UNIVERSITY OF LIVERPOOL

Research Support Office

Procedure for

End of Study Procedures for University of Liverpool Sponsored Studies

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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 (v3.2 10th October 2017), 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 Joint Research Office (JRO) Sponsorship Committee or Non-Interventional Sponsorship Sub Committee. End of Study notifications for clinical trials (including CTIMPs) will be reviewed by the JRO Sponsorship Committee.

2. Scope of Procedure

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 HRA Research Ethics Committee (REC), MHRA and Sponsors.

3. Procedure

3.1. 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.

3.2. 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 University Research Support Office (RSO).

3.3. How

The CI or designated member of the study team (e.g. Trial Manager/Co-ordinator), who will be responsible for informing the Sponsors of the end of the study. The CI or designated other will also

complete the necessary steps to formally provide notification of the end of study to REC and MHRA (where appropriate).

The CI must ensure that all End of Study Notifications are sent to the Sponsor at the time of submission to REC and MHRA (where appropriate). The End of Study report will then be discussed at the next JRO Sponsorship Committee.

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.

3.3.1 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.

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.

3.3.2 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[1].

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 HRA[2]. End of Trial Declarations must be submitted via CESP (Common European Submission Portal)[3]. User accounts can be requested from the Clinical Research Governance Team in the Research Support Office [REDACTED]. 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.

[1] https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues
[2] http://www.hra.nhs.uk/resources/during-and-after-your-study/end-of-study-notification-clinical-trials-of-investigational-medicinal-products-ctimps-eudract-form/
[3] https://cespportal.hma.eu/Account/Login

The sponsor is responsible for uploading the end of trial summary results to EudraCT as per the commission's guidelines[4] on posting and publication of result-related information. The time frame for posting the summary is within six months of the end of trial for paediatric clinical trials or within one year of the end of trial for non-paediatric clinical trials.

This function is delegated to the CI, or CTU managing the trial. The end of trial summary report must be submitted to the Sponsor(s) and REC upon upload to EudraCT.

It is not required to submit this clinical trial summary report to the MHRA as well however you must send a short confirmatory email to CT.Submxxxxxx@xxxx.xxx.gov.uk once the result-related information has been uploaded to EudraCT, with 'End of trial : result-related information: EudraCT XXXX-XXXXXX-XX' as the subject line. You will not get an acknowledgment email or letter.

3.3.3 Notification of end of study for all other research (non-CTIMPs)

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[5].

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.

3.3.4 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.

4. Roles and Responsibilities

It is the CIs responsibility to:

- Inform the Sponsors, the REC and MHRA of;
    - end of study within 90 days
    - amendments to the definition of end of study
    - early termination of study within 15 days

[4] http://ec.europa.eu/health//sites/health/files/files/eudralex/vol-10/2012_302-03/2012_302-03_en.pdf
[5] http://www.hra.nhs.uk/research-community/end-of-study-and-beyond/notifying-the-end-of-study/

- non commencement of study

- Submit End of Study Report to (co-)sponsors, REC and MHRA 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 University'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 JRO Sponsorship Committee.

5. Abbreviations

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

6. 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

UK Policy Framework for Health and Social Care Research (v3.2 10th October 2017) http://beta.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/

UK Statutory Instrument 2004 No 1031: Medicines for Human Use (Clinical Trials): Schedule 3, Part 4 http://www.legislation.gov.uk/uksi/2004/1031/pdfs/uksi_20041031_en.pdf

7. Training and Resources

Members of University staff involved in the set-up, management and conduct of research sponsored by the University read and fully understand this SOP. If any further training is required, this can be arranged with the RSO Research Integrity and Governance Manager.

8. Monitoring and Audit

Compliance with this SOP will be audited by the RSO Research Integrity and Governance Manager as part of regular audit procedures.