STANDARD OPERATING PROCEDURE (SOP)

SOP Number: NCP/R&D_008

SOP Title: Code Breaking

Role	Name	Signature	Date
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SOP Review Date			Effective date stamp

Review History

Version	Effective Date	Review Undertaken/Significant Changes	Date Approved
1		Initial Version	

1. PURPOSE AND CONTEXT

1.1. This standard operating procedure (SOP) describes the process which must be followed for when a clinical trial involves an Investigation Medicinal Product (IMP) where at times safety data will be limited. Depending on the nature of the study, a study patient may be randomized to receive an active IMP or a placebo/active comparator in a blinded manner so that both the Principal Investigator (PI) and patient are not aware which arm of the trial they are randomized to.

1.2. When there are concerns in relation to safety concerns, a situation may be required where it is necessary and in the patient's best interest to break the randomization code and unblind the patient's medication. This SOP sets out the steps to be taken to break a randomization code or unblind a patient in an emergency.

1.3. Additional information on Code Breaks can be found in Pharmacy SOP CP R&D 006 – Code Breaks.

2. DEFINITIONS

- *When appropriate, a list of definitions should be included for terms used in a SOP.*

3. PROCEDURE and RESPONSIBILITIES

3.1 General Information

3.1.1 If a study involves IMP, the R&D team will assess the risk of the drug for patients at the beginning of the study, using NCF-R&D_012 – Risk Assessment Tool. This will be done to anticipate whether it is likely code breaking will be required for the duration of the study and provide a written document of any risk.

3.1.2 Unless otherwise specified in the study protocol, the Principal Investigator (PI) at Southern Health NHS Foundation Trust will be delegated the task of unblinding authorization as part of 24 hour cover. In some cases this task may be delegated to a member of the Research & Development team if agreed by the PI. A back up should be identified for when this person is on leave.

3.1.3 The study protocol emergency code breaking procedure should be reviewed by the Pharmacy team before the study begins recruitment to ensure that any queries in relation to the process are answered before the study begins.

3.1.4 In accordance with CP R&D_006 – Code Breaks, it is the responsibility of the Lead Pharmacist to ensure that all relevant code breaking information is easily accessible for the on-call Pharmacist.

3.2 When to break a code

3.2.1 A code should be broken if at any time there are concerns in relation to patient safety and the involvement of the treatment they are receiving. Some examples of situations where code breaking is required are below but this is list is not exhaustive:-

a) If a patient experiences a Suspected Unexpected Serious Adverse Reaction (SUSAR), this being if the reaction is unexpected and unlisted in the study protocol and Investigator's Brochure (IB) or Summary of Product Characteristics (SmPC).

b) If a patient is admitted to hospital in an emergency and the treating clinician needs to know whether the active drug or placebo/comparator is being taken to rule out any side effects or potential risks of concomitant medications.

c) In the event that a patient's medication is accidently taken by another household member i.e. a child.

d) For submission of study data to the Data Monitoring Committee (DMC) or other regulatory bodies for the monitoring of safety or efficacy.

e) If the patient has an Adverse Event (AE) or Adverse Reaction (AR) (even if expected in IMP) where there are concerns for the patient's wellbeing and safety.

3.3 Requesting a code break

3.3.1 If the code break is thought necessary, the Chief Investigator and/or Sponsor should be contacted if possible before the unblinding. If they are not available or this is not possible due to the emergency of the situation, they must be contacted as soon as possible afterwards (within 24 hours of the next working day).

3.3.2 Requests should be made to the Lead Pharmacists in writing using NCF-R&D_018 – Emergency Code-Breaking Reporting Form by the Principal Investigator (or delegate) unless the nature of the emergency makes this this impossible. If this is the case a verbal request is acceptable but the conversation must be document in a Site File Note (NCF-R&D_019).

3.3.3 When the Pharmacist receives a code break request on the Emergency Code-Breaking Reporting Form (NCF-R&D_018), they must identify/check the requester and establish whether the reasons for breaking the code are warranted. If the code break is requested by anyone other than the PI (unless otherwise specified in the study protocol), the PI should be consulted for guidance on the appropriateness of breaking the blind.

3.3.4 If the local PI is not available, the Pharmacist will refer to the specific study protocol for instructions and contact information.

3.3.5 The Pharmacy team will have the authority to break the blind if s/he deems appropriate and must notify the PI within 24 hours or by the next working day after the code breaking.

3.3.6 The Pharmacy team should follow CP R&D_006 – Code Breaks SOP and refer to the study protocol for study specific procedures.

3.3.6 A copy of the Emergency Code-Breaking Reporting Form should be held in the patient notes and also in the study Pharmacy Site File.

3.4 Post Code Breaking

3.4.1 If the code breaking goes ahead, the PI should decide if the patient needs to be withdrawn from the study based on the details released of their randomization. As necessary, this decision should be discussed with the Chief Investigator/Sponsor and should be documented for the site file.

3.4.2 If the R&D team has not already been made aware during the code breaking process, the R&D Manager should be notified and a copy of the Emergency Code-Breaking Reporting Form provided. If the patient is due to be withdrawn, R&D should also be notified to update the study recruitment records.

	Responsibility	Undertaken by	Activity
1	R&D Office	R&D Manager	• Risk Assessment for study need for Code Breaking based on treatment type.
2	R&D Office	R&D Office/Principal Investigator	• Identification of person responsible for unblinding requests and back-up.
3	Pharmacy	Lead Pharmacist	• Review the study protocol and raise any queries in relation to code-breaking process. • Document discussion points for reference of Pharmacy team.
4	R&D Office/Principal Investigator	R&D Office/Principal Investigator	• As possible notify the Chief Investigator/Sponsor **before** the code breaking occurs.
5	Principal Investigator	Principal Investigator/delegate	• Complete the Emergency Code-Breaking Reporting Form and provide to the Pharmacy team for urgent review. **In the case of an emergency, this can be done verbally but should be documented.**
6	Pharmacy	Pharmacist	• Prompt action on receipt of Code-Breaking request • Verify person requesting code break • Review to see that code breaking is warranted. Discuss with PI/CI as appropriate. • Confirm and arrange the code break. • Document the code break in the Pharmacy Site File. • Provide a copy of the Emergency Code-Breaking Form to the PI and R&D team.
7	Investigators	Principal Investigator/Chief Investigator	• As required, confirm to the Pharmacist any additional details to justify the need for a code break. • If code break happens, discuss if patient should continue on the study. • Notify the R&D team accordingly.
8	R&D Office	R&D Manager/delegate	• Notify the Sponsor/CI if not already aware or check this has taken place. • Document in the study documents the Emergency Code-Breaking Form.

			• Update records if patient is withdrawn on study.

4. SUPPORTING MATERIAL and ATTACHMENTS

The following documents can be used in conjunction with this SOP:

SOPs

- CP R&D_006 – Code Breaks

Forms

- NCF-R&D_018 – Emergency Code-Breaking Reporting Form
- NCF-R&D_019 – Site File Note

5. TRAINING

5.1 All R&D staff are required to read and understand the content within this SOP. Staff should sign to confirm that the SOP has been read and document this within the R&D SOP file. When a SOP is updated or each 2 years (as appropriate), staff will be notified and will need to re-read and sign against the SOPs within the R&D SOP file.

6. REFERENCES

Department of Health Research Governance Framework for Health and Social Care

https://www.gov.uk/government/publications/research-governance-framework-for-health-and-social-care-second-edition

The Medicines for Human Use (Clinical Trials) Regulations 2004
http://www.legislation.gov.uk/uksi/2004/1031/contents/made

The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006
http://www.legislation.gov.uk/uksi/2006/1928/contents/made

Medicines for Human Use (Clinical Trials) Amendment (No.2) Regulations 2006, Statutory Instrument 2006/2984
http://www.legislation.gov.uk/uksi/2006/2984/contents/made

Medicines for Human Use (Clinical Trials) and Blood Safety and Quality (Amendment) Regulations 2008, Statutory Instrument 2008/941
http://www.legislation.gov.uk/uksi/2008/941/pdfs/uksi_20080941_en.pdf

Medicines for Human Use (Marketing Authorisations Etc) Amendment Regulations 2008, Statutory Instrument 2008/3097

http://www.legislation.gov.uk/uksi/2008/3097/made

Medicines for Human Use (Advanced Therapy and Miscellaneous Amendments) Regulations 2010, Statutory Instrument 2010/1882
http://www.legislation.gov.uk/uksi/2010/1882/pdfs/uksi_20101882_en.pdf

NIHR Research Support Services Framework, May 2011

http://www.nihr.ac.uk/policy-and-standards/framework-for-research-support-services.htm

Government GCP Guidance

https://www.gov.uk/good-clinical-practice-for-clinical-trials