University of Hertfordshire UH

Clinical Trials Unit

University of Hertfordshire Clinical Trials Unit (CTU)

END OF STUDY PROCEDURES

Standard Operating Procedure for Closure of and End of Study Reports for University of Hertfordshire Sponsored/Co-sponsored and UH CTSN adopted Studies

SOP Number: gSOP-24-02	**Effective Date: 2nd December 2025**
Version Number: 2.0	**Review Date**: 3 years (or as required)

1.0 BACKGROUND

This is a University of Hertfordshire (UH) standard operating procedure (SOP).

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. It aims to provide clear guidance on how participants, staff and study related documentation is managed during close-out to ensure compliance with the University's Information Governance Policies, the Data Protection Act 2018, and the UK Policy Framework for Health and Social Care Research (2017). Where there are potential conflicts between different collaborating organisations' SOPs, project level working instructions should be developed, to determine precedence.

Research transparency is central to ethical research practice. Research studies should be registered, and the results made public, so that participants are protected from unnecessary studies and research funding maximised. Investigators have an obligation to the scientific community, current and future patients to provide full and open disclosure of research project results, whatever the findings. Research projects with null results, those which failed to recruit to target and those which were unexpectedly terminated all need to be reported in accordance with national transparency requirements.

The University is committed to the immediate, unrestricted, online public availability of its peer-reviewed research outputs free-of charge, to enhance intellectual inquiry, support new research, enrich education and maximise the impact and value of its research for wider economic and social good.

2.0 PURPOSE

To ensure all UH sponsored/co-sponsored and adopted research studies are closed, and end of study reports are submitted according to protocol, regulatory and sponsor requirements. This document aims to ensure end of study reports are appropriately reported and disseminated within the required timeframe.

3.0 APPLICABLE TO

This applies to all staff involved with research sponsored/co-sponsored by UH and/or adopted by the UH CTU 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, Research Assistants and students.

4.0 RESPONSIBILITIES

The Chief Investigator (CI)/Principal Investigator (PI) or Delegated Individual (DI) is responsible for the closure of the research study and end of study reports according to regulatory and sponsor requirements. The CI/PI/DI should ensure for UH sponsored/co-sponsored studies, that the end of study definition is agreed and documented clearly in both the protocol and any corresponding agreements before the study starts.

For UH sponsored clinical trial of investigational medicinal products (CTIMP) trials, the sponsor's representative will ensure that the approved protocol provides adequate detail regarding end of trial (gSOP-14) and the UH CTU/R&D Office will ensure that these trials are closed according to the protocol, regulatory and sponsor/co-sponsor requirements. If the end of trial is amended during the course of the study 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.

The CI has responsibility to ensure that study findings are reported and disseminated as appropriate and in accordance with national requirements. The CI also has responsibility to be aware of the funder requirements in respect of study reports and publications and to inform them of any impending publications. The CI should ensure the posting of reports and publications to any relevant research databases.

For clinical trials, it is the sponsor's responsibility to ensure that the CI uploads the clinical trial summary results in EudraCT where applicable and /or any research database to which the study has been registered (e.g. ISRCTN - International Standard Registered Clinical/Social Study Number, ClinicalTrials.gov).

5.0 PROCEDURE

5.1 Closure to Recruitment

5.1.1 A study is said to be "Closed to Recruitment" when a study has recruited its target number of participants as detailed in the protocol. If the study is multicentre this must mean that no further participants can be recruited at any of the participating sites, however, where applicable participants may still be on treatment/intervention when the study is closed to recruitment.

5.1.2 Once a study has completed recruitment, but participants are still on treatment/intervention, the CI/PI/DI or delegate should notify the UH CTU (if adopted by the UH CTU) and Trust R&D office (if co-sponsor), where applicable.

5.1.3 The UH CTU and Trust R&D office will acknowledge the change in status and update their respective databases.

5.1.4 For multicentre studies, the CI/DI should ensure that the end to recruitment is clearly communicated and subsequently documented at each site. It is the PI's responsibility to ensure that, where applicable, 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 study's closure to recruitment.

5.1.5 Once the study is ready to close, as defined in the protocol, the research team should start close out procedures.

5.2 Participating site closure

5.2.1 The participating site may only be closed when all data queries have been answered, resolved and documentation returned to the coordinating team as necessary.

5.2.2 Once all required documents have been provided to the participating sites for inclusion in the ISF, the CI or delegate will arrange for a site close-out via:

- On-site visit, or
- Remote monitoring

5.2.3 The coordinating team will distribute the site close out checklist to participating sites for completion. Upon receipt, participating sites are expected to complete and return the completed form in advance of site closure.

5.2.4 The site close out checklist should be completed for all site close-out visits. During close out procedures, specific attention should be paid to:

- Confirmation of archiving arrangements for the ISF and associate files at the participating site.
- Discrepancies in the ISF documentation and arrangements for resolution.
- Specific requirements of the site staff including the publication rights and procedures, dissemination of information to trial participants etc.
- On-going responsibilities of the site staff or the site for example collection of patient long-term follow-up data, provision of information in the event of an Audit or Inspection or long-term safety reporting for patients included in the trial.
- Where applicable, Investigational Medicinal Product (IMP) accountability including the return or destruction of IMP which was provided specifically for use in the trial (this excludes hospital stock).

5.3 Notification of End of Study or Early Termination

5.3.1 The CI/DI should declare a study completed when it reaches the end of study as defined in the protocol, or it has been terminated prematurely.

5.3.2 All study activities (including follow-up visits and procedures) must be completed before a study can be declared completed to regulatory authorities and participating sites.

5.3.3 Where applicable, the sponsor/co-sponsor should liaise with the Trust NHS pharmacies to ensure accountability is performed and excess IMP are returned or destroyed as detailed in the protocol, legal requirements and relevant pharmacy SOPs. The TMF/ISF and Pharmacy files including drug accountability logs and records of returns or destruction should be up to date before closure.

5.3.4 For CTIMPs, the CI/DI should complete the Declaration of End of Trial Form, from the MHRA website, and send to the MHRA and Research Ethics Committee (REC) that gave the trial favourable opinion within 90 days of the end of the trial, including an end of trial form and a covering letter. For CTIMPS submitted via Combined Review Service, the End of Trial Form can be completed and submitted in the new part of the Integrated Research Application System (IRAS).

5.3.5 For all other research, the end of study declaration form should be completed and emailed to the REC (can be downloaded from the HRA website) within 90 days of the end of the study, as follows :

- Where a project has HRA approval and has been reviewed by a REC, only the REC needs to be informed that the study has ended.
- For those studies that do not require HRA approval but have received UH Ethics approval **and** involves invasive procedures or has a high risk of physical/mental harm an EC7 protocol monitoring form should be submitted to UH Ethics once the study has ended.
- Where a project has HRA approval and was not reviewed by a REC, the HRA must be informed when the project has ended. This notification should be sent by email to approvals@hra.nhs.uk including the study IRAS ID and main contact information (phone and email).
- All studies formally adopted by the UH CTU should send a copy of the end of study declaration to uhctu@herts.ac.uk including those who do not fall within the above criteria.

5.3.6 For CTIMPs that are terminated early, the MHRA, REC, sponsor, co-sponsor and UH CTU should be informed within 15 days, and the CI/DI should clearly explain the reasons for the early termination.

5.3.7 For all research, the CI/DI should send a copy of the end of study notification documents to the sponsor/co-sponsor and participating site R&D departments where applicable. A copy of the Declaration of End of Study form and the R&D acknowledgement is to be sent to the Trust NHS Pharmacies, if required, for their records.

5.3.8 Once the End of Study acknowledgements have been received from the appropriate ethics committee or regulatory agency (e.g. REC, MHRA), R&D and co-sponsor where applicable, the study can be considered closed and can be archived following the SOP for archiving (see gSOP-17).

5.3.9 Final reports should be submitted within one year of study closure.

5.3.10 Please refer to the sponsored study closure procedure in the appendix for a flow diagram of the process (Appendix 2).

5.4 End of Study Report

5.4.1 Results of all studies should be reported within 12 months of the published definition of the end of the study. This may be defined as 'Last patient, Last Visit' (LPLV), or any other variation including submission of the 'End of Study Report'. Where a definition has not been provided, the End of Study Declaration will be taken as the end of study date.

5.4.2 For CTIMPS, the CI/DI is responsible for submitting a final research report to the MHRA and REC within 12 months of trial having ended. The submission email and subsequent acknowledgement of receipt should be filed in the TMF.

5.4.3 The end of trial report should be prepared using the TP-60 End of Study Report Template and the GCP guidance document "structure and content of clinical study reports" (CPMP/ICH/137/95). As a minimum, the end of study report must contain the following information:

- Study title
- Name and address of the sponsor or sponsoring group's legal representative in the UK
- Study Protocol code number if any
- Date of end of study including all participating centres in all countries within and outside the EU if relevant. Note: specific requirements may vary across different countries;
- Whether the study achieved its objectives;
- The main findings of the study;
- A listing of all the significant non-compliances that occurred during the trial and how these contributed to the analysis;
- Details of any serious breaches reported during the study;
- Arrangements for publication;
- Dissemination of the research including feedback to participants.
- Additional information to be included for CTIMPS:
  - EudraCT number:
  - The IMPs tested in the trial:

5.4.4 For non-CTIMPS, a summary of the final research report should be sent to the REC within 12 months of the end of the study. The submission email and subsequent acknowledgement of receipt should be filed in the TMF.

5.4.5 There is no standard format for final reports for the REC. As a minimum, the report should state whether the study achieved its objectives, the main findings, and arrangements for publication or dissemination of the research, including any feedback to participants. Please refer to TP-60 End of Study Report Template.

5.4.6 Where appropriate, reports should be uploaded to the publicly accessible platform detailed in the initial application e.g., ClinicalTrials.gov/ISRCTN/ EudraCT. In addition, many funding bodies will require a final report. The format and deadline for these may differ depending on the funder.

5.4.7 Final reports for studies sponsored by UH must also be sent to UH Research Sponsorship.

5.5 End of Trial Summary Results to MHRA (for CTIMPs)

5.5.1 Publication of full dataset on EudraCT

- The CI will ensure the full dataset is finalised and ready for posting within 12 months following the conclusion of a clinical trial.
- The CI or delegate will upload the full dataset as required by EudraCT.
- In order to report results via EudraCT, the user must be registered with the system as a results reporter.
- Results can be directly entered into the system using the fields provided or uploaded via an .xml file.
- Once data has been successfully uploaded and the results become public (approximately 15 days after upload), the CI or delegate will send a short confirmatory email to CT.Submission@mhra.gsi.gov.uk stating “End of trial study report: EudraCT XXXX-XXXXXX-XX” in the subject line.
- The datasets posted with confirmatory email will be filed.

5.6 Following Submission of the End-of-Trial Study Report to the MHRA and the REC

5.6.1 No further amendments can be made to the study once the “Declaration of the end of a clinical trial form” has been submitted.

5.6.2 Clinical trial documents should not be archived until the final report has been submitted.

5.7 Publications

5.7.1 In addition to the study report, many CIs and funders will submit to peer reviewed scientific journals. Publications may occur at any time point during the lifetime of a study e.g., protocols may be published during recruitment phase. If a study is closed prematurely, it may still be published, giving such results and conclusions as possible and discussing why the trial was closed. This ensures that data is still available for subsequent meta-analysis. The benefits and hazards of treatment policies are equally important; both must be reported.

5.7.2 The format and deadlines for these publications may differ depending on the requirements of the journal. Publications of trials should conform to the CONSORT (Consolidated Standards of Reporting Trials) statement guidelines. CONSORT comprises a checklist and flow chart to provide a standard way for researchers to report studies. Full details including a downloadable checklist and flow diagram may be found from the CONSORT website.

5.7.3 The contribution of funders should be clearly acknowledged. Where the format of this acknowledgement has been specified by the funder(s), the CI must ensure that this is followed. If there is no funder specification, please follow UH guidance on acknowledgement. The CI must also ensure that any contractual obligations to

the funder relating to publications are met. This may include prior notification of the publication.

5.7.4 The publication must include details of the sponsor and any ethics committee and other review bodies i.e. MHRA within the manuscript. Where applicable all study reference numbers i.e. IRAS, REC, MHRA, EudraCT, ISRCTN etc. should be stated in the publication.

5.8 Dissemination

5.8.1 Dissemination to Participants

- It is good practice to disseminate the results of research to those who participated as well as other interested groups or communities. Providing participants with a summary of the findings acknowledges and appropriately respects the contribution they have made. Information about the findings of the research should be available, in a suitable format and timely manner, to those who took part in it, unless otherwise justified.

- There is no standard format for providing information to participants at the end of a study, however the process for dissemination of results to participants will have been addressed at the of ethical approval and detailed in IRAS/the protocol and publication/dissemination policy. Evidence of completion should be filed in the TMF. Any deviations from this should be discussed and agreed with the sponsor.

5.8.2 Dissemination to the Public

- Consideration should be given to the format of dissemination. The CI must ensure that any contractual obligations to the funder are met including any prior approval of press releases or other media material. All relevant parties, including the funder, should be approached for approval in advance of any press release(s) being issued. If the press release contains research project results the press release must be embargoed until the date and time of publication.

5.8.3 Open Access

- CIs must follow the UH Open Access Policy (UPR IM18). The University will normally make its research outputs available in electronic formats that support searching, downloading, text and data-mining, and re-use of their content, providing that any such re-use is subject to full and proper attribution.

- The ‘green’ open access deposit of all research outputs in the UH Research Archive (UHRA) is mandatory. Deposit is to be carried out by the author or relevant PI.

- For research data there are various repositories into which data can be deposited. UHRA is a depository which allows the researcher greater control over the process as the Research and Scholarly Communications Team support this. A DOI will also be assigned. To deposit data into the

UHRA a UH Data Deposit Form should be completed. Once data has been made available it should be linked by including a data access statement in the publication.

- Research output will be uploaded to the University's Research Information System (RIS). Deposit must be made at the time the research output is accepted for publication.

5.8.4 Data Sharing

- Requests to access data may be received at the end of the study. Please refer to gSOP-27 Data Sharing for details of the process.

5.9 Archiving

- The trial can be archived when all the end of trial documentation and end of trial reports have been written, submitted and filed.
- Any publications received after the files have been archived will be added to the archive at the time.
- The trial documentation must be archived in accordance with SOP-17 Archiving Essential Documents

6.0 RELATED DOCUMENTS

- gSOP-09 Amendments
- gSOP-13- Research Applications
- gSOP-14 Writing Research Protocols
- gSOP-24 Training for Research Staff
- gSOP-27 Data Sharing in UH Sponsored and CTSN supported Clinical Studies
- gSOP-17 Archiving Essential Documents
- TP-60 End of Trial Study Report Template
- GU06 Site Close out Guidance
- HRA Ending your Project Guidance https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/ending-your-project/
- Data Deposit Form
- CONSORT (Consolidated Standards of Reporting Trials) statement guidelines http://www.consort-statement.org/
- UH guidance on publication acknowledgement https://herts365.sharepoint.com/sites/UHResearch/SitePages/Acknowledgement-in-Scholarly-Work.aspx

7.0 APPENDICES

- Appendix 1 - Definitions
- Appendix 2 - Study Closure Procedure Flow diagram

8.0 VERSION HISTORY

Revision Chronology:		
Version Number	**Effective Date**	**Reason for Change**
2.0	**02/12/25**	Review

9.0 AUTHORSHIP & APPROVAL

Author Megan Smith

Signature  **Date** **19 February 2025**

Pro-Vice Chancellor (Research & Enterprise) Approval

Signature 

Date 02/12/2025

Signed by Dr Susan Grey, Chair of the Governance of Clinical Studies Group (GCSG), on behalf of the Pro-Vice Chancellor (Research & Enterprise)

10.0 AGREEMENT

Please detach and retain within <u>your training files</u>

I have read and understood the contents and requirements of this SOP (ref gSOP-24-02) and accept to follow UH policies implementing it.

Recipient

Signature: ……Date: ……..

Name & Position: ……

Appendix 1.0 Definitions

Chief Investigator (CI) - An individual who is responsible for the conduct of the whole project in the UK. 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.

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) - 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) - 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

Study Closure Procedure Flow diagram