University of Hertfordshire UH

Clinical Trials Unit

University of Hertfordshire Clinical Trials Unit (CTU)

Registration/ Randomisation, Blinding and Un-blinding

Standard Operating Procedure for the Registration/ Randomisation, Blinding and Un-blinding at the University of Hertfordshire

SOP Number: gSOP-47-02	**Effective Date:** 2nd December 2025
Version Number: 2	**Review Date:** 2-3 years (or as required)

1. BACKGROUND

This is a University of Hertfordshire (UH) standard operating procedure.

This document sets out the procedures to be followed by all UH staff who are responsible for randomisation, blinding and unblinding for research studies run at UH.

Clinical trials are often blinded to hide the treatment group assignment from participants and/or investigators in order to prevent the unintentional biases of either party affecting participant data.

Clinical trials comparing one or more treatments or placebo may be randomised such that participant treatment allocation occurs at random.

At the start of any clinical trial, the Chief Investigator (CI) should have a written procedure for the randomisation, blinding and related processes, as well as the details of authorised personnel who will have access to un-blinded data.

Where there are potential conflicts between different collaborating organisations' SOPs, project level working instructions should be developed, to determine precedence.

2. PURPOSE

To describe the steps required in setting up a participant registration/randomised treatment allocation system that is transparent and unbiased.

3. APPLICABLE TO

This applies to all staff involved in clinical research sponsored/co-sponsored by UH and/or adopted by the UH CTU, including but not limited to: Chief Investigators (CIs), Principal Investigators (PIs) Research Fellows, Consultants, Statisticians, Clinical Trial Pharmacists, Research Managers, Research Nurses, Clinical Trial Practitioners, Allied Health Professionals, Trial Co-ordinators/Managers, Clinical Studies Officers, Data Managers, Research Assistants and Students.

4. RESPONSIBILITIES

- All staff are responsible for ensuring research is conducted in accordance with the clinical trial regulations and adhere to all current UH CTU SOPs and have signed to confirm that these documents have been viewed/understood.
- The Statistician is responsible for ensuring the type of randomisation is appropriate for the trial design.
- The CI is responsible for ensuring all research personnel in the trial team are trained on the trial specific SOP on randomisation, blinding and unblinding (if applicable).
- For multi-centre trials the CI is responsible for ensuring all PI and trial teams at participating sites are familiar with the trial specific SOP on randomisation, blinding and unblinding (if applicable).

5. PROCEDURES

5.1. PREPARATION

- Random allocation of a clinical trial's participants to the treatments under study aims to ensure that any differences between the treatment groups are due to chance alone. The randomisation procedure must be determined during the design phase of the trial and detailed in the trial protocol. The trial statistician should be involved at this stage to ensure that the type of randomisation is

appropriate for the trial design. The randomisation schedule should be produced and implemented once funding for the trial is confirmed and prior to participant recruitment. Consideration should be given to the following:

- Type of randomisation and description of the randomisation process, allocation ratios, block sizes, and stratification variables and any other variables used in the randomisation procedure to be recorded.
- The level of blinding as required by the trial's protocol (e.g., unblinded, single-blind or double-blind) and how it will be implemented (e.g., using an identical placebo). The level of the blinding must be maintained for the entire duration of the trail.
- Allocation concealment, a technique used to prevent selection bias by concealing the allocation sequence from those assigning participants to intervention groups, until the moment of assignment. Allocation concealment prevents researchers from (unconsciously or otherwise) influencing which participants are assigned to given intervention group. Allocation concealment is possible with all types of trials, including unblinded trials, and is therefore universally recommended.
- Unblinding/code breaking: for blinded trials, randomisation system should include a mechanism that permits rapid identification of the allocated treatment in case of a medical emergency, but one that does not permit undetectable breaks of the blinding in order to protect the integrity and the validity of the data. To ensure this, the code break procedures must be clearly established and the circumstances where unblinding can be performed should be detailed in the protocol, e.g., treating an individual for an adverse event or for the submission of trial data to the Data Monitoring and Safety Committees (DMSC).
- Method of implementation (e.g., web based, password protected lists).
- Responsibilities for each stage of the process should be clearly defined.

- The process of producing the randomisation schedule should be documented including the following:
  - Method of producing the schedule and rationale for its choice.
  - If the randomisation is produced in-house, the code for generating the sequence should be documented and stored.
  - Person responsible for preparing and checking the schedule.
  - Person responsible for implementing and using the schedule.
  - Guidelines for the user (including storage and access control methods).
  - Unblinding arrangements.
  - Details of documentation to be completed for randomisation (e.g., signed informed consent form, randomisation checklist/eligibility checklist).

5.2. SPECIFICATION TEMPLATE

- The sequence of allocations must be truly random. It must be based on random number generation or other random process. Allocation must be concealed in advance of randomisation, and it must not be possible to know in advance what the next allocation in the sequence will be.
- When developing the randomisation specification (TP-85), the following factors should be included, as appropriate:
    - Definition of any strata (e.g., to handle randomisation in a multi-centre trial and to ensure balance for baseline prognostic factors).
    - Any factors that may be the subject of blocking. The clinical staff involved in the study shall not be informed of the block size(s) used.
    - Number of groups (and strata where appropriate).
    - Number of participants to be randomised to each group.
    - Method of allocation (e.g., simple randomisation, blocked randomisation, minimisation, etc.).
    - Method of implementation (e.g., web-based system, telephone-based system, etc.).
    - How the allocation method is to be tested (e.g., by means of simulations).
- The statistician or delegate responsible for randomisation shall document all relevant information in a randomisation protocol, with consideration of the following:
    - Method of production of the allocation list/algorithm.
    - Persons responsible for preparing and checking the allocation list/algorithm.
    - Outputs from any testing and simulation.
    - Person(s) responsible for the implementation and use of the allocation list/algorithm.
    - Guidelines for users of the allocation list/algorithm.
    - Storage and access control for any copies of the allocation list/algorithm.
    - The randomisation protocol must be produced and implemented prior to recruitment.
- A description of the randomisation procedure must be included in the trial protocol, although it may not be appropriate to include all details from the randomisation protocol; for example, to avoid intervention allocation bias.
- Any deviations from or failures of the randomisation procedures during the recruitment phase shall be documented in the Trial Master File (TMF) by the research team using a file note.

5.2.1 Blinding

- In blinded trials, adequate steps shall be taken to ensure that the interventions are indistinguishable, as specified by the trial protocol.
- The trial protocol shall define any individuals involved in the trial who should not/cannot be blinded to treatment. For example, laboratory staff may have access to laboratory measurements which would unblind the trial. Such data shall be withheld from other research team members until the end of the trial.

5.2.2 Un-Blinding

- Unblinding of participants during the conduct of a blinded trial is not permitted unless there are compelling medical or safety reasons to do so (e.g., knowledge of the treatment allocation is necessary for treatment of serious adverse advents (SAEs)).
- If participant unblinding is permitted during the conduct of a trial, the protocol must state procedures for obtaining permission to unblind.
- Where possible the CIs advice should be sought before requests for unblinding are made.
- If a participant has been unblinded, the participant should be encouraged to remain in the trial and, if possible, on trial treatment, unless medically contraindicated. All unblinding of the randomisation code for specific participants shall be fully documented and justified.
- In the event of individual unblinding, knowledge of the intervention allocation shall be restricted as far as is practical until the trial is fully unblinded.
- Any un-blinding should be recorded within the study Record of Unblinding Log (TP-46).

5.3. VALIDATION SPECIFICATION

- Referring to gSOP-42 Data Management System Validation, the same steps will be taken to test the system with the same documentation and approval forms.
- Both Functional and User Acceptance Testing may require a mock concealment list and randomisation list to be provided.
- When the system is under development by the Programmer, the system will be in Development status [*Study acronym* Development].

- For functional testing by the Trial Statistician or delegate, the system will be published to Test [*Study acronym* Test] to be accessed by the Trial Statistician and Data Manager for functional testing.
- The Test system will be used for the final User Acceptance testing stage involving the Chief Investigator or delegate and any other parties involved as required.
- Once the system has been completed including Acceptance testing, the associated documents will be signed off by the Programmer and the Trial Statistician.

6. RELATED DOCUMENTS

- SOP-42-01 Data Management System Validation
- TP-85 Randomisation Specification Template
- TP-46 Record of Unblinding Log

7. APPENDICES

- Appendix 1 – Definitions

8. VERSION HISTORY/REVISIONS

Version Number	Effective Date	Reason for Change
2.0	02/12/25	Periodic review – no changes required other than minor grammar/stylistic amendments

9. AUTHORSHIP & APPROVAL

Author Karen Irvine

Signature  **Date** 24/04//25

Pro-Vice Chancellor (Research and Enterprise) Approval

Signature 

Date 02/12/2025

Signed by Dr Susan Grey, Chair of the Governance of Clinical Studies Group (GCSG), on behalf of the Pro-Vice Chancellor (Research & Enterprise)

10. AGREEMENT (MOVE ON TO A SEPARATE SHEET BEFORE PRINTING)

Please detach and retain within <u>your training files</u>

I have read and understood the contents and requirements of this SOP (ref gSOP-47-02) and accept to follow University of Hertfordshire policies implementing it.

Recipient

Signature: ……Date: …….

Name & Position: ……

Please retain copy of the signed form for your reference in your training file

Appendix 1- Definitions

Chief Investigator

An individual who is responsible for the conduct of the whole project in the UK. In a multi-site study, the CI has co-ordinating responsibility for research at all sites. All applications for ethical review should be submitted by the CI.

Clinical Trial

A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or control) to evaluate the effects of those interventions on health outcomes.

Principal Investigator (PI)

The investigator responsible for the research site. There should be one PI for each research site. In the case of a single-site study, the chief investigator and the PI will normally be the same person.

Randomisation

The act of allocating a treatment to a trial subject using an element of chance to determine which treatment to allocate

Blocked Randomisation

A method of randomisation where a short sequence of treatments e.g., AAABBB, is repeatedly permuted at random e.g., ABBABA, to define a list of treatments, and a new trial subject receives the next treatment in the list.

Minimisation

A family of methods of treatment allocation where each new patient is allocated to a treatment in a manner that attempts to minimise the degree of imbalance in treatment allocations within stratification factors.

Human readable

An electronic document that can both be understood by a user of the document and be processed directly by a computer