TRIAL CLOSURE

Research & Development

Standard Operating Procedure for Closure of West Hertfordshire Hospitals NHS Trust Sponsored and Hosted Clinical Trials

SOP Number : SOP-21-05	**Effective Date:** October 2021
Version Number: v05	**Review Date:** 2-3 years

1.0 BACKGROUND

This document sets out the procedures to be followed by all West Hertfordshire Hospitals Trust (WHHT) staff who are involved in the close-down, termination, suspension or final reporting of research studies and clinical trials.

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

2.0 PURPOSE

To ensure all WHHT sponsored and hosted trials are closed according to protocol, regulatory and sponsor requirements.

3.0 APPLICABLE TO

Any Trust employee involved with clinical research including, but not limited to, Unit Heads, Chief Investigators (CI), Principal Investigators (PI), Consultants, Co-Investigators, Clinical Trial Pharmacists, Research Managers, Statisticians, Research Nurses, Allied Health Professionals, Trial Coordinators, Data Managers & R&D Administrative Staff.

4.0 RESPONSIBILITIES

The CI/PI or Delegated Individual (DI) is responsible for the closure of the trial according to regulatory and Sponsor requirements (see SOP-08). The CI/DI should ensure for WHHT sponsored trials that the end of trial is detailed in the approved protocol.

For WHHT sponsored Clinical Trials of an Investigational Medicinal Product (CTIMPs), the R&D Office,

as the Sponsor's representative, will ensure that the approved protocol provides adequate detail regarding end of trial (see SOP-14). The R&D Office will ensure that these trials are closed according to the protocol, regulatory and Trust 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 definition of the end of trial is amended during the course of the trial this should be submitted as a substantial amendment (see SOP-09).

5.0 PROCEDURES

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 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.

5.1.2 Once a trial has completed recruitment, but patients are still on treatment the CI/PI/DI should notify the R&D Office.

5.1.3 R&D will acknowledge the change in status and update the R&D database.

5.1.4 For WHHT 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 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 WHHT 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 patient has received their last treatment including any patients at multicentre sites.

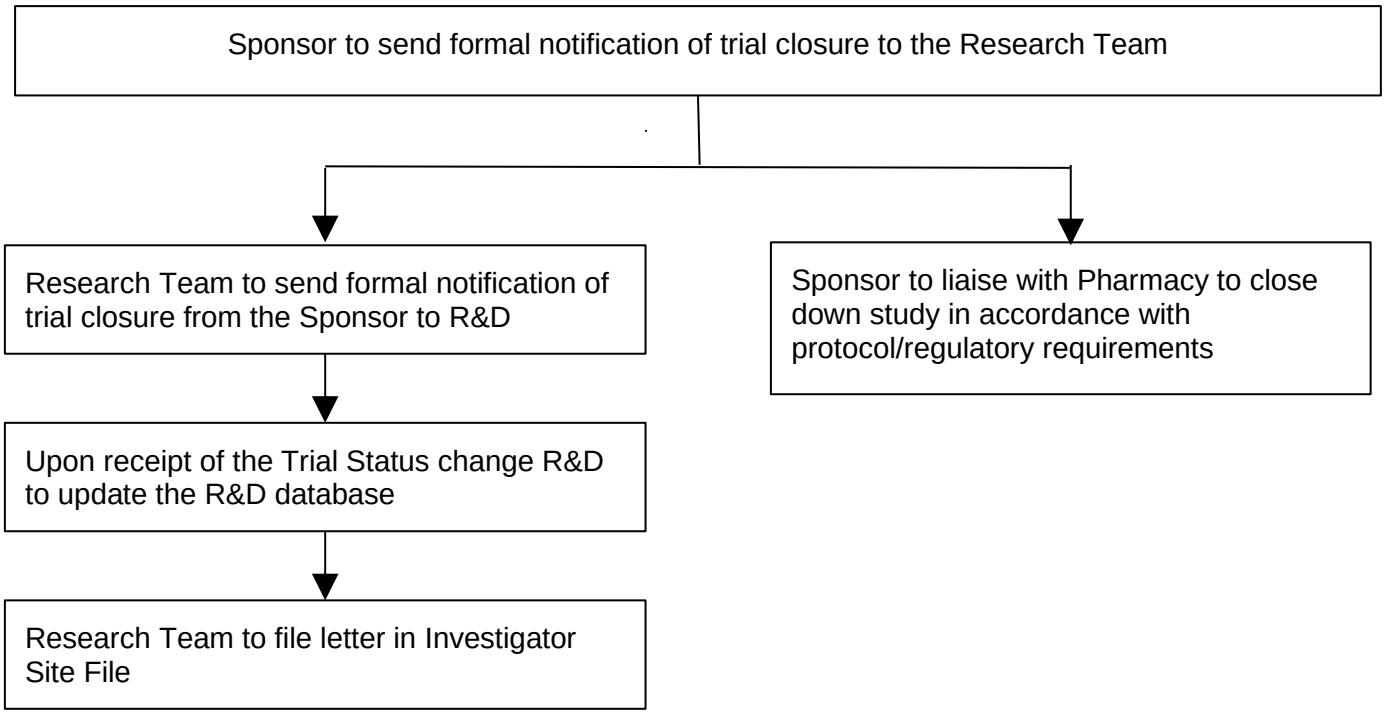
5.2.2 The Research Team should send a copy of the formal notification of study closure received from the Sponsor to the R&D Office.

5.2.3 The Sponsor will liaise with the Trust pharmacy to ensure that they are closed in accordance with regulatory and protocol requirements.

5.2.4 Once R&D has received the Sponsor's notification of study closure they will close the study on the R&D database.

5.2.5 If WHHT has accepted responsibility for trial closure then certain sections below may be applicable depending on the type of trial.

5.2.6 Flow Diagram: Trial Closure Procedure for Hosted Studies



5.3 WHHT 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 Research and Development Steering Group (RDSG) informing them of the reasons for study closure before the End of Trial Notification Form is submitted to the regulatory authorities. The date of this letter will then determine the deadline for the End of Trial Report (see SOP-22).

5.3.2 The CI/DI should inform the R&D Office 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 Pharmacy to ensure accountability is performed and excess Investigational Medicinal Product (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 R&D Office has given permission the CI/PI/DI should complete the End of Trial Notification Form.

5.3.7 For multicentre studies the End of Trial Notification Form should be submitted when the trial has

ended at all of the sites.

5.3.8 The End of Trial Notification Form must be sent to the Medicines and Healthcare Products Regulatory Agency (MHRA), main Research Ethics Committee (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/DI must ensure that the ISF/TMF is kept up-to-date with all End of Trial Notification Forms and final reports.

5.3.12 Once R&D has received the End of Trial Notification Form they will close the study on the R&D database. Once the study has been closed the R&D Office 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 End of Trial Notification Form and the R&D acknowledgement letter to 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 (see SOP-17).

5.3.15 End of Study Reports should be submitted within 1 year of study closure (see SOP-22).

5.3.16 Please refer to the sponsored trial closure procedure for a flow diagram of the process (Appendix 2).

5.3.17 The CI will ensure that all transparency requirements are met including:

- the results of individual research studies are shared publicly- at a minimum the record in the registry should be updated with a lay summary of the results
- participants are informed of the findings as outline in IRAS during application, if applicable

5.4 WHHT 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 Study.

5.4.3 For multicentre studies the Declaration of End of Study should be submitted when the trial has ended at all of the sites.

5.4.4 The Declaration of End of Study must be sent to the main REC and R&D within 90 days of the trial ending.

5.4.5 For trials that are terminated early the main REC, and R&D should be informed within 15 days and the CI/PI should clearly explain the reasons for the early termination.

5.4.6 If the trial did not start the CI/PI must notify the main REC and R&D and provide an explanation.

5.4.7 The CI/PI/DI must ensure that the ISF/TMF is kept up-to-date with all Declaration of End of Study forms and final reports.

5.4.8 Once R&D has received the Declaration of End of Study they will close the study on the R&D database.

5.4.9 The R&D team will also forward a copy of the Declaration of End of Study and the R&D acknowledgement letter to Pharmacy (if required) for their records.

5.4.10 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 (see SOP-17).

5.4.11 End of study reports should be submitted within 1 year of study closure (see SOP-22).

5.4.12 Please refer to the sponsored trial closure procedure for a flow diagram of the process (Appendix 2).

5.4.13 The CI will ensure that all transparency requirements are met

6.0 RELATED DOCUMENTS

- SOP-08- Role of CI, pharmacy, nuclear medicine and R&D
- SOP-09- Amendments
- SOP-14- Writing Research Protocols
- SOP-17- Archiving of Essential Documents
- SOP-22- End of Study Reports
- Make it Public: transparency and openness in health and social care research

7.0 APPENDICES

Appendix 1.0 - Definitions
Appendix 2.0 - WHHT Sponsored Trial Closure Procedure Flow diagram

8.0 VERSION HISTORY

Revision Chronology:		
Version Number	**Effective Date**	**Reason for Change**
SOP-21-05	**October 2021**	1. Change from general Standard Operating Procedures (gSOP) to SOP 2. Removal of the '10.0 Agreement' from the template - all

		agreement signatures will be collated on a new 'SOP Signature Sheet Document' 3. Addition of transparency requirements 4. Other minor changes and clarifications of terms following review
gSOP-21-04	**10/2017**	Minor amendments following review
gSOP-21-03	**22/05/2014**	Minor amendments following review
gSOP-21-02		SOP modified for implementation at ENHT/WHHT
gSOP-21-01 (MVCC)		SOP modified for implementation at MVCC

9.0 AUTHORSHIP & APPROVAL

Author

Signature  **Date** 28/10/2021

R & D Steering Group Approval

Signature  **Date** 28/10/2021

Appendix 1: Definitions

Chief Investigator (CI)
The investigator with overall responsibility for the research. In a multi-site study, the CI has co-ordinating responsibility for research at all sites. All applications for ethical review should be submitted by the CI. For Trust sponsored trials, the CI had been delegated the pharmacovigilance responsibility for identification, recording and reporting of safety events, including submission of Development Safety Update Reports (DSURs) to the MHRA and REC.

Clinical Trial
A clinical study in which participants are assigned to receive one or more interventions (or no intervention) so that researchers can evaluate the effects of the interventions on biomedical or health-related outcomes. The assignments are determined by the study protocol. Participants may receive diagnostic, therapeutic, or other types of interventions. A Study Type.

End of Trial
When the study has been notified as closed to the MHRA and/or ethics committee by sending the End of Trial Notification Form. The end of trial definition 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. The archiving period should be for minimum of five years from this date. Any change to the definition of 'End of Trial' in the protocol must be submitted as a substantial amendment.

Investigational Medicinal Products (IMP)
A pharmaceutical form of an active substance or placebo being tested, or to be tested, or used, or to be used, as a reference in a Clinical Trial, and 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)
The investigator responsible for the research site. There should be one PI for each research site. In the case of a single-site study, the chief investigator and the PI will normally be the same person.

The Medicines & Healthcare products Regulatory Agency (MHRA)
The MHRA is the competent authority for the UK in relation to the Directive 2001/20/EC and the Clinical Trials Regulations, and for Medical Devices, the competent authority in relation to the Medical Devices Regulations 2002.

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.

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: WHHT Sponsored Trial Closure Procedure Flow diagram