Standard Operating Procedure:

Healthy Volunteers and Medical Oversight

# Purpose

This standard operating procedure (SOP) describes the procedures for the recruitment, management and medical oversight of healthy volunteers in clinical research.

# Scope

This SOP is applicable to all University of Birmingham (UoB) sponsored clinical research involving healthy volunteers, with the exception of Phase I clinical trials. Where clinical research is (co-)sponsored by another institution, this procedure should be followed as far as possible, and in line with the contractual agreement between the UoB and the other institution. This SOP also applies to clinical research approved by UoB Research Ethics Committee (REC) that are required to follow the UoB Principles of Good Clinical Practice (GCP) for Clinical Research (UoB-GCP-POL-001). This SOP may be used as a guidance document in all other cases.

# Implementation plan

This SOP will be implemented directly after its effective date for any clinical research that is still in the set-up phase. For existing clinical research that has already been set up and is in the recruitment phase (or further) at the time of implementation, the list of expected outputs (see below) should be followed as far as possible.

# Stakeholders

Note that where a clinical trials unit (CTU) is involved, the CTU may take on responsibility for aspects related to the procedures for healthy volunteers and medical oversight. The CTU may delegate these duties further to their trials team(s). All delegation of duties will be documented e.g. using the Clinical Trials Task Delegation Log (UoB-SPO-QCD-001).

* Chief investigator (CI): the CI may delegate activities to members of their research team, although evidence of CI involvement and approval is still expected and may not be delegated where ‘no delegation allowed’ is indicated. The SOP will state where delegation is possible. For clinical research approved by UoB REC, the role of CI may be termed the principal investigator, or the supervisor for the postgraduate research student.
* Healthcare professional (see ‘Abbreviations and Definition’ section below). This may be the CI where they are a healthcare professional.

# Background and rationale

For the purpose of this SOP, a healthy volunteer is defined as an individual who has either no known significant health problems or does not suffer any significant health problems relevant to the proposed research, and consents to participate in the research. A healthy volunteer may participate in research ranging from non-invasive observational studies to a Phase I clinical trial testing a new drug. However, Phase I clinical trials involving healthy volunteers are beyond the scope of this SOP. For more information, see guidance provided by the Health Research Authority (HRA) on [Phase I clinical trials](https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/phase-1-clinical-trials/).

Healthy volunteers do not typically benefit (therapeutically) from taking part in clinical research. It is also common for healthy volunteers who take part in clinical research to be compensated financially for their participation. Therefore, it is important to have mechanisms in place to monitor healthy volunteers who participate recurrently in clinical research (e.g. through a database or questionnaire). It is imperative that the safety and well-being of the individual prevails over the interests of science and society as per the UoB Principles of GCP for Clinical Research (UoB-GCP-POL-001). There are various scientific, medical and ethical reasons why healthy volunteers must not participate in clinical research too often, for example:

* if the gap between two studies is too short or the studies overlap, the interventions might interact
* taking too many blood samples could cause anaemia
* it is unethical and scientifically questionable to expose healthy people too often to interventions (medicines) they do not need
* it may be dangerous to expose healthy people to radiation that is not necessary.

Where clinical research with healthy volunteers also involves one or both of the activities listed below, see the section on Clinical Research in the Laboratory within the [UoB Quality Management System (QMS)](https://www.birmingham.ac.uk/research/activity/mds/mds-rkto/governance/qms.aspx).

* Handling, processing, receipt, storage or analysis of samples of human tissue
* Laboratories performing analyses that contribute to the (primary, secondary and exploratory) endpoints of a clinical trial of an investigational medicinal product.

In the event of an adverse event, see the Adverse Event Reporting SOP (UoB-AES-SOP-001) for reporting requirements.

For deviation and serious breach reporting, see the Deviations and Serious Breach Reporting SOP (UoB-DSB-SOP-001).

# Procedures

## Set-up phase

1. During the protocol design phase, the CI (or delegate) will determine the inclusion and exclusion criteria for the volunteers. Where the criteria involve healthcare-related measures (such as blood pressure, blood results or electrocardiogram readings), the CI (or delegate) will consult with an appropriate healthcare professional to determine the appropriateness/suitability of each healthcare-related criterion and how these are verified (e.g. self-reported versus confirmation by a general practitioner (GP)).

* Where required, the CI (or delegate) will include appropriate funding for confirming the healthcare-related criteria with a GP.
* It is recommended that the items below are considered when a GP is to be contacted.
* Obtaining specific consent from the participant to contact their GP.
* How will the contact details for the GP be collected?
* Timeframe for contacting the GP and receiving a response (if required).
* A process to deal with no response from a GP (if required).

1. The CI (or delegate) will decide on and document (e.g. in the protocol) the level of ongoing input required from an appropriate healthcare professional. For example, in determining the eligibility of a volunteer for healthcare-related measures as evidenced on the eligibility checklist.
2. The CI (or delegate) will develop and implement an appropriate method for confirming whether the volunteer has previously participated in clinical research and, where applicable, when and what the research involved.

* Where blood is donated, the CI (or delegate) will ensure that volunteers only donate a maximum of 500 millilitres of blood in any six month period as per the [UoB Health and Safety Policy for Blood Taking from Volunteers for Research (PDF – 58 KB)](https://intranet.birmingham.ac.uk/hr/documents/public/hsu/hsupolicy/Blood-taking-from-Volunteers-Policy.pdf). It is expected that this limit is stated as an exclusion criterion.

1. The CI (or delegate) will develop and implement an appropriate method for confirming the volunteer’s relevant medical history. As a minimum, the CI (or delegate) will obtain a declaration from the volunteer to confirm that the information provided is correct (e.g. through a health screening questionnaire).
2. The CI (or delegate) will ensure that staff involved in the recruitment, management and medical oversight of healthy volunteers are appropriately trained and informed of their roles before undertaking their respective tasks. See also the Training SOP (UoB-TRN-SOP-001).

## Recruitment phase (and further)

1. The CI (or delegate) will identify potentially eligible volunteers in accordance with ethically and regulatory approved procedures (i.e., the protocol).
2. The CI (or delegate) will recruit and consent volunteers according to the procedures in the Participant Engagement and Informed Consent SOP (UoB-PEI-SOP-001).
3. The CI (or delegate) will assess and document the eligibility of the volunteer against the inclusion and exclusion criteria. Where a decision is required on the volunteer’s medical condition/history, the CI (or delegate) will consult with the healthcare professional, and will evidence the healthcare professional’s approval to include/exclude the volunteer.
4. Where human biomaterial is collected, processed and/or stored on UoB premises, the CI (or delegate) will follow the [UoB health and safety policies and guidance for biological safety](https://intranet.birmingham.ac.uk/hr/wellbeing/worksafe/biological/index.aspx), including performing a risk assessment for work with biological materials. Where applicable, the CI (or delegate) will follow the procedures detailed in the Laboratory Facilities SOP (UoB-CRL-SOP-002) and Sample Management SOP (UoB-CRL-SOP-003).
5. The CI (or delegate) will archive any documentation relating to the healthy volunteer with the study/trial master file at the end of the project. See Archiving SOP (UoB-ARC-SOP-001) for further information on archiving requirements.

# List of expected outputs

* Evidence of clearly defined inclusion and exclusion criteria for the volunteers.
* Evidence of a process to determine if a volunteer has previously participated in clinical research.
* Evidence of the level of ongoing input required from a healthcare professional.
* Evidence of recruitment and consent processes as outlined the Participant Engagement and Informed Consent SOP (UoB-PEI-SOP-001).
* Evidence of an eligibility assessment for each volunteer, and that relevant medical history has been reviewed.

# Related documents

* UoB-AES-SOP-001 Adverse Event Reporting
* UoB-ARC-SOP-001 Archiving
* UoB-CRL-SOP-002 Laboratory Facilities
* UoB-CRL-SOP-003 Sample Management
* UoB-DSB-SOP-001 Deviations and Serious Breach Reporting
* UoB-GCP-POL-001 UoB Principles of GCP for Clinical Research
* UoB-PEI-SOP-001 Participant Engagement and Informed Consent
* UoB-SPO-QCD-001 Clinical Trials Task Delegation Log
* UoB-TRN-SOP-001 Training

UoB QMS documents can be found on the [Clinical Researh Compliance Team (CRCT) website](https://www.birmingham.ac.uk/research/activity/mds/mds-rkto/governance/index.aspx). Internal work instructions can be obtained from the CRCT ([crct@contacts.bham.ac.uk](mailto:crct@contacts.bham.ac.uk)) and/or from the Research Governance Team (RGT) ([researchgovernance@contacts.bham.ac.uk](mailto:researchgovernance@contacts.bham.ac.uk)).

# References and frameworks

* Allied health professions: <https://www.england.nhs.uk/ahp/role/>
* HRA guidance on Phase I clinical trials: <https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/phase-1-clinical-trials/>
* UoB health and safety policies and guidance for biological safety: <https://intranet.birmingham.ac.uk/hr/wellbeing/worksafe/biological/index.aspx>
* UoB Health and Safety Policy for Blood Taking from Volunteers for Research: <https://intranet.birmingham.ac.uk/hr/documents/public/hsu/hsupolicy/Blood-taking-from-Volunteers-Policy.pdf>
* UoB QMS: <https://www.birmingham.ac.uk/research/activity/mds/mds-rkto/governance/qms.aspx>

# Abbreviations and definitions

| Term | Description |
| --- | --- |
| **Authorised healthcare professional** | An authorised healthcare professional is defined as a doctor, dentist, nurse or pharmacist. |
| **CI** | Chief investigator |
| **Clinical study** | Any health-related research study on humans. This includes a study:   * administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology * involving qualitative methods only * limited to working with human tissue samples (or other human biological samples) and data (specific project only) * limited to working with data (specific project only). |
| **Clinical trial** | **For clinical trials using an investigational medicinal product:**  Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more investigational medicinal product(s), and/or to identify any adverse reactions to one or more investigational medicinal product(s) and/or to study absorption, distribution, metabolism and excretion of one or more investigational medicinal product(s) with the object of ascertaining its (their) safety and/or efficacy.  **For all other clinical trials:**  Prospective biomedical research on human subjects that are conducted to allow safety (or more specifically, information about adverse drug reactions and adverse effects of other treatments) and efficacy data to be collected for health interventions. Examples include devices, surgery and radiotherapy trials. |
| **CTU** | Clinical trials unit |
| **GCP** | Good Clinical Practice |
| **GP** | General practitioner |
| **Healthcare professional** | A healthcare professional is defined as an authorised healthcare professional, or a qualified and registered (or alike) [allied health profession](https://www.england.nhs.uk/ahp/role/) such as a physiotherapist, dietitian or radiographer. |
| **Healthy volunteer** | An individual who has either no known significant health problems or does not suffer any significant health problems relevant to the proposed research. |
| **HRA** | Health Research Authority |
| **ICF** | Informed consent form |
| **PIS** | Participant information sheet |
| **QMS** | Quality management system |
| **REC** | Research ethics committee |
| **SOP** | Standard operating procedure |
| **UoB** | University of Birmingham |

See also the [Glossary of Terms](https://www.birmingham.ac.uk/research/activity/mds/mds-rkto/governance/Glossary-of-Terms.aspx).