South Eastern Health and Social Care Trust

# Standard Operating Procedure (SOP) Research and Development Office

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| **Title of SOP:** | Preparation of a Study Specific Randomisation, Blinding and Emergency Unblinding Standard Operating Procedure |
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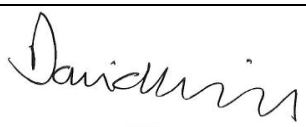
| Signed: |  |
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## 1. INTRODUCTION

Clinical trials are often blinded to hide the treatment group assignment from participants and investigators (in double-blinded studies) in order to prevent the unintentional biases of either parties affecting subject data.

In order to protect the well being and safety of the trial subject as required in the principles of GCP, the coding system for the Investigational Medical Product(s) in blinded trials should include a mechanism that permits rapid identification of the product(s) in case of a medical emergency, but one that does not permit undetectable breaks of the blinding in order to protect the integrity and validity of the data. To ensure this, emergency unblinding procedures must be clearly established.

At the start of any clinical trials the Chief Investigator (CI) should have a written procedure on the randomisation, blinding and process for rapidly identifying a blinded Investigational Medicinal Product(s), as well as the details of authorised personnel who will have access to unblinded data.

## 2. OBJECTIVE

This objective of this SOP is to describe the process that an investigator should follow to prepare a trial specific randomisation, blinding and emergency unblinding SOP.

## 3. SCOPE

This SOP applies to clinical trials/studies carried out in South Eastern Health and Social Care Trust where the Trust has accepted the role of 'Sponsor'.

## 4. RANDOMISATION

The CI needs to determine what type of method will be used to reduce the chance of imbalance between treatment groups. The design and type (simple, block, stratified, minimisation) should be detailed in the protocol and in the SOP. The CI should consult with a qualified statistician to determine the type of randomisation needed.

Once the design and type of randomisation has been established in the protocol, a randomisation list with details of the randomisation codes should be produced in accordance with the protocol. The list should be generated by a person who has no direct contact with the trial subjects or involvement with the assessment for eligibility in the trial. It is recommended that the CI considers using an external source to perform this task using either an Interactive Voice Response System (IVRS) or Interactive Web Response System (IWRS). In cases of trials that are single site involving small numbers and depending on the complexity of the randomisation required, a qualified statistician or data manager may perform this task.

The process used to produce the randomisation list and how randomisation will be implemented should be documented in the SOP with the following considerations made:

- A brief description of the randomisation process
- Variables used in the procedure to be recorded
- The name and job title of the person generating the randomisation list
- Computer software that will be used to generate the list and perform randomisation (if applicable) and details on the validation of the system before it is used.
- What approach will be used to conceal allocation (eg password protected electronic format), and details on location of the randomisation list and how it will be stored securely.
- If a system of sealed envelopes is used, the CI/PI should ensure that all seals of these envelopes are signed and dated and that the CI/PI collects the envelopes at the end of the trial to ensure that the seals have not been broken.
- The name and job title of the person who will have access to the randomisation list and will be responsible for randomisation (NB for double blinded trials the randomisation list should not be made available to the CI and their trial team until database lock and the codes are officially broken at the end of the trial).
- For blinded trials, will need to provide details on how the randomisation codes will be provided to the IMP manufacturer to ensure the IMP are packaged, coded and labelled in a manner that protects the blinding
- Details on the randomisation process (include telephone numbers and/or web links) and should include open times for randomisation and procedure to be used out of hours if applicable (ie randomisation hours between 9-5 Monday to Friday).
- Details of the documentation to be completed for randomisation (eg signed informed consent form, randomisation checklist/CRF or eligibility criteria checklist CRF)
- Details on how pharmacy will be informed of the randomisation treatment code allocation (eg fax sent to pharmacy)
- Should include the provision of a study specific patient card with contact details (including out of hours contact details) for emergencies.

## 5. BLINDING

The protocol and SOP should define the level of blinding eg unblinded, single-blind or double-blind and how the blinding will be implemented (eg through the use of an identical placebo).

For double blinded trials the SOP should include how the IMP will be packaged, coded and labelled in a manner that protects the blinding (NB labelling should not make reference to group allocation).

## 6. EMERGENCY UNBLINDING

The emergency unblinding process should be detailed in the protocol and the procedure thoroughly documented in the SOP and needs to include the following considerations:

Circumstances where unblinding of individual can be broken such as in a medical emergency where knowledge of the blinded treatment is necessary for the treatment of an adverse event, where a child in a participants household accidentally takes an IMP, in the event of a SUSAR needing expedited reporting or if requested by a Data Safety Monitoring Committee (DSMC).

Details on the format of the emergency unblinding (ie 24 hour telephone number, scratch cards, tear of labels, IVRS or IWRS system).

Sealed emergency unblinding envelopes could be considered for small non complex single site trials. The CI will need to detail in the SOP that the envelopes are to be signed on both seals, and in the event of an emergency unblind the name of the code breaker, the signature, date and time needs to be recorded on the outside of the envelope.

If the emergency unblind envelopes are used, the SOP should give details on the collection of envelopes by the CI/PI at the end of the study and provide information on where the emergency unblind envelopes will be held.

It is essential that, in the case of an emergency, there is a system in place for providing 24 hour cover to access the emergency unblind. The SOP needs to provide the step by step instructions on how to unblind in an emergency.

Specify what needs to be documented and how for any emergency unblind. The SOP should request this to be documented fully on a study specific unblinding form or file note and should contain: The date and time, reason for unblinding, name and signature of the person requesting the emergency unblind, name and signature of the person breaking the blind.

Detail where the written documentation of the emergency unblind should be filed.

For single site trials, the SOP needs to state that the investigator will notify the sponsor in writing following an emergency unblind, detailing the reasons for unblinding.

For multicentre trials, the SOP needs to state that the CI must inform other investigators in writing following an emergency unblind, with the reasons for unblinding.

Provide details on circumstances where patients will be able to remain on the trials following unblinding.

Provide details of unblinding after study completion, all data collected and queries resolved and the database locked, including the role of the DSMC and Statistician.

Consider the method of informing participants of their blinded treatment allocation, if applicable.

The procedure for emergency unblinding should be provided to the Trust pharmacy department before the trial commences.

## 7. REGULATIONS, GUIDELINES, REFERENCES, SOP LINKS ETC.

Statutory instrument 2004/1031: The Medicines for Human Use (Clinical Trials) regulations 2004.

Statutory instrument 2006/1928: The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006.

European Commission, The rules governing medicinal products in the European Union, Volume 4, Good manufacturing practices, Annex 13, Manufacture of investigational medicinal products, Revision 1 July 2003

## 8. APPENDICES

None