponsor review of the study. If it is deemed appropriate to implement the Over Volunteering Prevention System (TOPS), this must be documented in the feasibility and Sponsor Risk Assessment and Sponsor review documentation report.

As Sponsor, UHL expect that a separate TOPS consent form be used along side the study consent form and that within the Participant Information Sheet an explanation about the requirement to be registered onto TOPS and the information required to facilitate this be included. Suggested wording is as follows:

'You must not take part in too many studies because it's not good for you. So to help research units, the Health Research Authority keep a database of healthy volunteers and when they take part in studies, this is called TOPS.

We will enter into the database:

*Your National Insurance number (if you're a UK citizen); or your passport number and country of origin (if you're not a UK citizen); and the date of your last dose of study medicine
If you withdraw from the study before you receive any study medicine, the database will show that you never received a dose.*

Only staff at (insert the name of your unit) and other medicines research units can use the database. We may call other units, or they may call us, to check your details.

We will not keep your data for any longer than two years. If we need to contact you about the study after you've finished it, but we can't because you've moved or lost contact with your GP, we might be able to trace you through the information in the database

Access to the TOPS database will be administrated by the Research & Innovation (R&I) Office. User Names and Passwords for each study will be supplied to the Chief or Principal Investigator.

3.1 Identifying and Registering a Subject

- The individuals responsible for recruiting the healthy volunteers (e.g. investigators, research nurses) must make the volunteers aware that they will need their national insurance number or passport number to take part in a study that is using the TOPS scheme.
- Anyone named in the Delegation of Authority may not be entered as a subject
- Use of the TOPS database must also be included in the study specific Participant Information Sheet – please see suggested wording in *italics blue* above.
- A separate Consent Form must be included to be signed and dated by the volunteer indicating permission to enter their details on the TOPS database a suggested template is included in **Appendix 1**
- The first time the volunteer presents themselves for a relevant study, the responsible individual must ensure that the volunteer has consented for their details to be added to the TOPS database. If consent has been withheld, the volunteer must not be allowed to continue.
- Once consent to be included in the TOPS database has been confirmed, their unique identifier (NI Number or Passport Number) must be entered in to the TOPS database and must be before the first dose of IMP has been administered.

3.2 Identification of Existing Volunteer on TOPS

Occasionally a volunteer may already be registered on the TOPS system. A review of the existing record must be undertaken and a decision made and documented about whether or not a volunteer may continue in the study.

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

Information about the volunteer must be passed to the Principal Investigator. The Principal Investigator (PI) must discuss continuation of the volunteer with the Chief Investigator (CI) (if different to the PI). If the CI considers that it is not appropriate for the volunteer to continue in the study, the volunteer must be notified and reasons explained. The reasons for halting continuation into the study must be clearly documented in the volunteer notes or in the Case Report Form (CRF).

If the CI considers that it is appropriate that the volunteer continue in the study, the discussion must be clearly documented in the volunteer notes or in the CRF. The reason for halting the study procedures must be explained to the volunteer. The CI and PI may wish to proceed with the study following a review of the procedures that the volunteer has undergone within the other trial(s).

Further investigation (i.e. phoning the unit where the previous study was conducted) may reveal there is no need to exclude the volunteer. The CI and the PI must agree that continuation of the volunteer in the study is appropriate before further study procedures commence. The rationale for proceeding must be fully documented in a file note and in the volunteer research notes or CRF.

3.3 Steps to be taken after Registration

Once a subject has been consented to participate in the research activity, and their inclusion in the activity has been confirmed, every attempt to confirm relevant medical history must be made. It is not always necessary to contact the volunteers General Practitioner, but as a minimum a declaration from the volunteer confirming that the information they have given is correct must be obtained.

Confirming medical history with a GP may be costly and adequate provision must be made in the funding for this where required.

A set of volunteer notes must be generated for each volunteer. In some cases it may be appropriate to generate a set of hospital notes where none exist. The appropriateness of records will be discussed at the Sponsor Review meeting.

It is possible that other units registered on TOPS may make contact to discuss the study and the volunteers' involvement. Every effort must be made to assist them and the appropriate investigator contacted.

4. Responsibilities

	Responsibility	Undertaken by	Activity
1	R&I Office	Head of Research Operations or their delegate	Register the study requiring access to TOPS onto the database
2	R&I Office	Head of Research Operations or their delegate	To ensure that appropriate wording in PIS and separate consent form are present and reviewed during the Sponsor Review Process
3	Chief Investigator	Chief Investigator or their Delegate	Appropriately delegate individuals to operate the TOPS database

	Responsibility	Undertaken by	Activity
4	Chief Investigator	Chief Investigator or their Delegate	Ensure all personnel trained to consent to TOPS registration
5	Chief Investigator	Chief Investigator or their Delegate	Discuss with PIs or responsible individuals the continuation of volunteers on the study
6	Principal Investigators	Principal Investigator	Discuss with CI continuation of volunteers on study
7	Chief Investigator	All Investigators	Ensure adequate documentation maintained of volunteer medical record, and continued agreement to be registered on TOPS.

5. Supporting Documents and Key References

SOP S-1037 Appendix 1

6. Key Words

Research, Innovation, Volunteers, Participants, CTIMPS, Trials, Monitoring, Bioequivalence, Pharmacokinetics, Pharmacodynamics, Healthy Volunteers, ADME, REC, HRA, TOPS, IMP, CRF

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