York Foundation Trust R&D Unit
SOP
Pharm/S89

Maintaining the blind for clinical trials in Pharmacy

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 Unit's website and R&D Newsletter 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 Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded versions are promptly withdrawn from use unless notified otherwise by the SOP Controller.

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This SOP will normally be reviewed every 2 years unless changes to the legislation require otherwise

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.

Version	Date Implemented	Details of significant changes
1.0	20th August 2015	

Contents

1 Introduction, Background and Purpose

The MHRA Good Clinical Practice Guide states that 'Blinding is the process that keeps one or more parties involved in a trial (for example, the Sponsor, the Investigator team and/or the subject) unaware of what treatment arm subjects have been randomised to. It is vital that the blind is maintained throughout the trial to ensure that no bias is introduced when making safety and efficacy statements'.

Maintaining the blinding for a clinical trial is described in section 6.6.3 of the MHRA Good Clinical Practice guide and it lists the processes for handling the following items as being important in achieving this purpose;

- code break envelopes
- randomisation lists and envelopes
- Drug administration records (and preparation records)

Pharmacy may have a role in handling these items (and in some circumstances therefore be un-blinded to patient treatment allocation) and therefore have an important role in maintaining the blinding arrangements in a studies which are designed in this manner. The study design and therefore the specific blinding arrangements for a trial should be apparent when completing a Pharmacy risk assessment form for a clinical trial.

The purpose of this SOP is to describe the procedures or actions that should be considered or undertaken within Pharmacy to ensure that blinding for a trial is maintained, and in particular, Pharmacy take appropriate action to prevent inadvertent un-blinding of the trial. This SOP also describes how these actions should be documented for a particular study as appropriate. This SOP is intended to provide guidance on this subject and its content should not be considered as exhaustive.

2 Who Should Use This SOP

This SOP should be used by all members of the Pharmacy clinical trials team at York and Scarborough hospitals, which form part of the York Teaching Hospital NHS Foundation Trust.

There may be circumstances where this SOP is also applicable to the Principal Investigator and other members of the local research team e.g. Research Nurses and Clinical Trials Assistants.

3 When this SOP Should be Used

This SOP should be used whenever it has been identified that Pharmacy will have a role in one or all of the following activities;

- Sourcing IMP for a blinded trial.
- Randomisation of participants from a randomisation list that identifies patient treatment allocation.

- Handling of code break envelopes, or a role in other methods of un-blinding the trial.
- Preparation of Investigational Medicinal Products in an un-blinded manner.
- Taking a role to be part of an un-blinded team in the trial.

This SOP should be used when preparing Pharmacy trial instructions to ensure that blinding for a relevant trial is maintained.

4 Procedure(s)

The arrangements for maintaining the blind for a clinical trial should be considered in detail and those arrangements carefully planned, documented and communicated to ensure inadvertent un-blinding is avoided.

To this aim, the Pharmacy trial instructions should be written to detail what actions will be taken to maintain the blind for a clinical trial and who will be responsible for these actions. These are likely to be very specific to each relevant trial.

Therefore for each clinical trial that involves an activity within the scope of this SOP, the Pharmacy trial instructions, created by the Pharmacy clinical trials team, should cover the following subjects (as applicable to the trial in question);

- Manufacture of the Investigational Medicinal product
- Handling of code break envelopes and other methods used for un-blinding
- Handling of an open randomisation list and other methods used for randomisation
- Aseptic preparation of IMP
- Communication with the Research Team
- Communication with the Sponsor
- Invoicing and stock management for blinded trials
- Destruction of IMP
- Training

The relevant template should be chosen to incorporate the relevant information e.g. Pharm/T41 – Pharmacy study specific trial instructions - Aseptic dispensing and release of IMP – should be used to describe procedures for maintaining the blind where the trial involves Aseptic preparation of IMP.

The Pharmacy trial instructions should be created, reviewed and approved in line with those procedures detailed in Pharm/S50 – Preparation, review and approval of Pharmacy study specific trial instructions.

The following sections contain guidance on what should be considered when writing the Pharmacy trial instructions to maintain the blind for a study. This guidance is not intended to be universally applicable and there may be study specific arrangements in this respect that are not covered here. The Sponsor should be consulted as appropriate.

4.1 Manufacture of the Investigational Medicinal product

Correct manufacturing and assembly processes are vital in ensuring that the blind is maintained. If Pharmacy is involved in sourcing IMP for use in a blinded trial, this should be considered as part of the Technical agreement put in place to

cover IMP manufacture for the clinical trial. Further information can be found in section 6.6.1 of the grey guide.

4.2 Handling of code break envelopes and other methods of un-blinding

Consideration should be given as to;

- How code break envelopes are reconciled at the end of the trial to ensure that they have not been tampered with.
- The process of Un-blinding a subject in the trial. This process should not un-blind the whole trial, and where possible the trial team should not be informed.
- How code break envelopes are to be controlled in a manner so that, once opened, they are not available to any members of the blinded Research Team.

Refer to Pharm/S54 – Managing Code Break Procedures for further information.

4.3 Handling of Randomisation lists and other methods used for randomisation

Consideration should be given as to;

- How these will be stored and controlled so that they are kept under the control of those personnel un-blinded to treatment allocation.
- When IRT (Interactive Response Technologies) systems for randomisation are being employed, how to ensure that un-blinded information is not sent to those who are supposed to be blinded in the trial.

4.4 Aseptic preparation of IMP

The following should be considered here:

- Training to ensure that Pharmacy staff in Aseptics units do not inadvertently un-blind the study if contacted by the Research team.
- Procedures and worksheets designed to ensure labelling of the prepared product does not inadvertently un-blind the clinical trial.
- The procedure for blinding any prepared infusions should be documented and where possible tamper proof tape should be used to ensure that the blinding has been maintained during the process of IMP administration.
- How preparation worksheets should be controlled in such a manner that they are only available to be viewed by un-blinded personnel.

Where un-blinded members of the research team have been delegated to prepare study drug outside Pharmacy, the trial treatment should be prepared in a quiet area, out of site from the blinded research team and the patient (if they are blinded also). A member of the un-blinded research team (who is listed on the delegation log as being responsible for this activity) should prepare the infusion.

4.5 Communication with the Research Team

The Following should be considered here:

- Which members of the Research team are un-blinded and blinded. Some studies may have separate blinded and un-blinded members of the Research team.
- How Pharmacy is made aware of any changes in which members of the Research Teams are blinded and un-blinded (blinded and un-blinded team members should not switch roles during the study).

- How to ensure that patient treatment is only discussed with those un-blinded to patient treatment allocation.

In studies that involve Pharmacy dealing with a blinded and un-blinded research team, the following should also be considered:

- Prescribing study treatment (if applicable)

If this is being done by an un-blinded Principal Investigator, consideration should be given as to the handling of the prescription in such a manner as to not indicate treatment allocation to blinded members of the research team

- Dispensing study treatment

In trials, where Pharmacy are un-blinded and giving out to an un-blinded member of the research team, the medication dispensed should be given to a member of the un-blinded research team in an opaque bag to ensure that the contents cannot be seen by members of the blinded research team, or the patient. A photocopy of the prescription should not be given to the un-blinded research team, unless it is clear how this information will be handled in a way that doesn't un-blind the study.

- Disposal and/or return of prepared products

Care should be taken to ensure that the study medication is disposed of by un-blinded staff in line with standard hospital procedures, and in a concealed manner. Signature of staff to prompt and confirm this activity is often useful to support compliance.

Consideration should be given as to how items will be returned to pharmacy to prevent inadvertent un-blinding of the trial. In this circumstance, an opaque bag could be used to prevent the medication being viewed by blinded members of the research team.

4.6 Communication with the Sponsor

Consideration should be made for those studies in which there is an un-blinded and blinded Clinical Research Associate (CRA). In these circumstances the trial instructions should document:

- How to ensure Pharmacy staff are aware which CRA's are blinded and un-blinded.
- That un-blinded information e.g. patient treatment should not be shared with the blinded CRA.
- What should be made available to whom during monitoring visits, and other contact, with Pharmacy (e.g. files may be marked as containing un-blinded information to prevent inadvertent un-blinding).

4.7 Invoicing and stock management for Blinded trials

Consideration should be given to those trials involving commercial hospital stock and the use of computer dispensing systems e.g. JAC where IMP will need to be booked out to a Consultant during the process of preparation. The trial instructions should consider a process whereby this does not un-blind the study at a later date e.g. when Finance reports are run detailing what was booked out on the dispensing system.

Invoicing the Sponsor for the drug costs associated with blinded trials should be carefully considered in these trials and potentially conducted at the end of the study. This will ensure that the Sponsor and the Trial Management team are not un-blinded to the treatment each patient has received.

4.8 Training

Training (of the Pharmacy clinical trials team) should be conducted in the Pharmacy trial instructions, once approved, prior to the start of the trial. All training should be recorded on a Pharmacy Training log (Pharm/F61).

5 Related SOPs and Documents

MHRA Good Clinical Practice Guide, 2012.

Pharm/S50	Preparation, review and approval of Pharmacy study specific trial instructions
Pharm/S54	Managing Code Break Procedures
Pharm/F61	Pharmacy Training Log