Clinical Directorate Clinical Research Governance Team

Standard Operating Procedure

End of Study Procedures for University of Liverpool Sponsored Studies

SOP021

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Document Control

Issue Date	21/02/2023
Effective Date	21st February 2023
Review Date	21st February 2025
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Document History can be viewed on Q-Pulse

Review Process Prior to Sign Off

Name of Committee	**Date**
Sponsorship Review and Approval Committee – v1	8th March 2013
Joint Research Office Sponsorship Committee – v2	9th June 2015
Joint Research Office Sponsorship Committee – v3	11th May 2017
Chair of Joint Research Office Sponsorship Committee – v4	13th September 2017

SPARK Sponsorship Committee - Version 5	15th November 2022
Chair of SPARK Sponsorship Committee - Version 6	21st February 2023

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1. Introduction

The UK Statutory Instrument 2004 No 1031: Medicines for Human Use (Clinical Trials) Regulations 2004 (the Regulations) define reporting requirements at the end of a Clinical Trial of an Investigational Medicinal Product (CTIMP). Reports should be submitted to the UK Competent Authority - the Medicines and Healthcare products Regulatory Agency (MHRA) and the relevant Research Ethics Committee (REC).

The end of a trial or study should be defined in the protocol; it is normally the date of data lock or last patient last visit. A trial however may be closed prematurely by the Trial Steering Committee (TSC), the Sponsor or the research team for reasons such as clear issues with efficacy or safety of trial treatments.

The Regulations and the Health Research Authority (HRA) state that for all studies covered under the UK Policy Framework for Health and Social Care Research, written notification of the end of study should be notified within 90 days of the end of project, or within 15 days if the project is terminated early.

All End of Study notifications will be reported to the Liverpool Health Partners (LHP) Single Point of Access to Research and Knowledge (SPARK) Sponsorship Committee or Non-Interventional Sponsorship Sub Committee (NISSC). Reporting will be made to the committee that initially reviewed and approved the study.

2. Scope

To describe the procedure for closure of all research Sponsored by the University of Liverpool (University) and ensuring that the notification of study closure is communicated appropriately to Research Ethics Committee (REC), MHRA, Sponsors and other required bodies.

3. Who

The Chief Investigator (CI) or delegated individual is responsible for confirming all appropriate actions have been completed prior to final data lock.

The Sponsor, or delegated individual, is responsible for reporting the end of a study to REC, MHRA and other required regulatory authorities.

4. When

The Sponsor must notify the end of the study *within 90 days* of the study ending (as defined in the protocol). If the study is terminated prematurely, it is the responsibility of the sponsor to notify the REC and MHRA within 15 days with clear justification for the early termination. This action is delegated by the University to the CI with appropriate oversight from the Clinical Research Governance Team.

The CI or designated member of the study team (e.g. Trial Manager/Co-ordinator), who will be responsible for informing the Sponsor, REC, MHRA and other required bodies of the end of the study.

The CI or delegated individual will collect all outstanding case report forms (CRFs) and equipment, resolve outstanding data queries, discuss how any long-term follow-up will be coordinated, ensure local archiving procedures are followed and reconciliation/destruction of trial drug supplies are undertaken as per protocol.

5. When is the end of the study?

The definition of the end of the study should be provided in the protocol and any change to this definition for whatever reason should be notified as a substantial amendment.

Please consider this carefully as after the end of study is declared no study activity, other than final analysis of the data (following 'lock' of the study database) and report writing, should be undertaken. For studies involving human tissue, the analysis of the samples should be undertaken as part of the data collection **before** the end of study is declared. Final analysis of the data (following 'lock' of the study database) and report writing is normally considered to occur after formal declaration of the end of the study.

The following sections detail the timelines required for the submission of end of study declarations and reports, and so it is essential that study teams take these timelines into account when defining the end of the study or trial.

Each study will have a proposed end date defined in the applications to Sponsor, REC, MHRA and other appropriate bodies. The Sponsor will use this date to provide early notification of the requirement to submit the end of study declaration. Any extension to the proposed end date needs to be submitted as an amendment. See SOP018[1] for more information.

6. Notifying the end of a CTIMP

For CTIMPs an 'End of Trial' form should only be completed at the end of the trial when the trial has completed in all participating countries. Information on the procedure for declaring the end of a CTIMP is available from the MHRA[2].

It is required that a 'Declaration of the end of a Clinical Trial' form should be sent to the MHRA within 90 days of the trial conclusion. The declaration of the end of a clinical trial form is available from the MHRA[3]. End of Trial Declarations must be submitted using MHRA Submissions via the Human Medicines Tile. Please select 'Clinical Trial' as the Regulatory Activity and 'CT – EOT' from the Regulatory sub activity dropdown list. User accounts can be requested from the Clinical

[1] Procedure for the Submission of Amendments
[2] https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues
[3] https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#end-of-trial

Research Governance Team (sponsor@liverpool.ac.uk). The MHRA will acknowledge receipt of the End of Trial Declaration.

A copy of the End of Trial Declaration and end of trial study report must be submitted to REC and Sponsors in parallel to MHRA submission.

For research that involved the collection, use and storage of human material it is also required to complete and submit a Human Material End of Study Declaration (HTAFORM001). This form will be provided by the Clinical Research Governance Team.

Once the declaration of the end of a clinical trial form has been received by the MHRA, REC and Sponsor it is not possible to submit any further amendments to the trial.

It is a requirement to publish a summary of results for clinical trials of an investigational medicinal products (CTIMPs) within 6 months of the end of trial for paediatric clinical trials or within one year of the end of trial for non-paediatric clinical trials.

The clinical trial summary report should be posted on the public register(s) where the trial was originally registered. The MHRA do not require a copy of the clinical trial summary report but do require the sponsor (or their delegate) to send a brief confirmatory email to CT.Submission@mhra.gov.uk once the result-related information has been uploaded.

7. Notification of end of study for all other research (non-CTIMPs) approved by an NHS REC

The REC which gave a favourable opinion of the research and the Sponsors should be notified in writing of the conclusion or early termination of a project using the appropriate form. This must be submitted within 90 days of the conclusion of the study, or 15 days for early terminations. Clear justification for the early termination must be provided. Further details are available from the HRA[4].

A summary of the final report on the research should be sent to the REC and Sponsors within 12 months of the end of the project. There is no standard format for final reports. As a minimum, the REC and Sponsor should receive information on whether the project achieved its objectives, the main findings and arrangements for publication or dissemination of the research, including any feedback to participants.

All documents must also be sent to the Sponsors.

For research that involved the collection, use and storage of human material it is also required to complete and submit a Human Material End of Study Declaration (HTAFORM001). This form will be provided by the Clinical Research Governance Team.

8. Notifying the Confidentiality Advisory Group (CAG)

If your study required Confidentiality Advisory Group (CAG) approval you need to ensure the end of the study is notified to them, along with confirmation that you will no longer be processing

[4] http://www.hra.nhs.uk/research-community/end-of-study-and-beyond/notifying-the-end-of-study/

confidential patient or service user information without consent, and therefore no longer require support from CAG under the regulations.

You should complete a Section 251 Support End Closure Report Form and submit it to CAG by email (cag@hra.nhs.uk) along with all relevant supporting documentation.

Once this closure report has been acknowledged, 'Section 251 support' will no longer be in effect and there will be no lawful basis to process identifiable information without consent.

9. Notification of end of study for research not approved by an NHS REC

The University also Sponsors studies that do not require approval from an NHS REC. These studies are usually approved by the University of Liverpool Ethics Committee, and may have approvals from other bodies (e.g. international ethics committees).

These studies are also required to formally declare the end of the study to the Sponsor, using FORM008[5]. The same timeframes and requirements apply to these studies as described in earlier sections.

For research that involved the collection, use and storage of human material it is also required to complete and submit a Human Material End of Study Declaration (HTAFORM001). This form will be provided by the Clinical Research Governance Team.

10. Study Does Not Commence

If, after receiving approvals, the CI decides not to commence a study, they should notify the MHRA, REC and Sponsors and clearly explain the reasons for not starting the study. There is no defined time period for reporting of the decision to not begin a study, but if a study has not commenced following 12 months of receiving the required approvals the University, as Sponsor, may undertake an assessment of continued Sponsorship.

11. Sponsor Requirements

Once you have notified your study as complete the Sponsor team will complete FORM011[6] and request documentation and information to close the Sponsor file. This information must be provided within 12 months of the study ending.

The Sponsor will require copies of notifications submitted to other bodies, as outlined above, as well as;

- Archiving arrangements for paper documentation
- Archiving arrangements for electronic data and/or documentation
- Confirmation of results being posted on appropriate trial register

[5] Sponsor End of Study Declaration
[6] Sponsor End of Study Checklist

12. Roles and Responsibilities

It is the CIs responsibility to:

Inform the Sponsor(s), the REC, MHRA and any other required bodies of;

- end of study within 90 days
- amendments to the definition of end of study
- early termination of study within 15 days
- non-commencement of a study

Submit End of Study Report to the sponsor(s), REC, MHRA, CAG and any other required bodies within 12 months of the study completion.

Collect all outstanding CRFs and equipment, resolve outstanding data queries, and discuss how any long-term follow-up will be coordinated, ensure local archiving procedures are followed and reconciliation/destruction of trial drug supplies are undertaken as per protocol.

It is the Sponsor's responsibility to:

Record the end of study dates

Receive end of study notification and reports

Ensure that required timescales are met

Ensure End of Study reports and notifications are reviewed at the appropriate SPARK Sponsorship Committee.

13. Abbreviations

CI	Chief Investigator
CTIMP	Clinical Trial of an Investigational Medicinal Product
CRF	Case Report Form
HRA	Health Research Authority
IMP	Investigational Medicinal Product
MHRA	Medicines and Healthcare products Regulatory Agency
REC	Research Ethics Committee
SOP	Standard Operating Procedure
TSC	Trial Steering Committee
University	University of Liverpool

14. Associated Documents and References

SOP018 Procedure for the Submission of Amendments

SOP020 Archiving of Essential Documents for University Sponsored Studies

HTAFORM001 Human Material End of Study Declaration

FORM011 Sponsor End of Study Checklist

UK Policy Framework for Health and Social Care Research

The Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004 No. 1031)

15. Training and Resources

CIs, students, trial coordinators and other members of University Staff involved in the set-up, management and conduct of research sponsored by the University should be aware of and familiar with this SOP. Training can be provided by the Clinical Research Governance Team upon request.

16. Monitoring and Audit

An internal audit of Clinical Directorate SOPs will be conducted at a minimum of every two years.