BU RDS SOP 023 V1

Title: Randomisation and Blinding	
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1. Scope

1.1 This Standard Operating Procedure (SOP) applies to all randomised controlled trials sponsored or co-sponsored by Bournemouth University, and to any personnel delegated to undertake duties involving randomisation or blinding, or those involved in the development of such procedures.

1.2 A randomised controlled trial is defined, by the National Institute for Health and Care Excellence (NICE) as:

> *'A study in which a number of similar people are randomly assigned to 2 (or more) groups to test a specific drug, treatment or other intervention. One group (the experimental group) has the intervention being tested, the other (the comparison or control group) has an alternative intervention, a dummy intervention (placebo) or no intervention at all. The groups are followed up to see how effective the experimental intervention was. Outcomes are measured at specific times and any difference in response between the groups is assessed statistically. This method is also used to reduce bias.' (NICE, 2018)*

The procedure for randomisation should be decided before the start of the trial, and should be ethically approved, being outlined within the study protocol.

2. Responsibilities

The *Chief Investigator (CI)/Researcher,* or delegated individual is responsible for producing and implementing the randomisation requirement and study protocol – ensuring that these are ethically approved. They are also responsible, alongside the Sponsor for ensuring that the randomisation aspect of the study will be hosted via an adequate randomisation service provider.

3. Procedure

3.1 The randomisation procedure must be truly random, and therefore employing a piece of randomisation software is advisable (e.g. *Sealed Envelope*), rather than more manual systems, such as alternate allocation. Allocation should be obscured prior to randomisation so that it is not possible to assume in advance what the next allocation will be.

3.2 The CI/Researcher should ensure that a trial statistician is consulted and advice sought on the most appropriate randomisation procedure. The procedure selected should

then be documented. The following factors should be considered when considering the best method for the given study:

- The sample size;
- The number of groups;
- The number of participants to be randomised to each group;
- Method of allocation (e.g. block randomisation, 1:2:1 randomisation etc.);
- Method of randomisation (e.g. web based, telephone based etc.);
- Processes for blinding (single blind, double blind etc.);
- Processes for un-blinding
- Processes surrounding accidental un-blinding.

The following information should likewise be discussed, agreed and documented:

- Method of generating a randomised code list;
- Name and job title of the person responsible for preparing and checking the randomised code list;
- Any factors that may be subject to blocking, in addition to stratification variables, e.g. algorithms used;
- The staff member(s) that will have access to the randomisation codes throughout the study and where they will be stored.

3.3 The procedure for randomisation of participants should be well documented in the trial protocol and should be ethically approved. In the case of double blind studies, the treatment allocations must be held securely by a carefully chosen individual until the codes are broken at study end.

3.4 The method chosen for randomising trial participants must ensure that each participant is allocated a unique study identifier, clearly showing the allocated treatment. In the case of blinded studies, allocations should be kept hidden from the investigators and research team. In some studies, it may be advisable to have certain individuals aware of the allocated treatment, but this is on a case by case basis.

3.5 Any deviations from or failures of the randomisation process should be documented in the Trial Master File (TMF) through use of a file note.

3.6 <u>Blinding</u>

3.6.1 Blinding is the process whereby one or more parties involved within a given trial, are unaware of what treatment group the participants have been randomised to. Blinding ensures that there is no bias, and so it is vital to maintain this throughout the trial, with one of the following methods being employed:

Open-label trial – both the research team and the participants know the treatment being administered.

Single-blind trial – one party, either the Investigator or the trial participant, is unaware of the treatment.

Double-blind trial – neither the participants nor the study team know what the participant is receiving.

3.6.2 The protocol should outline all the individuals involved in the study that will be blinded, and those that will not. In the case of studies involving placebos as the control, then extra steps should be taken to ensure that the treatments are indistinguishable, i.e. identical in smell, colour and texture to the Investigational Medicinal Product (IMP).

3.7 Un-blinding

3.7.1 In the interest of safety, un-blinding may be required, however prior to this being undertaken, the Sponsor should be consulted, as un-blinding one participant, could un-blind the whole study. In this situation, there should be procedures in place to access the randomisation list, in either paper version, or electronically.

3.7.2 There may be other situations, in which un-blinding is necessary, such as at the end of a trial or for interim analyses. In both of these situations, a formal process should be documented. For interim analyses, this process should be carried out by personnel who have no further involvement in the conduct of the trial, or the final analysis.

3.7.3 Prior to commencing a blinded trial, the Principal Investigator must ensure that:

- a comprehensive un-blinding process has been implemented and documented;
- the code breaks are in a designated place on site – e.g. code break envelopes, a master list held by Pharmacy etc.;
- the whole research team involved in the given trial are aware of the process and arrangements.

3.7.4 If a trial participant has been un-blinded, then the participant should be encouraged to remain in the trial, on the trial treatment, if safe.

4. Abbreviations and definitions

CI	Chief Investigator
IMP	Investigational Medicinal Product
NICE	National Institute for Health and Care Excellence
TMF	Trial Master File

5. Related documentation and references

NICE. (2018). Glossary. [online] Available at: https://www.nice.org.uk/Glossary?letter=R [Accessed 18 Jun. 2018]