ECTU Central Office SOP ECTU_SOP_TM_14: End of Trial Notification and Close-out

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Document Revision History		
Version No.	Effective Date	Summary of Revisions
1.0	27 Sep 2017	Initial creation
2.0	21 Oct 2019	Updates after scheduled review. Content moved to new ECTU SOP template v 2.0. Minor changes throughout, updated section 4.
3.0	15 Jun 2022	Updates after scheduled review. Content moved to new ECTU SOP template v 3.0. Minor changes throughout, updated section 4.

1.0 PURPOSE

This SOP outlines the procedures for preparing to close out trials that are managed by Edinburgh Clinical Trials Unit (ECTU).

2.0 SCOPE

This SOP applies to all clinical studies adopted by ECTU where trial closeout has been delegated to the Trial Manager (TM) or designee within ECTU. This SOP should be used in conjunction with any relevant sponsor SOPs relating to trial close-out.

3.0 RESPONSIBILITIES

End of trial responsibilities are detailed in the co-sponsorship agreement. These may be delegated to the TM or designee who is responsible for coordinating this process. Trial Management responsibilities may include some or all of those listed below:

- Ensure that all relevant sponsor/ECTU guidance and SOPs are followed during the close-out process
- Ensure that all end of trial notifications are sent to the relevant bodies in a timely manner.
- Timelines for data cleaning/database lock/data analysis are agreed
- A plan for dissemination of results including to trial participants has been determined by the chief investigator after discussions with the Trial Steering Committee and documented.
- Relevant final meetings e.g. TSC/DMC are organised and reports are submitted to relevant bodies.
- Ensure that all finances have been reconciled before the grant end date.
- Prepare and archive the Trial Master File.

4.0 PROCEDURE

There are a number of actions to be performed as part of the trial closeout, these will vary according to the type of trial and the requirements of the Sponsor and Funder. The Trial Manager or designee is responsible for identifying the specific actions for each trial.

4.1 Preparation for End of Trial Meeting

4.1.1 The trial end date should be defined in the latest version of the trial protocol. If this is not specified in the protocol then the date of the last patient, last visit should be used.

4.1.2 The primary members of the trial team who should be invited by TM or designee and attend this meeting are:

- Trial Manager or designee
- Chief Investigator
- Trial Statistician
- Sponsor representative e.g. Clinical Trials monitor (if applicable)
- Data Management

- IT Programmer
- Any other appropriate trial team member (e.g. Research Nurse)

4.1.3 The Trial Manager or designee should prepare an agenda to cover the main end of trial actions and close-out procedures (see Section 4.2). ECTU End of Trial Meeting Agenda Template (TM-T2X) should be used and adapted as required.

4.2 End of Trial Meeting

The TM is responsible for ensuring that minutes are taken during and circulated after the meeting to all members of the team who attended or who were invited but unable to attend. The minutes should be filed in the Trial Master File.

The following should be discussed at the End of Trial Meeting. This list is not exhaustive and may vary according to the nature of the trial.

4.2.1 End of Trial Notifications

4.2.1.1There may be several different organisations who require a formal End of Trial Notification procedure to be followed when the trial ends. These will often require notification from the Chief Investigator but the Trial Manager will be responsible for ensuring these requirements are identified and discussed at the End of Trial Meeting and co-ordinating the submission in a timely manner as required.

4.2.1.2The main organisations that will need to be informed are listed below, however, this is not an exhaustive list and will vary from trial to trial.

- Trial Sponsor
- MHRA (for CTIMP/device studies)
- Research Ethics Committee (REC)
- NHS Research and Development
- Trial Funder(s)

4.2.1.3 End of trial notifications should be carried out following the Sponsors appropriate Study closure and archiving SOPs .

4.2.2 Data Cleaning

4.2.2.1 The Trial Manager should discuss with the Data Manager, prior to the End of Trial Meeting, how long they estimate the data cleaning and reconciliation will take (based on current outstanding data, volume and type of queries). A minimum of six weeks would usually be practical for this but this should be finalised with the data management team and trial statistician to avoid unachievable dates being set. The Trial Manager should also ensure that the final QC check of the data is performed as agreed if this applies to the trial.

4.2.2.2.The IT Programmer should be made aware that there may be requests for reports or amendments to the database during the final data cleaning process, e.g. primary outcome reports, AE reports, reports for QC checks, uploading spreadsheets

4.2.2.3 The data should be cleaned and ready to be handed over to the Trial Statistician two weeks prior to the database lock date to allow for any final queries or anomalies that may require resolution. Any informal discussion regarding data cleaning should be documented.

4.2.3 Database Lock

The Trial Statistician should advise on a date for the database lock based on the length of time required to carry out the data analysis in relation to any reporting and publication deadlines and individual schedules.

This should be agreed upon by the Chief Investigator, Data Management team, Trial Management team, Trial Statisticians and Health Economics team if applicable.

4.2.4 Final Data Monitoring Committee (DMC) and/or Trial Steering Committee (TSC)

Trial specific TSC and/or DMC Charters should be followed along with the current protocol and funder requirements paying particular attention to the requirements for the release of trial results and dissemination.

4.2.5 Publications and Dissemination of Trial Results

The Trial Manager should discuss the publication plan with the Chief Investigator including establishing the authorship of the final paper, which publications the final paper will be submitted to, any conference presentations etc. The process of dissemination of trial results to participants and uploading results to relevant protocol registration databases (e.g. ISRCTN, ClinicalTrials.gov) should be established and responsibilities agreed.

4.3 Notification to sites and trial teams

The following teams should be notified as appropriate:

- Sponsor Pharmacovigilance

The Trial Manager should inform the Pharmacovigilance team, by email, of the agreed database lock date and the date the analysis is to start. The Pharmacovigilance team will be responsible for reconciling and locking their database in accordance with this timeline.

- Principal Investigators and Site Teams

The Trial Manager should inform the Principal Investigators and Site Teams via email of the final data deadlines and database lock dates. They should advise them of the final data cleaning process and what that will entail. The sites should also be informed of any final actions they are responsible for (e.g. final sample shipments, archiving etc.)

4.4 Site and Pharmacy Close-Out

4.4.1 Trial Sites should be closed out as soon as it is practical to do so.

4.4.2 For sites that have recruited participants to the trial and have collected data for the final analysis, the site should remain open until the database lock is complete in case any further action is required during this time.

4.4.3 In studies that are monitored by Clinical Trial monitors, close-out visits should be scheduled prior to database lock to ensure that any site-specific data related issues identified during close-out are addressed prior to statistical analysis.

4.4.4 Sites and Pharmacies should be closed out according to the Sponsor guidelines. The Sponsor, or if delegated to the trial management team, will arrange for a final close-out visit if required according to the study monitoring plan.

4.4.5 The Principal Investigator is responsible for ensuring that all actions are completed in accordance with Sponsor close-out procedures. Trial Manager will have oversight of this process to ensure it is completed appropriately. The sponsor Study Closure Checklist (if available) should be used to document these actions have been completed.

4.4.6 The ECTU Close Out Tracker should be adapted and used to aid this process.

4.4.7 The Trial Manager should ensure that arrangements are made for any final sample shipments if this applies to the trial. This includes liaising with the receiving site to ensure they can accept the samples, arranging a timeframe for shipments and arranging courier services.

4.4.8 The Trial Manager should also ensure final invoices have been received from the site if appropriate.

4.5 Archiving

4.5.1 The table of responsibilities in the site agreement will specify who is responsible for archiving which documentation (e.g. sites may be responsible for archiving their own data or this may have been delegated to ECTU). The sponsor guidelines on archiving should be followed.

4.5.2 The protocol should state the archiving period (the funder may have specific requirements for this). If not stated in the protocol, the data should be archived according to the Sponsors requirements as detailed in their archiving guidelines.

4.5.3 The Chief Investigator is responsible for meeting the costs for archiving and this must be paid in advance. The trial manager or designee should ensure the invoice for archiving costs is submitted before the grant end date.

4.6 Financial Close-out

4.6.1 The UoE will officially close down the trial grant three months after the trial end date. The Trial Manager will be responsible for ensuring that all finances have been reconciled by that point.

4.6.2 If any further expenses are expected after the grant closure, the Trial Manager should confirm how much of the funds can be held back for this.

4.6.3 All financial reporting will be compliant with the research funders' requirements and relevant UoE policy and procedures.

4.6.4 The Trial Manager should remind UoE Finance approximately 3 months before the financial reconciliation report is due to ensure they have it scheduled.

5.0 RELEVANT DOCUMENTS AND REFERENCES

ACCORD SOPs for UoE/NHSL Sponsored studies
(available at http://www.accord.scot/research-access/resources-researchers/sop)

- CR009 Study Closure and Archiving
- GS005 Archiving Essential Study Documentation
- CM003 Closeout Visits
- CR009-F01 Study Closure Checklist

ECTU Templates

- TM-T24 ECTU Close Out Tracker
- TM-T28 ECTU End of Trial Meeting Agenda