Document Title: Trial Closure and End of Trial Reporting

Document Number: PTUC SOP021

Staff involved in development: *Job titles only*	Senior R&D Manager, R&D Administration Manager, Research Officers
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Summary of Significant Change(s) (for this version only)

Section(s):	Modification:
	Added section reagrding handling of samples at the end of a study

Key Points of this Document

- This document sets out the procedures to be followed by all Staff who are involved in the close-down, termination, suspension or final reporting of research studies and clinical trials.
- It provides guidance on how patients, staff and trial related documentation is managed during close-out so as to ensure compliance with the Trust's Information Governance Policies, the Data Protection Act (2000), and the Research Governance Framework (2005).

1 Purpose and Content

a. This document defines the Trust's research procedures for trial closure and end of trial reporting of Research Studies and Clinical Trials managed by Royal Papworth Trials Unit Collaboration (PTUC) and sponsored / hosted by Royal Papworth NHS Foundation Trust.

b. The definition of the end of trial is outside the scope of this SOP and is described in PTUC SOP019: Research Protocol Design.

c. The document describes the responsibilities and actions of the Investigator and Sponsor in the event of premature termination or suspension of a trial. The archiving of study data is outside the scope of this SOP and is described in PTUC SOP011: Archiving SOP.

2 Roles & Responsibilities

a. This Policy applies to all personnel who are conducting research at the Trust.

b. Staff involved in running or managing research studies must comply with the requirements set out in section 4.

c. It is the responsibility of the Principal Investigator based at Royal Papworth, or the Trial Manager, to inform the Sponsor, PTUC and Royal Papworth's R&D Department (if different) of trial closure or suspension at Royal Papworth Hospital.

d. The Chief Investigator, or their designee, is responsible for informing the applicable regulatory authorities of the end of trial and submitting the necessary end of trial reports.

3 Policy

a. This SOP is mandatory and, as per the Trust's Information Governance and Records Management framework, non-compliance with may result in disciplinary procedures.

4 Procedure for studies managed by PTUC or sponsored by Royal Papworth

4.1 Early termination or temporary suspension of a trial

a. For temporary suspension of studies the main REC (and MHRA if the study is a CTIMP) should be notified within 15 days

1. The notification should be made as a substantial amendment to the ethics committee (via IRAS) and for CTIMPs the MHRA (using the notification of amendment form) clearly explaining the reasons for the suspension.
2. Substantial amendments relating to temporary suspension and urgent safety measures must be submitted to the MHRA using CESP.
3. To restart a trial that has been temporarily suspended, you should make the request as a substantial amendment using the notification of amendment form, providing evidence that it is safe to restart the trial.

b. For early termination (closure) of studies the main REC (and MHRA if the study is a CTIMP) should be notified within 15 days

1. For CTIMPs, the notification should be made by using the Declaration of End of Trial form (https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues) and include a brief explanation of the reasons for ending the trial. This form should be submitted using CESP.
2. For all other studies, the end of study report should be emailed to the REC which approved the study (http://www.hra.nhs.uk/resources/during-and-after-your-study/end-of-study-notification-studies-other-than-clinical-trials-of-investigational-medicinal-products/).

c. The Sponsor and R&D Unit should be notified immediately. This can be by telephone but must be followed up by a written report.

d. All investigators must be informed of the trial termination/suspension using expedited means of communication and receipt of notification acknowledged. The reasons for early termination (or temporary suspension) must be made clear.

e. The Chief Investigator and Sponsor must decide if participants need to be contacted to tell them of the termination or suspension of the study and any actions that need to be carried out. This decision must be documented.

f. Documentation and all records should be archived according to PTUC SOP011: Archiving SOP.

4.2 End of trial

4.2.1 Regulatory Reporting

a. The Chief Investigator (or their delegated individual) is responsible for informing the following that the trial is closed, by using the appropriate Declaration of End of Clinical

Trial Forms which are available from http://www.hra.nhs.uk/research-community/end-of-study-and-beyond/ . This should be submitted within 90 days of the end of the study.

i) Ethics Committee which approved the research

ii) HRA (where a study has HRA approval but did not require REC approval)

iii) Regulatory bodies (e.g. MHRA)

iv) Royal Papworth CTU

v) Royal Papworth R&D Unit

vi) Sponsor

b. The Chief Investigator, or their designee, should submit the End of Study report (there is no defined format for this report) to the REC and MHRA within 12 months of the end of the study.

4.2.2 Closure of sites:

a. The Chief Investigator, or their designee, should inform the Principal Investigators at other sites, in writing, that the trial has closed. The letter should:

1. summarise patient status (recruitment, withdrawals, SUSARS, SEAs etc)
2. remind the investigator of any continuing trial obligations (e.g. archiving)
3. advise of the dates of site closure, audit or inspections visits
4. solicit any queries in procedure
5. arrange for the return of trial supplies and/or drug supplies, if applicable
6. outline the results of the trial or provide a copy of the report
7. inform the investigators, if possible, of the timing of publication

b. Site closure - a study visit may be necessary to verify or complete the closure process at a participating site and will be conducted by either the Chief Investigator, or their designee. A site can be deemed to be closed once the following are reconciled or complete:

1. Investigator/institution and sponsor files are reviewed and all essential documentation for a particular site are present in the relevant files to ensure a clear audit trail of study conduct at the site
2. All site data are collected, entered, validated and all data queries resolved where feasible. This includes queries resulting from reconciliation of the clinical and safety database
3. For studies using electronic data capture, the sponsor or their delegate has provided copies of final study data relating only to participants at that site for local study files
4. All issues from previous study monitoring procedures are resolved or documented

5. All financial matters are resolved and all site payments are complete as agreed and documented in study contracts/agreements/approvals. Finance to be notified that all financial matters are resolved and that the study site has closed.
6. All unused trial supplies are returned or destroyed according to study and/or sponsor requirements
7. All samples collected during the trial have been sent to the agreed location for analysis/storage (usually the sponsor), along with a fully completed sample log.
8. For a CTIMP final drug accountability is complete and destruction of unused study drug is documented in the site file (if destroyed locally at site)
9. Investigators are aware of the study publication policy, as documented in the study protocol and/or study contracts/agreements
10. Investigator(s) are aware of and have implemented relevant ongoing requirements such as site archiving, subsequent audit/inspection procedures and any ongoing reporting requirements

c. Details of site closure visits must be documented, normally in the form of a written report, and any issues raised must be followed up promptly. It should be clear who reviews closure reports to ensure that feedback is provided to the site and sponsor (where applicable).

d. A site closure visit may not be necessary for a non-commercial study. In such cases, confirmation/agreement letters can be signed to document that all activities related to study close out are complete, copies of essential documents are held appropriately and a site visit was not required. This must be documented in the Trial Master File.

e. There is no regulatory requirement for the sponsor or delegate to notify routine closure of active sites at the conclusion of a study.

f. Upon closure of the trial, all study documentation is retained in the trial office until such time as all data queries are resolved and the database is closed. Final analysis of the data (following 'lock' of the study database see SOP 077 Data Management Overview) and report writing may occur after formal declaration of the end of the project. At this time all trial documentation should be archived according to the study protocol.

4.2.3 Early closure of participating sites

g. It may be necessary for a site to prematurely close; for example a site withdraws from a trial because it can no longer recruit participants as the protocol stipulates because of changes to its treatment pathway. If this occurs then the procedures for closing the site should be followed as in 4.1.1.

h. Once the Chief Investigator, or their designee formally closes the site the Sponsor or a delegate must notify the main REC, MHRA and other relevant bodies.

4.3 Planned closure of hosted studies at Royal Papworth

a. Upon closure of the trial, all study documentation is retained in the trial office until such time as all data queries are resolved and the trial sponsor's database is closed. At this time all trial documentation is archived according to the study protocol.

4.4 Trial closure and study samples

a. Upon closure of the trial all remaining study samples must be stored/destroyed in accordance with the conditions of the research ethics approval, trial protocol and individual signed consent forms.

b. A fully completed sample log must be saved in the study TMF (see SOP 013 and FRM021 Sponsor File Index) prior to archiving.

c. If consent was given for the remaining samples to be stored for future use the samples should be transferred to the appropriate freezer, the freezer sample log must be updated and proof of consent electronically stored.

d. If samples are to be transferred to a Biobank (e.g. Royal Papworth Hospital Research Tissue Bank), this should be completed prior to archiving of trial

e. The member of study team delegated to take responsibility for the samples at the end of the trial must complete the Sample Declaration (FRM 069) and this must be counter signed by the Investigator

4.5 End of Trial Reporting

Royal Papworth Sponsored Studies

a. It is the responsibility of the Chief Investigator to ensure the results of the study are analysed and reported within a reasonable timeframe.

b. A summary of the final report on the research should be sent to the MHRA ,as required, main REC and R&D Unit within 12 months of the end of the trial.

c. The Chief Investigator should make all necessary efforts to get the results reported in a peer reviewed journal.

5 Risk Management / Liability / Monitoring & Audit

a. The R&D SOP Committee will ensure that this SOP and any future changes to this document are adequately disseminated.

b. The R&D Department will monitor adherence to this SOP via the routine audit and monitoring of individual clinical trials and the Trust's auditors will monitor this SOP as part of their audit of Research Governance. From time to time, the SOP may also be inspected by external regulatory agencies (e.g. Care Quality Commission, Medicines and Healthcare Regulatory Agency).

c. In exceptional circumstances it might be necessary to deviate from this SOP for which written approval of the Senior R&D Manager should be gained before any action is taken. SOP deviations should be recorded including details of alternative procedures followed and filed in the Investigator and Sponsor Master File.

d. The Research and Development Directorate is responsible for the ratification of this procedure.

Further Document Information

Approved by: *Management/Clinical Directorate Group*	Research and Development Directorate
Approval date: *(this version)*	[Current active version approved date]
Ratified by Board of Directors/ Committee of the Board of Directors:	STET
Date:	N/A
This document supports: *Standards and legislation*	Medicines for Human Use (Clinical Trials) Regulations 2004 and all associated amendments. Research Governance Framework for Health and Social Care (2005)
Key related documents:	Trust Research Policy [Insert list of linked or relevant documents to this SOP]

Equality Impact Assessment: Does this document impact on any of the following groups? If YES, state positive or negative, complete Equality Impact Assessment Form available in Disability Equality Scheme document DN192 and attach.

Groups	Disability	Race	Gender	Age	Sexual orientation	Religious & belief	Other
Yes/No	NO	NO	NO	NO	NO	NO	NO
Positive/Negative							

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Version Control

Version	Date effective	Valid to	Approved by	Date of approval
1.0				
2.0				
3.0				
4.0				

I certify the contents of this SOP has been reviewed and ratified

..... 13th April 2018.

Signed by Dr Ian Smith, Clinical Director of R&D — Date

SOP release date: 18th April 2018