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SOP 335 Research Project Closure (Including Procedure for Suspension or Early Termination)

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2	Nov 23	NA	New template Addition of combined review information HRA approvals email to be used for end of study notification where a project was not reviewed by REC	Jackie Orford

This Standard Operating Procedure (SOP) is available on the Research & Development pages on the NNUH website

Copies downloaded from the website are only valid on the day of downloading.

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1. Contents

2. Definitions of Terms Used / Glossary

CI	Chief Investigator
CTIMPs	Clinical Trial of Investigational Medicinal Products
HRA	Health Research Authority
ICH GCP	International Conference on the Harmonisation of Good Clinical Practice
IDMC	Independent Data Monitoring Committee
IMP	Investigational Medicinal Product
IRAS	Integrated Research Application System
MHRA	Medicines and Healthcare Products Regulatory Agency
PI	Principal Investigator
R&D	Research and Development
REC	Research Ethics Committee
RIN	Research & Innovation Services
SI	Statutory Instrument
SOP	Standard Operating Procedure
TMF	Trial Master File

Temporary halt to a study:

- This is a stoppage (suspension) which was not envisaged in the approved protocol and where there is an intention to resume the study
- A temporary halt applies when the suspension is imposed on all sites; suspension of the study at a single site due to logistical reasons is not considered a temporary halt (unless the study is a single-site study)

Possible suspension reasons:

- On the recommendation of the Independent Data Monitoring Committee (IDMC) on review of new safety information
- Serious Breach
- Investigational Medicinal Product (IMP) supply issues
- Recruitment has to be halted for other reasons

Early termination of a trial (close down of the study prior to official End of Study date) Examples of reasons for premature termination include:

- Safety concerns
- Poor toleration of the study intervention
- Difficulty with recruitment
- Sponsor decision
- Investigator decision
- Regulatory decision
- IDMC recommendation

3. Objectives

To describe the process for closure of research projects, including suspension and early termination, in accordance with the protocol and regulatory requirements, ICH GCP E6/SI 2004/1031

4. Scope

The definition of the end of the study must be documented in the protocol. In most cases, this will be the date of the last visit of the last participant or the completion of any follow-up monitoring and data collection described in the protocol.

If there is any change to this definition, the Clinical Investigator (CI) should notify this as an amendment to the appropriate review bodies ensuring the relevant research office is similarly notified.

5. Purpose

To provide clear guidance on the procedure required to close a trial, including those that are suspended or closed early.

6. Notifying End of Study

The Sponsor (or delegate) must declare the end of study to the Research Ethics Committee (REC) within 90 days of the end of the study

- Final analysis of the data (following ‘lock’ of the study database) and report writing should usually happen after formal declaration of the end of the study

For clinical trials of investigational medicinal products (CTIMPs) the same end of trial form is used to notify both the REC and the Medicines & Healthcare products Regulatory Agency (MHRA). For trials submitted through **combined review,** the end of trial form should be completed and submitted view the Integrated Research Application System (IRAS). For CTIMP and Device trials that were not submitted through combined review, the form available on the MHRA website should be used and the CI or delegate should email this to the MHRA and REC with a copy to the relevant research office.

For all other research, the end of study declaration form should be completed and emailed to the REC.

Before the declaration of the end of the study is completed, the CI or delegate should:

- Review the plans that have been approved by the REC for: use of tissue, data collected in the course of the study, providing information to participants, and dissemination of results
- If any changes are required the CI or delegate must consider whether a substantial amendment is required before the end of study notification is submitted

7. End of study under Health Research Authority (HRA) Approval

- Where a project has HRA/HRCW approval and has been reviewed by a REC the Sponsor (or delegate) need only inform the REC when the study has ended as described above
- Where a project has HRA Approval and was not reviewed by an NHS REC, the Sponsor (or delegate) will need to notify the HRA when the project has ended. An email should be sent to approvals@hra.nhs.uk including IRAS ID and CI contact information (phone and email)

8. Research Final Report

The CI (or delegate) must send a final research report to the REC (and MHRA for clinical trials of investigational medicinal products) within 12 months of the end of the study.

If application was submitted via combined review, the final report should be completed in the IRAS system. For all other project-based research reviewed by a REC the HRA webform should be used https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/ending-your-project/final-report-form/

MHRA may request a copy of the final report of a clinical investigation of a device. It is likely that a copy would be requested under certain circumstances, e.g. where a serious adverse event has occurred associated with a CE-marked device which had undergone clinical investigation authorised by the MHRA, or where a novel technology has been investigated.

See **SOP 340 Clinical Trial Reporting**.

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9. Temporary halt of a study or early closure of a study

A substantial amendment requiring both authorisation and a favourable REC opinion is required for:

- Temporary halt of a trial or temporary halt at a trial site, and restart of the trial following a temporary halt
- Change of the protocol definition of the end of a trial
- For a CTIMP trial MHRA notification is required within 15 days of the submission of the notification of substantial amendment form. The Sponsor (or delegate) is responsible for ensuring this happens

10. Early Termination of a trial

The protocol definition of the end of trial

- describes when a trial shall end. If the trial ends early then a substantial amendment will need to be issued to the REC who provided the favourable opinion and to the MHRA if the trial is a CTIMP
- Notification is required within 15 days of the date of termination. The Sponsor is responsible for ensuring this happens. The notification must include a clear explanation of the rationale for ending the trial prematurely and shall describe the follow-up measures, if any, to be taken for safety reasons

The circumstances that have led to the research terminating early will need to be documented in the Trial Master File (TMF)

- Any potential implications for participants (e.g. if the study is terminated on safety grounds) and potential consequences on the results and their interpretation in terminating the trial early must be detailed in the end of study declaration form

11. Site Close Out

For all CTIMPs sponsored by NNUH, a trial close-out visit shall be conducted by the Monitor(s) at each site or remotely

For all NNUH sponsored studies the CI shall contact the R&D office, via email, prior to the scheduled end of the trial, or as soon as possible if the trial has been terminated early, in order to arrange a suitable time for the close-out visit. For UEA sponsored studies, Research Innovation Services (RIN) shall be notified by the CI once a site has been closed out.

Where monitoring activities are delegated to a UKCRC accredited Clinical Trials Unit, risk appropriate onsite and/or virtual monitoring activities will be agreed with the Sponsor on a trial specific basis.

12. Database System

In order to support accurate oversight and reporting of research activity in the organisation, the R&D Office and RIN are required to maintain up-to-date records on their database systems on study status, including study end dates.

13. Archiving

The CI / PI is responsible for archiving all records at the end of the study according to the Sponsor Standard Operating Procedure where available.

14. Delegation of Research Project Closure Activities

Where a UKCRC accredited Clinical Trials Unit is delegated Sponsor responsibilities, reporting and monitoring activities will be delegated in the 'Delegation of Trial Activities', and detailed in the Monitoring Plan on a trial by trial basis.

15. References and Related Documents

References
ICH GCP E6 / SI 2004/1031

SOP No.	**SOP Title**
SOP 340	Clinical Trial Reporting

16. Approval

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17. Training Implication

Training Implication	**Yes**
Actions required	• Familiarisation with new procedure