Emergency Code Break in Clinical Trials

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CHANGE HISTORY			
Date	Version Number	Change details	Approved by
11/11/2013	2.0	Scheduled Review and change of branding from JCTO to KHP-CTO and ESMS to MTIS	Jackie Powell
17/03/2015	3.0	Clarification of the scope of this SOP. This SOP is only mandatory for those trials choosing to use MTIS.	Jackie Pullen
28/04/2017	4.0	Scheduled review and change of name from MTIS to ESMS Global Ltd. Update to glossary section and ESMS setup procedure.	Jackie Pullen

21/08/2018	5.0	Procedure updated to include trials not using ESMS for the provision of emergency code break services. Information added regarding how the randomisation data would be obtained and securely delivered to ESMS.	Jackie Pullen
24/10/2018	5.1	Minor amendment to include trials managed by KHP-CTO	Jackie Pullen
13/10/2021	5.2	Minor amendment to ESMS processes	Jackie Pullen
20/10/2025	6.0	Regularly Scheduled review	Ann-Marie Murtagh

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1.0 BACKGROUND AND PURPOSE

The investigator site should have the ability to unblind a trial participant immediately in the case of a medical emergency. The purpose of this SOP is to describe the process for emergency code break (unblinding) of treatment within clinical trials of IMPs sponsored or co-sponsored by King's Health Partner Organisations.

2.0 SCOPE

Clinical trials of IMPs sponsored by one or more of King's Health Partner Organisations, or clinical trials where the sponsor responsibilities are managed by the KHP-CTO, where one or more parties involved in the trial is unaware of the treatment assignments (blinded).

3.0 AUTHORISED USERS

The only people authorised to perform emergency unblinding are healthcare professionals who have direct responsibility for the care of the trial participant concerned. Clinical Trial Investigators, or pharmacists calling on their behalf, are also recognised as authorised users. KHP-CTO staff are authorised to request unblinding for expedited reporting of SUSARs.

- The trial participant themselves, their relatives, or other members of the public are not authorised users and an emergency unblinding cannot be performed upon their request. If such a request is made the caller will be referred to their Clinical Trial Investigator, GP or their nearest A&E Department, as appropriate.

- During normal office hours, requests for information about the trial (e.g. study visits/appointments medication queries etc.) should be referred to the local site Investigator Team: contact details supplied during set-up.

- In extraordinary circumstances or incidents where there may be a public health concern, other professional individuals, e.g. police, teacher, may be authorised to request emergency unblinding by King's Health Partner CTO Director or Quality Manager

4.0 PROCEDURE FOR TRIALS NOT USING ESMS FOR EMERGENCY UNBLINDING SERVICES

4.1 Set Up

- Breaking the treatment code may be conducted by the use of physical code breaks or electronically via an internet or automated telephone-based system.

- In case of electronic system, a back-up system is required so the code break can be performed manually in the event that electronic system fails.

- Code breaking instructions will be specified clearly in the clinical trial protocol. Additional instructions detailing steps and contacts for emergency unblinding may be filed in the Investigator Study File i.e. when emergency unblinding is provided by a local pharmacy and site-specific contact details are required.

- Where appropriate, participants will be issued with emergency cards to be carried at all times. The cards should include the trial identifier such as number from the IRAS submission, emergency contact number and patient's unique trial number as a minimum. A successful test of the system – both in and out of normal working hours - must be performed by the KHP-CTO CRA or delegate , including contact via the electronic system if applicable, prior to recruitment of the first participant. Evidence of the test(s) should be filed in the TMF.

4.2 Process

- Any code break intentional or accidental will be documented. The record will include as a minimum the date, time, reason for unblinding, name of the person requesting and person breaking the code. Care must be taken when filing documentation and communicating an unblinding event to ensure that there is no potential for those with TMF access to be unblinded .

- The KHP-CTO will be informed, in writing, of the code break as soon as possible.

- The KHP-CTO CRA or delegate will ensure that the service provider will be informed of any applicable updates to the study protocol and/ or unblinding documents

4.3 End of the Trial

- The KHP-CTO CRA will perform reconciliation of physical code breaks at the end of the study. The CRA will verify whether code envelopes are still intact and any code that has been broken or lost during the study has been appropriately documented.

- When using an electronic system confirmation will be obtained from the service provider that the blinding has not been compromised.

5.0 PROCEDURE FOR TRIALS USING ESMS Global Ltd. FOR EMERGENCY UNBLINDING SERVICES

- ESMS Global Ltd. provide a 24-hour emergency medical response service. They operate on-site 24 hours a day, 365 days a year. Information scientists have immediate access to all study documentation, including randomisation information. Under the terms of the master service level agreement in place between the KHP-CTO and ESMS Global Ltd., the procedure below should be followed.

5.1 Set Up

- The KHP-CTO CRA will email ESMS Global Ltd. with notification of a new trial set up once the MHRA CTA application has been submitted and all final documents uploaded onto MATTS or EDGE
- This email will include a list of study document titles (according to the MATTS naming conventions), version numbers and issue dates as follows:-
    - Investigator's Brochure, Summary of Product Characteristics or other source of relevant Reference Safety Information, as appropriate.
    - An approved protocol summary and any relevant amendments;
    - Trial specific participant information leaflets
    - Contact details of Chief Investigator and Principal Investigators.
- A trial-specific work order will be prepared by ESMS Global Ltd. and sent to the KHP-CTO CRA for due diligence checking. Once confirmed as correct, this Work Order will be signed by the KHP-CTO Director or delegate prior to the trial commencing recruitment. A fully executed copy of each trial-specific work order will be sent to the ESMS Global Ltd. Head of Services and one copy filed in the trial Sponsor File.
- The KHP-CTO CRA will ensure that the randomisation data (code-break envelopes, randomisation schedules) are delivered to ESMS Global Ltd prior to recruitment The data will be provided by either physical code break (list, envelopes) or access to an electronic randomisation system and reception of randomisation emails. The CRA will request an email confirmation from ESMS Global Ltd. once physical randomisation data is received. If an electronic system used the CRA will ensure that unblinded access to the randomisation system has been obtained and designated username and password provided to ESMS Global Ltd by the randomisation system provider.
- ESMS Global Ltd. will provide 24hr contact details to be entered on patient cards. These cards will be given to each patient when consent has been obtained.
- Services will only commence when the work order is fully signed and ESMS Global Ltd. has received all necessary trial documentation. ESMS Global Ltd. will set up the trial as defined within their internal SOPs and will confirm setup completion to trial contact. The KHP-CTO CRA will perform the testing of unblinding system prior to recruitment of the first participant. This will be documented in Site Initiation Visit Checklist. A notification of ESMS readiness to provide service will be sent to the KHP-CTO CRA for inclusion in the trial sponsor file.

5.2 The Service

- ESMS Global Ltd. is first on-call to break randomisation codes and provide medical support at all times.
- The KHP-CTO CRA is responsible for informing ESMS Global Ltd. of any updates to study documents.
- ESMS Global Ltd. will conduct all code break activities according to their SOP's.

5.3 Process

- The completed Clinical Trial Enquiry form *(see related templates)* is emailed along with a request for acknowledgement of receipt to the KHP-CTO Pharmacovigilance inbox.
- The KHP-CTO Clinical Trials Administrator (or delegate) will return the acknowledgement of receipt form to ESMS Global Ltd. and inform the KHP-CTO CRA of the request for code break and the outcome.
- The CRA will inform the Chief /Principal Investigator(s) of the code break request.
- All completed Clinical Trial Enquiry forms, Clinical Trial Reports and receipts will be filed in the trial Sponsor file.

5.3 End of Trial

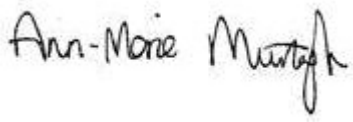
- The KHP-CTO CRA will provide ESMS Global Ltd. with written notification of the end of the trial, confirmation of receipt by ESMS Global Ltd. will be forwarded to the KHP-CTO and placed in the sponsor file.

6.0 RELATED TEMPLATES

6.1 ESMS Clinical Trial Enquiry Form

6.2 ESMS Clinical Trial Enquiry Report

7.0 APPROVAL AND SIGNATURE



_____ ____20/10/2025
Ann-Marie Murtagh Date
Director KHP Clinical Trials Office

Appendix 1

GLOSSARY

Blinding – The practice of keeping the trial participants, care providers, those collecting data, and sometimes those analysing data unaware of which intervention is being administered to which trial participant. Binding should be maintained unless unblinding is necessary to protect participant safety or well-being. Blinding is intended to prevent bias on the part of study personnel.

Chief Investigator (CI) – The chief investigator is the overall lead researcher for a research project (Outside the UK the term Coordinating Investigator or Investigator may be used). In addition to their responsibilities if they are members of a research team, chief investigators are responsible for the overall conduct of a research project

Clinical Research Associates – (CRAs) – A professional who organises and monitors clinical trials to assess the safety and effectiveness of new or existing drugs, medical devices, or treatments. CRAs play a vital role in ensuring that clinical trials are conducted ethically, safely, and in accordance with established protocols and regulations. CTO CRA's monitor compliance, for clinical trials where regulatory oversight has been delegated to the KHP CTO.

Clinical Trial - Any investigation in human participants, other than a non-interventional trial, intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more medicinal product and/or to identify any adverse reactions to one or more such products and/or to study absorption, distribution, metabolism and excretion of one or more such products with the object of ascertaining the safety and/or efficacy.

Code Break – breaking the blind. This is the mechanism that permits the rapid identification of the trial treatment in case of a medical emergency but does not permit undetectable breaks of the blinding.

Emergency Scientific and Medical Services Global Ltd. (ESMS) – an independent provider of emergency code break and medical information services.

Investigational Medicinal Products (IMP) – a pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial. This includes products with marketing authorisation when used in a way different from the approved form, for an unapproved indication, or to gain further information about an approved use.

King's Health Partners (KHP) – King's Health Partners brings together research, education and clinical practice across three NHS Foundation Trusts - Guy's and St Thomas', King's College Hospital and South London and Maudsley - and a world-leading university, King's College London

King's Health Partners Clinical Trials Office (KHP-CTO) – Established in 2006 by King's College London, Guy's & St Thomas' NHS Foundation Trust, South London and Maudsley NHS Foundation Trust and King's College Hospital NHS Foundation Trust to provide a streamlined approach for all aspects of trial administration. The King's Health Partners CTO has two sections: the Commercial Team which provides a single interface for those wishing to conduct trials sponsored by the pharmaceutical industries and the Quality Team that supports investigators at King's Health Partners institutions who undertake CTIMP trials where King's Health Partners are the sponsor or co-sponsor.

KHP-CTO Quality Team – Comprises the Quality Manager, Clinical Research Associate(s), Clinical Trial Administrator(s), Systems Executive, and Training Executive(s).

MedSciNet Active Trial Tracking System (MATTS) –The electronic Clinical Trial Portfolio Management System used by the KHP CTO.

Medicines & Healthcare products Regulatory Agency (MHRA) - the UK's regulatory body responsible for ensuring the safety and effectiveness of medicines, medical devices, and blood components for transfusion. It operates as an executive agency sponsored by the Department of Health and Social Care.

Principal Investigator (PI) - the individual primarily responsible for the conduct of a research study at a specific research site

Standard Operating Procedures (SOPs) - detailed, written instructions to achieve uniformity of the performance of a specific function, SOPs are the basis on which Quality Systems and Processes are conducted and monitored.

The Regulations - The Medicines for Human Use (Clinical Trial) Regulations 2004 which transposed the EU Clinical Trials Directive into UK legislation, as Statutory Instrument 2004 no 1031**.** An amendment to implement Directive 2005/28/EC was made to the Regulations as Statutory Instrument 2006 no 1928. As amended from time to time.