York Foundation Trust R&D Unit
Standard Operating Procedure
Pharm/S50

Preparation, Review and Approval of Pharmacy Trial Instructions

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 Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded versions are promptly withdrawn from use unless notified otherwise by the SOP Controller.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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Approved by:	Name/Position:	Jax Westmoreland, Principal Pharmacist, Clinical Trials & Research
	Signature:	
	Date:	11th January 2016
	Name/Position:	Sarah Sheath, SOP Controller
	Signature:	
	Date:	11th January 2016

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

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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 March 2012	
2.0	16th April 2012	Correction of spelling mistake. Removal of North and East Yorkshire R&D Alliance references.
3.0	8th February 2016	To include new templates and new process for writing trial specific instructions

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Contents

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1 Introduction, Background and Purpose

All Pharmacy study files should contain comprehensive trial instructions and checklists specific to that trial.

This SOP describes how pharmacy trial instructions should be prepared, reviewed, approved and implemented for Clinical Trials of Investigational Medicinal Product (CTIMP) studies.

The pharmacy trial instructions and checklists should cover trial activities specific to that trial such as:

- Trial Details and Summary (including unblinding)
- Dispensing
- Clinical and Accuracy Checking
- Trial Stock Management
- Aseptics Unit Instructions (where applicable)

The purpose of the trial instructions is to ensure that:

- Investigation Medicinal Products/Non-Investigational Medical Products (IMPs/NIMPs) are appropriate for use, procured, handled, stored and used safely and correctly.
- IMPs are managed and dispensed in accordance with the protocol.
- Trial procedures comply with relevant guidelines and regulations; The Medicines for Human Use regulations (as amended), Good Clinical Practice (GCP) and Annex 13 of Good Manufacturing Practice.

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2 Who Should Use This SOP

This SOP should be used by all members of the clinical trials team involved in initial study set up or checking and authorising of a new pharmacy clinical trial study file. This applies to all staff working within the Pharmacy clinical trials teams in York Teaching Hospital NHS Foundation Trust.

3 When this SOP Should be Used

Use this SOP when writing, reviewing and approving trial instructions for CTIMP studies.

4 Procedure(s)

Pharmacy trial instructions should be based upon the study protocol or other documentation provided by the Sponsor for the purposes of running the trial e.g. Pharmacy manual or sponsor provided SOPs. These can be referred to and referenced.

Templates Pharm/T39, Pharm/T40, Pharm/T41, Pharm/T42, Pharm/T43 contain guidance and instructions to assist with writing Pharmacy trial instructions for a trial. These templates are available from the R&D Unit website www.northyorksresearch.nhs.uk/sops.html.

4.1 How to Create New Trial Instructions

The following process will apply when Pharmacy Trial Instructions need to be prepared:

1. The Pharmacy Trial Manager will take responsibility for ensuring all pharmacy trial instructions are up-to-date, implemented, tracked and reviewed appropriately.

2. The Pharmacy Trial Manager will identify an appropriate lead for the trial.

3. The lead will collate the information and documentation required to prepare the SOP (e.g. protocol, sponsor instructions) and is responsible for contacting the Sponsor or Sponsor's representative (Clinical Research Associate or Trial Manager), to obtain any missing information.

4. The lead should ensure that the Pharmacy checklist for the trial is completed to capture the information required to assist with preparing the Pharmacy Trial Instructions (see Pharm/F32).

5. The lead will write a draft of the trial instructions using the above templates.

6. Guidance within the templates should be deleted and replaced with appropriate text.

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Pharmacy trial instructions will therefore be made up of the following documents (created using the following templates):

- Pharm/T40 - Trial Details and Summary (including unblinding)
- Pharm/T42 - Dispensing
- Pharm/T43 - Clinical and Accuracy Checking
- Pharm/T39 - Trial Stock Management
- Pharm/T41 - Aseptics Unit Instructions (where applicable)

Each of the above will be an individual document with a unique reference number, this number is the next sequential number obtained from the Trial Instructions spreadsheet (this is located on the X drive in the clinical trials folder).

4.1.1 Trial Details and Summary

Using template Pharm/T40, create a short summary of the purpose or objectives of the study, the possible treatment arms or randomisations involved and the medication involved in the study. The appropriate section of Pharm/F28 (Pharmacy Assessment Form) may be inserted here.

Indicate whether the trial is open label or blinded and in the case of blinded studies include a full description of the code break procedure specific to the study.

4.1.2 Dispensing

Using Pharm/T42, create a clear and accurate dispensing procedure for all IMPs/NIMPs involved in the trial to ensure any member of Pharmacy clinical trials staff that has been trained in clinical trials can follow the procedure and dispense the trial medication with confidence. Provide a brief, clear and concise description of the study drugs involved, where they can be found and whether they are open label or blinded supplies, details of accountability logs that need to be completed, any IXRS/IVRS process required at the time of dispensing and the labelling process.
Include any other information you feel appropriate in this section but keep the description brief.

Ensure that the complete dispensing process is documented in the dispensing checklist.

4.1.3 Clinical and Accuracy Checking Checklists

Using Pharm/T43, create checklists for clinical and accuracy checking, using the template as guidance.

4.1.4 Trial Stock Management

Using Pharm/T39, complete instructions for each task. These instructions should be brief, clear and concise and should reflect each step involved.

4.1.5 Aseptics Unit Instructions

Using Pharm/T41, create clear and concise instructions for preparation/dispensing within the aseptics unit. This should include where stock is located, any additional labels to be applied to medication and which accountability logs will need completing. Then complete a checklist for the pharmacist to use when checking and releasing aseptic products.

Once the instructions/templates have been written, the following applies:

1. The draft trial instructions must be reviewed by at least one other member of the Pharmacy clinical trials team, preferably one from each site. The review process and the identity of those involved must be clearly documented and this documentation retained as evidence of appropriate review.

2. The lead will collate reviewers responses and incorporate them (if appropriate) into a revised draft of the trial instructions. Note that it may be appropriate to review multiple drafts of a trial instruction. Ensure that draft versions are named as draft versions and the first version number will be 1.0 at the time of publishing.

3. The lead will send the latest draft of the trial instructions incorporating the reviewers comments back to the reviewer(s).

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4. The reviewer(s) may chose to submit further comments on the latest draft. In this case the process reverts to number 2 above. Alternatively the reviewer(s) may confirm that the latest draft is acceptable. Approval of the trial instruction and the names of those who gave approval must be documented. Copies of all draft trial instructions produced must be stored on the Pharmacy X drive /clinical trials folder/draft trial instructions.

5. The lead (or delegated individual) will prepare the trial instructions for publishing and implementation.

6. To prepare the trial instructions for publishing, the lead (or other delegated individual) will (i) update the version number of the trial instructions, (ii) amend the watermark, and (iii) insert appropriate implementation and review dates.

7. A paper copy of the final trial instructions will be printed on yellow paper, then approved, signed and dated by the Pharmacy Trial Manager or Senior Pharmacy Technician and the Research Pharmacist or Directorate Pharmacist with responsibility for this trial.

8. This is then laminated and filed in section 1 of the pharmacy file.

9. On the trial instructions spreadsheet record the implementation date, version number and review date (this would normally be every 2 years).

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4.2 How to formally review Pharmacy Trial Instructions

All trial instructions should have a review date. Review schedules will be modified should changes to legislation, study amendments or study arrangements necessitate expedited or immediate revision.

All trial instructions should be reviewed on or before their designated review date regardless of whether changes are envisaged.

If revision of a trial instruction is required for any reason (e.g. amendment, change to trial procedures or review date reached) a new version of the instruction should be created and the previous version superseded.

If an existing trial instruction is due for review or has been identified as requiring review:

1. The original lead will review the trial instruction and determine whether an update is required. If the original author is unavailable then an alternative author will be identified by the Clinical Trials Manager. The author may review and decide that there is no update required at that time. If this were the case the version number would change to reflect the change in review date e.g version 1.0 to version 2.0.

2. The lead will identify appropriate reviewer(s) and will organise a formal review. If possible, previous reviewers and current users should be included in the review team. The review process and the identity of those

involved must be clearly documented and this documentation retained as evidence of appropriate review.

3. The review team will return comments to the author (who will collate the responses and incorporate the comments from the review team into the final version).

4. If the review team confirm that they are happy with the draft trial instructions then the author will prepare the trial instructions for publishing.

5. To prepare the trial instructions for publishing, the author (or other delegated individual) will (i) update the version number of the trial instructions (ii) amend the watermark, and (iii) insert appropriate implementation and review dates.

6. A paper copy of the final trial instructions will be printed on yellow paper, then approved, signed and dated by the Pharmacy Trial Manager or Senior Pharmacy Technician and the Research Pharmacist or Directorate Pharmacist with responsibility for this trial.

7. This is then laminated and filed in section 1 of the pharmacy file.

8. On the trial instructions spreadsheet record the implementation date, version number and review date (this would normally be every 2 years).

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4.3 How to Manage Pharmacy Trial Instructions

All pharmacy trial instructions must be retained in the Pharmacy Clinical Trial File and archived as *Essential Documents*. Where paper/laminated copies of older versions of an trial instruction exist a line should be placed through the front page of the superseded version and “superseded” written across the top and signed and dated. Superseded versions should be kept in Pharmacy study files to enable identification of the version in use when any particular step was taken in the research.

Draft trial instructions should have a Draft watermark. Trial instructions under review should have a watermark stating that they are ‘under review’. Published trial instructions should have an ‘Uncontrolled document when printed’ watermark.

The standard style, layout and content of trial instructions are defined in the trial instructions Templates which is available on the SOPs page of the York R&D website (www.northyorksresearch.nhs.uk/sops.html).

4.4 Training

When a new Trial instruction is authorised, or when an existing trial instruction is revised, as a minimum self directed training must be carried out by all staff to which the trial instruction is relevant and this training documented on the study personnel training log. There should be adequate time for appropriate training for all relevant staff before the trial instruction is formally implemented. Staff should take time to read and fully understand the trial instruction and relevant documents, ensuring that they are able to implement it when required.

4.5 Archiving

Paper/laminated copies of all signed, approved and published study-specific trial instructions will be stored in Pharmacy Clinical Trial Files while the study is ongoing. At the end of the study, all trial instructions will be archived with the TMF in accordance with R&D/S11 (archiving).

5 Related SOPs

Pharm/T39	Trial Stock Management
Pharm/T40	Trial Summary and Unblinding Trial Instructions Template
Pharm/T41	Dispensing and Checking of Aseptic Trial Instructions Template
Pharm/T42	Dispensing Trial Instructions Template
Pharm/T43	Clinical and Accuracy Checking Checklist Template
R&D/F01	SOP Review Form
Pharm/F32	Clinical Trials Pharmacy Checklist
R&D/S11	Archiving of Essential Documents
Pharm/S44	The Pharmacy Clinical Trial File

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