Standard Operating Procedure CCTU/SOP077

End of Trial Procedures for CCTU Led Non-CTIMPs

1. Scope

This SOP applies to Cambridge Sponsored Non-CTIMP clinical research trials conducted in collaboration with the CCTU.

This SOP does not cover commercial research or international trials

2. Purpose

To ensure that end of trial procedures for CCTU managed Non-CTIMPs are in accordance with relevant regulatory, Research Governance and GCP requirements.

3. Definitions and Abbreviations

The headings below contain the definitions of terms and meaning of abbreviations used within the document.

3.1. Definitions

Term	Definition
Cambridge Sponsored	Sponsored by Cambridge University Hospitals NHS Foundation Trust (CUH); or the University of Cambridge (UoC); or jointly by CUH and UoC OR Sponsored by: Cambridge University Hospitals NHS Foundation Trust (CUH) or CUH jointly with the University of Cambridge or Cambridgeshire & Peterborough NHS Foundation Trust (CPFT) or CPFT jointly with the University of Cambridge
Archiving	The process of preparing and storing documents for a defined period of time to preserve their integrity and readability
Early Termination	An earlier end of the clinical trial, based on grounds of safety. Other grounds, such as faster recruitment than anticipated, are not considered an 'early termination'
End of Trial	The date of the last visit of the last participant or the completion of any follow-up monitoring and data collection as described in the protocol.
Essential Documents	Those documents that individually or collectively permit the evaluation of the conduct of a trial and the quality of the data generated. Essential documents include the trial master file, investigator site file, source documents, case report forms, sponsor file and the pharmacy file. (Section 8, ICH-GCP E6 (R1).
Investigator Site File (ISF)	The investigator site file is a standard filing system which allows the effective storage and location of essential documents relating to the conduct of a clinical trial at a participating site. The filing system can be in the form of a single project file or a

	number of files. The ISF also encompasses the participating site pharmacy files.
Trial Master File (TMF)	The trial master file is filing system which allows the effective storage and location of essential documents relating to the conduct of a clinical trial. This can be in the form of a single project file or a number of files. The TMF also encompasses the site information file for every participating site involved.
TMF: Site Information	Participating site information and local essential documents held by the co-ordinating centre. Technically part of the TMF, these files can be held separately for ease of use.

3.2. Abbreviations

Abbreviation	Meaning
CONSORT	Consolidated Standards of Reporting Trials
HRA	Health Research Authority
ISF	Investigator Site File
PS	Participating Site
REC	Research Ethics Committee
TMF	Trial Master File

4. Undertaken by:

The Chief Investigator is responsible for end of trial activities but some of these activities may be delegated to members of the CI's trial team.

5. Items Required

CCTU/TPL082 CCTU Led Non- CTIMP Monitoring Plan

CCTU/FRM017 Site Archiving Location Form

HRA Declaration of End of Trial Form

https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/ending-your-project/

CCTU/TPL061 Remote Monitoring Report

CCTU/TPL037 End of Trial Report

CCTU/TPL069 Close out Monitoring Report

6. Summary of Significant Changes

New

7. Method

The following sections provide a description of the processes to be followed when implementing this document's procedures.

7.1. Notification of End of Trial

The definition of the end of the trial should 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

7.2. End of Trial Responsibilities

It is the CI's responsibility to declare a trial completed when it reaches the end of trial as defined in the protocol. The CI/delegate will:

- Ensure the HRA Declaration of End of Trial Form is completed and sent it to the REC via e-mail within 90 days of the end of trial. The form is available from the HRA website at:

  https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/ending-your-project/

- For Medical device trials, manufacturers are required to notify the MHRA when a clinical investigation comes to an end
- File the end of trial notification, submission email and subsequent acknowledgement of receipt in the TMF
- Check the terms of the funder's contract to check whether they require a review
- Provide a copy of the completed end of trial notification form to:
  - The funder
  - All the participating sites for inclusion in the ISF
  - The Sponsor
  - Any labs involved in sample analysis
- Inform collaborators, suppliers, sub-contractors etc. as applicable that the trial is completed
- Ensure that
- All essential documents are present and correct in the TMF including superseded versions
- The close out monitoring report (CCTU/TPL069) has been completed
- All outstanding remote monitoring reports (CCTU/TPL061)from sites are collected and all queries resolved
- All SAEs, SADES and USADES have been collected, entered into the DB reported as appropriate, queries resolved and data cleaning has been completed
- All participating sites have been closed appropriately and have been instructed to archive their trial related documentation (ISF, pCRFs etc.)
- The randomisation system (if applicable) is closed
- Sample analysis has been completed
- Stored samples are either destroyed or put into long term storage according to details stated in the IRAS application

Within 12 months of the end of trial ensure that:

- The statistical analysis is complete and the database has been hard locked
- In collaboration with the trial team, the End of Trial Report (CCTU/TPL037) is completed and provided to the CCTU Operations Director for review who will grant Sponsor's permission to submit to REC (and to MHRA for medical devices
- Prepare and submit end of trial reports to the funder according to their instructions and template (if required)
- Ensure that all trial publications are notified to the sponsor and ensuring these are filed/archived as appropriate

7.2.1. Early Termination

The Chief Investigator (CI) should explain clearly the reasons for early termination. The CI should notify:

- The REC as directed by the HRA website
- The Funder
- HRA (via hra.approval@nhs.net, only for trials exempt from REC approval)
- The Sponsor
- The Confidentiality Advisory Group (CAG) (if applicable)
- MHRA (for medical device investigations). This responsibility is usually delegated to the manufacturer

7.2.2. Change to end of trial definition

If the end of trial has not been completed prior to the current end of trial definition a substantial amendment must be submitted for an extension to the duration of the trial.

This should be submitted and approved within 90 days of the end of trial definition, as stated in the protocol

7.3. Lead Site Closure

The lead sites may only be closed after the close out monitoring visit refer to:

- CCTU/TPL082 CCTU Led Non-CTIMP Monitoring Plan
- CCTU/TPL 069 Close- Out Monitoring Report

All monitoring queries must be answered, resolved and documentation returned to the coordinating team.

Specific attention should be paid to reconciliation of:

- Data queries
- Sample management if appropriate
- Medical devices if appropriate

Once all required documents have been provided for inclusion in the TMF, the CI/designee will arrange for site close-out as specified in CCTU/TPL082 CCTU Led Non-CTIMP Monitoring Plan

7.4. Participating Site Closure

Close out monitoring can be on site or remote as specified in the trial specific Non-CTIMP monitoring plan.

If monitoring is remote, the Coordinating team will distribute CCTU/TPL0061 Remote Monitoring Report to participating sites.

Participating sites must complete and return the form in advance of site closure

Specific attention should be paid to:

- Confirmation of archiving arrangements for the ISF Complete form CCTU/FRM017
- Checking ISF documentation according to the trial specific monitoring plan
- On-going responsibilities for the site staff for example collection of patient long-term follow-up data, provision of information in the event of an Audit or Inspection or long term safety reporting for patients included in the trial
- Clinical device reconciliation (for device investigations only)
- Laboratory sample reconciliation if applicable as detailed in the trial specific monitoring plan

Participating Sites may only be closed when all monitoring queries have been answered, resolved and documentation returned to the coordinating team.

7.5. Financial Closure

Financial closure can only be conducted when all milestones with the funder(s) have been met and payments received.

When the end of trial definition is met any outstanding payments should be made and confirmation of account closure obtained.

The funder will request a report for trial expenditure. This should be reconciled at the end of the trial once all payments are complete.

7.6. Trial Publications

- At the request of the Research Compliance Committee, the Sponsor will review any publication prior to submission and all reasonable comments from the Sponsor will be incorporated prior to publication
- The publication policy should be detailed in the protocol and IRAS form submitted to REC
- The CI should refer to the funding contract where appropriate to ensure that they comply with the terms and conditions of the report publication policy.
- For any publication or dissemination of clinical trials and clinical research follow the guidance given by the Consolidated Standards of Reporting Trials (CONSORT), http://www.consort-statement.org/consort-2010
- Publications should be sent to the sponsor with a copy placed in the TMF

7.7. End of Trial Confirmation

Once the End of Trial acknowledgements have been received from the main REC and R&D the trial can be considered closed and archiving procedures can be initiated.

CCTU/FRM017 must be completed and sent to the Coordination team for inclusion in the TMF

8. Monitoring Compliance with and the Effectiveness of this Document

a. Process for Monitoring Compliance and Effectiveness

As part of routine monitoring visits, audit and inspection

b. Standards/Key Performance Indicators

This process forms part of a quality management system and is reviewed according to CCTU procedures. Standard Operating Procedures are reviewed every two years.

9. References

The Institute of Clinical Research, Abbreviations used in Clinical Trials.

MHRA, Good Clinical Practice "Grey Guide"

10. Associated Documents

CCTU/SOP006 CCTU Archiving Process

11. Equality and Diversity Statement

This document complies with the Cambridge University Hospitals NHS Foundation Trust service equality and diversity statement.

12. Disclaimer

It is the user's responsibility to check against the electronic library that this printed out copy is the most recent issue of this document.

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