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

1. Purpose and Definitions

This Standard Operating Procedure (SOP) describes the procedure of randomisation 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.

2. Background

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. 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).

3. Roles and Responsibilities

The randomisation for individual studies may be developed internally using STU systems and expertise. There may also be instances where external organisations or individuals are delegated responsibility for generating the randomisation. In such instances agreements with delegated responsibilities will be developed.

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 **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.

The **Information Technology** (**IT) Manager** is responsible for oversight of any IT issues arising from the development of the trial randomisation. If an external vendor is used they may have a delegated development or oversight role.

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.

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 randomisation specification must be approved by the CI.

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 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.

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.

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.

4.4 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.

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.

4.5 Close down of randomisation system

Following last patient last visit, it is usual for randomisation systems to be closed. TM would contact the system provider and formally request closure. 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 2004 - http://www.legislation.gov.uk/uksi/2004/1031/contents/made
- ICH E9 statistical principles for clinical trials - Scientific guideline | European Medicines Agency (europa.eu)

It is assumed that by referencing the principal regulations that all subsequent amendments are included in this citation.

6. Associated Documents

Number	Title	Location
STU-AD-TMP-007	Randomisation Specification Template	Q-Pulse

7. Abbreviations

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

8. Appendices

Appendix 1: Document History

Version No:	3	**Effective Date:**	26-Mar-2024
Description of changes:	Addition of ICH E9 reference Reordering of procedure steps and addition of 'close down of randomisation system' Updated to SOP Template v5		

Appendix 2 – Randomisation Process Flowchart