TRIAL CLOSURE
Research & Development

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

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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 gSOP-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 gSOP-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 gSOP-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.

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should be accessed via the hospital intranet
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 gSOP-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.

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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 gSOP-17).

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

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

**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 gSOP-17).

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

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

6.0 RELATED DOCUMENTS

- gSOP-08- Role of CI, pharmacy, nuclear medicine and R&D
- gSOP-09- Amendments
- gSOP-14- Writing Research Protocols
- gSOP-17- Archiving of Essential Documents
- gSOP-22- End of Study Reports
- gSOP-24- Research Staff Training

7.0 APPENDICES

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

8.0 VERSION HISTORY

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<th>Version Number</th>
<th>Effective Date</th>
<th>Reason for Change</th>
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9.0 AUTHORSHIP & APPROVAL

Author

Signature  Date

R & D Steering Group Approval

Signature  Date

10.0 AGREEMENT

Please detach and retain in your training file

I have read and understood the contents and requirements of this SOP (gSOP-21-04) and accept to follow by Trust policies implementing it.

Recipient

Signature: .................................................................Date: .................................

Name & Position: .................................................................
Appendix 1: Definitions

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

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

Investigational Medicinal Products (IMP)
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 -

- used or assembled (formulated or packaged) in a way different from the form of the product authorised under the authorisation,
- used for an indication not included in the summary of product characteristics under the authorisation for that product, or
- 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 Nurse who has responsibility for the conduct of the trial at a host site.

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.

The Medicines & Healthcare products Regulatory Agency (MHRA)
UK competent authority responsible for regulation of clinical trials.

The Regulations

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

Is study CTIMP or Non-CTIMP?

CTIMP

Contact R&D to arrange close out visit

Close out visit. Once all issues are resolved following the close out visit the R&D Office will permit formal closure of the trial

CI or delegate completes End of Trial Notification form and sends to MHRA, REC and R&D within 90 days or 15 days if terminated early.

Pharmacy sent a copy of end of trial notification and R&D acknowledgement

Non-CTIMP

CI/PI completes Declaration of End of Study and sends to REC and R&D within 90 days or 15 days if terminated early.

Receive End of Trial Acknowledgement letters

Study Reports within 12 months of completion. Send a copy to MHRA (if appropriate), REC and R&D.

Database analysis after database lock

Dissemination of results

Archiving (gSOP-17)