End of Study Procedures

NJRO-REG-SOP-003

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1. Background/Introduction

End of study procedures must be completed to ensure the correct, and where applicable, legal processes are finalised once a study has ended.

2. Purpose

This Standard Operating Procedure (SOP) describes the end of study procedures to be performed by sponsors and investigators at the conclusion of a research study.

3. Scope of Document

This SOP is applicable to all personnel involved in clinical research sponsored or hosted by The Newcastle upon Tyne Hospitals NHS Foundation Trust (NuTH). It is particularly applicable to Chief Investigators (CIs) of NuTH sponsored studies and members of the NJRO team who have responsibility for performing sponsor-related duties.

'End of Study Procedures' SOP should be read in conjunction with SOP 'Publications' for research sponsored by NuTH.

4. Definitions

ATIMPs	Advanced Therapy Investigational Medicinal Products
CI	Chief Investigator
CTIMPs	Clinical Trials of Investigational Medicinal Products
CTU	Clinical Trials Unit
HRA	Health Research Authority
HTA	Human Tissue Authority
MHRA	Medicines and Healthcare products Regulation Agency
REC	Research Ethics Committee
SAE	Serious Adverse Event
NuTH	The Newcastle upon Tyne Hospitals NHS Foundation Trust

5. Roles & Responsibilities

It is the sponsor's responsibility to notify the relevant review bodies and compile the final study report to ensure that study documentation is archived appropriately. For studies sponsored by NuTH the responsibility is delegated to the CI or NuTH project manager (if applicable) except where a Clinical Trials Unit (CTU) has been contracted to manage the study.

6. Procedures

6.1 Defining the End of the Study

6.1.1 The definition of the end of the study must be specified in the study protocol e.g. last patient, last visit or completion of study follow-up.

6.1.2 Changes to the definition are classified as a substantial amendment requiring notification to the NHS REC, HRA and to MHRA where applicable.

6.1.3 Final analysis of the data, following database lock, is normally considered to occur after the formal declaration of the end of the study.

6.2 End of Study Notification

For all studies the appropriate review bodies must be informed of the end of a study within **90** days of the study conclusion or within **15** days if the study terminated early (early termination does not include completion of recruitment earlier than anticipated).

For those studies sponsored by NuTH the responsibility for submitting the end of study documentation is delegated to the CI except when a CTU or NuTH Project Manager is involved, in which case the responsibility is delegated to appropriate personnel within the CTU.

The CI or CTU must inform the appropriate NuTH sponsor team when a study has ended, specifying the date the study closed and highlighting if the study terminated early (where applicable).

An electronic copy of the end of study documentation must be sent to the appropriate NuTH sponsor team at the same time as it is sent to the review bodies.

For studies within the remit of the Regulatory Compliance Team, send to

tnu-tr.sponsormanagement@nhs.net

For studies within the remit of the Governance Team send to nuth.nuthsponsorship@nhs.net

6.2.1 CTIMPs and ATIMPs

The CI or Trial Manager must complete the Declaration of the End of Trial form available via the HRA website

Ending your project - Health Research Authority (hra.nhs.uk)

The completed form must be uploaded via the Common European Submission Portal (CESP) and a copy of the form also forwarded to the relevant REC and MHRA where applicable, both within the appropriate timeframe.

Once the declaration form is submitted, no further documentation will be accepted by the REC or MHRA except the end of trial report. A copy of the completed form must also be submitted to the appropriate NuTH sponsor team.

6.2.2 Medical Device Trials

The CI or Trial Manager must complete the NRES Declaration of the End of Study form available via the HRA website.

The completed form must be submitted to the relevant REC within the appropriate timeframe. If the investigation required a Notice of No Objection, the MHRA must also be informed in writing of the end of the investigation.

6.2.3 Other Studies

The CI or Trial Manager must complete the NRES Declaration of the End of Study form available via the HRA website.

The completed form must be submitted to the relevant REC within the appropriate time frame.

Where a project has HRA Approval and was not reviewed by an NHS REC, the HRA must be informed that the study has ended. Notification should be sent by email to hra.approval@nhs.net including relevant IRAS ID contact information.

6.2.4 Tissue Samples

If tissue samples have been taken as part of the research study then investigators must comply with the conditions of the favourable ethical opinion and the informed consent document signed by the participants.

Where the intention was to store the samples pending a favourable ethical opinion for another research project (as detailed in the NHS REC form) then this must be in place within 7 days of the end of the study, otherwise the tissue samples must be either be moved to a biobank licenced by the HTA or destroyed. Failure to do this is a breach of the favourable ethical opinion and of the Human Tissue Act.

6.2.5 Informing the Clinical Research Network

The CI or Trial/Project Manager should ensure that the Network is informed of closure to studies ensuring CPMS is also updated with all recruitment activity (cpms.nihr.ac.uk). The notification should include:

- Confirmation date of when recruitment ceased,
- Confirmation of final recruitment total,
- If there is any patient/participant follow up associated with the study, and what the duration is,
- If the study is associated with any ongoing or future sub-studies included in the original IRAS submission,
- If you expect this study to open further recruitment in the future?

6.2.6 Confidentiality Advisory Group (CAG)

If you have an application with the Confidentiality Advisory Group (CAG), when your study is completed, you should email the confidentiality advice team as soon as possible. The confidentiality advice team will review the information provided, update the approval register and email to confirm they have received the notice.

The application will remain on the approval register for at least 12 months following notification of closure.

6.3 Study Reports

Transparency in clinical research is vitally important and the publication of results from research studies forms part of this process. For all studies a final report should be compiled to detail the conduct and findings of the study, regardless of whether the study was deemed successful or not.

For those trials sponsored by NuTH the responsibility for compiling and submitting the final study report is delegated to the CI (with Trial Manager support). A copy of the final study report must be forwarded to NuTH sponsor team for review prior to submission to the REC or MHRA.

6.3.1 Clinical Trials of Medicinal Products

A copy of the final study report must be submitted within 12 months of the end of trial unless the study is a paediatric trial falling within the scope of the Paediatric Regulation (1901/2006) in which case the report should be submitted within 6 months.

Investigators are expected to take into account the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Guideline E3 – Structure and Content of Clinical Study Reports when preparing the final study report.

The report should be uploaded via CESP, with a copy forwarded to the relevant REC. A copy must also be submitted to the appropriate NuTH sponsor team.

In addition to the final report, clinical trial summary results must also be uploaded to the European Clinical Trials Database (EudraCT) as per the Commission's Guidelines EudraCT Public website - Home page (europa.eu) https://eudract.ema.europa.eu on posting and publication of result-related information. This must be within 12 months (6 months for trials falling within the scope of the Paediatric Regulation).

Responsibility for upload of EudraCT results lies with the sponsor but may be delegated to the CI (with support from the Trial Management Team). The clinical trial summary report does not need to be submitted to the MHRA as well, however a short confirmatory email must be sent to CT.Submission@mhra.gsi.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. (An acknowledgment email or letter will not be returned.)

6.3.2 Medical Devices

For those device trials subject to a Notice of No Objection from the MHRA, the outcome of the clinical investigation must be documented in a final study report.

Investigators should follow the structure proposed in EN ISO 14155:2011 – Clinical Investigation of Medical Devices for Human Subjects – Good Clinical Practice. The MHRA may request a copy of the final report of a clinical investigation of a device. A copy may be requested under certain circumstances, e.g. where a SAE has occurred associated with a CE-marked device which had undergone clinical investigation authorised by the UK Competent Authority, or where a novel technology has been investigated.

6.3.3 Other Studies

A copy of the final study report should be submitted to the REC within 12 months of the end of the study. There are a number of guidelines in place to aid investigators with the format of their end of study report, depending upon the type of study conducted.

Randomised Controlled Trials may be reported in accordance with the CONSORT Statement and extensions which was developed to aid author to prepare reports of trial findings in a complete and transparent manner - http://www.consort-statement.org/extensions

Qualitative research may be reported in accordance with the consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups - http://intqhc.oxfordjournals.org/content/19/6/349.long

For all other studies, investigators should use the search function on the Equator Network to identify any applicable guidelines for reporting their specific research study - http://www.equator-network.org/?post_type=eq_guidelines&eq_guidelines_study_design=experimental-studies&eq_guidelines_clinical_specialty=0&eq_guidelines_report_section=0&s

If there are no applicable guidelines, then investigators should follow the HRA advice regarding the minimum content for a final study report:

- whether the study achieved its objectives
- what the main findings of the study were
- any arrangements for publication or dissemination of the research, including any feedback to participants.

6.4 Dissemination of Results to Participants

Increased transparency in clinical research also extends to informing the participants of the results of the study, both at an individual level (i.e. informing participants of blinded studies what intervention they had been randomised to) and the overarching findings of the study.

Investigators should consider compiling a lay summary of the study report for review by the participants. This can then be distributed to participants or, for those studies looking at potentially sensitive topics or disease areas, be placed somewhere participants can access them if they choose to (e.g. study website).

6.5 Archiving

Following submission of the final study report, all of the study related and essential documents must be archived. For those studies sponsored by NuTH, investigators and trial teams must follow the 'Archiving Clinical Research Documents' SOP.

7 References

7.3 Health Research Authority - http://www.hra.nhs.uk/research-community/end-of-study-and-beyond/notifying-the-end-of-study/

7.4 MHRA: Clinical trials for medicines: manage your authorisation, report safety issues - https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues

7.5 Common European Submission Portal - https://cespportal.hma.eu/Account/Login?ReturnUrl=%2f

7.6 Human Tissue Authority - https://www.hta.gov.uk/

7.7 EudraCT - https://eudract.ema.europa.eu/

7.8 Clinical Investigations of Medical Devices - https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/508494/Guidance_for_mfrs_on_clinical_trials__GN1__-_16_Mar_2016.pdf

7.9 Commission Guideline — Guidance on posting and publication of result-related information on clinical trials - European Commission, official website (europa.eu)
7.10 Equator Network - http://www.equator-network.org/library/
7.11 ICH GCP E3 – ICH Official web site : ICH
7.12 MHRA Good Clinical Practice Guide Good clinical practice: guidance and inspections - GOV.UK (www.gov.uk)
7.13 HRA – guidance on dissemination of information Publication and dissemination of research findings - Health Research Authority (hra.nhs.uk)
7.14 NJRO SOP for Archiving Documents - Newcastle Joint Research Office (NJRO) (newcastlejro.com)