STU-SOP-DMS-001 – Standard Operating Procedure on Randomisation and Blinding

Version No:	4	**Effective Date:**	20-Mar-2026
Description of changes:	Merger of randomisation (STU-SOP-DMS-001) and blinding SOPs (STU-SOP-DMS-002) into a single document. SOP reviewed in light of clinical trial regulations 2025 and GCP updates. Specific references to QPulse as the QMS have been removed. We now only refer to a QMS system.		

List of Abbreviations	
CI	Chief Investigator
CONSORT	Consolidated Standards of Reporting Trials
CTIMP	Clinical Trial of an Investigational Medicinal Product
DM	Data Manager
DMC	Data Monitoring Committee
GCP	Good Clinical Practice
IDs	Identifiers
IMP	Investigational Medicinal Product
IS	Independent Statistician
PI	Principal Investigator
SOP	Standard Operating Procedure
STU	Swansea Trials Unit
SU	Swansea University
TM	Trial Manager
TS	Trial Statistician

1. Purpose and Definitions

This Standard Operating Procedure (SOP) describes the procedure of randomisation, blinding, and unblinding within all randomised controlled trials adopted or managed by Swansea Trials Unit (STU).

Definitions	
Randomised controlled Trial	A randomised controlled trial assigns human participants or groups of participants to one or more interventions prospectively, to evaluate the effects on health or other research outcomes.
Randomisation	The act of allocating a trial participant to a treatment (active or control) using an element of chance to determine assignments to reduce bias.
Simple randomisation	Randomisation using a single sequence of random numbers to assign intervention allocation to subjects.
Blocked randomisation	A method of randomisation which uses short pre-specified sequences of allocations, known as blocks, to ensure balance between groups.

Minimisation	A method of ensuring balance between groups for several prognostic factors. Allocation of the next participant enrolled in the study depends (wholly or partly) on the characteristics of those participants already enrolled. The aim is that each allocation should minimise the imbalance across multiple factors whilst preserving balance between allocation groups.
Blinding	The process of concealing the treatment allocation from one or more parties involved in a clinical trial in order to prevent bias. Blinding ensures that relevant individuals involved with a trial do not know which intervention a participant is receiving.
Unblinding	The authorised process by which a concealed treatment allocation is revealed to an appropriate individual(s).
Single blinding	A participant is unaware of the treatment allocation but trial staff and investigators are aware of treatment allocation.
Double blinding	The participant, trial staff and investigators are unaware of treatment allocation
Open label trial	The participant, trial staff, and investigators are aware of the treatment allocation.

2. Background

2.1. Randomisation

Randomisation is the process by which participants in a trial are assigned to either the intervention or control groups. The aim of randomisation is to remove the potential of systematic bias in the conduct of the trial.

The randomisation procedure must be determined during the design phase of the trial and detailed in the trial protocol, including any stratification or minimisation factors, and any planned emergency or back up randomisation procedures. This will enable the generation of the trial specific randomisation list or algorithm.

The method of randomisation can vary from a simple pre-specified static process through to more complex mechanisms involving algorithms used for adaptive designs.

Clinical Trials of Investigational Medicinal Products (CTIMPs) will have consideration for the statistical principles required by Good Clinical Practice (GCP).

2.2 Blinding

Blinding is a procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s) to remove the potential of bias arising from the influence of knowing the assignment(s). Unblinding is the process by which the treatment allocation code is broken, revealing the intervention allocated to a trial participant.
Unblinding may take place:

1) in medical emergencies
2) for the purpose of notification to the Data Monitoring Committee (DMC)
3) in error
4) for analysis purposes at the end of the trial.

The trial protocol must define the level of blinding (e.g. open label, single blind or double blind) and the process to manage emergency unblinding. Measures should be agreed during the design phase of the trial to prevent unblinding the entire treatment arm and the entire study in the case of a two-armed study when the treatment allocated to a trial participant has to be revealed for clinical and safety reasons.

3. Roles and Responsibilities

The **Chief Investigator (CI)** is responsible for ensuring that the production and implementation of the randomisation is assigned to individuals (or external organisations) with appropriate training. The CI is also responsible for determining the type of randomisation to be used, and for ensuring that a randomisation specification is produced as necessary and documented for the trial in conjunction with a statistician. When an external vendor or individual is used, the CI in conjunction with a statistician is responsible for indicating the trial requirements to the external party. This task may be delegated to an appropriate research team member. The CI is responsible for ensuring arrangements for blinding and unblinding are in place and to liaise with the DMC and Sponsor as required.

The **Trial Statistician (TS)** is responsible for generating the randomisation specification and overseeing the testing of the randomisation. If an external vendor is used the TS will have an oversight role and test/validate the randomisation as appropriate. The TS ensures the delivery of the randomisation list and is responsible for liaising with a suitably qualified peer, herewith referred as the Additional Statistician, for blinding and unblinding.

The **Independent Statistician (IS)** is independent of the trial team and will liaise with the TS to test/validate the randomisation procedure as appropriate, generate allocation sets, safeguard the integrity of blinding, log the location of all documentations relevant to blinding and unblinding, and carry out necessary independent analysis requested by the DMC.

The **Trial Manager (TM)** is usually the delegate of the CI with the authority to discuss and agree with a suitably qualified statistician the randomisation specification. If an external vendor is used they may be delegated the task of liaising with the vendor. The TM is additionally responsible for overseeing that randomisation and allocation systems work properly e.g. packaging, coding and labelling of treatments to protect blinding; delivery of randomised treatments to trial participants; ensure unblinding logs are properly kept and transmitted to the relevant parties.

The **Data Manager (DM)** is responsible for ensuring the database is designed to manage the randomisation procedure as required, preserve blinding and to ensure that the entire randomisation list, as available, is covered, unique trial participant identifiers are generated and transmitted to the IS for mapping to allocation sets.

External use of SOP: This SOP and Associated Documents (AD) may be used for research projects not adopted by STU where Swansea University (SU) staff and associated NHS

organisations require guidance. In such instances, oversight responsibility for any associated tasks will not be the responsibility of STU.

4. Procedure

4.1 Develop a randomisation specification

An outline description of the randomisation procedure must be included within the trial protocol. The randomisation specification and development of the trial allocation list should only be implemented when funding for the trial has been confirmed.

The TS (or individual assigned the responsibility) must develop the randomisation specification using the trial protocol and the Randomisation Specification Template (STU-AD-TMP-007) as appropriate, following guidance e.g. CONSORT. The method used for randomisation will be specific to each study and is usually determined by the study statistician with input from the study CI and other members of the trial co-investigators.

The randomisation specification must be approved by the CI jointly with the Senior Statistician on the trial/ study, who will ensure that the method used is appropriate for the research project and reduces the chance of imbalance between treatment groups (e.g. simple, block, stratified randomisation).

4.2 Identify Randomisation Service

The TS with the CI will identify whether randomisation will be developed in house or using a external randomisation service. The methods of preparing the randomisation schedule (or randomisation list) can vary and include random number tables, online randomisation programs and/or bespoke programs/macros.

The decision will be based on the complexity of the research project and randomisation, whether the project is multi-centre and the requirement to follow appropriate regulatory guidance for Clinical Trials of Investigational Medicinal Products (CTIMPs).

4.3 Generate the randomisation list

The TS (or external organisation) using the completed trial randomisation specification (STU-AD-TMP-007) will generate the randomisation.

Computer generated schemes (such as Sealedenvelope.com) are an acceptable method of sequence generation for randomisation. When the service is provided by an organisation external to STU, the external vendor in conjunction with the TS (or delegate), is responsible for generating and testing the randomisation. The TS will oversee this step.

As a minimum, a documented check should be completed before the randomisation goes live. For more complex studies (including those involving stratified randomisation) a dummy study should be run before the study is set up. These checks should confirm, through direct examination, that the proposed method of randomisation has been tested using the same

parameters as the actual study, and ensure that the procedure produces a valid randomisation specification (e.g. total randomisations, block sizes). All supporting documentation should be held securely in the TMF.

For studies which are blinded (concealed intervention allocation), additional considerations should be made to ensure the robustness of the chosen method of randomisation. Procedures to control the randomisation schedule to prevent accidental or deliberate unblinding should be implemented and enforced for blinded protocols e.g., access restrictions for electronic schedules. See STU-SOP-DMS-002 'Blinding' for further details.

If the randomisation sequence is generated by a computer, the random seed should be fixed and documented to allow the sequence to be reproduced if required. Care must be taken to ensure that restarting the computer does not automatically generate the same sequence each time.

A backup procedure will be in place to enable uninterrupted delivery of randomisation.
Both normal and emergency methods of access to randomisation will be detailed within the TMF.

The randomisation schedule/list should be version controlled so that it is clear which the final version is.

4.4 Coding of treatments

After generating the randomisation list, the TS should liaise with the IS to produce a Treatment Coding Document. The Coding Document will contain a set of codes for each treatment in the study. For example:

- 1 = Paracetamol
- 2 = Ibuprofen
- 3 = Placebo
- 4 = Aspirin

Any subsequent documentation of the trial should then use these codes instead of the direct names of the treatment, to help preserve blinding.

During a double-blind trial of an IMP it is not sufficient to label each drug kit with an anonymised label stating a code for the treatment as any emergency unblinding of any single patient will unblind the entire treatment arm and the entire study in the case of a two-armed study. Instead, each drug kit should be labelled with a unique label or number that is linked to the anonymised treatment labels in a concealment list along with any other information required, for example batch number.

The IS should have the only access to the Treatment Coding Document and is responsible for its maintenance and security. The Coding Document should be stored electronically in a password-protected manner and as a hard copy in a secure and confidential area with restricted access. Location details will be held in the TMF.

4.5 Implementation of randomisation checks

As required (e.g. Data Monitoring Committee reports) and at the end of the trial the randomisation shall be checked by the TS (or delegate) to determine that it has been followed.

These checks should ensure that:

- Any eligibility criteria are met
- Appropriate consent (e.g. informed consent, deferred consent) has been obtained.
- All pre-randomisation documentation is completed as per study requirements.

The CI (or delegate) will ensure the allocation of a unique identifier for each participant (i.e. a trial/study number) and that methods are in place to prevent the same participant being randomised more than once.

During the trial recruitment phase any deviations or failures of the randomisation procedures shall be documented in the Trial Master File (TMF) by a file note generated by the research team.

4.6 Manage unblinding

The blinding of the trial must be maintained throughout the trial until all data entry and processing are complete and the database has been locked.
Circumstances for breaking the randomisation code must be clearly described in the protocol, and the trial procedure for unblinding documented. These should be in place at the start of the trial to ensure readiness if unblinding becomes necessary.

The unblinding request log (STU-AD-FRM-012) should be completed. The method to be used for office and out of hours unblinding must be tested, documented and filed in the Trial Master File.

The details of all unblinding, including the revealed codes, shall be included in the statistical report at the end of the trial.

4.6.1 In medical emergencies

Any member of the medical team, or a health care professional involved in the care of a participant, may request unblinding in an emergency situation.

Arrangements for 24-hour emergency unblinding should be made before the trial commences. Details of the revealed allocation will be transmitted to the requesting party by the IS or delegate. Details of the request must be documented using the Unblinding Log (STU-AD-FRM-012) and stored in a confidential section within the Investigator Site File.

It must be ensured that in blinded trials that emergency unblinding of one participant does not unblind all participants in the trial.
The trial office will be informed about all unblinding requests.

4.6.2 For the purpose of requested notification to relevant safety committees

The IS shall request and receive copies of the relevant unblinding log(s) and perform any interim analyses described in the protocol or subsequently requested for safety purposes. The IS shall prepare an unblinded report which should include the date of code breaking and the reasons for the unblinding request. A record shall be kept in the TMF of the name of the statistician, the date

they were supplied with the relevant code breaks and the location of the results. The unblinded data and the results supplied shall not be accessible to the CI or trial staff.

4.6.3 Erroneous unblinding

Details of any erroneous unblinding shall be documented using the Unblinding Request Log (STU-AD-FRM-012) and completing a file note where relevant.

4.6.4 For analysis purposes at the end of the trial

The randomisation list should not be made available to the CI and their trial team until the database has been locked and analysis has been completed by the statistician.
The Statistical Analysis Plan must be finalised prior to the release of the allocation IDs. A record shall be kept in the TMF detailing who requested and when the allocation IDs were provided.

4.7 Close down of randomisation system

Following last patient last visit, it is usual for randomisation systems to be closed. The TM would contact the system provider and formally request closure. All recruiting sites should be informed of the timeframes for closing recruitment, and confirmation received from sites that the timeframes have been understood. The provider will forward audit logs and all relevant randomisation data for inclusion in the TMF.

5. References

Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. BMJ 2010;340:c332.

Health Research Authority website (HRA) – http://www.hra.nhs.uk/

Medicine and Healthcare products Regulatory Agency website (MHRA) - https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency/services-information

UK policy framework for health and social care research (2017) - https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/

UK Medicine for Human Use (Clinical Trials) Regulations 2025 - https://www.legislation.gov.uk/uksi/2025/538/contents

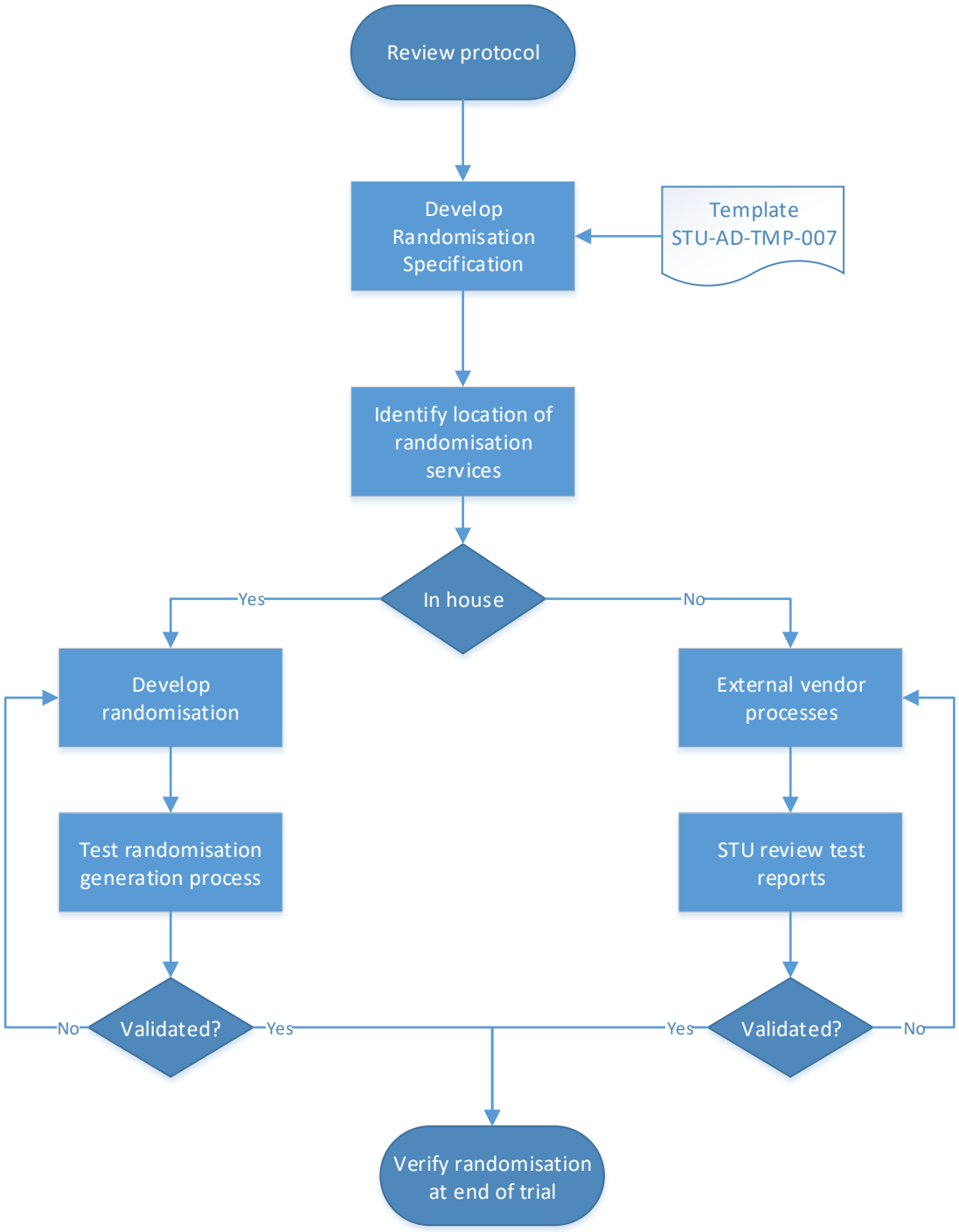
Guideline Statistical Principles for Clinical Trials http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E9/Step4/E9_Guideline.pdf

6. Associated Documents

Number	Title	Location
STU-AD-GDN-004	Recommendations for Generating Allocation Identifiers	QMS
STU-AD-TMP-007	Randomisation Specification Template	QMS
STU-AD-TMP-013	Allocation to Randomisation Checklist	QMS
STU-AD-FRM-012	Site Unblinding Request Form	QMS

7. Appendices

Appendix 1 – Randomisation Process Flowchart



Appendix 2: Blinding and Unblinding Flowchart