

University of Hertfordshire

TRIAL CLOSURE

Clinical Trials Support Network (CTSN)

Standard Operating Procedure for Closure of University of Hertfordshire
Sponsored/Co-sponsored and Hosted clinical studies

SOP Number: gSOP-21-01	Effective Date: 26 th April 2018
Version Number: 1.0	Review Date: 3 years (or as required)

1.0 BACKGROUND

This is a University of Hertfordshire standard operating procedure. UH acknowledges WHHT R&D which has allowed UH to use the SOPs developed by WHHT where possible, modified for local implementation.

This document sets out the procedures to be followed by all staff who are involved in the close-down, termination, suspension or final reporting of research studies and clinical trials. Where there are potential conflicts between different collaborating organisations' SOPs, project level working instructions should be developed, to determine precedence.

It provides guidance on how participants, staff and trial related documentation is managed during close-out so as to ensure compliance with UH's and the Trust's Information Governance Policies, the Data Protection Act (2000), and other relevant legislation and policy.

2.0 PURPOSE

To ensure all UH sponsored/co-sponsored and hosted trials are closed according to protocol, regulatory and sponsor requirements.

3.0 APPLICABLE TO

This applies to all UH staff involved with clinical research including, but not limited to: Chief Investigators, Principal Investigators, Research Fellows, Consultants, Statisticians, Clinical Trial Pharmacists, Research Managers, Research Nurses, Clinical Trial Practitioners, Allied Health Professionals, Trial Coordinators, Clinical Studies Officers, Data Managers and Research Assistants.

4.0 RESPONSIBILITIES

The Chief Investigator/Principal Investigator or Delegated Individual (DI) is responsible for the closure of the trial according to regulatory and sponsor requirements. The CI/DI should ensure for UH sponsored/co-sponsored trials that the end of trial definition is detailed in the approved protocol.

For UH sponsored CTIMP trials, the sponsor's representative will ensure that the approved protocol provides adequate detail regarding end of trial (gSOP-14) and the CTSN/R&D Office will ensure that these trials are closed according to the protocol, regulatory and Sponsor/co-sponsor requirements.

The definition of the end of study should be agreed and documented clearly in both the protocol and any corresponding agreements before the study starts. If the end of trial is amended during the course of the trial this should be submitted as a substantial amendment (gSOP-09). Study closure responsibilities should be clearly documented in the trial delegation log and this will be verified during monitoring and audit of the sponsored CTIMP trials.

5.0 PROCEDURE

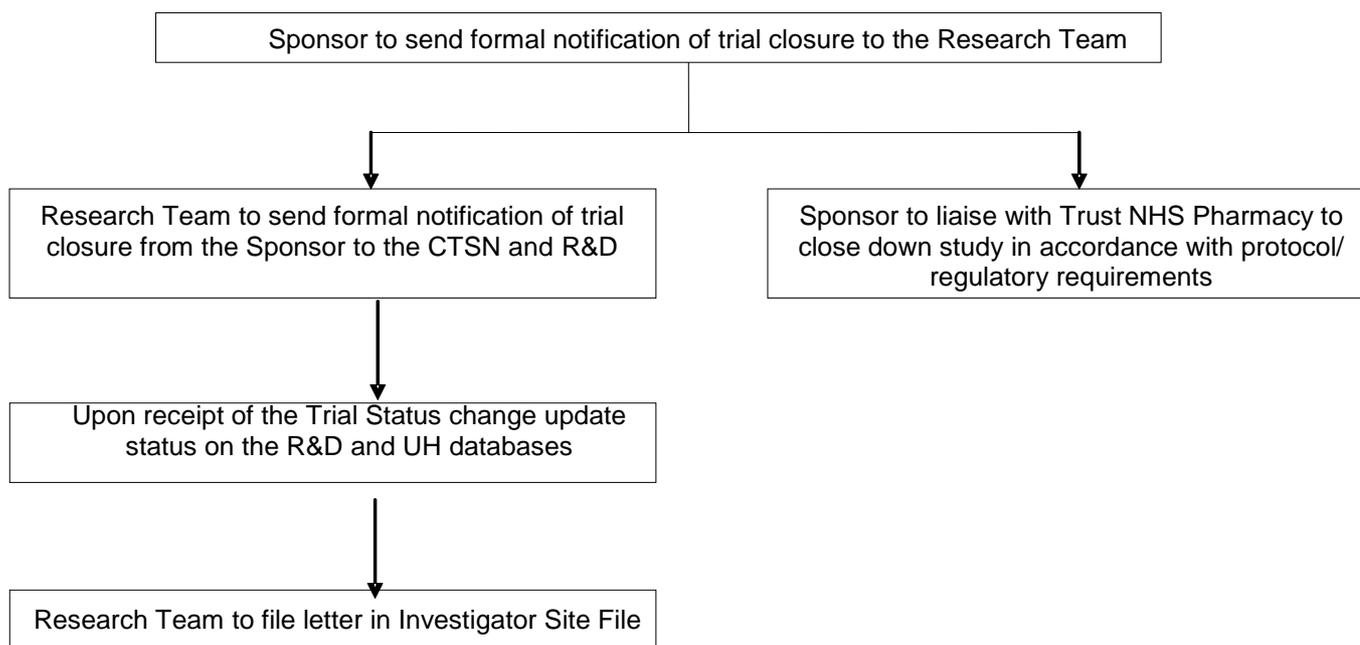
5.1 Closure to Recruitment

- 5.1.1 A trial is said to be “Closed to Recruitment”: when a trial has recruited its target number of participants as detailed in the protocol. If the trial is multicentre this must mean that no further participants can be recruited at any of the participating sites, however, participants may still be on treatment when the trial is closed to recruitment.
- 5.1.2 Once a trial has completed recruitment, but participants are still on treatment the CI/PI/DI or delegate should notify the CTSN/Trust R&D office
- 5.1.3 The CTSN/Trust R&D office will acknowledge the change in status and update their respective databases.
- 5.1.4 For UH sponsored/co-sponsored multicentre studies it is important to ensure that the end to recruitment is clearly communicated and subsequently documented at each site. It is the PI’s responsibility to ensure that the participating site’s R&D office is informed about the change in status and that evidence of this is kept in the Investigator Site File (ISF). The Trial Master File (TMF) should also contain documentation to show that each site was informed of the trial’s closure to recruitment.
- 5.1.5 Once the trial is ready to close as defined in the protocol or the research team should start close out procedures as detailed in sections 5.2, 5.3 or 5.4 depending on the type of study.

5.2 Externally sponsored UH Hosted Trial Closure Procedures

- 5.2.1 The end of trial should be detailed in the protocol, but where this is not the case the trial should be closed 30 days after the last participant has received their last treatment including any participants at multicentre sites.
- 5.2.2 The Research team should send a copy of the formal notification of study closure received from the sponsor to the R&D office and CTSN.
- 5.2.3 The Sponsor will liaise with the Trust NHS pharmacy to ensure that they are closed in accordance with regulatory and protocol requirements.
- 5.2.4 Once the R&D office and CTSN has received the Sponsor’s notification of study closure they will close the study on the respective databases.
- 5.2.5 If UH has accepted responsibility for trial closure then certain sections below may be applicable depending on the type of trial.

Flow Diagram: Trial Closure Procedure for Hosted Studies



5.3 UH Sponsor/Co-sponsored CTIMP Trial Closure Procedures

- 5.3.1 Where studies have closed before the expected date of closure a letter should be sent by the CI/DI to the R & D Office and the CTSN informing of the reasons before the Declaration of End of Trial form is submitted to the regulatory authorities. The date of this letter will then determine the deadline for the final report (see gSOP-22).
- 5.3.2 The CI/DI should inform the R & D office and the CTSN of the intention to close the study.
- 5.3.3 For multicentre studies evidence must be available in the TMF that all of the sites are ready to close out.
- 5.3.4 CI/PI/DI should liaise with Trust NHS pharmacy to ensure accountability is performed and excess IMP is returned or destroyed as detailed in the protocol, legal requirements and relevant pharmacy SOPs. Drug accountability logs and records of returns or destruction should be filed in the TMF/ISF.
- 5.3.5 The Trial Co-ordinator will ensure that the TMF and Pharmacy files are up-to-date and will then inform the team that they have permission to close the trial as detailed in section 5.2.
- 5.3.6 Once the Sponsor's representative has given permission the CI/PI/DI should complete the Declaration of End of Trial form.
- 5.3.7 For multicentre studies the Declaration of End of Trial form should be submitted when the trial has ended at all of the sites.

- 5.3.8 The Declaration of End of Trial form must be sent to the MHRA, main REC and R&D office within 90 days of the trial ending.
- 5.3.9 For trials that are terminated early the MHRA, main REC, and R&D should be informed within 15 days and the CI/PI should clearly explain the reasons for the early termination.
- 5.3.10 If the trial did not start the CI/PI must notify the MHRA, main REC and R&D and provide an explanation.
- 5.3.11 The CI/PI or delegate must ensure that the ISF/TMF is kept up-to-date with all End of Trial Declaration forms and final reports.
- 5.3.12 Once the CTSN/R&D has received the Declaration of End of Trial form they will close the study on the respective databases. Once the study has been closed the R&D office/CTSN will request any outstanding annual progress reports before sending to the research team.
- 5.3.13 The R&D team will also forward a copy of the Declaration of End of Trial form and the R&D acknowledgement to the Trust NHS Pharmacy, if required for their records.
- 5.3.14 Once the End of Trial acknowledgements have been received from the MHRA, main REC and R&D, the study can be considered closed and can be archived following the standard operating procedure for archiving (see gSOP-17).
- 5.3.15 Final reports should be submitted within 1 year of study closure (gSOP-22).
- 5.3.16 Please refer to the sponsored trial closure procedure in the appendix for a flow diagram of the process (Appendix 2).

5.4 UH Sponsored/Co-sponsored Non-CTIMP Trial Closure Procedures

- 5.4.1 For multicentre studies evidence must be available in the TMF that all of the sites are closed to recruitment and are ready to close out.
- 5.4.2 The CI/PI should complete the Declaration of End of Trial form.
- 5.4.3 For multicentre studies the Declaration of End of trial form should be submitted when the trial has ended at all of the sites.
- 5.4.4 The Declaration of End of Trial form must be sent to the main REC, R&D and CTSN within 90 days of the trial ending.
- 5.4.5 For trials that are terminated early the main REC, R&D and CTSN should be informed within 15 days and the CI/PI should clearly explain the reasons for the early termination.
- 5.4.6 If the trial did not start the CI/PI must notify the main REC and provide an explanation.
- 5.4.7 The CI/PI or delegate must ensure that the ISF/TMF is kept up-to-date with all Declaration of End of Trial Forms and final reports.

- 5.4.8 Once R&D and the CTSN has received the Declaration of End of Trial form they will close the study on the respective databases.
- 5.4.9 Once the End of Trial acknowledgements have been received from the main REC and R&D the study can be considered closed and can be archived following the standard operating procedure for archiving gSOP-17.
- 5.4.10 Final reports should be submitted within 1 year of study closure (gSOP-22).
- 5.4.11 Please refer to the sponsored trial closure procedure in the appendix for a flow diagram of the process.

6.0 RELATED DOCUMENTS

- gSOP-09 Amendments
- gSOP-14 Writing Research Protocols
- gSOP-17 Archiving
- gSOP-22 End of Trial Reports
- gSOP-24 Training for Research Staff

7.0 APPENDICES

- Appendix 1 - Definitions
- Appendix 2 – UH Sponsored/Co-Sponsored/Hosted Trial Closure Procedure Flow diagram

8.0 VERSION HISTORY

Revision Chronology:		
Version Number	Effective Date	Reason for Change

9.0 AUTHORSHIP & APPROVAL

Author

Signature

Date

Pro-Vice Chancellor (Research & Enterprise) Approval

Signature

Date

10.0 AGREEMENT

Please detach and retain within your training files

I have read and understood the contents and requirements of this SOP (ref gSOP-21-01) and accept to follow UH policies implementing it.

Recipient

Signature:Date:

Name & Position:

Appendix 1.0. Definitions

Chief Investigator (CI) - A Registered Physician, Dentist, Pharmacist or Registered Nurse who has overall responsibility for the conduct of the trial.

Clinical Trial - A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or control) to evaluate the effects of those interventions on health outcomes.

Clinical Trial of Investigational Medicinal Product (CTIMP) - A study that looks at the safety or efficacy of a medicine/food stuff/placebo in humans as defined by the Medicines for Human Use Regulations (2004).

Investigational Medicinal Products (IMP) - means a pharmaceutical form of an active substance or placebo being tested, or used as a reference in a clinical trial. This includes a medicinal product which has a marketing authorisation but is, for the purposes of the trial -

(a) used or assembled (formulated or packaged) in a way different from the form of the product authorised under the authorisation,

(b) used for an indication not included in the summary of product characteristics under the authorisation for that product, or

(c) used to gain further information about the form of that product as authorised under the authorisation

Principal Investigator (PI) - A Registered Physician, Dentist, Pharmacist or Registered Nurse who has responsibility for the conduct of the trial at a host site.

The Medicines & Healthcare products Regulatory Agency (MHRA) - UK Competent Authority responsible for regulation of clinical trials.

The Regulations - Medicines for Human Use (Clinical Trial) Regulations 2004 transposed the EU Clinical Trials Directive into UK legislation, as Statutory Instrument 2004 no 1031. This became effective on the 1st May 2004. An amendment to implement Directive 2005/28/EC was made to the Regulations as Statutory Instrument 2006 no 1928.

Regulatory End of Trial: The end of trial should be detailed in the protocol, but where this is not the case the trial should be closed 30 days after the last patient has received their last treatment/visit including any patients at multicentre sites.

Trial Closed to Recruitment: When a trial has recruited its target number of patients as detailed in the protocol. If the trial is multicentre this must mean that no further patients can be recruited at any of the participating sites, however, patients may still be on treatment when the trial is closed to recruitment.

Appendix 2.0

UH Sponsored/Co-sponsored/Hosted Trial Closure Procedure Flow diagram
