STANDARD OPERATING PROCEDURE FOR RANDOMISATION, BLINDING AND CODE BREAKING IN CLINICAL RESEARCH

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1. PURPOSE

This Standard Operating Procedure (SOP) describes the processes to be followed in research studies which require participants to be randomised to receive one or more interventions.

Blinding of randomisation, when required, is described as the process for unblinding randomised participants.

2. SCOPE

This document applies to all randomised controlled research studies sponsored or co-sponsored by the University of Dundee and/or NHS Tayside. Unless otherwise specified in a clinical trial site agreement, this SOP applies to personnel involved in the development or implementation of randomisation and/or blinding and unblinding procedures.

3. RESPONSIBILITIES

Chief Investigator (CI): production and implementation of the randomisation specification and protocol (can be delegated to an appropriately qualified and trained individual).

Statistician (or other appropriately qualified individual): provide advice on the appropriate randomisation method for the trial and ensure that the schedule is produced and documented.

4. PROCEDURE

4.1 Randomisation Procedure

Prior to study start

4.1.1 A randomisation service provider, who has no direct contact with the study subjects or involvement with the assessment for eligibility in the study, shall be involved in the development, validation and review of the randomisation method.

4.1.2 The randomisation system used shall be detailed in the study protocol and agreed by the Sponsor prior to study start up.

4.1.3 Any stratification and/or minimisation to be included in the randomisation process

should be detailed in the protocol.

4.1.4 The sequence of allocations shall be random and based on random number generation or other random process. The program and seed number must be documented to ensure that a randomisation can be reproduced if required.

4.1.5 Non-random processes, such as alternate allocation, are not acceptable unless by prior agreement with Sponsor.

4.1.6 It should not be possible to know in advance what the next allocation will be.

4.1.7 In trials of medicinal products, the randomisation system must be compatible with the arrangements for drug delivery systems, packaging and distribution.

Prior to recruitment

4.1.8 The randomisation provider shall provide relevant information, including but not limited to:

- Method of production of the allocation list/algorithm.
- The name and job title of the person generating the randomisation list.
- Any outputs from testing, including the use of test participants where relevant (dynamic randomisation).
- Guidelines for users.

4.1.9 Distribution of electronic and paper copies of the allocation list/algorithm including storage and access control methods and the method by which emergency access to an individual allocation is managed must be documented.

4.1.10 A description of the randomisation procedure shall be included in the approved protocol.

4.1.11 Any breach of the randomisation procedure shall be notified to the Sponsor following the TASC SOP for Breach Reporting for Clinical Research.

During recruitment

4.1.12 Periodic checks of the randomisation allocation/algorithm should be incorporated to ensure compliance with the protocol. Unusual activity, such as unrestricted access or unusual patterns of randomisation must be documented and accounted for by the CI and notified to the Sponsor Research Governance Manager and Data Safety Monitoring Committee (DSMC) if in place.

4.1.13 Any changes to the randomisation system through the course of the study, along with the date when the change becomes active, will be documented.

4.2 Blinding of the Investigational Medicinal Product (IMP)

4.2.1 The protocol should define if the trial is double-blind, single blind or open label.

4.2.2 The randomised treatment allocation must be provided to the organisation responsible for packaging and/or labelling the IMP and the location documented in the Trial Master File(TMF).

4.2.3 For **double-blind trials,** the IMP must be manufactured, packaged, coded and labelled in a manner that protects the blinding. IMP labelling should not make reference to group allocation (e.g. Group A, Group B). Treatment packs should be

identified either by unique numbering of each pack, or packs should bear the participant number of the participant for whom they are intended.

4.3 Code-breaking/Unblinding

4.3.1 Participants receiving treatment should be provided with contact details of the study team.

4.3.2 In trials of medicinal products, the unblinding mechanism must be specified in the IMP Management Plan and protocol. Details of how to use the unblinding service must be provided to sites prior to any IMP being delivered.

4.3.3 Unblinding should be performed in accordance with the protocol and only in the following circumstances:

- Immediate Unblinding in an emergency situation.
- Unblinding to provide required non-emergency medical care which might be incompatible with the trial treatment.
- Unblinding for Suspected Unexpected Serious Adverse Reaction (SUSAR) reporting to National Competent Authorities (NCA) e.g. The Medicines and Healthcare products Regulatory Agency (MHRA) which approved the study and to the Research Ethics Committee (REC) which provided a favourable ethical opinion. This is usually performed by TASC Pharmacovigilance.
- Unblinding data for the purpose of notification to a DSMC (see TASC SOP for Creating Reports for the Independent Data Monitoring Committee).
- Unblinding at the end of the trial for analysis purpose (see TASC SOP on Performing Database Lock).

4.3.4 Other than in an emergency situation, any requests for unblinding must be discussed with the Cl and Sponsor before the treatment allocation is revealed. Details of all unblinding incidents must be recorded.

4.3.5 Care must be taken to ensure that no unnecessary unblinding of the study team occurs. Any intentional or accidental unblinding before the end of the study should be notified to Sponsor following the TASC SOP for Breach Reporting for Clinical Research.

4.3.6 Incidences of unblinding must be recorded and provided to the person performing the analysis to add to the Statistical Report.

4.3.7 24-hour access to the unblinding mechanism (either web-based or paper copy) must be in place and tested to ensure that it is accessible for each study. Documented procedures for authorised users must be provided for whichever system is used.

5. ABBREVIATIONS & DEFINITIONS

CI	Chief Investigator
DSMC	Data Safety Monitoring Committee
IMP	Investigational Medicinal Product
MHRA	Medicines and Healthcare products Regulatory Agency
NCA	National Competent Authority
REC	Research Ethics Committee

SOP	Standard Operating Procedure
SUSAR	Suspected Unexpected Serious Adverse Reaction
TASC	Tayside Medical Science Centre
TCTU	Tayside Clinical Trials Unit
TMF	Trial Master File

6. ASSOCIATED DOCUMENTS & REFERENCES

None

7. DOCUMENT HISTORY

History prior to 2021 is in the archived SOPs available from TASC Quality Assurance Dept.

Version Number:	Reviewed By (Job Title):	Effective Date:	Details of editions made:
8	Margaret Band (Senior Trial Manager)	12/12/2022	Biennial review. Text refreshed. Comment on stratification added (section 4.1.3).
9	Margaret Band (Senior Trial Manager)	11/12/2024	Biennial review. No changes required.

8. APPROVALS

Approved by:	Date:
Dr Valerie Godfrey, TASC Quality Assurance Manager, on behalf of TASC Clinical Research Guidelines Committee	10 Dec 2024