LOUGHBOROUGH UNIVERSITY RESEARCH OFFICE
STANDARD OPERATING PROCEDURE

Loughborough University (LU) Research Office
SOP–1024 LU

Study Closedown and End of Study Reporting for NHS Research Sponsored by Loughborough University

Effective Date: October 2015

1.0 Introduction

This Standard Operating Procedure (SOP) describes the procedures for reporting and documentation requirements for the closure of research sponsored by Loughborough University (LU). The document covers closure as defined in the protocol, along with early termination for safety, ethical or logistical reasons and closure of individual sites in Multi-centre studies.

The outcome is that the Sponsor is able to confirm study closure.

2.0 Scope

This SOP applies to all research sponsored by Loughborough University.

3.0 Procedure

Trial closure should be performed as defined in the study protocol and in accordance with regulatory requirements and Good Clinical Practice guidelines (GCP). Any planned changes to the end of study should be submitted as a Substantial Amendment to the REC, appropriate regulatory bodies, and the NHS Trust R&D in accordance with SOP -1026 LU Sponsor Approval Process for Amendments.

The objective of trial closure is to ensure that:

- The rights and wellbeing of all participants have been protected
- All essential documents have been stored appropriately in the Trial Master File (TMF) and Investigator Site Files (ISF)

- The correct approved version of the protocol was used and adhered to
- Any SAEs (Serious Adverse Event), and SUSARs (Suspected Unexpected Serious Adverse Reaction) have been reported appropriately
- Source Data Verification (SDV) has been undertaken
- Monitoring has been performed as described in the study monitoring plan
- All contractual requirements have been met
- Any outstanding queries between the Sponsor and sites are resolved
- A study close-out report is produced

Plans for close down should be included in the monitoring plan and discussed during the Sponsor Risk Assessment and Approval Process (Appendix 1).

Archiving is covered in the Archiving SOP-1032 LU Archiving of Essential Documents.

3.1 Planned closure

It is expected that the definition of planned study closure will be outlined in the study protocol. The end of study would usually be described as the last visit of the last patient or the final follow-up completion and data collection. Plans for closing the study should be discussed during the Sponsor Risk Assessment and Approval Process, and included in the monitoring plan.

Final analysis of the locked database should occur after a study close down report has been completed. In cases of unblinding for randomised studies, written approval will be required.

It is the responsibility of the Sponsor to ensure that study closure tracking and study end dates are maintained on the database. The aim is to support the production of an accurate overview and reporting of research activity sponsored by LU.

It is the responsibility of the Chief Investigator to discuss study closure with the Sponsor and to complete relevant required documentation. The Sponsor will ensure that the regulatory authorities and REC receive completed documentation within 90 days in accordance with required timelines.

Where required, a study close down visit will be performed. The site close down report (Appendix 2) and site close down visit logs (Appendix 3) must be completed and appended to the monitoring reports / monitoring plan.

Database lock, validation and cleaning, must be done in accordance with SOP -1036 LU Data Management Process.

3.2 Premature Termination / Early Closure

As Sponsor LU has a legal responsibility to notify the Research Ethics Committee (REC) as relevant that a study has terminated early at a site within 15 days of the termination, irrelevant of reason. It may also be necessary to notify the following:

- Trial Management Group / Data Safety Monitoring Committee (where they have not been involved in the decision)
- Funding body / study finance staff
- All site investigators for multi centre studies

Research can be terminated prior to the planned closure date or event because of:

a. Adverse Events
b. Slow recruitment
c. Sponsor decision
d. Investigator decision
e. Regulatory decision

It is essential that the CI discuss the process with the Sponsor to ensure that appropriate documentation is completed and submitted within the required timelines.

3.2.1 Multi-centre studies

Closure of multi-centres must be documented and retained in the Investigator Site Files (ISF) and within the site section of the Trial Master File (TMF).

Confirmation of closure must include the justification of the closure, the number of participants still receiving treatment and the proposed management of those participants where appropriate.

A letter thanking the site for their contribution with an overall summary of the participants must be sent by the CI. The correspondence must include a reminder that the PI will be required to comply with any future audits or inspections of the closed study. There must be an agreed plan to resolve any financial balances, and information about the publication process.

The expectation will be that archiving of site study documentation be managed by the individual site. This will be discussed at the initial set up of the study along with the process to be used, and individuals responsible for close down of individual sites.

3.3 Final Report

A report of the study findings, negative and / or positive must be produced within one year of the closure date.

LU as Sponsor will track this date using the database and will remind the investigator at least 30 days prior to the due date.

4.0 Archiving

Essential Documents must be archived in accordance with the Archiving SOP 1032 LU. Details of what documents are regarded as ‘essential’ are detailed in the SOP 1015 LU.

5.0 Responsibilities

	Responsibility	Undertaken by	Activity
1	Chief Investigator (CI) in collaboration with Sponsor	CI & Sponsor	Determine whether the Study: • Is due to conclude as described in the study protocol; OR • Requires an extension to the end date; OR • Is to terminate early, and why.
2	CI	CI / PI	Discuss with Sponsor regarding study conclusion or extension requirement. Complete required documentation.
3	Sponsor	Research Governance Officer or their delegate	Maintain the relevant database/s with the end date and study status related to closure or extension based on information from the CI and set reminders for final reports
4	Sponsor / CI	CI	Inform the regulatory authorities and the REC, and all other relevant parties as necessary copying in the Sponsor to all correspondence.
5	Sponsor	Research Governance Officer or their delegate	Ensure that all relevant parties are informed within the required timelines.
6	Sponsor/CI	Research Governance Officer or their delegate /CI	Finalise the study files ensuring all necessary documents are present in TMFs / ISFs and ensuring all end of study procedures are completed.

6.0 Monitoring and Audit Criteria

Key Performance Indicator	Method of Assessment	Frequency	Lead
All research sponsored by LU has appropriate study close down procedures in place.	Included in the monitoring / audit programme.	Random audits / monitoring conducted on 10% of research activity.	Research Governance Officer or their delegate

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This table is used to track the development and approval of the document and any changes made on revised / reviewed versions

DEVELOPMENT AND APPROVAL RECORD FOR THIS DOCUMENT		
Author / Lead Officer:	Jackie Green	**Job Title:** Research Governance Officer

Approved by:	Ethics Committee	**Date Approved: 23/10/15**

REVIEW RECORD			
Date	**Issue Number**	**Reviewed By**	**Description Of Changes (If Any)**

DISTRIBUTION RECORD:			
Date	**Name**	**Dept**	**Received**

Appendix 1

Sponsor End of Study / Close-down Proforma

Study Title (in full):	
Reference No:	

	Yes	No	In progress	Date Completed
Has an appropriate public database been identified for registration of the study?	☐	☐	☐	
Is the end of study defined in the Protocol?	☐	☐	☐	
Are the plans for archiving study documentation from all sites clear?	☐	☐	☐	
Is there adequate funding available for archiving for all sites or centrally?	☐	☐	☐	
Is there a named individual responsible for study close down at each site?	☐	☐	☐	
Has the individual responsible for authoring the end of trial reports been identified?	☐	☐	☐	
Has the individual responsible for ensuring publication been identified?	☐	☐	☐	
Has individual responsible for database 'lock' at each site been identified?	☐	☐	☐	
Has appropriate electronic storage been identified at each site or centrally?	☐	☐	☐	
Has study close out been included in the Monitoring Plan?	☐	☐	☐	

Appendix 2

LU Site Close Down Report

Site Information

Site:	
Study title:	
Study number:	
Centre name:	
Investigator name:	
Date of visit:	

List of site and monitoring personnel in attendance

Name	**Position**

Study Status

Planned patient number	
Number of patients randomised	
Number of patients completed	
Number of patients withdrawn	
Number of patients lost to follow up	
	Comments:

1. Protocol

Items Discussed/verified	**Yes**	**No**	**Version/comment**
Is the current approved protocol on file?			
Is the protocol signed and dated?			
Are superseded protocols on file?			
Is there a protocol deviation log on file?			
Have protocol deviations been reported/reviewed by PI?			
Comments/Findings			

2. Ethics

Items discussed/verified	Yes	No	Comments
Are all original applications/submissions/approvals on file?			
Are all substantial amendments complete and on file?			
Are all non substantial amendments complete and on file?			
Ethics correspondence on file?			
Notification of trial completion on file?			
Comments/Findings			

3. Competent Authority

Items Discussed/verified	Yes	No	N/A	Comments
Are all original applications/submissions/approvals on file?				
Is there CTA acknowledgement of amendment letter/s?				
Notification of trial completion on file?				
Comments/Findings				

4. R&D

Items Discussed/verified	Yes	No	Comments
Are all original applications/submissions/approvals on file?			
Are all substantial amendment/s complete and on file?			
Are all non substantial amendment/s complete and on file?			
Notification of trial completion on file?			
R&D Correspondence on file?			
Comments/Findings			

5. Investigator Site Personnel

Items Discussed/verified	Yes	No	Comments
Is the delegation of authority and signature log updated to reflect end of study			
Confirm that all CVs/GCP/training records are up to date and on file			
Comments/Findings			

6. Standard Operating Procedures

Items Discussed/verified	Yes	No	Comments
Is the delegation of authority and signature log updated to reflect end of study			
Confirm that all CVs/GCP/training records are up to date and on file			
Comments/Findings			

7. Study Documentation

Items Discussed/verified	Yes	No	Versions/Comments
Is the current approved patient documentation on file?			
Are all superseded patient documents on file?			
Are previous versions of study documentation marked as superseded?			
Is there a copy of the current Case Report Form on file?			
Are all superseded Case Report Forms on file?			
Comments/Findings			

8. Subject Documentation

Items Discussed/verified	Yes	No	Comments
Is there a current screening log template on file?			
Is the Subject Screening log complete?			
Is there a current Enrolment Log template on file?			
Is the Enrolment Log complete, including an outcome for each subject?			
Comments/Findings			

9. Randomisation

Items Discussed/verified	Yes	No	N/A	Comments
Is there documentation of the Randomization Process on file?				
Where is the Master Randomization List held?				
Evidence of correct blinding as per study protocol?				
Comments/Findings				

10. Informed Consent

Items Discussed/verified	Yes	No	Comments
Are all consent forms present and correctly completed?			
Has 100% consent audit been undertaken and documentation of the audit on file?			
Is informed consent process properly documented in the medical/trial records			
Comments/Findings			

11. Safety Reporting/Pharmacovigilance

Items discussed/verified	Yes	No	N/A	Comments
Are SAE reporting Guidelines/SOP and Pharmacovigilance/Governance contact on file?				
Is there a Current SAE form Template on file?				
Are SAE reports and associated acknowledgement correspondence from Sponsor/R&D on file?				
Are SUSAR reporting guidelines on file?				
Are SUSAR reports and associated acknowledgement correspondence from Sponsor/ R&D on file?				
Are there signed and dated annual Development Safety Update Report(s) on file?				
Comments/Findings				

12. Monitoring

Items Discussed/verified	Yes	No	Comments
Is study initiation and subsequent monitoring visit documentation on file?			
Is the monitoring log complete and on file?			
Comments/findings			

13. Clinical Laboratory/Specimen Collections

Items Discussed/verified	Yes	No	N/A	
Have central Labs been used?				
Are the current and previous Central Lab accreditations on file?				
Is Central Lab normal reference ranges on file?				
Are there signed and dated copies of CVs of Heads of departments?				
Have Local Labs been used?				
Are the Local Laboratory current and previous accreditation certificates on file?				
Local Lab normal reference ranges				
Are sampling and sample handling procedures documented/is there a lab manual on file?				
Are specimen results reviewed and signed and dated by PI?				
Are specimen results that are out of range marked as clinically significant or not clinically significant?				
Are sample logs/records complete and on file?				
Is there on going storage of samples for future research?				
If yes; Are storage conditions monitored and recorded?				
Have all samples been analysed and destroyed as per protocol?				
Have the retained samples been sent to Central Labs or destroyed? (Unless permission to keep samples for future research)				
Has all supplied equipment been returned?				
Comments/Findings				

14. Pharmacy

Items Discussed/verified	Yes	No	N/A	Comments
Are Pharmacy Staff GCP and CVs up to date and on file?				
Is the Delegation of Authority and signature log updated to reflect end of study?				
Are instructions in place with regards to handling trial medication and trial related materials? Dispensing procedure Randomization/resupply/returns and destruction?				
Is there a Pharmacy approved Prescription template on file?				
Records of drug dispensing on file and has the drug been correctly dispensed with all completed prescriptions on file?				
Have drug accountability records been completed?				
Have any drug excursions been recorded?				
Have any drug been quarantined?				
Are all required GMP, certificate of analysis and QP release documents on file?				
Comments/Findings				

15. Financial/Legal agreements

Items Discussed/verified	Yes	No	N/A	Comments
Are all completed documents relating to contracts, finance, funding, indemnity and sponsorship on file?				
Comments/Findings				

16. Study Related Supplies

Items Discussed/verified	Yes	No	N/A	
Are all study related supplies documents completed and on file?				
Are all maintenance and calibration records completed and on file?				
Comments/Findings				

17. Annual/Final Reports

Items Discussed/verified	Yes	No	
Are annual progress and where applicable safety reports to the Ethics Committee on file?			
Are R&D confirmations of annual report receipt on file?			
Comments/Findings			

18. Publication

Items Discussed/verified	Yes	No	
Are copies of all study analysis publications on file?			
Comments/Findings			

19. Correspondence

Items Discussed/verified	Yes	No	
Is all study related correspondence on file?			
Comments/Finding			

20. Source Data Verification

Items Discussed/verified	Yes	No	Comments
Are all CRFs complete and all data queries resolved?			
Has all patient identifiable data been removed?			
Where required, has a 'do not destroy' dated sticker been added to the patient notes?			
Comments/Findings			

21. Data Protection

Items Discussed/verified	Yes	No	Comments
Are computer records and files containing identifiable data stored on a remote and secure server?			
Is the emergency recovery procedure for retrieving data available?			
Is access to electronic study records and files password protected?			
Are electronic data files for analysis anonymised?			
Is there provision in place for suitable archiving?			

If yes are details logged with the R&D office?			
Comments/Findings			

22. Other – if not covered above

Items Discussed/verified	**Yes**	**No**	
Comments/Findings			**Category**

Additional Comments/Overview

Confirmation by Sponsor/Sponsors delegate that the study is ready for closure.
Name (Print) ……..
Signature ……..
Role ……..

LU Site Closedown Visit Log

Date of Visit:

Chief Investigator:

LU Sponsor Reference:

Principle Investigator:

Study Title:

Site :

Name	Role in study	Signature