STANDARD OPERATING PROCEDURE

DO NOT USE THIS SOP IN PRINTED FORM WITHOUT FIRST CHECKING IT IS THE LATEST VERSION

The definitive versions of all UHPNT RD&I Dept SOPs appear online, not in printed form, to ensure that up to date versions are used. If you are reading this in printed form check that the version number and date below is the most recent one as shown on the Trust's website: https://www.plymouthhospitals.nhs.uk/researchers

Study Closure

SOP No: SC1

Version No: 3.1

Effective Date: Jan 2019

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Page: **1** of **12**

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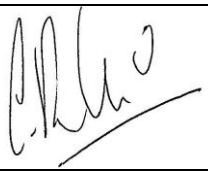
Signature:	
Date:	18th Jan 2019

1 Purpose and Scope

The purpose of this Standard Operating Procedure (SOP) is to describe the requirements relating to the end of a clinical trial.

In accordance with The Medicines for Human Use (Clinical Trial) Regulations (2004) and the Health Research Authority Standard Operating Procedures, written notification for the End of Trial shall be given for all CTIMPs and non-CTIMPs within 90 days of the global end of trial, or within 15 days if the trial is terminated early.

Final analysis of the data and report writing is normally considered to occur after formal declaration of the end of trial. A summary of the final research report must be sent to the REC (and MHRA for CTIMPs and Medical Devices) within 12 months of the end of the trial.

In scope: research hosted by, and/or sponsored by University Hospitals Plymouth NHS Trust (UHPNT).

Definitions

CI	Chief Investigator
ClinicalTrials.gov	is a registry of clinical trials. It is run by the United States National Library of Medicine (NLM) at the National Institutes of Health, and is the largest clinical trials database, currently holding registrations from over 230,000 trials from 195 countries in the world.
CONSORT	Consolidated Standards of Reporting Trials
CTIMP	Clinical Trial of an Investigational Medicinal Product
CTU	Clinical Trials Unit
GCP	Good Clinical Practice
HCA	Health Care Assistants
HRA	Health Research Authority
ICH	International Council for Harmonisation
ISF	Investigator Site File
ISRCTN	International Standard Randomized Controlled Trial Number registry is a primary clinical trial registry recognised by WHO and ICMJE that accepts all clinical research studies (whether proposed, ongoing or completed), providing content

	validation and curation and the unique identification number necessary for publication. All study records in the database are freely accessible and searchable.
LVLP	Last Visit of the Last Patient
MHRA	Medicines and Healthcare products Regulatory Agency
UHPNT	University Hospitals Plymouth NHS Trust
PI	Principal Investigators
RD&I	Research Development & Innovation
REC	Research Ethics Committee
RO	Research Office
SOP	Standard Operating Procedure
TMF	Trial Master File

2 Who should read this document?

All staff involved in conducting research e.g. Chief Investigators (CI), Principal Investigators (PI), Research Nurses & Midwives, Health Care Assistants (HCA), RD&I Managers and Clinical Trial Administrative staff

3 Procedure to Follow

3.1 Responsibilities:

Sponsor: Regulation 27 of The Medicines for Human Use (Clinical Trials) Regulations 2004 (Statutory Instrument 2004/1031) states that 'within 90 days of the conclusion of a clinical trial the sponsor shall notify the licensing authority and the relevant ethics committee in writing that the trial has ended.'

In trials where UHPNT takes on the sponsor responsibility for End of Trial management the UHPNT will delegate the duties to the CI, who may delegate these duties further to their trials team, or to a Clinical Trials Unit (CTU), where appropriate.

Chief Investigators (CI): The CI takes on responsibility for procedures surrounding the end of the trial. The CI may delegate specific tasks to members of their team. It is strongly recommended to have delegation of tasks documented, e.g. on the trial delegation log.

3.2 Procedure:

3.2.1 Defining End of Trial

The European Commission guidance on the End of Trial states that the protocol should include:

- a clear and unambiguous definition of the end of the trial in question. In most cases this will be the date of the last visit of the last patient (LVLP) undergoing the trial. Any exceptions to this should be justified in the protocol; and
- a description of the plan for the provision of any additional care for the trial participants once their participation in the trial has ended, where it differs from what is normally expected according to the medical condition of the clinical trial participant.

Where a trial is multi-national the declaration refers to the End of Trial in all participating countries and not just in the UK.

3.2.2 End of Trial declaration

As soon as the End of Trial has been reached the following should be undertaken:

For CTIMPs:

- Notify the Competent Authority (MHRA in the UK) and the REC within 90 days of trial conclusion via a 'Declaration of the End of Trial Form'
- For CTIMPs where the UHPNT is the Sponsor or has accepted Sponsor responsibilities for End of Trial reporting send a copy of the ' Declaration of the End of Trial Form' to the RD&I Office (RO) at time of sending to the MHRA and REC
- For trials sponsored externally refer to their own procedures
- Ensure other organisations are notified as defined in contractual agreements
- The MHRA and REC should acknowledge receipt of the declaration; ensure acknowledgment is received and filed in the Trial Master File (TMF).
- For CTIMPs the CI must liaise with pharmacy to ensure that study drug accountability is performed and excess study drug is returned or destroyed as appropriate. The CI should ensure drug accountability logs and records of drug returns and or destruction are filed in the TMF and locally by the PI in the Investigator Site File (ISF), or where these documents will be retained by pharmacy, a file note should be filed in the TMF and ISF to document the location of these documents.

For non-CTIMPS:

- Notify the REC within 90 days of trial conclusion using the HRA 'Declaration of the end of a study' form

- For non-CTIMPs where the UHPNT is the Sponsor or has accepted Sponsor responsibilities for End of Trial reporting, send a copy to the RO at time of sending to the REC
- For trials sponsored externally refer to their own procedures
- Ensure other organisations are notified as defined in contractual agreements
- The REC should acknowledge receipt of the declaration; ensure acknowledgment is received and filed in the TMF.

3.2.3 Early Termination

For CTIMPs:

- Notify the Competent Authority (MHRA in the UK) and the REC within 15 days of trial conclusion *via* a 'Declaration of the End of Trial Form'.
- For CTIMPs where the UHPNT is the Sponsor or has accepted Sponsor responsibilities for End of Trial reporting send a copy of the ' Declaration of the End of Trial Form' to the RO at time of sending to the MHRA and REC
- For trials sponsored externally refer to their own procedures
- Ensure other organisations are notified as defined in contractual agreements
- The MHRA and REC should acknowledge receipt of the declaration; ensure acknowledgment is received and filed in the Trial Master File (TMF).

For non-CTIMPS:

- Notify the REC within 15 days of trial conclusion using the HRA 'Declaration of the end of a study' form
- For non-CTIMPs where UHPNT is the Sponsor or has accepted Sponsor responsibilities for End of Trial reporting, send a copy to the RO at time of sending to the REC
- For trials sponsored externally refer to their own procedures
- Ensure other organisations are notified as defined in contractual agreements
- The REC should acknowledge receipt of the declaration; ensure acknowledgment is received and filed in the TMF.

3.2.4 Abandoned trials

It is recommended that if a trial is abandoned prior to commencement (where commencement is defined as the study having all approvals in place to start) the Chief Investigator notifies the Sponsor within 30 days of the decision to abandon the study. The sponsor will then notify the main REC and the MHRA by letter outlining the reasons for abandoning the trial. This should be done before the Annual Progress Report and/or Development Safety Update Report is due. If the REC/competent authority subsequently request that a specific form be provided, this should be sent within requested timelines.

For trials abandoned post-commencement for any reason the 'Early Termination' process described above must be followed.

- Ensure any relevant documentation including confirmation of receipt from MHRA and REC is filed in the TMF.

3.2.5 Trial analysis

Following the End of Trial notification, trial analysis is expected to occur as described in the protocol and/or the Statistical Analysis Plan. Other activities will be ongoing at this point, such as data entry, analysis and report writing. Quality activities can be ongoing, the expectation is that the authorities are informed when the trial conduct has completed, the trial does not have to be closed out and reported at the point of the end of trial notification. Following the end of both CTIMP or non-CTIMP trials, the sponsor has one year to provide the authorities with a report on the trial outcome.

3.2.6 Trial Reports

Following the trial analysis, a trial report has to be generated. This may take the form of a publication. For publications of randomised trials, the CONSORT (Consolidated Standards of Reporting Trials) statement guidelines should be followed http://www.consort-statement.org/ .

In addition, a summary report must be provided to the REC and for CTIMPs to the MHRA; this summary report must be generated within 12 months of the End of Trial date.

Summary reports for CTIMPs

- Collate the summary report taking into account the ICH guidelines for structure and content
- Provide the summary report to the MHRA and REC within 12 months of the actual End of Trial date
- For CTIMPs where the UHPNT is the Sponsor or has accepted Sponsor responsibilities for End of Trial reporting send a copy of the summary report to the RO at time of sending to the MHRA and REC
- For trials sponsored externally refer to their own procedures
- Ensure other organisations are notified as defined in contractual agreements
- Ensure all correspondence with the MHRA and REC is retained in the TMF
- At the time of reporting to the MHRA and REC, the CI must ensure the clinical trial summary results are also be posted in EudraCT and should be completed within twelve months following the End of Trial (six months for paediatric CTIMPs). Further information can be found on the European Medicines Agency webpages
- If agreed, send a copy of the summary of the End of Trial report to trial sites.

Summary reports for Non-CTIMPs

- For non-CTIMP research, the HRA website sets out the minimum requirements for the final summary report
- Provide the summary report to the REC within 12 months of the actual End of Trial date
- For non-CTIMPs where UHPNT is the Sponsor or has accepted Sponsor responsibilities for End of Trial reporting send a copy of the 'Declaration of the end of a study' Form to the RO at time of sending to the REC
- For trials sponsored externally refer to their own procedures
- Ensure other organisations are notified as defined in contractual agreements
- Ensure all correspondence with the REC is retained in the TMF
- If the study has been registered on a clinical trials registry (International Standard Randomized Controlled Trial Number (ISRCTN) or ClinTrials.gov) the CI must ensure the clinical trial summary results are also be posted on the relevant site and this should be completed within twelve months following the End of Trial. A clinical trials registry is an official platform and catalogue for registering a clinical trial and allows free public access. Further information can be found on the www.isrctn.org, https://clinicaltrials.gov/ webpages or the HRA webpage http://www.hra.nhs.uk/about-the-hra/our-plans-and-projects/transparency/
- If agreed, send a copy of the summary of the End of Trial report to trial sites.

3.2.7 Publications

The HRA has set out its expectations for the publication and dissemination of research. Researchers and sponsors are expected to ensure, as a minimum:

- Registration of research, including publication of summary results, on a suitable publicly-accessible register (ISRCTN or ClinTrials.gov)
- Reference to the IRAS ID number in publications and reports to allow tracking of fulfilment of transparency commitments made to the funder and REC

3.2.8 Patient and public involvement activities

At the end of the research study you will be expected to fulfil commitments made to research participants. This may include:

- Care after research
- Providing information about the outcome of a study

Participants in clinical trials and other interventional studies including diagnostic studies should be given information at the end of a study explaining:

- How their care might change i.e. do they return to treatment as usual or will the study drug / intervention still be available for their continued treatment?
- When they can expect the summary findings to be made available

- How they will be given access to the summary findings

For further information please see the HRA webpage guidance on participants at the end of the study.

3.2.9 Archiving

Following the end of study closeout visit the trial maybe archived. The CI is responsible for ensuring that the study documentation including source data are archived for a minimum of five years (longer if required by the regulation or the study funder). The trial report is added to the archived study on its completion; see SOP SC2 Archiving for further details.

4 Document Ratification Process

The review period for this document is set as ***default of three*** years from the date it was last ratified, or earlier if developments within or external to the Trust indicate the need for a significant revision to the procedures described.

This document will be approved by the ***RD&I Manager or their Deputy***.

Non-significant amendments to this document may be made, under delegated authority from ***a Senior RD&I manager***, by the nominated author. These must be ratified by ***a Senior RD&I manager***.

Significant reviews and revisions to this document will include a consultation with ***appropriately knowledgeable staff***. For non-significant amendments, informal consultation will be restricted to ***staff*** who are directly affected by the proposed changes.

Dissemination and implementation

4.1. Dissemination of this SOP

4.1.1. New SOPs and new versions of existing SOPs: The Research Governance Manager will be responsible for ensuring authorised SOPs are uploaded on the RD&I intranet site. Internal Trust Staff are expected to use the RD&I intranet site to access latest versions of SOPs and to check the website regularly for updates.

Notice of new or amended procedural documents that have undergone a major amendment will be given *via* the following routes:

- Inclusion in the Trust weekly e-bulletin Vital Signs
- Direct email to Trust Researchers and or teams

4.2. Training in this SOP

4.2.1. All staff whose activities are subject to this SOP should ensure that they read and understand the content of the SOP.

5 Reference material

EudraLex - Volume 10 - Clinical trials guidelines:
https://ec.europa.eu/health/documents/eudralex/vol-10_en

Clinical Trials Toolkit
http://www.ct-toolkit.ac.uk/routemap/clinical-trial-summary-report/
http://www.ct-toolkit.ac.uk/routemap/unique-trial-number/

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

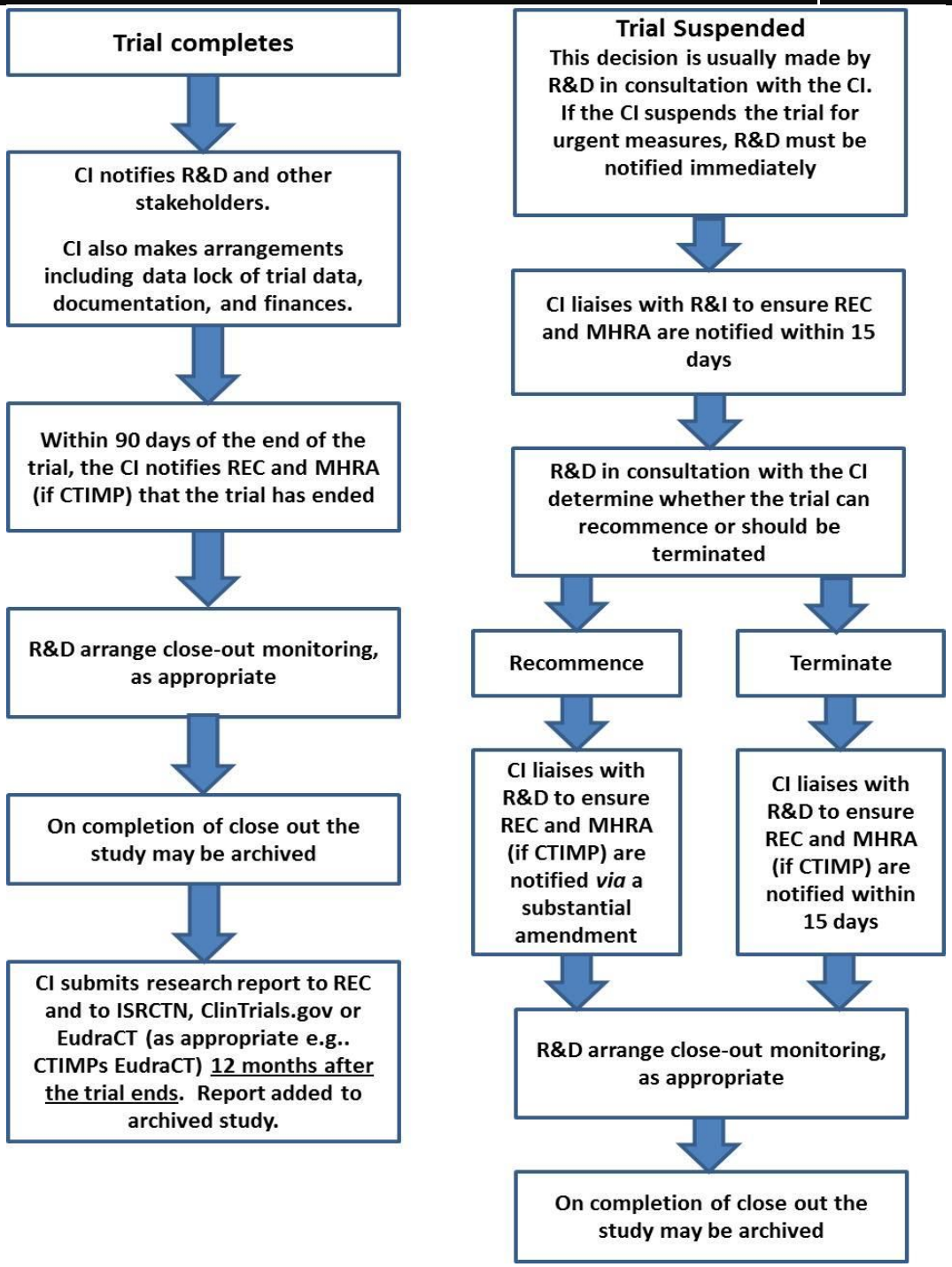
ICH E3 Guideline: Structure and Content of Clinical Study Reports:
http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500002832.pdf

European Medicines Agency: 'Posting of clinical trial summary results in European Clinical Trials Database (EudraCT):
https://eudract.ema.europa.eu/
http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2014/06/news_detail_002127.jsp&mid=WC0b01ac058004d5c1

MHRA webpage including guidance on withdrawal of trial before a decision on authorisation is reached:
https://www.gov.uk/clinical-trials-for-medicines-apply-for-authorisation-in-the-uk

HRA webpage guidance on participants at the end of the study:
http://www.hra.nhs.uk/research-community/end-of-study-and-beyond/participants-at-the-end-of-study/

Appendix: Flow chart for study closure of Trust Sponsored studies — Appendix 1



6 Amendment History

Version Number:	3.1
Date of Amendment:	Jan 2019
Details of Amendment:	Updated Trust and Dept. name; Reduce signature requirement to single senior RD&I Manager.

Version Number:	3.0
Date of Amendment:	Aug 2017
Details of Amendment:	Updated SOP template and numbering system. Reviewed and updated SOP.

Version Number:	2.2 (minor amendment)
Date of Amendment:	Jan 2015
Details of Amendment:	Add the requirement of end study reports to submitted to the MHRA within 12 months of the study completion. Add the requirement to upload study results onto the EudraCT database within 12 months of the study completion. Remove templates from SOP

Version Number:	2.1 (minor amendment)
Date of Amendment:	Mar 2012
Details of Amendment:	Cover page - Change of SOP location address.

Version Number:	2.0
Date Of Amendment:	September, 2010

Details Of Amendment: Appendix 1 updated with latest version of the Declaration of the End of Trial Form.