noclor
RESEARCH SUPPORT

NHS

Amendments

Sponsored Research

SOP Reference ID:		Noclor/Spon/S07/02	
Version Number	2.0	**Effective Date:**	15th June 2016

It is the responsibility of all users of this SOP to ensure that the correct version is being used. The definitive versions of Noclor SOPs are available from the Noclor website https://www.noclor.nhs.uk/training-resources either by checking the document library or by carrying out a specific document search

Standard Operating Procedure: Amendments

Version History

SOP Reference ID	Effective Date	Reason for Change
Noclor/Spon/S07/01	01/03/2016	
Noclor/Spon/S07/02	15/06/2016	SOP content (and associated templates) relating to HRA approval/ NHS permissions have been revised further to full implementation of HRA Approval Systems from 31/03/2016.

Authorship and Authorisation

Author Job Title:	Noclor Sponsor Representative			
Reviewed by:	Noclor Senior Management Group		Date:	24th May 2016
Authorised by:	Lynis Lewis, Noclor Service Director			
	Signature:	Signed copy held by Noclor	Date:	8th June 2016

SOP Content

Standard Operating Procedure: Amendments

1. Purpose

The Chief Investigator (CI) must keep the sponsor and all relevant review and approval bodies informed of any changes to their research study post-approval. Changes to the study are defined as either substantial or non-substantial. Substantial amendments require approval (from the relevant bodies) before they can be implemented except in the case of Urgent Safety Measures (Noclor/Spon/S08/0X).

This Standard Operating Procedure (SOP) describes the procedures for managing amendments in research sponsored by a Noclor Partner NHS Trust.

2. Scope

This SOP should be followed by Chief Investigators (CIs) that are responsible for setting up and managing health research that is sponsored by a Noclor Partner NHS Trust to ensure that any changes to the research post-approval are managed in accordance with sponsor procedures.

3. Abbreviations

CI	Chief Investigator
CTIMP	Clinical Trial of Investigational Medicinal Product(s)
HRA	Health Research Authority
ISF	Investigator Site File
PI	Principal Investigator
SOP	Standard Operating Procedure
S/TMF	Study/Trial Master File

4. Procedure and Responsible Personnel

It is the responsibility of the sponsor to determine whether an amendment is substantial and confirm which approvals are required prior to any submission being made by the delegated responsible party.

	Procedure	Responsible Personnel
4.1	**Classifying the amendment** The Chief Investigator (CI) is responsible for initially classifying the proposed amendment as substantial or non-substantial and assessing what approvals are required. For further guidance on classifying the proposed changes the CI should refer to: relevant HRA Guidance; the MHRA (Grey Guide) for Clinical Trial of Investigational Medicinal Products (CTIMPs) and/or contact the Noclor Sponsor Representative directly for advice or opinion prior to preparing the amendment submission. For clinical trials, where a substantial amendment relates to an	Chief Investigator (CI)

	Urgent Safety Measure (USM) or Temporary Halt please also refer to relevant SOPs (USM Noclor/Spon/S08/0X and Temporary Halts Noclor/Spon/S09/0X).	
4.2	**Preparation of amendment submission** **Substantial amendments** forms should be prepared through IRAS (the system automatically generates the type of notice of substantial amendment form that is appropriate to the project category) **Non-substantial amendments** require a Non-Substantial/Minor Amendments(s) for NHS Studies Form to be completed and authorised as part of the amendment submission pack. This form (current version) is available on the HRA website and must be authorised by the Noclor Sponsor Representative. The CI or member of the study team (as delegated by CI) should prepare the amendment submission documents for sponsor review (substantial or non-substantial) as below : 4.2.1 A complete amendment pack should be submitted by email for review to the Noclor Sponsor Representative. The pack should include the following as relevant to the amendment : ▪ draft cover letter(s)/summary of changes ▪ new or revised supporting documents (tracked changes version and clean version for revised documents) ▪ if the protocol has been revised - tracked changes version and a clean new version authorised by the CI should be submitted ▪ draft notice of substantial amendment form (where relevant) **OR** ▪ Non-Substantial/Minor Amendments(s) for NHS Studies Form, completed and CI authorised (where relevant) 4.2.2 All amendments should be given a unique sequential study amendment reference code, this reference should be referred to in the cover letter (and in the notice of substantial amendment form OR Non-Substantial/Minor Amendments(s) for NHS Studies Form) and tie in with the details of the amendment added to the Amendment Log Noclor/Spon/T06/02 and NHS/R&D Substantial Amendment Approval /Implementation Form Noclor/Spon/T13/02 (where relevant)	Chief Investigator (CI)

	4.2.3 All study documents must be version controlled. For clinical trials the details of revised study documents must be added to the Document Inventory Log Noclor/Spon/T07/0X The CI is responsible for consistency checking across all documents to ensure that information is consistent and accurate before submitting an amendment to sponsor for review.	
4.3	**Sponsor Review** The Noclor Sponsor Representative will : 4.3.1 confirm receipt of amendment submission by return of email 4.3.2 confirm classification of the amendment (substantial or non-substantial) 4.3.3 confirm which review bodies the amendment should be submitted to 4.3.4 review the amendment documents for completeness (the CI is responsible for accuracy, consistency and version control) *4.3.5* review risks as required (refer to Noclor/Spon/S03/0X)	Noclor Sponsor Representative
4.4	**Sponsor Authorisation** 4.4.1 If any comments/revisions are required prior to sponsor authorisation these will be communicated to CI/trial manager via email. 4.4.2 The Noclor Sponsor Representative will provide sponsor authorisation for the amendment to be submitted (this will be via email in response to amendment submission). 4.4.3 For substantial amendments 4.4.3.1 CTIMPs ▪ The notice of substantial amendment form reviewed by sponsor can be submitted via IRAS for electronic authorisation by CI (for amendment notification to REC and HRA/NHS organisations) and Sponsor (for MHRA amendment submission) ▪ Where revision has been made to the trial protocol the Noclor Sponsor Representative will authorise the revised protocol and send the original wet signed protocol signature page back to the CI by tracked post for filing in the Trial Master File (TMF)	Noclor Sponsor Representative

4.4.3.2 All other research

The notice of substantial amendment form can be submitted via IRAS for electronic authorisation by sponsor.

4.4.4 For non-substantial/minor amendments(s) the sponsor will authorise the Non-Substantial/Minor Amendments(s) for NHS Studies Form and return it to the CI

4.5 **Submit**

Once authorised by the sponsor the amendments should be submitted by the delegated responsible person as follows:

Approval /Review Body	Amendment Type	Party Responsible for Submission
REC	▪ Substantial Amendments that require favourable REC ▪ *Non-substantial amendments for notification only (at sponsor's discretion)*	Chief Investigator (CI) to send approved submission to REC (the REC that approved study) by email, the Noclor Sponsor Representative should be copied in
MHRA	▪ Substantial Amendments that require authorisation from Competent Authority	Noclor Sponsor Representative (or delegate) will submit via Common European Submission Platform (CESP).
HRA[1] (for participating NHS organisations)	▪ Substantial amendments for studies with HRA approval that included NHS REC review only need to submit amendment to REC ▪ Substantial amendments for projects that did not require NHS REC and non-substantial amendments for all project types should submit amendment to hra.amendments@nhs.net	Chief Investigator (CI) to send approved submission to relevant party (and copy in Noclor Sponsor Representative)
National Offender Management Service (NOMS)	▪ The National Research Coordinator should be notified of all amendments. It is not necessary to submit a Notice of Substantial	Chief Investigator (CI) to notify amendment by email to the National Research Coordinator and copy in Noclor Sponsor

As indicated in table

		Amendment form for this review body.	Representative
	Other	▪ Amendment approval or notification by specific organisations as required (e.g funder)	Chief Investigator (CI) to notify amendment by email as relevant and copy in Noclor Sponsor Representative

[1]Amendments for studies set-up pre-HRA approval should be submitted in exactly the same way as HRA approval studies.

4.6 **Amendment Approvals and Acknowledgements** — Chief Investigator (CI)

Amendments requiring approval cannot be implemented until the relevant approvals are in place except in the case of Urgent Safety Measures (Noclor/Spon/S08/0X).

4.6.1 HRA/NHS Permissions and Notifying Sites

4.6.1.1 HRA will confirm receipt of the amendment submission and inform the applicant (CI) of the 'category[2]' of the amendment within 5 days.

4.6.1.2 The applicant (CI) can/should send the amendment documentation and categorisation information to participating NHS sites (investigators and R&D) at this stage (copy in the Noclor Sponsor Representative) so that, where necessary, arrangements can be put in place to continue the sites capacity and capabilities to deliver the study/prepare for the amendment

4.6.1.3 The amendment will be assessed by HRA and once any regulatory requirements are in place a letter confirming continuing HRA Approval (or outcome of the amendment assessment) will be sent to the applicant (CI).

4.6.1.4 The outcome of HRA assessment should be shared with the participating NHS sites (investigators and R&D).

4.6.1.5 CI/Sponsors can assume continuing permission for the study/permission to implement the amendment at a specific participating NHS organisation 35 days after the NHS organisation has been notified, subject to other required approvals being in place (including HRA approval), unless the NHS organisation raises an objection within this period.

- It is considered good practice for a letter to be issued to the CI/Sponsor to confirm continuing permission NHS

	permission within the 35 days, however where a letter is not issued and no objection is raised amendment approval is presumed. ▪ All communications in regards to HRA/NHS organisations and whether permission is presumed or evident for an amendment of a specific participating NHS organisation should be retained in the S/TMF 4.6.2 Amendment approvals, acknowledgements and all related communications should be filed in Study/Trial Master File (S/TMF) with the amendment submission documentation. 4.6.3 For clinical trials, the CI should provide the Noclor Sponsor Representative with copies of all approvals/acknowledgments (where the sponsor has not been copied in on correspondence) [2]*Categories* *A - Amendment to a research study that ALL participating NHS organisations are expected to consider to determine whether they are able to continue NHS research permission.* *B - Amendment to a research study that only those participating NHS organisations affected by the amendment are expected to consider to determine whether they are able to continue NHS research permission.* *C - Amendment to a research study that participating NHS organisations are not expected to consider. This category includes any amendment to a research study that has no implications that require management or oversight by the participating NHS organisations hosting the research study.*	
4.7	**Amendment Documentation** 4.7.1 The Amendment Log Noclor/Spon/T06/02 should be updated and filed in the S/TMF. 4.7.2 Details of approval of substantial amendments to the level of participating NHS organisations should be recorded on the NHS/R&D Substantial Amendment Approval /Implementation Log Noclor/Spon/T13/02 by the CI/study team and filed in the S/TMF 4.7.3 For clinical trials, the document inventory log Noclor/Spon/T07/0X should be updated with details of new or revised study documents 4.7.4 For clinical trials, a copy of all three updated logs should be sent to the Noclor Sponsor Representative 4.7.5 Amendment packs sent to participating sites by CI/study team should contain all information/documentation relevant	Chief Investigator (CI)

	to the amendment (including amendment forms, revised documents, HRA categorisation information, all approvals/acknowledgements, completed amendment logs as above etc). 4.7.6 For CTIMPs, Principal Investigators (PIs) will be required to confirm that they will comply with the revised protocol by signing a protocol signature page (either as part of the revised protocol itself or as separate signature page which details the protocol version etc). Original PI signature pages should be retained at site in the Investigator Site File (ISF) and a copy returned to CI/study team for filing in the TMF.	
4.8	**Implementation of Substantial Amendments** Substantial amendments can be implemented once the above steps have been completed successfully (and are evidenced on file). Note:- external sites are delegated responsible through their mNCA for ensuring that substantial amendments to the protocol are not implemented prior to the relevant approvals being evident.	Investigators
4.9	All documents and correspondence pertaining to an amendment must be filed by the CI in the S/TMF and at participating sites in the ISF by the local investigator.	Chief Investigator (CI)/Principal Investigator (PI)
4.10	Details of the amendment will be uploaded to the study record on the Noclor IMS system	Noclor Sponsor Representative

5. Deviation from SOP

Noclor Sponsor SOPs define working methods which should be adhered to. However, occasionally for specific projects it may be necessary to deviate from the Sponsor SOP.

Formal written explanations/justifications of such deviations must be approved by Noclor Sponsor Representative prior to implementation (or they will be considered a non-compliance to sponsor procedures requiring reporting according to SOP Noclor/Spon/S10/0X).

The deviation from Sponsor SOP should be recorded on the SOP Deviation Form (Noclor/Inter/T12/0X) and sent to the Sponsor Representative for review. A copy of the completed and signed form should be filed with the S/TMF.

6. SOP Storage and Archive

For clinical trials, the details of this SOP should be included on the study specific document inventory log (Noclor/Spon/T07/0X).

The Chief Investigator (CI) is responsible for retaining and archiving Sponsor SOPs (and the associated training records) that have been worked to for the duration of a research study in the Study/Trial Master File (S/TMF).

7. Associated Documents

Document Reference ID	Document Type	Document Title
Noclor/Spon/T06/02	Template	Amendment Log
Noclor/Spon/T07/0X	Template	Document Inventory Log
Noclor/Spon/T13/02	Template	NHS/R&D Substantial Amendment Approval /Implementation Log

8. Appendices

9. Confirmation of Training

This SOP will be provided to the Chief Investigator (CI) and he/she will have the opportunity to ask specific questions to the author of the SOP.

For clinical trials, the CI must e-sign the confirmation of self-training below prior to the study commencing.

The CI is responsible for ensuring that members of his/her study team are trained in the sponsor procedures (SOPs) that are relevant to their specific roles and responsibilities on the study.

I,

confirm that I have read and understood the content of this SOP and will work according to it.

Sponsor SOPs should be filed in the relevant section of the Study/ Trial Master File (S/TMF). If this SOP replaces a previous version, the previous version should be retained in the S/TMF and marked through as superseded.

For clinical trials, the SOP details should be added to the document inventory log (Noclor/Spon/T07/0X).

10. SOP Training Log

All members of the co-ordinating trial team concerned by this SOP (according to the role and responsibilities they are being delegated by the CI and as they appear on the co-ordinating trial team delegation log) should sign the SOP training log.

	Full Name	By signing below I confirm that I understand and agree to work to this SOP	
		Signature	Date

This training log should be filed in the relevant section of the S/TMF.