York Foundation Trust R&D Unit
Standard Operating Procedure
Pharm/S79

Receipt and review of Protocol amendments 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 Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded versions are promptly withdrawn from use unless notified otherwise by the SOP Controller.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

SOP Reference:	Pharm/S79
Version Number:	2.0
Author:	Richard Evans
Implementation date of current version:	19th January 2016

Approved by:	Name/Position:	Jax Westmoreland, Principal Pharmacist, Clinical Trials and Research
	Signature:	Signed copy held by R&D Unit
	Date:	22nd December 2015
	Name/Position:	Sarah Sheath, SOP Controller
	Signature:	Signed copy held by R&D Unit
	Date:	22nd December 2015

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	22nd November 2013	Introduction of amendment checklist Pharm/F106 & Red, Amber & Green light amendment letters are now provided as separate templates (Pharm/T44, Pharm/T45 & Pharm/T46). Other minor process changes and clarifications.
2.0	19th January 2016	

Contents

1 Introduction, Background and Purpose

The procedures describing processing and implementation of amendments for Clinical Trials of Investigational Medicinal Products (CTIMPs) being conducted within York Teaching Hospital NHS Foundation Trust are described in the following SOPs;

- Implementing amendments for research studies NOT sponsored by the Trust (R&D/S07)
- Making amendments to Trust Sponsored Research studies (R&D/S74)
- R&D processing of amendments (R&D/S75)

These procedures stipulate that Pharmacy be informed of any amendments being processed within the Trust that relate to CTIMPs. There is also a requirement that Pharmacy authorisation, for the amendment to proceed, is obtained prior to its implementation.

Pharmacy should be notified of amendments to ensure that;

- any changes are made to the Pharmacy Trial Instructions, trial prescription, accountability logs and other trial documentation e.g. aseptic worksheets that may be required as a result of the amendment, and
- Pharmacy are in receipt of all of the correct versions of study documentation e.g. Protocol & Investigator Brochure, that may have changed as a result of the amendment.

The purpose of this SOP is to describe the process for reviewing an amendment to a clinical trial protocol within the York Teaching Hospital NHS Foundation Trust Pharmacy department.

2 Who Should Use This SOP

This SOP should be used by all members of the Pharmacy clinical trials team at York and Scarborough Hospital, which form part of the York Teaching Hospital NHS Foundation Trust.

3 When this SOP Should be Used

This SOP should be used upon receipt of an amendment to a clinical trial within Pharmacy. This may be in the form of a new protocol or other changes to the documentation being used to conduct the study.

The member of staff who receives the amendment / updated protocol is responsible for reviewing any changes that have been made, or asking an appropriately qualified colleague to do so, and initiating any changes to pharmacy documentation required as a result of the amendment.

Any Pharmacy documentation that changes as a result of the amendment e.g. Pharmacy Trial Instructions or study-specific SOP must be authorised in line with the existing procedures for those documents.

4 Procedure(s)

Due to the complexity of aspects of this process, an amendment checklist is available and should be used in conjunction with this SOP to ensure all appropriate actions are carried out. This is entitled Pharm/F106 – Pharmacy Amendment Checklist Form.

4.1 Receipt of an amendment

1. Protocol amendments are usually received either by post or e-mail. On receipt of a letter or e-mail containing an updated protocol/study documentation, locate the Protocol Amendment Receipt Record Form (Pharm/F94).

2. Complete the header on the Protocol Amendment Receipt Record Form (electronically or by hand after printing the blank form) with the following details:
    a. Trial title
    b. Protocol number
    c. Investigator
    d. EudraCT number
    e. Sponsor amendment number
    f. Version number (of new protocol)
    g. Date of new version
    h. Date amended protocol received
    i. Name of person who received

    Please note: There may be occasions where an amendment does not change the study protocol in use. In these circumstances, note the details of the documentation received in the *version number* box and complete the remaining sections accordingly.

3. If the amendment has not been received from the R&D department, confirm receipt of the amendment to R&D (to the nominated individual who processes amendments).

4. Print the documents supplied with the amendment and file in the clinical trials office/room together with any relevant correspondence.

5. Save the documentation supplied, in a sub folder bearing the relevant amendment number, on the Pharmacy X drive (or I drive) in the amendments folder (X:\Clinical Trials*Trial Name*\amendments*amendment number)*of the relevant trial*.*

6. Complete the amendment tracker on the Pharmacy X drive (or I drive) with the following details (there is completion guidance on the tracker; X/I drive location of the amendment tracker is X/I:\clinical trials trackers\clinical trials amendment tracking):
    a. Date received
    b. Received from
    c. Study title
    d. R&D Number
    e. New version number of the protocol (if applicable) & amendment number

f. Documents supplied

7. When a protocol undergoes a substantial amendment, the new version must be approved by the:
    a. Medicines and Healthcare products Regulatory Agency (MHRA)
    b. Research Ethics Committee (REC)

    In addition, all amendments should be acknowledged by the Trust Research and Development (R&D) department who provide continuing NHS permission in the form of an R&D No objection letter

8. Obtain a copy of each of the above documents (as applicable, from either the sender of the amended protocol, the Research Nurse or Principal Investigator) and indicate this on the Protocol Amendment Receipt Record Form with a tick next to the relevant approval. Add the dates of the approval letters to the form. These letters should then be filed in the trial specific Pharmacy File.

    Substantial amendments should not be implemented until MHRA, REC approval and Trust R&D approval/No objection has been granted, unless they are urgent safety amendments which should be implemented immediately.

9. Proceed to follow section 4.2 below to process the amendment within Pharmacy.

4.2 Review of an amendment

1. Wherever possible, obtain a summary of changes or a “tracked changes” version of the revised protocol (if applicable). Review each one of these changes (or any other changes detailed in the amendment received) and decide if any of them impact on:
    a. Drug dosing (has there been a change to the strength/form/dose or frequency of any of the drugs in the protocol? Or has a new drug been added?)
    b. Treatment thresholds (blood counts, liver/renal function or biochemistry) - either for eligibility or subsequent cycles
    c. Supportive care
    d. Concomitant medication
    e. Potential interacting medication
    f. Drug preparation
    g. Drug storage or expiry
    h. Drug formulation, packaging or labelling
    i. Drug funding / potential excess treatment costs or cost savings

2. Once all the changes have been reviewed and potential impacts assessed, decide whether any of the following trial documentation needs to be amended:
    a. Pharmacy Trial Instructions/dispensing procedure/checking procedure
    b. Trial specific prescription
    c. Aseptics/technical services worksheet
    d. Labels
    e. Accountability logs
    f. Drug order forms

3. Complete the Protocol Amendment Receipt Record Form section entitled "protocol amendment reviewed by" with your name and the date on which you reviewed the amendment.

4. If, based on your assessment, Pharmacy cannot authorise the amendment to proceed, complete a Pharmacy 'red light' amendment letter (See Appendix 2) and send to the Research and Development (R&D) Department, Principal Investigator and Research Nurse for the study. This is likely to be in exceptional cases only, and in such cases, a meeting will be held with the above to agree the way forward, and what communication is required with the Sponsor.

5. If, based on your assessment, Pharmacy authorisation remains for the study to continue, and **no changes** are required to be made to any of the trial specific documentation:
    a. Complete a Pharmacy 'green light' amendment letter , and send to the nominated individual who processes amendments in R&D. Indicate on the Protocol Amendment Receipt Form that you have completed this by signing and dating the form in the 'Pharmacy green light letter sent' section. This can be done by the Pharmacist, Clinical Trials Manager or Senior Pharmacy Technician.
    b. Tick the "no changes required" box in the table on the Protocol Amendment Receipt Record Form.
    c. Upon receipt of R&D no objection letter, agree the implementation date for the amendment with the Research team (it may be appropriate for this to be the same date as the R&D letter).
    d. On the agreed implementation date, replace the protocol in the Pharmacy trial file with the new version, and supersede any other documents as required.
    e. Draw a diagonal line across the front page of the previous protocol, and write in block capitals "SUPERSEDED BY VERSION X (*insert new version number*)" and the date on which you are undertaking this process. Initial this annotation.
    f. Indicate on the amendment receipt form that you have completed this by signing and dating the form.
    g. File the superseded protocol in the appropriate section of the Pharmacy trial file.
    h. Attach an amendment sticker (see template in Appendix 1) to the trial instructions, and complete the boxes on the sticker with the following details:
        1. Date of new protocol.
        2. Version number of new protocol.
        3. Initials of the person who confirmed no changes to the documentation were required.
        4. Initials of the person who marked the previous version of the protocol as superseded.
        5. Date that the process of replacing and superseding was undertaken.
    i. If an electronic protocol has also been provided, ensure the previous version has been moved to the superseded folder in the appropriate electronic trial folder. Supersede any other electronic protocols stored elsewhere in a similar manner e.g. Satellite Unit folder on the X drive.
    j. Update the amendment tracker on the X (or I drive) in the location (X:\clinical trials trackers\clinical trials amendments tracking\amendments tracker*)*

6. If **changes are required** to trial specific documentation, indicate on the Protocol Amendment Receipt Record Form, what changes are required and who will be responsible for completing the action (see below).
   Complete a Pharmacy 'amber light' amendment letter, noting the changes required in the space provided, and send to the nominated individual in R&D who processes amendments. Indicate on the Protocol Amendment Receipt Form that you have done this by signing and dating the form in the 'Pharmacy amber light letter sent' section.

7. Depending on the changes required, send a copy of the Protocol Amendment Receipt Record Form and the new version of the protocol to the appropriate people from the list below and request that the trial specific documentation be updated:
   - Dispensing procedure, checking procedure, trial specific prescription, labels, accountability logs, drug order forms – Lead Senior Pharmacy Technician for Clinical Trials at the relevant hospital site who has responsibility for this study.
   - Chemotherapy Prescription - Chemocare Pharmacist or Technician.
   - Aseptics/Technical Services Worksheet and labels – Aseptics/Technical Services Principal/Senior Technician.

   Add the appropriate person's initials to the actions table on the Protocol Amendment Receipt Record Form.
   Any amendment to trial specific documentation requires creation of a new version. This new version should be approved as per the standard operating procedures for creating such documents. Changes to the dispensing procedures or trial instructions should be actioned in line with those procedures described in SOP Pharm/S50 - Preparation, Review and Approval of Pharmacy Study Specific Trial Instructions.

   Discuss any changes to drug funding, particularly if there are going to be new excess treatment costs, with the Clinical Trials Manager/Pharmacist, who will discuss with the Head of R&D.

8. Ensure the Directorate Pharmacist is notified where appropriate (usually by email) of any changes to the protocol resulting from the amendment. Complete the Protocol Amendment Receipt Record Form with your initials and the date to confirm this has been done.

9. Once any changes to the trial specific documentation have been authorised by the Clinical Trials Pharmacist, the person who has completed this action should complete the Protocol Amendment Receipt Record Form with the date they completed their action and their initials.

10. At this point, complete a Pharmacy 'green light' amendment letter, and send to the nominated individual who processes amendments in R&D. Send a copy also to the Principal Investigator, Directorate Pharmacist (where appropriate) and Research Nurse.

11. Once all changes have been made, ensure the other actions are carried out, as per the instructions above in point 5 (c – j, exclude section h however, if a new version of the Trial Instructions is authorised an amendment sticker is not required in these circumstances).

12. Once all actions have been completed, the Protocol Amendment Receipt Record Form should be filed with the approval documents in the appropriate section of the trial specific Pharmacy file.

13. For any amendments involving a change in the version number of the study Protocol &/or Investigator Brochure, ensure the Pharmacy Trial Status Inventory List is also updated with this new information (refer to Pharm/S61 – Maintenance of the Trial Status Inventory Dispensary List).

Templates for Red, Amber and Green light Pharmacy amendment letters are available and should be used to support this process as follows;

Pharm/T44 - Pharmacy Green Light Amendment Letter Template
Pharm/T45 - Pharmacy Amber Light Amendment Letter Template
Pharm/T46 - Pharmacy Red Light Amendment Letter Template

The person processing the amendment in Pharmacy should seek appropriate advice if required from the Clinical Trials Manager &/or Principal Pharmacist (Clinical Trials & Research) or Senior Pharmacy Technician, prior to sending a Pharmacy amendment letter.

5 Red/amber/green light Pharmacy amendment letters must also be copied to the Principal Pharmacist, Clinical Trials and Research or other Pharmacist with delegated responsibilities for the study to ensure oversight of amendment processing within Pharmacy. Related SOPs and Documents

Pharm/S50 - Preparation, Review and Approval of Pharmacy Study Specific Trial Instructions

Pharm/F94 – Protocol Amendment Receipt Record Form

R&D/S07 - Implementing amendments for research studies not sponsored by the Trust

R&D/S74 - Making amendments to Trust Sponsored Research studies

R&D/S75 - R&D processing of amendments

Pharm/S61 – Maintenance of the Trial Status Inventory Dispensary List

Pharm/T44 - Pharmacy Green Light Amendment Letter Template

Pharm/T45 - Pharmacy Amber Light Amendment Letter Template

Pharm/T46 - Pharmacy Red Light Amendment Letter Template

Pharm/F106 – Pharmacy Amendment Checklist Form

6 Appendix 1 – Amendment sticker contents

Date of new protocol ……..

Version number of new protocol…….

No changes to the documentation were required (Initial)……..

Previous version of the protocol marked as superseded (Initial)……..

Date superseding took place …….