Sheffield Teaching Hospitals NHS
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Research Department

STANDARD OPERATING PROCEDURE

Research Department & STH Researcher

Code break procedures for STH Sponsored IMP clinical trials

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Standard Operating Procedure: Research Department

Code break procedures for STH Sponsored IMP clinical trials

This SOP has been produced in accordance with Medicines for Human Use (Clinical Trials) Regulations 2004. This SOP will outline the procedure for breaking the study code in a STH Sponsored blinded randomised IMP clinical trial.

Background

Clinical trials are often blinded to prevent the unintentional biases of either the patient or the investigator affecting subject data. Blinded studies, unlike open-label studies (in which treatment assignment is known), hide treatment group assignment from participants in the study.

Code break procedures must be clearly established to ensure that no unnecessary or unintentional un-blinding occurs and to protect the integrity and validity of the data. If un-blinding of participants is allowed during the conduct of a clinical trial other than for an emergency situation, the protocol must state the procedures for obtaining permission to break the blind.

Definition

Code break is also known as breaking the blind and involves un-blinding a participant so that the treatment allocation is made known. Only the pharmacy Clinical Trials Manager, or delegate may break the code, as per Pharmacy SOP

Procedure

1. For STH Sponsored IMP blinded studies the Pharmacy Clinical Trial Manager holds the study codes in a study specific file. The study file is held in a secure area in Pharmacy, with access only provided to those persons to whom permission has been delegated. This permission is documented on the delegation list on a study by study basis.
   1.1. For studies using WPH Pharmacy, code breaks are kept in the emergency cupboard on Ward 3, due to the pharmacy not having a 24 hour resident service. For IVRS access code breaks, the medical oncologists rotate availability to perform this action.

2. The Principal Investigator (PI) may only break the study code under the following circumstances; per protocol, in an emergency or at the end of the study.

3. **Breaking the blind per protocol**

   3.1. The PI contacts the holder of the code break envelope/list. During office hours the Pharmacy Clinical Trials Manager at the relevant STH site should be contacted by phone.
   3.2. The Pharmacy Clinical Trials Manager (or delegate) provides the PI with the information as requested.
   3.3. The PI documents the breaking of the code per protocol in the site file.
   3.4. The Pharmacy Clinical Trials Manager (or delegate) documents the breaking of the code per protocol on the code list within the Pharmacy study file.

4. Breaking the blind in an emergency

   4.1. The study code should only be broken for valid medical or safety reasons e.g. in the case of a severe adverse event where it is necessary for the PI or treating physician to know which treatment the patient is receiving before the participant can be treated.
   4.2. The PI or treating physician contacts the holder of the code break envelope/list. During office hours the Pharmacy Clinical Trials Manager at the relevant STH site should be contacted by phone, out of hours on-call pharmacist via switchboard should be contacted.
   4.3. The Pharmacy Clinical Trials Manager (or delegate) provides the PI or treating physician with the information as requested.

4.4. On receipt of the treatment allocation details the PI or treating physician deals with the participant's medical emergency as appropriate.

4.5. If the treating physician is not the PI, the treating physician must inform the PI of the code break and the reasons for the actions taken as soon as possible.
4.6. The PI documents the breaking of the code and the reasons for doing so on the CRF and in the site file.
4.7. The Pharmacy Clinical Trials Manager (or delegate) documents the breaking of the code and the reasons for doing so on the code list within the Pharmacy study file.
4.8. The PI notifies the Research Coordinator (acting on behalf of the Sponsor) in writing as soon as possible following the code break detailing the necessity of the code break.
4.9. The PI notifies the Research Ethics Committee of the protocol deviation and copies the letter to the Research Coordinator

5. Breaking the blind at the end of the study

5.1. The un-blinding of participants cannot occur until all participants have completed the final data collection visit (also know as Last Patient Last Visit, LPLV).
5.1.1. It is best practice to un-blind after the database has been locked i.e. all data entered, validated and no further changes are expected.
5.1.2. Furthermore, it is best practice for the person performing the statistical analysis to remain blinded until after the analysis has been completed.
5.2. The PI contacts the Research Coordinator (acting on behalf of the Sponsor) confirms that data collection is complete, provides the date of LPLV and requests permission for the un-blinding of the study.
5.3. The Research Coordinator confirms that the study may be un-blinded by email to the PI, copying in the Pharmacy Clinical Trials Manager (or delegate).
5.4. The Pharmacy Clinical Trials Manager (or delegate) provides treatment allocation details to the PI as requested.
5.5. The PI makes every effort to inform all-participants of their individual treatment assignment.
5.5.1. The PI determines the appropriate method of informing participants of the blinded random assignment. If disclosure of the random assignment requires counselling of the participant or could cause distress, the PI (or delegate) does this in person.