Unblinding Procedures

IT IS THE RESPONSIBILITY OF ALL USERS OF THIS SOP TO ENSURE THAT THE CORRECT VERSION IS BEING USED

All staff should regularly check the R&D Department’s webpage for information relating to the implementation of new or revised versions. Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded versions are promptly withdrawn from use unless notified otherwise by the SOP Controller.

The definitive versions of all R&D Department SOPs appear online. If you are reading this in printed form check that the version number and date below is the most recent one as shown on the R&D Department webpage.

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Date: 11.10.17

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Signature: 
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This SOP will normally be reviewed every 3 years unless changes to the legislation require otherwise

Version 1.0 13/10/17
Version History Log

This area should detail the version history for this document. It should detail the key elements of the changes to the versions.

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1 Introduction, Background and Purpose

PURPOSE/INTRODUCTION

This Standard Operating Procedure (SOP) details the procedures to followed to:
1) Unblind a subject in an emergency situation,
2) Unblind data for the purpose of notification to DMC,
3) Manage accidental unblinding,
4) Unblind a research project for analysis purposes at the end of the trial.

For the purpose of this SOP, ‘Un-blinding’ is synonymous with ‘Code Breaking’ and with ‘Unmasking’, all terms that are frequently used in research protocols.

Treatment codes shall be broken before reporting a SUSAR to the MHRA and REC.

2 Who Should Use This SOP

This SOP is applicable to research staff undertaking randomised blinded projects sponsored by ABM UHB.

ABM UHB SOPs may also be used by staff from other NHS areas, or organisations, with prior agreement.

This includes clinical trials of investigation medicinal products (CTIMPs) covered by the UK Medicines for Human Use (Clinical Trials) regulations or equivalent local legislation outside the UK.

3 When this SOP Should be Used

A ‘blind’ study is a clinical trial in which the subject or the Investigator (or both) are unaware of which trial product/drug the subject is taking.

When only one is blinded to the data this is a ‘single blind’ study. When both do not know the treatment, the study is ‘double-blind’.

Studies in which the participant takes part in three arms, such as placebo, active drug and comparative drug remain as double blind.

Unblinding is the process by which the allocation code is broken so that the CI and/or trial statistician becomes aware of the intervention.
4 Procedure(s)

4.1 Definition:

A ‘blind’ study is a clinical trial in which the subject or the Investigator (or both) are unaware of which trial product/drug the subject is taking.

When only one is blinded to the data this is a ‘single blind’ study. When both do not know the treatment, the study is ‘double-blind’.

Studies in which the participant takes part in three arms, such as placebo, active drug and comparative drug remain as double blind.

Unblinding is the process by which the allocation code is broken so that the CI and/or trial statistician becomes aware of the intervention.

4.2 RESPONSIBILITIES

-The CI shall include on the Delegation Log names of research staff that will have access to the treatment randomisation codes for purposes of unblinding. The CI shall include on the Delegation Log names of researchers who may request unblinding.
- Prior to the initiation of the research project, the CI shall ensure that the process for Emergency Unblinding is in place, including a system for ‘Out of Hours’ access to the codes (i.e. the code-breaks are in a designated secure area on site).

- The CI is responsible to ensure that all trial staff, irrespective of location, involved in the process shall be aware of the arrangements.

- All researchers, delegated tasks within the project, shall follow the trial’s randomisation procedures and shall ensure that unblinding takes place only in accordance with the protocol.

- Participants in CTIMPs are to be issued with ‘In case of emergency’ cards to be carried at all times. Minimum details on the card shall include the trial emergency contact number, name of CI, study identifier and details of the potential IMP (IMP name or Placebo) plus the name of the participant.

- Consideration shall be given to testing the Emergency Phone number and the Unblinding system prior to recruitment of the first participant. When this occurs, the process shall be documented.

- If the trial or single subject is prematurely unblinded (e.g. accidental unblinding or unblinding due to a serious adverse event) the CI or delegate is responsible for promptly documenting the series of events and notifying the sponsor.

- The CI is responsible for notifying REC and the MHRA of any premature unblinding, using SOP02 Breaches and Urgent Safety Measures and associated documents.

4.3 Emergency unblinding of individuals

- All care shall be taken to ensure that the study team are kept blinded.

- Details of any emergency unblinding shall be documented fully in the Sponsor file, Investigator TMF and Pharmacy and Site File(s). This includes, but may not be limited to:
  1) Date,
  2) Subject details,
  3) Reason for unblinding,
  4) The results,
  5) Name and role of the individual requesting the unblinding,
  6) Name and role of the individual carrying out the unblinding.

The information shall be transmitted to the requesting party.
-If the Clinical Trials Pharmacy or an individual as named on the Delegation Log has performed the procedure, they will inform the Sponsor the trial identifier, subject number and name and title of the person making the request, but NOT the result. The details shall be included in the statistical report.

4.4 Unblinding for DMC

The protocol shall specify if an interim analysis is to be conducted and the statistical analysis to be performed. This can be predetermined at protocol stage or at the request of the DMC. Unblinded results supplied to the DMC can determine whether a trial should continue, be modified or recommend to TSC that the trial be halted earlier than intended.

A named statistician, not involved with the final data analysis or with the study, shall receive the relevant codes and perform the interim analysis. A record shall be kept in the Investigator TMF of the name of the statistician, the date they were supplied the relevant code breaks and the location of the results. The unblinded data and the results supplied to the DMC shall not be accessible by the CI or trial staff.

4.5 Accidental unblinding

Details of any accidental unblinding shall be documented fully. This includes, but may not be limited to:

1) Date,
2) Subject details,
3) Reason for accidental unblinding,
4) Name and role of the individual responsible for the unblinding,
5) Action taken to preventive recurrence,
6) Details on the CI’s decision for the subject to remain in the trial, or be withdrawn.

These details shall be forwarded to the sponsor using the Breach Report Form

The details shall be included in the statistical report and documented in the Sponsor File and Investigator TMF/ISF

4.6 Unblinding at end of trial

The Statistical Analysis Plan shall be provided in the protocol or be finalised prior to the release of the randomisation codes. Changes to the statistical analysis plan shall be version controlled. A record shall be kept in the Investigator TMF to confirm when the randomisation code was requested and when provided.
4 Related SOPs and Documents

R&D/SOP02   Serious Breach of GCP or the study protocol

R&D/SOP03/AD01 Unblinding Record