Sheffield Teaching Hospitals NHS
NHS Foundation Trust

Research Department

STANDARD OPERATING PROCEDURE

Amendments

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Approved by (name & role)	Dipak Patel R&D Manager	**Date:**	17/11/2015
Signature:	D Patel		

Standard Operating Procedure: Research Department

Amendments

This SOP has been produced in accordance with **Medicines for Human Use (Clinical Trials) Regulations 2004 and subsequent amendments, Good Clinical Practice (GCP) & Research Governance Framework.**

This SOP will outline the procedure for dealing with Study Amendments.

Background

The STH Research Department reviews and issues NHS Permission for all research that takes place within the Trust. If changes are made from the original application, the Research Department requires notification of the intended amendment, to enable review and confirmation of continued NHS Permission where applicable.

Index (if necessary)

Acronyms

CSP	Coordinated System for Gaining NHS Permission
CTIMP	Clinical Trial of an Investigational Medicinal Product
MHRA	Medicines and Healthcare products Regulatory Agency
REC	Research Ethics Committee
RMS	Research Management System

Definitions

An amendment is any change to the original study application during the life of the study. This includes but is not limited to: protocol amendments, updated study documentation, duration of the study, changes in study management (including sponsorship or funding) or changes to the research team (CI/PI). Amendments can be classified as Substantial or Non-Substantial, depending on whether they require approval either by the Research Ethics Committee (REC) and/or Medicines and Healthcare products Regulatory Agency (MHRA).

Procedure

1. Where STH is the Study Sponsor (CTIMP/device studies)

The CI or delegate informs the R&D Coordinator of a required amendment, forwarding a copy of all study documents containing the proposed changes and requests advice from the Coordinator regarding whether the amendment is classified as substantial for the purposes of the REC and/or MHRA.
The R&D Coordinator responds in writing to confirm whether the amendment is substantial or non-substantial for the REC and/or MHRA.

1.1 Where STH is the Study Sponsor (CTIMP/device studies): Substantial Amendments

1.1.1 The CI or delegate transfers the completed Amendment Notification Form to the R&D Co-ordinator who then reviews it in conjunction with the revised/new study documents, identifies any risks or implications of the amendment and ensures that these can be accommodated.

1.1.2 Where the responsibility for risk assessment and management has not been delegated to a CTRU or other body, the R&D Coordinator forwards the amendment to the Risk Assessment Lead or Deputy.

1.1.3 The Risk Assessment Lead or Deputy advises whether the amendment has any impact on the original risk assessment for the study and takes forward any necessary reassessment until all issues if any have been addressed in liaison with the CI and study team.

1.1.4 Once the amendment has been confirmed as substantial for the MHRA, the R&D Coordinator should complete the Finance memo for the MHRA fee and sends it to the Research Finance team for processing for submission to the MHRA.

1.1.5 The CTIMP Amendment Notification Form is signed only by the person responsible for submitting the amendment including any relevant documentation to the REC and/or MHRA. This should be the R&D Coordinator unless this responsibility has been delegated to a CTRU or other body. The R&D Coordinator or delegate/CTRU submits the amendment to the REC and/or MHRA, liaises with the CI and study team to address any requests for further information, disseminating the approval letters to the CI on receipt.

1.1.6 For CSP studies, the CI or delegate uploads the amendment documents to CSP as per the current CSP Operational Guidelines. The R&D Coordinator may assist with this task if the CI or delegate is unfamiliar with the process. The amendment will then be classified as Category A, B or C by the lead CRN according to the updated categorisation method (see section 4 below).

1.1.7 The R&D Coordinator asks the CI if the Case Report Form and/or any other study specific templates or SOPs will need updating as a result of the amendment. If the CI confirms that this is the case then the R&D Coordinator requests that the CI forward a copy of the updated templates for review by the Risk Assessment Lead or Deputy.

1.1.8 Where the amendment impacts upon the Support Services/Facilities (as determined by the CI or their delegate) and/or financial requirements for the study, the appropriate Support Service documents are updated by the R&D Coordinator or delegate and saved within Alfresco. In the instances where Support Service forms do not apply, the R&D Coordinator emails the Support Service contact a copy of an Amendment Summary and a tracked changes version of the protocol.

1.1.9 The R&D Coordinator requests the appropriate Support Services/Finance approval via document sharing in Alfresco and starts the Amendment task in the Research Management System (RMS).

1.1.10 Where Support Services and/or Finance review is not required, the R&D Coordinator starts the RMS Amendment task, changing the Support Services status to “approved”.

1.1.11 Once regulatory (REC/MHRA, as applicable), and Support Service/Finance approvals as applicable are in place, the R&D Coordinator or delegate issues a Letter of Continued NHS Permission to the CI, to list all associated updated study documents and templates, copying to all appropriate contacts and Support Services using the current template letter. (Appendix 1)

1.1.12 For CSP studies, the R&D Coordinator or delegate uploads the regulatory approvals and Letter of Continued NHS Permission to CSP as per the current CSP Operational Guidelines.

1.1.12.1 The R&D Coordinator or delegate subsequently completes allocated CSP amendment tasks for the amendment (this applies to Category A and where appropriate Category B amendments only, see section 4 regarding amendment classifications).

1.1.13 The R&D Coordinator or delegate completes the Amendment task in RMS and updates the RMS diary page accordingly.

1.1.14 For studies with an STH number >17000, all amendment documentation is saved in the STH electronic R&D Master File on Alfresco.

1.1.15 For studies with an STH number <17000, all amendment documentation is saved in the R&D S Drive folder.

1.1.16 A paper copy of the documentation is printed and filed in the R&D Master File and the yellow tracking sheet updated accordingly.

1.1.17 Where there are multiple sites, the CI or delegated CTRU is responsible for ensuring that the amendment is disseminated to the PI teams for review, local R&D approval (where the amendment is not classed as Category C, see section 4 below) and implementation.

1.1.18 Where the amendment involves a change in funding and STH is providing funding to other sites, the R&D Coordinator will liaise with the relevant contacts at the PI sites to update the financial agreements as necessary.

1.2 Where STH is the Study Sponsor (CTIMP/device studies): Non-substantial Amendments

1.2.1 The CI or delegate drafts the amendment and identifies any risks or implications of the amendment and ensures that these can be accommodated and then forwards the documentation along with any risks and implications of the amendment to the R&D Coordinator.

1.2.2 The R&D Co-ordinator reviews the revised/new study documents, identifies any risks or implications of the amendment and ensures that these can be accommodated.

1.2.3 Where the responsibility for risk assessment and management has not been delegated to a CTRU or other body, the R&D Coordinator forwards the amendment to the Risk Assessment Lead or Deputy.

1.2.4 The Risk Assessment Lead or Deputy advises whether the amendment has any impact on the original risk assessment for the study and takes forward any necessary reassessment until all issues if any have been addressed in liaison with the CI and study team.

1.2.5 For CSP studies, the CI or delegate uploads the amendment documents to CSP as per the current CSP Operational Guidelines. The R&D Co-ordinator may assist with this task if the CI or delegate is unfamiliar with the process. The amendment will then be classified as Category A, B or C by the lead CRN according to the updated categorisation method (see section 4 below).

1.2.6 Where the amendment impacts on the Support Services/Facilities (as determined by the CI or their delegate) and/or financial requirements for the study, documents are updated by the R&D Co-ordinator or delegate and saved within Alfresco. In the instances where Support Service forms do not apply, the R&D Co-ordinator emails the Support Service contact a copy of the Amendment Summary and a tracked changes version of the protocol.

1.2.7 The R&D Co-ordinator requests the appropriate Support Services/Finance approval via document sharing in Alfresco and starts the Amendment task in the Research Management System (RMS).

1.2.8 Where Support Services and/or Finance review is not required, the R&D Co-ordinator starts the Amendment task, changing the Support Services status to "approved"

1.2.9 Once Support Service/Finance approvals as applicable are in place, the R&D Co-ordinator or delegate issues a Letter of Continued NHS Permission to the CI, copying to all appropriate contacts and Support Services using the current template letter (Appendix 1)

1.2.10 For CSP studies, the R&D Co-ordinator or delegate uploads the Letter of Continued NHS Permission to CSP as per the current CSP Operational Guidelines.

1.2.10.1 The R&D Co-ordinator or delegate subsequently completes allocated CSP amendment tasks for the amendment (this applies to Category A and where appropriate Category B amendments only, see section 4 regarding amendment classifications).

1.2.11 The R&D Co-ordinator or delegate completes the Amendment task in RMS and updates the RMS diary page accordingly.

1.2.12 For studies with an STH number >17000, all amendment documentation is saved in the STH electronic R&D Master File on Alfresco.

1.2.13 For studies with an STH number <17000, all amendment documentation is saved in the R&D S Drive folder.

1.2.14 A paper copy of the documentation is printed and filed in the R&D Master File and the yellow tracking sheet updated accordingly.

1.2.15 Where there are multiple sites, the CI or delegated CTRU is responsible for ensuring that the amendment is disseminated to the PI teams for review, local R&D approval (where the amendment is not classified as Category C, see section 4 below) and implementation.

1.2.16 Where the amendment involves a change in funding and STH is providing funding to other sites, the R&D Co-ordinator will liaise with the relevant contacts at the PI sites to update the financial agreements as necessary.

1.2.17 The non-substantial amendment will be incorporated with the next substantial amendment to REC and MHRA. The R&D Co-ordinator will inform the CI of this and remind them of the next Annual Progress Report to REC.

2 Where STH is the Study Sponsor (non-CTIMP/non-device studies)

The CI or delegate informs the R&D Coordinator of a required amendment forwarding a copy of all study documents containing the proposed changes and requests advice from the Coordinator regarding whether the amendment is classified as substantial for the purposes of the REC.
The R&D Coordinator confirms whether the amendment is substantial or non-substantial.

2.1 Where STH is the Study Sponsor (non-CTIMP/non-device studies): Substantial Amendments

2.1.1 The CI or delegate drafts the Amendment Notification Form and revised/new study documents, identifies any risks or implications of the amendment and ensures that these can be accommodated. The CI or delegate then forwards the documentation along with any risks and implications of the amendment to the R&D Coordinator.

2.1.2 The R&D Co-ordinator reviews the amendment form for completeness and requests Sponsor signature on the Amendment Notification Form from the Research Manager or approved delegate.

2.1.3 The CI or delegate submit the amendment to the REC and addresses any requests for further information, forwarding the approval letter to the R&D Coordinator on receipt.

2.1.4 For CSP studies, the CI or delegate uploads the amendment documents to CSP as per the current CSP Operational Guidelines. The R&D Coordinator may assist with this task if the CI or delegate is unfamiliar with the process. The amendment will then be classified as Category A, B or C by the lead CRN according to the updated categorisation method (see section 4 below).

2.1.5 Where the amendment impacts upon the Support Services/Facilities (as determined by the CI or delegate) and/or financial requirements for the study, the appropriate Support Service documents are updated by the R&D Coordinator or delegate and saved within Alfresco. In the instances where Support Service forms do not apply, the R&D Coordinator emails the Support Service contact a copy of an Amendment Summary and a tracked changes version of the protocol.

2.1.6 The R&D Coordinator requests the appropriate Support Services/Finance approval via document sharing in Alfresco and starts the Amendment task in the Research Management System (RMS).

2.1.7 Where Support Services and/or Finance review is not required, the R&D Coordinator starts the RMS Amendment task, changing the Support Services status to “approved”.

2.1.8 Once REC and Support Service/Finance approvals as applicable are in place, the R&D Coordinator or delegate issues a Letter of Continued NHS Permission to the CI, to list all associated updated study documents and templates, copying to all appropriate contacts and Support Services using the current template letter.

2.1.9 For CSP studies, the R&D Coordinator or delegate uploads the regulatory approvals and Letter of Continued NHS Permission to CSP as per the current CSP Operational Guidelines.

2.1.9.1 The R&D Coordinator or delegate subsequently completes allocated CSP amendment tasks for the amendment (this applies to Category A and where appropriate Category B amendments only, see section 4 regarding amendment classifications).

2.1.10 The R&D Coordinator or delegate completes the Amendment task in RMS and updates the RMS diary page accordingly.

2.1.11 For studies with an STH number >17000, all amendment documentation is saved in the STH electronic R&D Master File on Alfresco.

2.1.12 For studies with an STH number <17000, all amendment documentation is saved in the R&D S Drive folder.

2.1.13 Where there are multiple sites, the CI or delegated CTRU is responsible for ensuring that the amendment is disseminated to the PI teams for review, local R&D approval (where the amendment is not classed as Category C, see section 4 below) and implementation.

2.1.14 Where the amendment involves a change in funding and STH is providing funding to other sites, the R&D Coordinator will liaise with the relevant contacts at the PI sites to update the financial agreements as necessary.

2.2 Where STH is the Study Sponsor (non-CTIMP/device studies): Non-substantial Amendments

2.2.1 The CI or delegate reviews the amendment to identify any risks or implications of the amendment and ensures that these can be accommodated. The R&D Co-ordinator advises the CI or delegate to submit the amendment to the Research Ethics Committee who provided the original favourable opinion, for information along with the next substantial amendment.

2.2.2 For CSP studies, the CI or delegate uploads the amendment documents to CSP as per the current CSP Operational Guidelines. The R&D Co-ordinator may assist with this task if the CI or delegate is unfamiliar with this process. The amendment will then be classified as Category A, B or C by the lead CRN according to the updated categorisation method (see section 4 below).

2.2.3 Where the amendment impacts on the Support Services/Facilities (as determined by the CI or delegate) and/or financial requirements for the study, documents are updated by the R&D Co-ordinator or delegate and saved within Alfresco. In the instances where Support Service forms do not apply, the R&D Co-ordinator emails the Support Service contact a copy of the Amendment Summary and a tracked changes version of the protocol.

2.2.4 The R&D Co-ordinator requests the appropriate Support Services/Finance approval via document sharing in Alfresco and starts the Amendment task in the Research Management System (RMS).

2.2.5 Where Support Services and/or Finance review is not required, the R&D Co-ordinator starts the Amendment task, changing the Support Services status to “approved”.

2.2.6 Once Support Service/Finance approvals as applicable are in place, the R&D Co-ordinator or delegate issues a Letter of Continued NHS Permission to the CI, copying to all appropriate contacts and Support Services using the current template letter (Appendix 1).

2.2.7 For CSP studies, the R&D Co-ordinator or delegate uploads the Letter of Continued NHS Permission to CSP as per the current CSP Operational Guidelines.

2.2.7.1 The R&D Co-ordinator or delegate subsequently completes allocated CSP amendment tasks for the amendment (this applies to Category A and where appropriate Category B amendments only, see section 4 regarding amendment classifications).

2.2.8 The R&D Co-ordinator or delegate completes the Amendment task in RMS and updates the RMS diary page accordingly.

2.2.9 For studies with an STH number >17000, all amendment documentation is saved in the STH electronic R&D Master File on Alfresco

2.2.10 For studies with an STH number <17000, all amendment documentation is saved in the R&D S Drive folder

2.2.11 Where there are multiple sites, the CI or delegated CTRU is responsible for ensuring that the amendment is disseminated to the PI teams for review, local R&D approval (where the amendment is not classified as Category C, see section 4 below) and implementation.

2.2.12 Where the amendment involves a change in funding and STH is providing funding to other sites, the R&D Co-ordinator will liaise with the relevant contacts at the PI sites to update the financial agreements as necessary.

3 Where STH is not the Study Sponsor

The R&D Coordinator is notified of an amendment and provided with the amendment documents via the Sponsor, PI team or CSP. The R&D Coordinator should be notified of whether the amendment is substantial or non-substantial (and in the case of CSP studies whether the amendment is Category A/B/C)

3.1 Where STH is not the Study Sponsor: Substantial and Non-Substantial Amendments

3.1.1 Where appropriate, the R&D Coordinator establishes CSP categorisation of the amendment (see section 4). If the amendment is Category A or Category B and applicable to STH, the R&D Co-ordinator ensures the PI team are happy to support the amendment as appropriate. If the study is a non-CSP study, the R&D Co-ordinator will confirm with the Sponsor if the amendment requires review at STH as appropriate.

3.1.2 Where the amendment impacts upon the Support Services/Facilities and/or financial requirements for the study, the appropriate Support Service documents are updated by the R&D Coordinator or delegate and saved within Alfresco

3.1.3 In instances where Support Service forms do not apply, the R&D Co-ordinator emails the relevant Support Service a copy of the available Amendment Summary and the tracked changes protocol, where there are financial implications.

3.1.4 The R&D Coordinator requests the appropriate Support Services/Finance approval via document sharing in Alfresco (or by email for older studies) and starting the Amendment task in RMS. Where Support Services and/or Finance review is not required, the R&D Coordinator starts the RMS Amendment task, changing the Support Services status to “approved”.

3.1.5 If there is an impact on the study costs, the R&D Co-ordinator may request a change to the site agreement for the study where appropriate.

3.1.6 Once regulatory (REC/MHRA as applicable), and Support Service approvals and confirmed funding as applicable are in place, the R&D Coordinator or delegate issues a Letter of Continued NHS Permission to the PI, copying to all appropriate contacts and Support Services using the current template letter

3.1.7 For CSP studies the R&D Coordinator or delegate uploads the Letter of Continued NHS Permission to CSP as per the current CSP Operational Guidelines and completes any outstanding CSP amendment tasks.

3.1.8 The R&D Coordinator or delegate completes the amendment task in RMS and RMS diary page updated accordingly.

3.1.9 For studies with an STH number >17000, all amendment documentation is saved in the electronic R&D Master File on Alfresco.

3.1.10 For studies with an STH number <17000, all amendment documentation is saved in the R&D S Drive folder.

4 CSP Categorisation of Studies

4.1 The CSP process classifies all amendments Category A, B or C – irrespective of whether these are substantial or non substantial, with exception to urgent safety measures. Urgent safety measures should be notified to all participating NHS organisations promptly to ensure participants safety; the new categorisation is based on the impact an amendment has on a site. This determines the need for review of an amendment by R&D offices at each participating site:

4.1.1 **Category A** (notifiable): An amendment that impacts or affects ALL participating NHS organisations and therefore needs to be considered and may need change control actions.

4.1.2 **Category B** (notifiable): An amendment that impacts or affects SPECIFIC participating NHS organisations. Only at these organisations does it need to be considered and take any change control actions required.

4.1.3 **Category C** (non-notifiable): An amendment that does not have an impact on NHS organisations that require management or oversight. Therefore R&D do not need to be notified of such amendments however they will have access to all documents within CSP Module.

4.2 For Category A and Category B (where applicable to STH) amendments where R&D offices are made aware of the amendment, see the processes as outlined in sections 1-3 above.

4.3 For Category B (where not applicable to STH) and Category C amendments, refer to the following process:

4.3.1 Where an amendment is classified as Category B (where not applicable to STH) or Category C within CSP and R&D offices are not notified by any route, no action can be taken by the R&D Coordinator.

4.3.2 Where an amendment is classified as Category B (where not applicable to STH) or Category C, but the R&D office is made aware of the amendment, an email of acknowledgement is issued (Appendix1) by the R&D Coordinator or delegate. The email is copied to the notifier. There is no requirement to upload the acknowledgement email to CSP or for the R&D Coordinator to review the amendment.

4.3.3 Where documents are received, they are stored on the Alfresco system for studies with an STH number >17000 or in the S Drive folder for studies with an STH Number <17000.

4.3.4 If no documents are received, no acknowledgement email is required.

4.3.5 Where the study is an STH Sponsored CTIMP/Device, the R&D Coordinator reviews the amendment following the process described above in Sections 1-3. A full Letter of Continued NHS Permission will be sent instead of the email notification process described above.

Appendix 1 Documents Associated with the SOP

	Document	S-drive	Website	RMS	Who
1	Letter of continued NHS permission	S:\General\Research Governance\Amendments	No	RMS 1, Alfresco section 5.2	ZW

Appendix 2 SOP revisions and history

SOP number	Effective date	Reason for change	Author
THIS SOP			
C105 V3.0	17 Nov 15	To incorporate use Support Service Forms for review, when an amendment impacts financially on a given Support Service. General reformatting.	RS
PREVIOUS SOPs			
C105 V2.0		To bring procedures in-line with the notifiable and non-notifiable processes.	MH, GK, JDM
C105 V1.0			AP, TL