Dorset HealthCare University NHS Foundation Trust

Breaking Randomisation Codes

Objectives	To ensure that the correct procedure is followed when receiving a request to break the randomisation code for a clinical trial participant.
Scope	This procedure is applicable to all Research & Development staff involved in the preparation, review, approval and issuing of SOPs.
Responsibility	The R&D Facilitator is responsible for ensuring implementation of this SOP within the Research & Development Department.
Related Documents	• SOP RES SA 017 - Study Files and Filing • SOP RES SA 019 - Adverse Event, Serious Adverse Event and Suspected Unexpected Serious Adverse Reactions Reporting.

1 Purpose

To ensure that the correct procedure is followed when receiving a request to break the randomisation code for a clinical trial participant.

2 Introduction

Trials may be 'blinded' to avoid the introduction of bias. If patient, Investigator or statistician knows which treatment the patient is receiving, it may influence response to the treatment, or the assessment of response and thus bias results. For example, if the Investigator gives a patient the new treatment, he/she may then observe the patient more closely or may communicate more positively with the patient. He/she may also evaluate the patient groups differently. If the patient knows they are receiving the new treatment and not the standard, this may also affect response (positively or negatively).

Placebos are often used when there is no standard therapy available, or the efficacy of the 'standard treatment' has not been established. When one group of patients receives treatment and the other receives nothing, it could be that the group on treatment shows an improvement compared to the control group. The problem is that you don't know if they showed the improvement just because they were being actively treated or whether it was due to a real effect of the substance, therapy or surgery. It has often been demonstrated that many minor illnesses could be effectively treated by placebos.

The reason for using placebo in clinical trials is therefore to attempt to make patient attitudes as similar as possible between the treatment groups. The patient should not be aware that they are receiving a placebo and therefore the trial should at least be designed as a trial that blinds the patient (single blind).

Double blind trials are those where neither the Investigator nor the patient know which treatment the patient is receiving. Most double blind trials involve therapy with a test treatment compared with a placebo. However, they can also consist of a test treatment and a standard treatment. To be properly blinded, the two blinded treatments must be perfectly matched for appearance, taste, smell etc. If this is not possible for practical reasons, a 'best attempt' is usually considered acceptable.

It is sometimes necessary to compare two treatments with different methods of application, e.g. comparing a tablet with a topical application. In this case, it may be necessary to have a 'double dummy' design, i.e. one treatment group receives the test tablet with a placebo cream, the other group a placebo tablet with the test cream. Here each placebo must be matched with the respective test substance.

Blinding often completes the randomisation procedure, and it is also necessary to have a coding procedure, identifying the patient number or the medication code number with the treatment. The patient number and medication code number may be the same.

In ophthalmological research the term double masked may be used, to avoid any disagreeable associations and possible confusion.

3 Training

New users must read and understand this SOP before carrying out this procedure. Existing users must read and understand the Revisions Section.

4 Revisions

This is the second version of this SOP.

5 Procedure

5.1 Only break open a randomisation code if it is essential to the welfare of the patient. They are usually only broken if a patient suffers a Serious Adverse Event (SAE) or is hospitalised as an emergency. Breaking a code invalidates the patient from the trial and may affect the statistics of the trial. Code breaks are only available when the trial is "blinded".

5.2 The pharmacy clinical trial summary located in the front of each pharmacy site file includes details of where the random code is stored and where to look for more information.

5.3 Randomisation codes or code breaks may be sealed 'envelopes' or in the form of labels, which, once the medication is dispensed, are usually fixed to the patients records in the pharmacy site file. If these have been generated via IVRS/IWRS, the randomisation codes will be broken by investigator and pharmacy intervention should not be required.

5.4 Always refer to company procedure for breaking the randomisation code. This can be found in the study protocol sometimes on the outer envelope containing the random codes, or in the specific section of the study file.

5.5 Contact the trial Sponsor before breaking the code to obtain permission.

5.6 Code breaking is usually undertaken by the Principal Investigator (PI), the Consultant in overall charge of the trial at this site. PIs must be contacted before the code break is undertaken.

5.7 Details of why the code was broken, the date and the signatures of the person breaking the code (pharmacy) and the relevant investigator should be recorded on the code break documentation. This information should be filed in the relevant pharmacy clinical trials folder and a copy should be sent to the trial Sponsor.

5.8 Wherever possible, the Clinical Trials team should perform the code break; if this is not possible, then they should be informed that the code has been broken as soon as possible.

N.B. If a patient has relapsed and wishes to know their treatment, under no circumstances is it permitted to give this information unless an SAE has occurred and has been graded as a SUSAR – SOP RES/009. In this case the SUSAR must be reported to the MHRA unblinded.

6 Appendices

None.

7 Responsibilities

The clinical trial Sponsor is responsible for planning and organising the procedures for un-blinding.

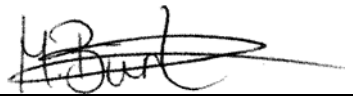
The Principal Investigator is responsible for breaking the code after consultation with the Monitor/Sponsor. The Pharmacist may be delegated this responsibility. Sub-investigators may also break the code if nominated to do so. The un-blinding may also be carried out centrally from the trial office.

8 Associated Documentation

SOP RES/004 – Study Files and Filing
SOP RES/009 – Adverse Event, Serious Adverse Event and Suspected Unexpected Serious Adverse Reactions Reporting.

9 Review

This SOP should be reviewed every two years unless new guidance or legislation dictates a review any sooner.
Date Reviewed: 12/04/19 Date of review: 12/04/21

Written By	Signature	Date
Hazel Burt		12/04/19
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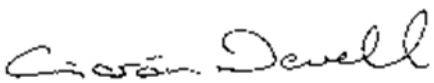
Dr Ciarán Newell		12/04/19
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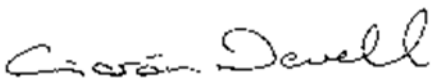
Dr Ciarán Newell		12/04/19