York Foundation Trust R&D Unit
Standard Operating Procedure
Pharm/S56

Trial Closedown in Pharmacy

IT IS THE RESPONSIBILITY OF ALL USERS OF THIS SOP TO ENSURE THAT THE CORRECT VERSION IS BEING USED

All staff should regularly check the R&D Unit's website and R&D Newsletter for information relating to the implementation of new or revised versions. Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded versions are promptly withdrawn from use unless notified otherwise by the SOP Controller.

The definitive versions of all R&D Unit SOPs appear online. If you are reading this in printed form check that the version number and date below is the most recent one as shown on the R&D Unit website: www.northyorksresearch.nhs.uk/sops.html

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This SOP will normally be reviewed every 2 years unless changes to the legislation require otherwise

Version History Log

This area should detail the version history for this document. It should detail the key elements of the changes to the versions.

Version	Date Implemented	Details of significant changes
1.0	1st February 2011	
2.0	22nd July 2013	Removal of references to the North and East Yorkshire R&D Alliance. Change of SOP Controller.
3.0	20th August 2015	Minor amendments

Contents

1 Introduction, Background and Purpose

Pharmacy is responsible for ensuring that accurate records exist to provide an audit trail from receipt of Investigational Medicinal Products (IMP) to their removal from site or destruction. During the closedown of a trial, it is an important requirement to ensure that all the documents that provide an audit trail are present in the Pharmacy clinical trial file. The Pharmacy trial file and documents contained within are required to complete the Trial Master File and therefore at all times should contain the essential documents relating to the clinical trial.

This SOP describes a procedure for the closedown of clinical trials of Investigational Medicinal Products to support compliance with the UK Clinical Trials regulations and Annex 13 of Good Manufacturing Practice.

This SOP should be used in conjunction with R&D/S21 – Trial Close Out and describes the procedures to follow when a clinical trial that is hosted or Sponsored by York Teaching Hospital NHS Foundation Trust closes or is terminated. A trial site can be considered closed when all study related activities at a particular site are reconciled and/or completed. For details of what should be actioned during trial close-out, refer to R&D/S21 section 4.

The exact date of closure of a clinical trial will be defined by the Sponsor, and the Pharmacy department will be notified by the Sponsor in advance of the closure of the trial in writing. For commercial trials, this communication may come from the Clinical Research Associate, or for non-commercial trials, the Trial Manager of the relevant study. For trials Sponsored by York Teaching Hospital NHS Foundation Trust, this notification will come from the R&D Unit.

The closure of a clinical trial within Pharmacy will usually take the form of a trial close-out visit conducted by the trial Sponsor. However, in some circumstances, the trial Sponsor will request confirmation from Pharmacy that all relevant close-out activities have been completed by the Pharmacy department at the trial site.

The purpose of this SOP is to ensure that the Pharmacy file is ready for archiving and contains all the relevant documents according to Pharm/S44 – The Pharmacy Clinical Trial File and Pharm/F52 – Pharmacy Clinical Trial File Contents. This SOP also describes what actions should be taken during the process of study closure or closedown visit conducted by the trial Sponsor.

The procedures for the processing of the final trial related payments are also described. For the procedures relating to the archiving of documents in York Teaching Hospital Foundation Trust, please refer to R&D/S11- Archiving of Research Study Documents and Pharm/S44 – The Pharmacy Clinical Trial File.

2 Who Should Use This SOP

This applies to all members of the clinical trials team within the Pharmacy department at York and Scarborough hospitals, which form part of the York Teaching Hospital NHS Foundation Trust.

3 When this SOP Should be Used

The procedure should be used;

- when requested to closedown a trial by the trial Sponsor.
- during the trial close-out visit by the trial Sponsor.
- when preparing the Pharmacy file for archiving.

4 Procedure(s)

The activities to be conducted at trial closedown are such that compliance with ICH-GCP (section 8.4) is ensured. This states that documentation should be provided to ensure that the Investigational Medicinal Product(s) have been used according to the protocol and that the final accounting of Investigational Medicinal Product(s) received at the site, dispensed to subjects, returned by the subjects, and returned to Sponsor (or destroyed at site) is documented.

Trial close-out will usually take the form of a close-out visit and the relevant member of the Pharmacy clinical trials team should follow the procedure outlined below.
In some circumstances, Pharmacy staff may be asked by the trial Sponsor to closedown the study in the absence of a Trial Monitor or Clinical Research Associate. This may include completion of a closedown checklist (provided by the trial Sponsor via post or email) which you are required to action, complete and return. In these circumstances you should comply with the request from the trial Sponsor and also follow the actions specified below, which would normally occur during the trial closedown visit. In this case, Pharmacy would assume the responsibility of performing these tasks. A copy of any completed closedown documentation should be filed with the Pharmacy trial file.

4.1 Final Pharmacy payments

Prior to the trial close-out visit, a member of the Pharmacy clinical trials team should prepare the final invoice for the study according to the procedures contained within Pharm/S42 – Pharmacy Financial Agreements and Invoicing.
At the trial close-out visit, agree with the Sponsor representative what the remaining payments are for the study and confirm the invoice has been prepared by the Pharmacy clinical trials team and will be sent to our Finance department at York Teaching Hospital NHS Foundation Trust.

4.2 The trial close-out visit

The trial close-out visit will be conducted by the Sponsor in the presence of a member of the Pharmacy clinical trials team at York Teaching Hospital NHS Foundation Trust. At the close-out visit the following activities should be carried out by the Sponsor representative with the support of a member of the Pharmacy clinical trials team:

- Reconciliation of the trial medication supplies or Investigational Medicinal Product (to ensure it has been used according to the protocol and all drugs have been comprehensively and accurately accounted for as described in section 8.4 of ICH-GCP). This should include a check that all IMP has been

returned by patients. All IMP accountability logs must be checked for accuracy and any discrepancies accounted for.

- Check all the essential documents are in the Pharmacy file

The file should be checked against the required contents of the Pharmacy file as described in Pharm/S44 and shown in Pharm/F52.

It is a Chief Investigator (CI)/Principal Investigator (PI) responsibility to ensure that all essential documents are archived as described in R&D/S11.

In preparation for this a member of the Pharmacy clinical trials team is responsible for ensuring that:

- copies of all storage temperature graphs covering the period the IMP has been stored on site are reviewed and archived centrally. A signed and dated filenote (R&D/T20) should be placed in the Pharmacy trial file documenting that the temperature graphs have been reviewed and describing where these can be obtained if required. Temperature graphs should be stored in York Teaching Hospital NHS Foundation Trust and archived by the Trust periodically. It is also acceptable for the temperature graphs to be stored in the Pharmacy file itself.

- all randomisation code break envelopes (if applicable) are present in the Pharmacy file.

- copies of all relevant correspondence are printed and filed in the relevant section of the Pharmacy file.

- all documentation is completed accurately and in full (any discrepancies in documentation and drug accountability must be accounted for and file notes written, as applicable, to describe these).

- all payments to Pharmacy have been made.

After the close-out visit, the Sponsor will write to Pharmacy to confirm that all activities required for trial close-out have been completed, or describe what actions are required by Pharmacy (i.e. if IMP discrepancies were noted during the Trial close-out visit then these will need to be satisfactorily explained). This will take the form of a final trial close-out monitoring report (usually a letter via post or email). Once confirmation of the trial close-out visit has been received from the Sponsor and all actions contained within have been completed as applicable, the report should be filed within the Pharmacy file and the following activities can take place;

- Removal or on-site destruction of trial medication supplies or Investigational Medicinal Product (if applicable) and documentation of this activity.

If no IMP discrepancies are noted during the trial close-out visit, the Sponsor representative may return IMP to the Sponsor during this visit. If IMP discrepancies are present then these must be satisfactorily explained and accepted by the Sponsor prior to return of the IMP. Returns to the Sponsor should be documented within the Pharmacy file (usually by obtaining a copy of the completed Sponsor provided returns documentation). Where IMP is to be destroyed on-site, destruction should only be conducted following written

authorisation from the Sponsor (as per Annex 13 of GMP). A certificate of destruction should be completed and filed within the Pharmacy trial file – see Pharm/S57 (Destruction of Investigational Medicinal Product) for more detail.

- the Pharmacy file can proceed to archiving. Archiving should be prompted by the CI/PI in line with in R&D/S11- Archiving of Research Study Documents.

4.3 Documents to be kept by Pharmacy

Prior to sending the Pharmacy file for archiving as described above, the financial information regarding the trial any relevant invoices and the Clinical Trials Pharmacy Checklist (Pharm/F32), should be removed from the Pharmacy file.

A member of the Pharmacy clinical trials team should:

1. Enter the date that the any financial documentation is removed from the Pharmacy file onto the Clinical Trials Pharmacy Checklist (Pharm/F32).
2. Ensure that all other sections of the Clinical Trials Pharmacy Checklist are completed.
3. Deliver the financial documentation relating to the trial to the R&D Unit's named archivist who will be responsible for ensuring that this information is placed in the appropriate R&D file. R&D files are archived by the Trust in line with R&D/S11. In some circumstances (e.g. when there are outstanding payments to Pharmacy), the financial documentation may be retained within Pharmacy (together with the completed Clinical Trials Pharmacy Checklist).
4. File the completed Clinical Trials Pharmacy Checklist in Pharmacy for future reference.
5. Complete any relevant tracking spreadsheets relating to this activity.

5 Related SOPs and Documents

R&D/T20	File Note Template
R&D/S11	Archiving of Research Study Documents
Pharm/S42	Pharmacy Financial Agreements and Invoicing
Pharm/F32	Clinical Trials Pharmacy Checklist
Pharm/S44	The Pharmacy Clinical Trial File
Pharm/S57	Destruction of Investigational Medicinal Product
Pharm/F52	Pharmacy Clinical Trial File Contents
R&D/S21	Trial close out; CTIMPs and other research studies

Practice Guidance on Pharmacy Services to Clinical trials, RPSGB, June 2005

Annex 13 of Good Manufacturing Practice

Section 8.4 of ICH-GCP