Title: Study Close Down

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For Trust-wide SOPs, please check this is the **latest version of the SOP** on the Joint Research Office website:www.ucl.ac.uk/joint-research-office.

For Departmental SOPs, please check this is the **latest version of the SOP** with the Research Unit QA Manager.

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Revision Chronology:

Version Number:	Effective date:	Reason for change:	Author:
1	26/09/2014	Initial standardised SOP for use within UCLH.	Patricia Galligan
2	06/11/2017	Entire SOP updated to reflect current processes. U.K Policy Framework for Health and Social Care Research (Version 3.2, 10/10/2017) incorporated into SOP revisions. Additional detail and clarification regarding processes provided. Updated to current UCLH SOP template. Reviewed by UCLH Research Unit Quality Assurance Managers (CCTU: Shivali Trivedi and NIHR CRF: Selvy Raju).	Mona Hassan
3	30/05/2020	Expired links updated and the use of a study close-down checklist for UCLH-hosted studies has also been referenced. This checklist, located on myUCLH, can be used if the Sponsor is unable to provide a study close-down checklist. SOP updated to current UCLH SOP template. Reviewed by Mona Hassan, JRO Research Quality and Safety Manager and UCLH Research Unit Quality Assurance Managers (CCTU: Celia St Clair and NIHR CRF: Kirsty Adams).	Arti Kara

ACRONYMS

CCTU	Cancer Clinical Trials Unit
CI	Chief Investigator
CRF_1	Case Report Form
CRF_2	Clinical Research Facility
CTIMP	Clinical Trial of Investigational Medicinal Product
HRA	Health Research Authority
IMP	Investigational Medicinal Products
ISF	Investigator Site File
JRO	Joint Research Office
LRN	Lead Research Nurse
MHRA	Medicines and Healthcare Products Regulatory Agency
Non-CTIMP	Any research study that is not a CTIMP
PI	Principal Investigator
QA	Quality Assurance
REC	Research Ethics Committee
RN	Research Nurse
R&D	Research & Development
SOP	Standard Operating Procedure
TMF	Trial Master File
UCLH	University College London NHS Foundation Trust

1. BACKGROUND

This Standard Operating Procedure (SOP) outlines the process for study close down for University College London NHS Foundation Trust (UCLH) hosted CTIMPs and non-CTIMPs, upon the end of the study. Effective study close down is essential to the overall quality management of the study, ensuring data and documentation is up to date, approved, verified and complete, to facilitate potential future audit(s) and/or inspections.

The definition of the 'end of the study' should be clarified within the protocol. In most instances, this will be the date of the last visit of the last recruited participant, or the completion of any follow-up monitoring and data collection described in the study protocol. Any change to this definition after approval for the research has been granted should be processed as an amendment. This route of study closure is classified as planned closure. As soon as the Sponsor confirms that a study has ended, they need to notify the REC (which originally issued favourable opinion of the study) and the MHRA (as applicable) within 90 days of the end of the study. There is no need to additionally notify the Health Research Authority (HRA), however if the study does **not** have an NHS REC approval but holds HRA Approval, the HRA will also need to be notified of the end of study via hra.approval@nhs.net.

Premature termination of a study may occur due to a number of reasons such as unsafe events attributed to the study's intervention or procedure, slow recruitment, Sponsor decision or regulatory decision (e.g. MHRA). If a study closes earlier than expected, the Sponsor has a legal responsibility to notify the HRA, relevant REC and MHRA (as applicable)within 15 days of termination, irrespective of the reason why early termination occurred.

The REC and MHRA (if applicable), will consequently issue a 'Declaration of the End of Study' acknowledgment letter, which may serve as the formal confirmation to sites of study closure.

Final analysis of the data (following 'data lock' of the study database systems, where applicable) and report writing is normally considered to occur after formal declaration of the end of the study. Data Locks to study database systems must be authorised and signed off by the Investigator(s), as a true and accurate reflection of the study specific data entry.

The Sponsor will notify the Principal Investigator (PI) of the end of the study and the research team will then need to proceed to close the study at the participating site. Upon this notification, site level actions at UCLH include forwarding a copy of the **Declaration of the End of a Study Form** (obtained from the Sponsor) to the UCLH/UCL Joint Research Office (JRO) and Pharmacy (if applicable).

2. PURPOSE

The purpose of this SOP is to describe how UCLH study teams should proceed once written confirmation of the end of study, or early termination, is received from the Sponsor.

This SOP should be used in conjunction with local NHS Trust wide and sponsor specific policies and procedures, and complies with the U.K Policy Framework for Health and Social Care Research (and subsequent amendments) and Good Clinical Practice as outlined by the Clinical Trial Regulations.

3. PROCEDURE

	Actions (When? How?)	Responsible persons (Who?)
1	When written confirmation of the end of study is received from the Sponsor by the PI, the PI or their delegate should inform all members of the Study team of the end of the study.	PI or delegated individual
2	A copy of the **Declaration of the End of a Study form** from the Sponsor should be forwarded to the JRO and Pharmacy (if applicable) as soon as possible. For CTIMPs the form is available from the following website: https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues	PI or delegated individual
3	Where UCLH is the Sponsor organisation (for non-CTIMPs), the Declaration of the End of a Study Form should be completed and submitted to the REC and JRO for information. For all other research (non-CTIMPs) the form is available from the HRA website at: http://www.hra.nhs.uk/resources/during-and-after-your-study/end-of-study-notification-studies-other-than-clinical-trials-of-investigational-medicinal-products/ For declarations of end of a **clinical investigation of a medical device**, manufacturers are required to notify the MHRA when a clinical investigation comes to an end. Following receipt of the Declaration of the End of a Study Form, a Declaration of End of Study acknowledgment letter will be issued by the REC (and MHRA if applicable), which may also serve as the formal notification to the participating site that the study has now closed.	CI or delegated individual Device Manufacturer
4	The study team should meet to confirm that all **study-related activities have stopped**. A record of the meeting should be included in the investigator site file/trial master file (ISF/TMF).	Study Team
5	The sponsor site file index should be used to carry out an Investigator Site File (ISF)/Trial Master File (TMF) review. **File notes** should be inserted into the ISF/TMF to explain any missing essential documents (refer to *UCLH SOP 8: Essential Documents and the Site File* for further information on what documents are considered 'essential'). It should be documented that an ISF review has been carried out to identify any discrepancies in documentation and study record keeping.	Delegated individual
6	All site data should be collected, entered, validated and all data queries resolved. **Case Report Forms (CRFs)** should be complete and accurate and the **Database** confirmed as closed.	Delegated individual
7	If applicable: The study monitor will close out all data queries and perform a Study Close Out Visit and produce a **Study Close Out Visit Report** which is to be filed in the ISF/TMF. For studies that do not have a monitor: Study teams can complete this task; templates for study close out reports/checklists should be obtained from the Sponsor. If this is not available from the Sponsor, the associated checklist corresponding to this SOP, the study close-down checklist for UCLH-hosted studies, could be used. This checklist can be found on myUCLH where this SOP has been saved.	Monitor/Study Team
8	All financial matters are resolved and all site payments completed as agreed in the study agreements and approvals.	Delegated individual
9	All unused trial supplies are returned or destroyed, according to the study protocol and/or study agreement and/or requirements of the Sponsor.	Delegated individual

10	Unused IMPs are returned to the Sponsor or destroyed locally on-site (as pre-arranged in the study Agreement and/or other arrangements made with Pharmacy onsite). If an IMP is destroyed on-site, the destruction should be documented in the ISF.	Pharmacy
11	**For trials that introduced a new interventional procedure at UCLH** The principal investigator or clinical lead for a study must refer to the *Introduction of New Interventional Procedures to UCLH* policy; any research that introduced a new interventional procedure to UCLH must obtain approval to continue using this intervention via the Clinical Effectiveness Steering Group (CESG) once this type of study completes. Refer to the policy for further details. **Medical Devices: Research that introduced a new medical device (CE marked and non-CE marked) to UCLH**. Notification must be made to the Medical Devices Committee in accordance with UCLH policy, prior to any devices being used as standard care at UCLH. Refer to guidance available on the Medical Physics and Biomedical Engineering myUCLH page.	Principal Investigator or clinical lead
12	**Use of human tissue/data after research** For studies that involve the collection of data/tissue for future use (i.e. secondary use), steps should be made to ensure these are used in line with the consent provided by participants. Where consent has **not** been obtained for future retention, only anonymised data and acellular material that is not relevant material under the Human Tissue Act 2004 can be retained. In England, Wales and Northern Ireland, samples may be held after the declaration of the end of the trial, for analysis or verification of research data for up to one year. After this period, legal authority to hold any human tissue under the ethical approval for the study will expire. To ensure that any continued storage is lawful, either the tissue must be held on premises with a storage licence from the Human Tissue Authority, or an application made for ethical approval of another study before the favourable ethical opinion of the existing study expires. Otherwise the tissue would need to be destroyed in accordance with the HTA Codes of Practice. Please refer to the Human Tissue Authority's website for further information: https://www.hta.gov.uk/hta-codes-practice-and-standards-0. The IRAS application should outline the study conditions for future use, and it should be determined whether samples or data can be contributed to an existing biobank or data-sharing repository. Otherwise, tissues should be disposed of in accordance with the relevant ethical approval and Human Tissue Authority guidance (as per the Human Tissue Act 2004).	CI & PI
13	**Participants following the end of study** Any commitments made to participants should be fulfilled, including providing information about the outcome of the study, and any care available following the end of the research. This could be in the form of a summary sheet of the findings or advising participants on where they can access the results of the study. Any end of study information sheets that are provided to participants should also be submitted with the final study report to the relevant REC. The HRA provides guidance on disseminating information to participants following the end of the study:https://www.hra.nhs.uk/planning-and-improving-research/best-practice/publication-and-dissemination-research-findings/	CI & PI
14	Investigators should comply with the study publication plan, as outlined in either the study protocol and/or study agreements; the HRA additionally sets out expectations	CI & PI

	for the publications and dissemination of research[1]. The results of the study should be outlined in the **Summary of the Final Research Report**, and submitted via email to the REC (and MHRA if applicable) within 12 months of the end of the study. There is no standard format for final reports, but as a minimum, the REC/MHRA should be informed of whether the study has achieved its objectives, the main findings, and arrangements for publication or dissemination of the research, including any feedback to participants. For medical device studies, according to the HRA, "MHRA (devices) may request a copy of the final report of a clinical investigation of a device. It is likely that a copy would particularly be requested under certain circumstances, e.g. where a serious adverse event has occurred associated with a CE-marked device which has undergone clinical investigation authorised by a UK Competent Authority, or where a novel technology has been investigated".[2] **Notification of end of study to Confidentiality Advisory Group (CAG):** for studies that have applied to the CAG, the HRA provides guidance on how and when to notify the CAG of study completion: http://www.hra.nhs.uk/research-community/end-of-study-and-beyond/notifying-the-end-of-study/.	
15	The Sponsor should be notified that the ISF/TMF is ready for archiving and request an email to confirm that the study team can proceed with archiving. UCLH study teams should refer to UCLH SOP 10 for further details regarding archiving of the ISF/TMF (available on myUCLH and the JRO website). Any queries regarding archiving of the Pharmacy Site File should be directed to uclh.PharmacyCT@nhs.net.	Delegated individual

4. IMPLEMENTATION & TRAINING

Staff following this SOP shall confirm they have read and understood the procedures outlined above by signing the SOP Log and/or completing their relevant training log as a record of acknowledgement (where applicable).

5. PUBLICATION & COMMUNICATION

This SOP is authorised and published on the JRO website: http://www.ucl.ac.uk/joint-research-office. The latest version of the SOP will be made available on the JRO website.

The original fully signed master copy is stored in a designated binder within the JRO and maintained by the JRO Research Quality & Safety Manager (or Research Unit QA Manager if a Departmental SOP).

[1] https://www.hra.nhs.uk/planning-and-improving-research/best-practice/publication-and-dissemination-research-findings/

[2] http://www.hra.nhs.uk/research-community/end-of-study-and-beyond/notifying-the-end-of-study/

6. REFERENCES

Joint Research Office:
http://www.ucl.ac.uk/joint-research-office/

Health Research Authority website (incl. REC and MHRA guidance):
http://www.hra.nhs.uk/research-community/end-of-study-and-beyond/notifying-the-end-of-study/

Human Tissue Act 2004
https://www.hta.gov.uk/policies/human-tissue-act-2004

ICH GCP:
https://www.ema.europa.eu/en/ich-e6-r2-good-clinical-practice

U.K Policy Framework for Health and Social Care Research (and subsequent amendments):
https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/

7. APPENDICES

APPENDIX A:

Study Close Down Checklist for UCLH Hosted Studies Template: the latest version can be found on the UCLH intranet, myUCLH, where this SOP has also been saved.