Close Out Visits

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1 Introduction

1.1 The Academic & Clinical Central Office for Research & Development (ACCORD) is a joint office comprising clinical research management staff from NHS Lothian (NHSL) and the University of Edinburgh (UoE).

1.2 As per ICH-GCP E6 (R2) guidelines, sites may require a close out monitoring visit to ensure that all trial documentation is completed prior to archiving. Close out visits will be scheduled according to the monitoring plan.

1.3 The end of a study will be defined in the study protocol. Studies may also finish early or specific sites may close ahead of schedule due to poor recruitment or the discovery of data indicating that the study should be stopped.

2 Purpose

2.1 To document the procedure for close out visits for NHSL and/or UoE sponsored studies selected for monitoring, both at a site level and at a study level to ensure all required actions are closed prior to final analysis.

3 Scope

3.1 This Standard Operation Procedure (SOP) applies to the Senior Clinical Trials Monitor, Clinical Trials Monitor or any other individual, who will conduct and document the close out visit (COV) on behalf of the sponsor(s).

4 Responsibilities

4.1 The Clinical Trials Monitor, or designee, is responsible for conducting the COV (including reporting and follow up).

4.2 The Senior Clinical Trials Monitor, or designee, is responsible for allocating a member of the monitoring team, or designee, to carry out the COV and for reviewing the COV report.

4.3 The Principal Investigator (PI), or designee, is responsible for completing the site level close out checks required by the site close out checklist (CM003-T03) during remote site close out and confirming that all site level close out actions are followed up to resolution.

5 Procedure

5.1 Close out Visit Preparation

5.1.1 For multi-centre trials the Clinical Trials Monitor will meet with the Trial Manager during the course of the study to agree a plan for site and study close out. Close out training for sites will be discussed and provided where necessary. This meeting will be documented in a contact report (CM002-T02). For single centre trials there is no requirement to meet with the Trial Manager prior to close out however this meeting can take place if required.

5.1.2 The Clinical Trial Monitor, or designee, will adapt the close out templates (CM003-T01-T06) to be study specific where required. Where this task is delegated, e.g to the Trial Manager, they will provide the study specific templates to the assigned Clinical Trial Monitor for review prior to use.

5.1.3 The Clinical Trials Monitor, or designee, will contact the site to schedule the COV (onsite or remote as required by the monitoring plan (CM004-T01).

5.1.4 Where the close out visit is to be conducted remotely the Clinical Trials Monitor, or designee, will provide the site with a copy of the study specific Site Level Close Out Checklist (CM003-T03) for completion by the Principal Investigator (PI), or designee. The PI, or designee, will complete the Site Level Close Out Checklist (CM003-T03) as fully as possible to confirm that all close out activities, as described in the COV report (CM003-T02), have been reviewed/completed prior to the close out visit (see section 5.2). If it is not possible to complete all actions listed in the Site Level Close Out Checklist (CM003-T03) prior to the remote close out visit, the outstanding actions will be discussed as part of this visit.

5.1.5 Where a site received Sponsor Authorisation to Open (SATO) but did not recruit, i.e. did not consent a participant, remote completion of CM003-T03 will be considered

sufficient for site close out. A close out visit is not required for these sites. Any required documents will be provided for filing in the TMF and the ISF will be managed as per local site policy.

5.1.6 Where a site has been sent clinical trial supplies e.g. Investigational Medicinal Product (IMP) or medical device for clinical investigation, but did not receive SATO, completion of CM003-T03 is still required to document full accountability for the clinical trial supplies provided to site. Any required documents will be provided for filing in the TMF and the ISF will be managed as per local site policy.

5.1.7 The Clinical Trials Monitor, or designee, will request that the PI ensure the Investigator Site File (ISF) is complete in accordance with the appropriate document checklist (CR001-T01, CR001-T02 or CR001-T03). Where the COV will be carried out remotely PI oversight of the ISF will be documented through signature of the PI Declaration in Section 1 of CM003-T03.

5.1.8 Where possible, the Clinical Trials Monitor, or designee, will schedule in advance time with the PI (either onsite or remotely) to ensure that any required signatures are obtained and to explain the close down procedure and the legal requirement to ensure documentation is complete.

5.1.9 Where required the Clinical Trials Monitor, or designee, will schedule time with any supporting departments (e.g. pharmacy, radiology) that participated in the trial to ensure their documentation is complete and that study materials and Investigational Medicinal Products (IMPs) / Investigational Agents / Medical Devices have been accounted for/reconciled.

5.1.10 The Clinical Trials Monitor, or designee, will review the most recent monitoring visit report and identify any outstanding actions to be resolved. These actions will be followed up with the PI for resolution before or during the COV, as appropriate.

5.2 During the Site Close Out Visit

5.2.1 The close out visit will be conducted remotely (e.g. by telephone or video call) or onsite according to the study monitoring plan (ACCORD SOP CM004). Where the visit is conducted remotely the completed Site Level Close Out Checklist (CM003-T03) will be reviewed prior to the visit by the Clinical Trials Monitor, or designee, where possible and any issues with completion noted for discussion during the site close out visit.

5.2.2 Where the visit is conducted onsite the Site Level Close Out Checklist (CM003-T03) will

be completed during the visit by the Clinical Trials Monitor, or designee.

5.2.3 The Clinical Trials Monitor, or designee, will discuss the archiving process and responsibilities with the PI, or designee. The outcome of the discussion will be documented in the COV report (CM003-T02) and also in the follow up letter (CM003-T06)

5.2.4 Where the site close out is for an NHS Lothian site the Clinical Trials Monitor, or designee, will contact the R&D Administration Manager, or designee, to initiate archiving procedures following the COV, where required, as specified in GS005 (Archiving Essential Study Documentation).

5.2.5 The COV Report (CM003-T02) and Site Level Close Out Checklist (CM003-T03) will be used by the Clinical Trials Monitor, or designee, as a guide to ensure that all site level close out activities are completed.

5.2.6 Where the visit is conducted onsite the Clinical Trials Monitor, or designee, will conduct a full and final review of the ISF, where required by the study source data verification (SDV) plan (CM004-T02).

5.2.7 The Clinical Trials Monitor, or designee, will advise the PI, where relevant, with regard to the requirements and timelines for writing the clinical study report, as specified in CR011 (Research Study Reports & Publication of Results).

5.2.8 The Clinical Trials Monitor, or designee, will meet with the PI or site contact at the end of the COV to discuss any findings and any actions. If there are any serious issues uncovered at the COV, these must be raised with the PI and Senior Clinical Trials Monitor as soon as possible. If the PI is not available in person then follow-up will be carried out via a phone call or e-mail. Any phone or e-mail contact must be documented in the COV report or Contact Report (CM002-T02).

5.2.9 Where a remote site close out visit cannot successfully verify that all close out requirements have been completed an onsite close out visit will be triggered.

5.3 Post Site Close Out Visit

5.3.1 If there are missing documents noted during final ISF review, the Clinical Trials Monitor, or designee, will refer to the TMF or other relevant sources to locate required documentation. Documents can be provided to the PI, or designee, with the final close out follow up letter, detailing in the follow up letter the document(s) enclosed.

Where essential documents are deemed absolutely unrecoverable, a file note can be used to detail attempts to locate the documents.

5.3.2 Subsequent to the visit, the COV report (CM003-T02) and follow-up letter will be prepared by the Clinical Trials Monitor, or designee, who conducted the visit. The report will be completed with factual information only. No personal opinions or comments will be documented in the report.

5.3.3 The COV report will be subject to review by the Senior Clinical Trials Monitor, or designee, in accordance with the monitoring plan, before the follow up letter is provided to the study site. Review must be completed by an individual who did not perform the COV.

5.3.4 The COV follow-up letter will be sent to the PI, by the Clinical Trials Monitor, or designee, copying in any relevant study team members. If any issues relate to supporting departments, these departments will also be copied in. In the follow-up letter it will be made clear which actions are intended for the study team.

5.3.5 Target times for completion of COV report, completion of review and sending follow up letter to PI are outlined in the monitoring plan. Where target times were not met justification will be documented.

5.3.6 The COV report will be made available to the sponsors' representative(s). Copies of the close out visit report and follow-up letter will be stored securely in the TMF and/or Sponsor File held within the ACCORD monitoring office.

5.3.7 Any significant findings identified at a COV will be highlighted to the sponsors' representative(s) as soon as possible and discussed at the Sponsorship Meeting.

5.3.8 Actions identified during the COV will be followed up until resolution using the COV actions log (CM003-T05). A copy of the action log will be provided to site with the follow up letter. Once all actions are resolved the PI will sign the close out statement to document oversight of close out and return to the Clinical Trial Monitor, or designee.

5.3.9 The Clinical Trials Monitor, or designee, will issue a Final Close Out Letter (CM003 - T08) to the site to confirm that close out for that site is complete.

5.4 Study Level Close Out Visit

5.4.1 During the course of close out, the Clinical Trials Monitor will complete the Study Level Close Out Checklist (CM003 - T04). This checklist will be used to track study level close out progress.

5.4.2 All sites will undergo a site close out visit, where appropriate, prior to final database lock and analysis of the trial dataset. This will ensure any data related issues identified at site close out are resolved prior to analysis of the dataset. Any actions identified at close out visits which impact the study dataset, pharmacovigilance (PV) or non-compliance line listings must be resolved prior to final database lock. The Site Level Close Out Checklist (CM003-T03) and Study Level Close Out Checklist (CM003-T04) highlight which actions require resolution prior to database lock. See Close Out Process Flow (CM003-T07) for further details on the sequence of study close out events.

5.4.3 The Clinical Trials Monitor will review the Trial master file (TMF)/Sponsor File (SF) held by ACCORD for completeness as part of the study level close out. Where the TMF is held external to ACCORD a review will be arranged to ensure the completeness of the TMF as part of the study close out process where required by the SDV plan. This review may be carried out onsite or remotely.

5.4.4 Once all tasks on the Study Level Close Out Checklist (CM003-T04) are complete the monitor will send the completed checklist to the Senior Clinical Trial Monitor, or designee, for review.

6 References and Related Documents

- CM003 -T02 Close Out Visit Report
- CM003 - T03 Site Level Close Out Checklist
- CM003 - T04 Study Level Close Out Checklist
- CM003 – T05 Close out action log
- CM003 - T06 Close Out Follow Up Letter
- CM003-T07 Close out Process Flow
- CM003-T08 Final Close Out Letter
- CM002-T02 Contact Report
- CM002-T03 Monitoring Visit Actions Log
- CR001-T01 Document Checklist (CTIMP)
- CR001-T02 Document Checklist (non-CTIMP)
- CR001-T03 Document Checklist (Medical Device)
- CR011 Research Study Reports & Publication of Results
- ICH-GCP E6(E2) Guidelines

7 Document History

Version Number	Effective Date	Reason for Change
1.0	14 SEP 2011	New procedure.
2.0	05 FEB 2016	Updated SOP template. Amalgamation of close out visit report (CM003-T02) and Close out Visit Checklist (CM003 –T01).
3.0	15 AUG 2018	Change of author. Routine review and update of SOP template and Close Out Visit Report (CM003 - T02)
4.0	13 JUN 2019	Section 5.2.2 updated to remove reference to the Business Research Manager. Minor administrative changes.
5.0	24 FEB 2022	Change of author. PI responsibilities added. Section 5.1 added to describe general close out preparation. Original section 5.1 and 5.2 (now section 5.2 and 5.3) updated to include remote close out visit preparation and completion. Section 5.3 (now section 5.4) updated to remove specific requirement to follow up AE reporting prior to COV report sign off, include references to the Close Out action log (CM003-T05), Close Out follow up Letter (CM003-T06) and Final Close Out Letter (CM003-T08). Original Section 5.4 removed as remote close out process is now embedded within main close out sections of SOP and replaced with study level close out process. Updates to close out visit report (CM003-T02) to make this more site close out specific. Addition of new templates CM003-T03 Site level close out checklist, CM003-T04 Study level close out checklist, CM003-T05 Close out action log, CM003-T06 Close out follow up letter, CM003-T07 Close out Process flow and CM003-T08 Final Close Out Letter.
6.0	23 MAY 2023	Sections 5.1.4, 5.2.1 and 5.4.2 updated to provide clarification to close out process.

		Site level close out checklist (CM003-T03) updated to provide clarification for use of template and update layout of checks to be performed. Study level close out checklist (CM003-T04) updated to add additional check that the ACCORD Pharmacovigilance (PhV) Team have confirmed all PhV documentation filed in TMF/SF.
7.0	08 JUL 2025	Section 5.1.5 updated to clarify process for sites that receive SATO but do not recruit. Section 5.1.6 updated to clarify process for sites that receive SIV but no SATO. Section 5.3.6 updated to clarify documents provided for sponsor representatives. Section 5.4.5 removed as this does not accurately reflect the close out process. Close Out Visit Report (CM003 – T02) updated to avoid repetition of information already captured in Site level close out checklist and streamline completion (CM003 – T03). SOP and associated templates (except CM003-T07 as n/a) transferred to current SOP template.

8 Approvals

Sign	Date
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Alice Graves Alice Graves (20-Jun-2025 13:42 GMT+1) APPROVED: Alice Graves, Senior Clinical Trials Monitor, NHS Lothian, ACCORD	20-Jun-2025
L. Mackenzie AUTHORISED: Lorn MacKenzie, QA Manager, NHS Lothian, ACCORD	20-Jun-2025

CM003 SOP Close Out Visits v7.0

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