1. Introduction

1.1 This Standard Operating Procedure (SOP) describes the procedures for reporting and details documents required to fully close research sponsored by the University Hospitals of Leicester NHS Trust (UHL). This document covers site/s closure as defined in the protocol, as well as procedures required implementing early termination for safety, ethical or logistical reasons and closure of individual sites in multi-centre studies.

1.2 The outcome is that the Sponsor is able to confirm that the study site/s has been fully closed prior to confirmation of end of sponsor green light

2. Scope

2.1 This SOP applies to all research sponsored by the UHL.

3. Procedure

3.1.1 Trial closure should be performed as defined in the study protocol and in accordance with regulatory requirements and Good Clinical Practice guidelines (GCP) as appropriate. Any planned changes to the closure of a study should be submitted as a Substantial Amendment to the HRA, REC, appropriate regulatory bodies, and the NHS Trust R&I in accordance with SOP S-1017 UHL.

3.1.2 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 as appropriate in the Trial Master File (TMF) and/or Investigator Site Files (ISF)
- The correct approved version of the protocol / clinical investigation plan was used and adhered to
- IMP accountability has been carried out where required
- Any SAEs, and SUSARs have been reported where appropriate
- Any SAE/SADE/USADEs and device deficiencies for medical device studies have been reported as appropriate
- DSURs have been submitted where required
- Source Data Verification (SDV) has been undertaken as appropriate
- Correct labelling, and accountability has been undertaken for medical device studies (where relevant)
- Monitoring has been performed as described in the study monitoring plan where relevant and all monitoring findings have been signed off
- All contractual requirements have been met
- Any outstanding queries between the Sponsor and sites are resolved
- A study end of study declaration has been submitted to the REC, HRA and MHRA (where applicable) and acknowledgement of declaration received.

3.1.3. Plans for site/s close-down should be included in a monitoring plan. Not all studies sponsored by UHL require a monitoring plan so closure processes should be discussed during the Sponsor Risk Assessment and Green Light Process as detailed in SOP S-1002 UHL, SOP S-1003 UHL, SOP S-1014 UHL, and SOP S-1007 UHL revisited as part of the Annual Reporting process.

3.1.4 The End of Sponsor Green light process is detailed in SOP S-1045. Archiving is covered in the Archiving SOP S-1029 UHL.

3.2 Planned Closure

3.2.1 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 Green Light Process and included in the monitoring plan where relevant.

3.2.2 Final analysis of a 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 in accordance with the UHL Pharmacy Unblinding SOP 412.

3.2.3 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 the UHL. This is carried out through Attributes and Workflows in EDGE.

3.2.4 It is the responsibility of the Chief Investigator (CI) to discuss study closure with the Sponsor and to complete relevant required documentation. The Sponsor will ensure that the Regulatory Authorities and HRA/REC receive completed documentation within 90 days of the agreed closure date in accordance with required timelines.

3.2.5 Where required, a study close-down visit will be performed. The site close-down report (Appendix 1, 1a) and site close-down visit logs (Appendix 2) must be completed and appended to the monitoring reports / monitoring plan.

3.2.6 For Non CTIMP/ CE marked Medical Device studies, where an on-site closedown visit is not undertaken, the Study Closedown checklist (Appendix 3,3a) must be completed and signed by the CI/Principal Investigator (PI), a copy sent to the Sponsor with a copy filed in the TMF/ISF. Database lock, validation and cleaning, must be done in accordance with SOP S-1031 UHL Data Management process for research Sponsored by UHL.

3.3 Premature Termination / Early Closure

3.3.1 As Sponsor the UHL has a legal responsibility to notify the Competent Authority (MHRA) HRA & Research Ethics Committee (REC) as relevant that a study has terminated early at a site within 15 days of the termination, irrelevant of reason.

3.3.2 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
- Medicinal product supplier

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

a. Unsafe events attributed to the Study IMP (Investigational Medicinal Products)
b. Poor toleration of the IMP
c. Unsafe events/ Device deficiencies attributed to medical device(s)
d. Poor tolerance related to use of medical devices
e. Slow recruitment
f. Sponsor decision
g. Investigator decision
h. Regulatory decision (e.g. MHRA)

3.3.4 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.

3.4 Multi-Centre Studies

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

3.4.2 Confirmation of closure must include the justification; the number of participant's still receiving treatment and the proposed management of those participants where appropriate.

3.4.3 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.

3.4.4 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.

3.5 Final Report

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

3.5.2 UHL as Sponsor will track this date using the EDGE database and will remind the investigator at least 30 days prior to the due date, further reminders will be sent as per sponsor SOP S-1030. A copy of the final report and any publication(s) must be supplied to the Sponsor and filed in the TMF.

3.5.3 CTIMP studies: the final report and any associated publications must be uploaded to the public database identified in the application. With effect from January 2021 EudraCT is not used by the UK to publish results. This should be done using either Clinicaltrials.gov or ISCRTN until the HRA have finalized an appropriate portal. The CI must ensure that study status is maintained and regularly updated on the relevant platform

3.5.4 Non-CTIMP studies / CE marked medical device studies: At study closure the study status must be updated on www.clinicaltrials.gov. This is the responsibility of the CI.

3.6 Sponsor Database

3.6.1 The Sponsor, or their delegate, will update the relevant Sponsor database (EDGE) workflows to record closure.

4. 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	R&I Deputy Chief Operating 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. For CTIMPs: update relevant registry with final study report and status. For both CTIMPs and non-CTIMPs, CE marked and Non CE Marked Device studies update the study status on the relevant public database.
5	Sponsor	R&I Deputy Chief Operating Officer or their delegate	Ensure that all relevant parties are informed within the required timelines.

	Responsibility	Undertaken by	Activity
6	Sponsor	R&I Deputy Chief Operating Officer or their delegate	Finalise the study files ensuring all necessary documents are present in TMFs / ISFs and ensuring all end of study procedures are completed. Update Sponsor database (EDGE).
7	Chief Investigator	Chief Investigator	Provide Sponsor with a copy of the final report/ publication. File a copy of the final report/ publication in the TMF.

5. Who Guideline Applies To

5.1 This guideline applies to all staff within UHL and external to UHL who are delivering research at Leicester's Hospitals.

6. Guideline Standards and Procedures

6.1 The SOP is detailed so the process can be clearly followed. No supporting flowchart is required / provided.

7. Education and Training

7.1 None.

8. Monitoring & Audit Criteria

Key Performance Indicator	Method of Assessment	Frequency	Lead
All research sponsored by UHL has appropriate study close down procedures in place.	Included in the monitoring / audit programme.	Random audits / monitoring conducted on 10% of research activity.	R&I Deputy Chief Operating Office or their delegate

9. Supporting Documents and Key References

SOP S-1024 Appendices 1, 1a, 2, 3 & 3a
SOP S-1002
SOP S-1003
SOP S-1007
SOP S-1014
SOP S-1017
SOP S-1029
SOP S-1030
SOP S-1031
SOP S-1045
UHL Pharmacy Unblinding SOP 412

10. Key Words

10.1 Research, Innovation, Volunteers, Participants, Trials, HRA, Sponsor, Closedown, Closure Termination, GCP, REC, TMF, ISF

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

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Author / Lead Officer:	Carolyn Maloney	**Job Title:** R&I Deputy Chief Operating Officer
Reviewed by:	R&I Governance Meeting	
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Date	**Issue Number**	**Reviewed By**	**Description Of Changes (If Any)**
May 2015	2	Carolyn Maloney	Changes to Logos and corporate identity
September 2016	3	CM, LW, JJ	Consistency checks and updates.
February 2017	4	Carolyn Maloney	Update to Logo
February 2021	5 & 6	CM JJ, LW	Updated R&I logo Update to include CE and NON-CE marked device studies Specified requirement to updated EudraCT, www.clinicaltrials.gov and any research database detailed in the REC/HRA/ MHR application. Requirement to provide final report to Sponsor & file in TMF Requirement to complete end of sponsor green light processes. Referenced EDGE Reformatting to new trust template
February 2022	7	LW, JJ	Update and title change and current changes in transparency requirements

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