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RESEARCH SUPPORT

NHS

Site Initiation and Activation

Clinical Trials

SOP Reference ID:		Noclor/Spon/S05/01	
Version Number	1.0	**Effective Date:**	23rd February 2016

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Standard Operating Procedure: Site Initiation and Activation

Version History

SOP Reference ID	Effective Date	Reason for Change
SOP CA012 Version 1.0	14/04/2009	
SOP CA012 Version 2.0	18/09/2011	Administrative change from Camden PCT to CNWL NHS Foundation Trust (Camden Provider Services). Minor revisions/clarifications to procedures.
Noclor/Spon/S05/01	23/02/2016	Newly created Noclor SOP (applicable to all Noclor partner NHS Trusts). New numbering system adopted so this SOP has been assigned first version. New SOP format and revised content.

Authorship and Authorisation

Author Job Title:	Noclor Sponsor Representative		
Reviewed by:	Noclor Senior Management Group	Date:	11th December 2015
Authorised by:	Lynis Lewis, Noclor Service Director		
	Signature: Signed copy held by Noclor	Date:	15th February 2016

SOP Content

Standard Operating Procedure: Site Initiation and Activation

1. Purpose

Clinical trials must be conducted in accordance with the protocol and all applicable guidelines, laws and regulations. This Standard Operating Procedure (SOP) describes the procedure to ensure that a site participating in a clinical trial sponsored by a Noclor Partner NHS Trust is initiated prior to the trial commencing and any procedures taking place.

2. Scope

This SOP should be followed by all personnel who are involved in preparing for or conducting trial initiation activities at participating research sites for clinical trials (CTIMPs and non-CTIMPs) where Noclor is representing the NHS Trust sponsor.

3. Abbreviations

CI	Chief Investigator
CTIMP	Clinical Trial of Investigational Medicinal Product
IMP	Investigational Medicinal Product
ISF	Investigator Site File
PI	Principal Investigator
PSF	Pharmacy Site File
SIV	Site Initiation Visit
SOP	Standard Operating Procedure
TMF	Trial Master File

4. Procedure and Responsible Personnel

Site initiation is the process by which the sponsor is assured that the Principal Investigator (PI) at site is trained in the protocol and other instructions (as relevant) prior to issuing a 'study activation notice' which permits the site to commence the study. The study activation notice must be issued prior to obtaining consent from the first subject.

Site Initiation can only be conducted after Ethics, Competent Authority [for Clinical Trials of Investigational Medicinal Products (CTIMPs)], sponsor and site permissions/ approvals have been received.

For CTIMPs, a visit to site [Site Initiation Visit (SIV)] to initiate the study is mandatory. Site initiation for non-CTIMPs may be conducted using formats other that site visits (for example: a video conference, investigator meeting or teleconference).

Site initiation should be conducted once all supplies (including study documentation) are available to the Investigator site. If certain supplies are not available to the site for any reason at the time of the site initiation then this should be documented in the site initiation report (a further visit /training may be required).

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Site initiation should be conducted by personnel who are familiar (trained) in the protocol and all other applicable documents, procedures and the relevant regulatory requirements. This is usually the Trial Monitor/Manager but maybe other personnel as appropriate (and as agreed with sponsor during trial set-up).

	Procedure	Responsible Personnel
4.1	Prior to site initiation [and for CTIMPs before Investigational Medicinal Product (IMP) supplies are shipped to the site], the following permissions should have been obtained : 4.1.1 For CTIMPs, Clinical Trial Authorisation (CTA) from Competent Authority (if any conditions to authorisation ensuring these have been met) 4.1.2 Ethics approval (with conditions of approval met) 4.1.3 Site-specific approval (with fully executed clinical trial agreement evident prior to this approval being obtained)	Chief Investigator (CI)
4.2	The following study documents should be provided to the sponsor for review prior to site initiation and before the study documents are made available to participating sites : 4.2.1 Final approved protocol 4.2.2 Study procedures manual(s)/Study specific SOPs [including details on consent procedures, assessment of eligibility, randomisation and unblinding, 24 hour medical cover (where relevant), protocol deviations, non-compliance, Urgent Safety Measure (USM) etc] 4.2.3 Safety Reporting Procedures and Forms 4.2.4 IMP Procedures and Logs (for management, accountability and storage of IMP for CTIMPs) 4.2.5 Blinded studies - procedures on how the randomisation list will be created and managed throughout trial 4.2.6 Completed Document Inventory Log (Noclor/Spon/T07/0X) 4.2.7 Completed Amendment Log (Noclor/Spon/T06/0X) and NHS/R&D Substantial Amendment Approval /Implementation Log (Noclor/Spon/T13/01) 4.2.8 Delegation of responsibilities ▪ Completed Co-ordinating Centre Delegation Log ▪ Site Specific Delegation and Signature Log Template (to be used at all sites) 4.2.9 Screening and Enrolment Log Templates (to be used at all	Chief Investigator (CI)

	sites) 4.2.10 The Case Report Forms (CRFs) and instructions on its handling and completion (evidence of input/review by trial statistician) 4.2.11 Oversight Committee - Charter(s) or Terms of Reference (as relevant) 4.2.12 Data management procedures (evidence of review /approval by trial statistician) 4.2.13 Statistical Analysis Plan (SAP) if not included in the protocol 4.2.14 Laboratory sample handling procedures including sample storage, processing and dispatch (where relevant) 4.2.15 Site initiation agenda and reference/training material that will be used at site initiation (e.g slide presentations)	
4.3	Prior to the trial being initiated/activated the sponsor will ensure that: 4.3.1 Funding is awarded (i.e for NIHR grants - prime contract is fully executed and start certificate issued) 4.3.2 Contracts/agreements are fully executed prior to contracted activities commencing 4.3.3 The CI has been provided with all mandated sponsor SOPs and templates for use in the trial 4.3.4 Relevant sponsor SOPs have been signed off by CI (evidence of self-training at the latest prior to study being activated) 4.3.5 Study documentation /procedures do not conflict with or contradict sponsor procedures (note- sponsor may request changes are made before documentation/ procedures are finalised and distributed to site) 4.3.6 IMP Management & Accountability Procedures have been approved by Sponsor Pharmacy Representative (CTIMPs) 4.3.7 Risks have been assessed/mitigation plans are in place 4.3.8 A trial specific monitor plan has been drafted (for CTIMPs the monitoring plan must be agreed to by the Noclor Sponsor Representative and the CI)	Noclor Sponsor Representative
4.4	**Regulatory Release of IMP (CTIMPs)** The Noclor Sponsor Representative will authorise release of IMP	Noclor Sponsor Representative

	to sites in accordance with the requirements of Article 9 (Commencement of a clinical trial or Regulatory Green light) of Directive 2001/20/EC prior to SIV	
4.5	Site initiation should be arranged for when trial supplies (including IMP for CTIMPs) have been sent to site. The agenda for site initiation should be sent to the PI/site staff in advance of the meeting/visit.	Trial Monitor/Manager
4.6	**Site Initiation Attendance** The PI must be in attendance at site initiation. If the PI is not available then another visit/meeting would need to be arranged before the site can be activated by sponsor. For CTIMPs, the clinical trial pharmacist (person being delegated overall responsibilities for IMP storage, management and accountability by PI) must also attend the SIV. A pharmacy initiation visit may take place separately to the main SIV (note- this would still require reporting prior to the site being activated by sponsor).	Trial Monitor/Manager
4.7	**Site initiation should cover the following :** 4.7.1 The procedure for study activation at site [i.e issue of activation notice by sponsor further to the site initiation being conducted and reported. No study procedures should be undertaken by sites until they have received this is notice] 4.7.2 The current approved protocol and any amendments (refer to Amendment Log). 4.7.3 PI Signature/Declaration page for current approved version of protocol should be signed, a copy collected for the Trial Master File (TMF), the original should be retained at site in the Investigator Site File (ISF) 4.7.4 Current approved documents with local details where appropriate (e.g Patient Information Sheets/Consent/GP letters) 4.7.5 Study supplies and documentation (e.g Document Inventory Log/ISF etc) 4.7.6 Delegation of Responsibilities. The site specific Delegation and Signature Log should be completed, signed by the PI and a copy collected for the TMF, the original should be retained at site in the ISF. [It is essential that the PI is aware of their role on the trial (in terms of PI oversight and	Trial Monitor/Manager

	how this should/will be evidenced). The PI should also understand the importance of keeping this log up to date throughout the life of the trial and delegating roles/responsibilities according to the individuals' training and experience (and this training and experience must be appropriate and evident on file). It should also be communicated that this log and supporting evidence (such as signed/dated CVs, SOP training logs and training certificates) should be made available to the trial team (monitor/manager) or sponsor at any point during study for monitoring or auditing purposes]. 4.7.7 Consent and eligibility (for CTIMPs, medical assessment/confirmation of eligibility and where this is evidenced). 4.7.8 The Screening and Enrolment Logs and maintaining subject confidentiality 4.7.9 24 medical cover, USMs, stopping rules (where relevant) and safety and incident reporting procedures. Refer to the forms and logs (use the document references) that will be used to record and report events. ▪ For CTIMPs, include details on the Reference Safety Information (RSI) that will be referred to during the trial (and how updates to this RSI should/will be communicated/evidenced and who will be responsible) 4.7.10 Randomisation procedures and code breaking (if applicable) 4.7.11 Procedures for reporting protocol deviations and non-compliance (refer to Noclor/Spon/S10/0X and associated templates Noclor/Spon/T04/0X and Noclor/Spon/T05/0X) 4.7.12 The data capture tools (pCRF/eCRF) – training/instructions on how to handle and complete 4.7.13 For CTIMPs, IMP handling, accountability and storage [pharmacy dept/out of pharmacy areas (if relevant to IMP/trial) should be visited at part of SIV] 4.7.14 Interactions with internal support department/external departments (e.g. imaging facilities, labs etc.) 4.7.15 Laboratory sample handling procedures including sample storage, processing and despatch [facilities for processing and storing samples should be checked/reported at SIV] 4.7.16 Study timelines, recruitment requirements and strategies	

	4.7.17 Source document verification procedures and access to source data (source data location logs completed) 4.7.18 Monitoring plans (and what to do if site is notified of an audit or inspection that will involve the study) 4.7.19 Review of facilities and equipment 4.7.20 End of study, close-out, archive and publication	
4.8	The Site Initiation/Monitor Log (Noclor/Spon/T09/01) should be completed for all personnel involved in the site initiation. The original document should be retained in the ISF at site and maybe requested by monitor/sponsor at intervals.	Trial Monitor/Manager
4.9	Following the site initiation a report should be written. 4.9.1 The Site Initiation Report template (Noclor/Spon/T08/01) should be completed by the person (Trial Monitor/Manager) who conducted/led the site initiation. 4.9.2 The report should be completed as soon as possible so as not to delay the study being activated at site (but no later than 10 working days from the site initiation date). 4.9.3 If there are actions outstanding at site further to the site initiation these should be documented in the report as outstanding issues/actions arising and the trial monitor/manager should follow these up to completion. The trial monitor/manager should send a letter/email to site within 48 hours of the site initiation to clarify any outstanding issues so that they can be dealt with promptly. All paperwork and correspondence relating to the actions arising should be retained with site initiation report. 4.9.4 The site initiation report should be signed and dated and sent to the Noclor Sponsor Representative for review.	Trial Monitor/Manager
4.10	The Noclor Sponsor Representative will review the site initiation report within 5 working days of receipt and sign off as reviewed (adding any comments to the report as appropriate). 4.10.1 A signed copy of the site initiation report will be sent to the Trial Manager/Monitor for filing in the TMF. 4.10.2 The trial manager is responsible for forwarding on copies of complete signed reports to the PI/site for filing in the ISF. 4.10.3 The Noclor Sponsor Representative will issue a study	Noclor Sponsor Representative Trial Manager

	activation notice to the Trial Manager/Monitor to forward on to the site. The activation notice is part of the Site Initiation Report template (Noclor/Spon/T08/01) that is signed off by the Noclor Sponsor Representative. 4.10.4 At this point the study can commence and the first patient can be consented. 4.10.5 If for any reason a site cannot be issued with an activation notice further to the review of the site initiation report then the CI/Trial Monitor/Manager will be notified by the Noclor Sponsor Representative.	
4.11	Records of site initiation including attendance logs, correspondence, what was covered (agenda, slides, documents referenced) and reports should be retained in the TMF and at site in ISF.	Trial Monitor/ Manager /Principal Investigator (PI)

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 TMF.

6. SOP Storage and Archive

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 controlled copies of Sponsor SOPs (and the associated training records) that have been worked to for the duration of a trial in the Trial Master File (TMF).

7. Associated Documents

Document Reference ID	Document Type	Document Title
Noclor/Spon/T08/01	Template	Site Initiation Report
Noclor/Spon/T09/01	Template	Site Initiation/Monitor 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.

The CI must e-sign the confirmation of self-training below prior to site initiation.

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.

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

The SOP details should be added to the document inventory log (Noclor/Spon/T07/0X).

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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 TMF.