Standard Operating Procedure

noclor RESEARCH SUPPORT

NHS

Research Management and Monitoring

Sponsored Research

SOP Reference ID:		Noclor/Spon/S06/01	
Version Number	1.0	**Effective Date:**	21st March 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: Research Management and Monitoring

Version History

SOP Reference ID	Effective Date	Reason for Change
SOP CA007 Version 1.0	14/04/2009	
SOP CA007 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/S06/01	21/03/2016	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:	8th March 2016
Authorised by:	Lynis Lewis, Noclor Service Director		
	Signature: Signed copy held by Noclor	Date:	14th March 2016

SOP Content

Standard Operating Procedure: Research Management and Monitoring

1. Purpose

All health research should be conducted in accordance with the approved protocol, relevant legislation, GCP, governance frameworks and Sponsor Standard Operating Procedures (SOPs).

This SOP describes the sponsor procedures for managing and monitoring research sponsored by a Noclor Partner NHS Trust from the point that the study is active until end of study notification.

2. Scope

This SOP should be followed by Chief Investigators (CIs) that are responsible for conducting and managing health research that is sponsored by a Noclor Partner NHS Trust to ensure that all research activities post-approval are managed, recorded and reported in accordance with sponsor procedures.

3. Abbreviations

CI	Chief Investigator
CRF	Case Report Form
CTIMP	Clinical Trial of Investigational Medicinal Product
ISF	Investigator Site File
PI	Principal Investigator
PSF	Pharmacy Site File
PV	Pharmacovigilance
SDV	Source Data Verification
SOP	Standard Operating Procedure
S/TMF	Study/Trial Master File

4. Procedure and Responsible Personnel

There are a number of steps that must be completed before a research study that is sponsored by a Noclor Partner NHS Trust can commence; refer to Study Set-Up and Approval Noclor/Spon/S04/0X. For clinical trials, the process of study activation is a formal one whereby the sites will be issued a study activation notice prior to any study procedures being undertaken; refer to Site Activation and Initiation (Clinical Trials) Noclor/Spon/S05/0X. For the purposes of this SOP (and assuming all required steps are completed) when a research study is ready to commence it is defined as being ‘active’.

This SOP provides a detailed breakdown of sponsor procedures for active research; in alphabetical order of research related activity (the SOP content table can also be used to navigate round this section of the SOP).

Not all procedures detailed here are relevant to all research studies, however, CIs of all research sponsored by a Noclor Partner NHS Trust are expected to review this SOP and work in accordance with the procedures that are relevant to their study and incorporate/outward communicate the requirements as appropriate to research study personnel via their own study procedures/documents/training material.

	Procedure	Responsible Personnel
4.1	**Abandoned Research** In the unlikely event that an 'active' research study is abandoned after approvals have been obtained but prior to any recruitment or study activities commencing, the CI should notify/discuss with the Noclor Sponsor Representative in the first instance. The Noclor Sponsor Representative will advise on the next steps (depending on outcome of discussions and reasons for proposed abandonment).	Chief Investigator (CI)
4.2	**Addition of New Sites/Change of PI** 4.2.1 Clinical Trials of Investigational Medicinal Products (CTIMPs) - the addition of a new site(s) or a change of Principal Investigator (PI) at a site is a substantial amendment requiring review by the REC and NHS permission (for NHS sites). Refer to 4.3 4.2.2 For further guidance regarding what is required for the addition of new sites/change of PI for all other research the Chief Investigator (CI) should refer to HRA website (or contact Noclor Sponsor Representative).	Chief Investigator (CI)
4.3	**Amendments** Once a study has been approved the CI must keep the sponsor and all relevant review bodies informed of any changes to the study. Refer to SOP Amendments (Sponsored Research) Noclor/Spon/S07/0X	Chief Investigator (CI)
4.4	**Archiving** When a study has declared ended, closed-out and reported, according to SOP End of Study Notification, Close-Out and Reporting (Sponsored Research) Noclor/Spon/S11/0X, the study files/essential documents should be prepared for archive. Refer to Archive (Sponsored Research) Noclor/Spon/S12/0X	Chief Investigator (CI)
4.5	**Audits and Statutory Inspections** The CI is responsible for communicating procedures/requirements to participating sites in regards to audit and inspection. For CTIMPs, these requirements should be covered at the site initiation visit, refer to Site Initiation and Activation SOP Noclor/Spon/S05/0X. **4.5.1 Audit** 4.5.1.1 Noclor apply a risk-based approach to the frequency and nature of audit activities of sponsored research	Chief Investigator (CI)

Audits are either:

- triggered 'for cause' as a result of reports of non-compliance refer to Protocol Deviations, Non-Compliance and Serious Breaches SOP Noclor/Spon/S10/0X)
- triggered for 'investigation' as a result of a 'red-flags' (i.e review of minutes of a meeting, a monitor report or email correspondence that raises concern or a formal complaint)
- routine /random - a site or study maybe selected for audit or one particular area across all sponsored studies may be audited (such as consent or document version control etc).

4.5.1.2 Where a study/site is selected for a Noclor audit the relevant investigator will be contacted to arrange a convenient date and then the audit will be conducted according to the following basic programme:

- Introductory Meeting
- Review of Site Files as relevant (S/TMF/ISF/PSFs)
- Interviews with key study personnel (as relevant)
- Review of CRFs and other documents and check against source records
- Visit to laboratory/pharmacy (if applicable)
- Audit close out meeting

4.5.1.3 Where a study has been audited by Noclor, the Noclor Sponsor Representative will disseminate the audit report as appropriate to other parties. Signed audit reports and correspondence relating to specific study should be retained by the CI in Study/Trial Master File (S/TMF) and by the PI in the Investigator Site File (ISF) as relevant.

4.5.1.4 Where a study sponsored by a Noclor partner is selected for audit by a party other than the sponsor:

- The Noclor Sponsor Representative should be notified (ideally in advance of the audit).
- A copy of the audit report should be provided to the Noclor Sponsor Representative (as this may flag up non-compliance or issues that are study-wide as opposed to site-specific and left unreported may escalate to serious breaches)
- Reports should be retained by the CI in the S/TMF and by the PI in the ISF as relevant.

4.5.2 Statutory Inspections

4.5.2.1 Clinical Trials that are within the scope of The Medicines for

	Human Use (Clinical Trials) Regulations 2004 (SI 1031) as amended may be subjected to MHRA inspection. UK Inspectors have statutory rights; these include the rights to enter premises involved in CTIMPs to carry out inspections, take samples, request documentation and take copies of the documentation and to seize substance, articles and documents. It is a criminal offence to obstruct an inspector during a statutory inspection. 4.5.2.2 If a third party (host site or vendor) is notified of a statutory/triggered MHRA inspection of a clinical trial that is sponsored by a Noclor Partner NHS Trust, the Noclor Sponsor Representative should be notified immediately as Noclor may need to assign specific resources to assist with the inspection preparation or advice on a particular course of action. 4.5.2.3 Reports of MHRA inspection findings that relate to a specific trial sponsored by a Noclor Partner NHS Trust should be communicated to the Noclor Sponsor Representative and CI. ▪ The sponsor /CI may need to be involved in any Corrective and Preventative Action Plans (CAPA)) ▪ Reports/CAPA should be retained by the CI in the S/TMF and by the PI in the ISF as relevant.	
4.6	**Chief Investigator Responsibilities** The CI is the person designated overall responsibility for the conduct of a study. 4.6.1 For clinical trials, the sponsor will formally delegate responsibilities to the CI through a Delegation of Responsibilities Agreement. Refer to Sponsorship Request and Approval Noclor/Spon/S02/0X 4.6.2 For all other research, the CI will be sent a letter declaring sponsorship which will detail any conditions of sponsorship and the responsibilities of the CI. Refer to Sponsorship Request and Approval Noclor/Spon/S02/0X 4.6.3 Any change to the CI's circumstances that are likely to significantly impact on the safety or management of the research study (for example planned change of Chief Investigator employer or absence due to ill health/sabbatical etc) must be notified to the Noclor Sponsor Representative immediately so that an assessment of the situation can be made and the appropriate decisive action can be taken.	Chief Investigator (CI)

	Changes to the Chief Investigator's circumstances may result in one of the following (with the ultimate decision being made by the sponsor): ▪ Replacing Chief Investigator (this would require a risk assessment and documented action plan which would include: notice of substantial amendment, possible amendment to contracts and a documented handover between outgoing and incoming CI for the S/TMF, possible revision of label of IMP etc) ▪ Temporary Halt, refer to SOP Noclor/Spon/S09/0X ▪ Early termination (in the event of no suitable replacement being found). Refer to SOP Noclor/Spon/S11/0X ▪ Transfer or withdrawal of sponsorship. Refer to SOP Noclor/Spon/S02/0X	
4.7	**Complaints** 4.7.1 For complaints that are in relation to the service provided by an NHS organisation the NHS organisation should be contacted directly. Every NHS organisation has a complaints procedure, refer to the NHS Trust's website. 4.7.2 Participants in research sponsored by a Noclor Partner NHS Trust should be provided with contact details in the Patient Information Sheet of who they should approach if they are unhappy with the study: this would be a contact if participants have any concerns about your study and their involvement in it. 4.7.3 Formal complaints can be submitted to Noclor via the website https://www.noclor.nhs.uk/submit-feedback-or-complaint All complaints received will be investigated and the appropriate action taken (where required) in a timely manner.	Investigators/Study Team
4.8	**Consent and Eligibility** 4.8.1 Enrolled participants must meet the eligibility criteria defined in the approved protocol. 4.8.2 Protocol waivers (i.e where a participant does not fully meet the eligibility criteria) are not acceptable for clinical trials sponsored by a Noclor partner NHS Trust and these types of events should be reported as protocol violations according to SOP Protocol Deviations, Non-Compliance and Serious Breaches Noclor/Spon/S10/0X. 4.8.3 For CTIMPs, the decision as to whether a participant is eligible for entry into the trial is considered a medical decision and must	Chief Investigator (CI)/Principal Investigators (PIs)

therefore be made, and evidenced as such, by a medically qualified doctor (as delegated and as they appear on the site delegation log) prior to participant enrolment /randomisation.

4.8.4 Participant consent forms should be completed accurately, taken at the time stipulated in the approved protocol and signed off by relevant (responsible) personnel.

4.8.5 Consent documentation should always be up to date and available to monitor, audit or inspect at any time. Sites should carry out routine self –monitor checks on their consent forms (check all consent forms are complete and filed).

4.8.6 Completed original consent forms should be filed together with the accompanying version of PIS on which the consent was taken in the Investigator Site File (ISF), a copy should be given to the participant and a further copy filed in the medical notes (where relevant).

4.8.7 Version control of consent documentation is of paramount importance in a clinical trial, copies of current approved and superseded versions of consent documentation should be retained in the Study/Trial Master File S/TMF (and in the ISF at site) any version changes should be included on the Amendment Log Noclor/Spon/T06/0X and the Document Inventory Log Noclor/Spon/T07/0X.

4.8.8 Informed consent is an ongoing process and over the duration of a study. Amendments to the protocol, PIS and/or consent forms may be made that may require participants to re-consent. Any requirements for re-consenting participants will be clearly instructed to site by the CI.

4.8.9 Participants may also withdraw their consent at any point. In the event that a participant withdraws their consent the CI must have systems in place to deal with these events (this should be incorporated in the protocol /data management procedures). The action taken should be according to what consent it being withdrawn (for example is consent being withdrawn from further treatment but participant still consents to follow-up; is consent being withdrawn for GP to be informed or medical notes to be followed up at the end of study or is consent being withdrawn for any data being used).

4.9	**Contracts** 4.9.1 Contracts must be fully executed prior to any contracted activities commencing. Refer to Set-Up and Approval Noclor/Spon/S04/0X 4.9.2 The CI should maintain a summary table of all contracts that are in place for his/her study in the contracts section of the S/TMF. It is useful to make note of contract execution/expiry dates (where relevant). 4.9.3 The CI is responsible for ensuring that all contracts and agreements reflect current practice and are amended, renewed and terminated as appropriate. 4.9.4 The CI should communicate with the Noclor Sponsor Representative where any Variation To Contracts VTC) needs to be initiated. 4.9.5 Noclor operates a 'wet ink signature' regime. ▪ Original (wet) signed contracts/agreements will be filed in the study file at the Noclor offices ▪ Scanned copies of fully executed contracts will be sent to the CI and should be retained in the contracts section of the S/TMF (along with the summary contracts table see 4.9.1) ▪ For clinical trials, when the study is declared ended original wet signed contracts will be reconciled into the S/TMF for archiving. Refer to Archive (Sponsored Research) Noclor/Spon/S12/0X. 4.9.6 The CI should raise any concerns over the service being provided/ conduct of a contracted third party to the Noclor Sponsor Representative in the first instance.	Chief Investigator (CI)
4.10	**Data Management** 4.10.1 The responsibilities for data management and statistical analysis are delegated to the CI (who is then responsible for onward delegation to an appropriately qualified member(s) of the study team) and would have been agreed during study set-up refer to Study Set-Up and Approval Noclor/Spon/S04/0X 4.10.2 Where a data management plan is in place, the data should be managed according to the agreed plan [the plan should be agreed prior to study activation and signed off by the relevant parties (which for CTIMPs includes the trial statistician)] 4.10.3 Data query resolution should be a formalised procedure; details should be included in the data management plan (with reference to data query/data clarification forms that will be used). Consistent delays with dealing with/responding to data queries should be escalated [the how and when and to who should be	Chief Investigator (CI)

	documented in the data management plan also]. 4.10.4 Revisions to the data management plan should be version controlled (for clinical trials the details should also be updated on to the Document Inventory Log Noclor/Spon/T07/0X) 4.10.5 The CI is responsible for checking consistency of the Case Report Form (CRF) version with the protocol. For example if there is amendment to the protocol, the CI must ensure any necessary changes to CRF are also made and implemented. Version control of data collection tools (CRFs) must be maintained and evidenced in the S/TMF.	
4.11	**Delegation of Responsibilities** ICH GCP guidelines state that 'each individual involved in conducting research should be qualified by education, training and experience to perform his or her respective task(s)'. ICH GCP also states that 'the Investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties'. 4.11.1 The Investigators (Chief and Principal) are responsible for delegating out tasks on the study to appropriately trained/qualified individuals and ensuring that these individuals have the 'appropriate' GCP and protocol-specific training/supervision required for their specific roles and responsibilities (and that this evidenced on file). 4.11.2 For some study roles it may be most 'appropriate' to tailor the GCP training so that it is specific to the individuals' role on the study (covering aspects such as documenting activities in source notes and recording adverse events). 4.11.3 All clinical trials sponsored by a Noclor partner NHS Trust are required to establish a study team delegation log (for delegation of responsibilities from CI to study team personnel) and a site-specific authorised delegation log on which each team member's responsibilities will be documented at participating sites. 4.11.4 The delegation logs should be supported by the following additional evidence on file: ▪ signed and dated CVs ▪ evidence of contract (where required) ▪ training certificates (as relevant to role and to study) ▪ attendance and notes from study initiation (where relevant) ▪ 1:1 supervision/training (where relevant) ▪ SOP signature pages (where relevant)	Chief Investigator (CI)/Principal Investigator (PI)

	4.11.5 Site delegation logs should clearly state the name of the person, their role and the activities they are delegated by the PI as well as being signed and dated by the PI prior to the activity being undertaken by the individual. The delegation is not just a paper exercise; it is documented evidence of appropriate delegation of investigator's responsibilities. 4.11.6 Delegation logs should be kept up to date at all times (real-time as demonstrates oversight), for example, when a member of staff leaves or is no longer working on the study in the same capacity this should be recorded. 4.11.7 Training should be an ongoing process during the study and should be documented accordingly, for example, updates to training of team when there are amendments to protocol or study procedures, new safety information (to inform study team of what to look out for), changes to legislation etc. 4.11.8 Delegation logs and all supporting evidence should be retained by the CI in the S/TMF for co-ordinating centre delegated activities and by the PI in the ISF for site delegated activities, all documents should be available for review (or provided) on request by trial manager /monitor or Noclor Sponsor Representative.	
4.12	**End of Study** Within 90 days of the research study concluding (as defined in the protocol) the CI must notify the appropriate bodies that the research has ended. Where a CTIMP has terminated earlier than as defined in the protocol the end of study must be notified within 15 days of decision being made to stop. Refer to End of Study Notification, Close-Out and Reporting (Sponsored Research) Noclor/Spon/S11/0X	Chief Investigator (CI)
4.13	**Enrolment Logs** Under ICH GCP the Principle Investigator (PI) should be able to demonstrate a potential for recruiting the required number of suitable subjects within the agreed recruitment period specified by the protocol (ICH GCP 4.2.1). This is achieved through the subject screening, enrolment and identification code logs. The logs can/should also serve the purpose to collect information on withdrawals and number of subjects who concluded the trial. 4.13.1 For all research , the CI is required to create and disseminate (to participating PIs) template logs for use as appropriate to the study type	Chief Investigator (CI) /Principal Investigators (PIs)

	4.13.2 For clinical trials, these logs will be reviewed by the Noclor Sponsor Representative to ensure they capture the details required, refer to Site Initiation and Activation SOP Noclor/Spon/S05/0X . 4.13.3 To ensure confidentiality, the PI should use the code instead of the subject's name on documents such as the Case Report Form (CRFs), samples, lab results and other documents to maintain patient confidentiality. Refer to 4.25	
4.14	**Equipment Maintenance** Some of the more general equipment that is used routinely in research (especially clinical trials) are things such as weighing scales, ECGs, thermometers, centrifuges, Blood Pressure machines, X-Rays , CT Scans etc. 4.14.1 The CI is responsible for ensuring that any equipment that they will utilised during their study is adequate for "the foreseen duration of the trial to conduct the trial properly and safely" (ICH GCP 4.2.3). 4.14.2 Any equipment that will be provided to /or used at site during a research trial should be assessed and confirmed as fit for purpose including review of maintenance records at site initiation. The equipment that is to be used should be listed in Section 3 of the Site Initiation Report Noclor/Spon/T08/0X 4.14.3 Monitor checks should be made (either via site visits or remotely through collection of records/logs etc) to ensure that equipment remains fit for purpose throughout the trial and for clinical trials these checks should be included in the trial specific monitor plan. Refer to Risk Assessment SOP Noclor/Spon/S03/0X	Chief Investigator (CI)
4.15	**Essential Documents (Study/Trial Master File)** The 'file' where study documentation is maintained and retained to allow for reconstruction of a research study (at any point in time) is referred to as the Study/Trial Master File (S/TMF). Maintenance and security of the S/TMF is essential for GCP compliance and for Clinical Trials of Investigational Medicinal Products (CTIMPs) is a legal requirement. 4.15.1 ICH Topic E6 (Section 8) defines the contents of the TMF as 'essential documents for the conduct of a clinical trial' and lists them in detail. The ICH principles of what documents should be retained in the S/TMF should be applied to all other research category (as relevant) 4.15.2 For clinical trials, the CI is delegated responsibility for maintaining the TMF through agreement and must use the	Chief Investigator (CI)

sponsor index templates as detailed below (refer to Study Set-Up and Approval SOP Noclor/Spon/S04/0X) :

- TMF Index Noclor/Spon/T02/0X
- TMF Sponsor Lead Site File Index Noclor/Spon/T02a/0X (where sponsor has lead site and the TMF is combined with the ISF)
- TMF Site File Index Noclor/Spon/T02b/0X
- ISF Index Noclor/Spon/T03/0X for sites

4.15.3 For all other research (non-clinical trials) the sponsor templates can be adapted for use (their use will not be mandated).

4.15.4 The S/TMF should be clearly referenced on the spine(s) so easily identifiable. Label with the study short title, unique registration identifiers (sponsor reference/IRAS ref as minimum and for CTIMPs the EudraCT ref must also be included on spine), Chief Investigator name and the number of files that constitute the S/TMF (for example file one of five would be File No:1/5)

4.15.5 Only restricted trial staff (and Noclor Sponsor Representative or delegate and inspectors) should be allowed to gain access to the documentation stored in the S/TMF.

4.15.6 The S/TMF must be kept up to date and inspection ready at all times and be available for review/inspection on request from Noclor Sponsor Representative

4.15.7 Strict version control should be applied to all key documents retained within the S/TMF.

4.15.8 Where possible study documents should be assigned unique document references ids/numbers to facilitate document management

4.15.9 For clinical trials, the document inventory log Noclor/Spon/T07/01is a mandatory sponsor template that should be maintained by the CI/study team throughout the trial to facilitate document management (centrally and at sites). This log can be used in non-clinical trials also.

4.15.10 Individual documents should be stored with the earliest material at the back and the most recent at the front.

4.15.11 Correspondence should be stored in the relevant correspondence sections.

4.15.12 During the study where documents or files are retained outside of the S/TMF they should be file-noted to detail their location (i.e audit trail of traceability).

	4.15.13 The S/TMF should be regularly monitored to check for completeness. For clinical trials, checks will be included in the trial-specific monitor plan, refer to Risk Assessment SOP Noclor/Spon/S03/0X. 4.15.14 The S/TMF files may be audited by Noclor on request (for clinical trials there will be an audit at some point) /ad hoc or inspected by the regulatory authority(ies) such as MHRA. 4.15.15 The S/TMF should be checked/reconciled to ensure for complete and legible prior to transfer to archive (all documents reconciled/filed) according to Archive (Sponsored Research) Noclor/Spon/S12/0X	
4.16	**Finances** 4.16.1 The CI is responsible for managing the resources required to deliver the study throughout the study life cycle ensuring that it is delivered to time, to target and within budget. 4.16.2 The responsibilities for managing funding/grant awards are retained by the budget holder (the Trust that has received the funding) in line with local Trust policies, Standard Financial Instructions (SFIs) and according to the requirements of the funder contract (prime contract). 4.16.3 The claiming (invoicing) procedures for a specific study should be clearly specified in the financial schedules of contracts/agreements. 4.16.4 The CI should review the research budget against expenditure on a quarterly basis (minimum requirement) and provide these budget reports to Noclor Service Director 4.16.5 The Chief Investigator should inform the Noclor Sponsor Representative of any changes to completion dates or budgets (as these may require amendments to the study or contracts). 4.16.6 Copies of all financial records and reports should be retained in the S/TMF.	Chief Investigator (CI)
4.17	**Fraud & Misconduct** The Fraud Act 2006 provides for a general offence of fraud with three ways of committing it, which are by false representation, by failing to disclose information and by abuse of position. Research misconduct would be for example, failure of researcher in obtaining ethical approval.	All parties

	4.17.1 Fraud and research misconduct that relates to any research sponsored by a Noclor Partner NHS Trust must be reported to Noclor. This should be reported directly to the Service Director by (Direct Line) Tel: 020 3317 3763 or email lynislewis@nhs.net 4.17.2 Refer also to Protocol Violations, Non-Compliance to Protocol/ GCP and Serious Breaches in 4.27	
4.18	**IMP Management and Accountability** 4.18.1 The trial specific procedures in regards to IMP management and accountability will be provided to participating sites by the CI/study team (having been reviewed and approved by the Sponsor Pharmacy Representative according to the sponsor procedures of Study Set-Up and Approval Noclor/Spon/S04/0X). 4.18.2 Where IMP is to being stored outside of the pharmacy department, the local pharmacy should have a formalised procedure for the assessment, approval and monitoring of the designated storage area and drug accountability records. 4.18.3 The site pharmacy must have a process in place to identify and manage temperature excursions in relation to on-site storage of the IMP which will include how affected stock will be quarantined (in a segregated area) and how the sponsor will be notified. This should be discussed at site initiation visit, refer to Site Initiation and Activation SOP Noclor/Spon/S05/0X. Failure to act on temperature excursions can have serious consequences; refer to Protocol Deviations, Non-Compliance and Serious Breaches (Clinical Trials) SOP Noclor/Spon/S10/0X. 4.18.4 IMP management and accountability will be monitored throughout the trial according to the trial- specific monitoring plan. Refer to Risk Assessment SOP Noclor/Spon/SA03/0X. 4.18.5 Unissued IMPs and returned used IMPs (returned by clinical trial subjects) will usually be disposed of locally on sponsor authorisation, in accordance with the trial specific instructions and Trust procedures.	Chief Investigator (CI)
4.19	**Incident Reporting** Research related adverse incidents encompass a whole range of research related activities, unlike safety reporting (refer to 4.31) which relates to medical events for participants receiving IMP or other interventions/study procedures.	All parties

	Incidents (or near misses) may include: incidents that involve staff or a carer/visitor during the course or a research study (for example: - a member of staff maybe injured whilst administering an intervention or the carer may take trial medication in error); an incident relating to the premises (for example: discovery of asbestos, burglary, fire); or incident relating to equipment failure, data loss and breaches in confidentiality etc. 4.19.1 Any research related incident reported locally (within a Trust according to local Trust policy) for a research study sponsored by a Noclor partner should also be notified to the Noclor Sponsor Representative. 4.19.2 Reporting should be through the incident reporting system where possible by including sponsor.noclor@nhs.net as one of the reviewers of the incident report. Where this is not possible a copy of the report or summary of incident reported should be sent to the same email address. 4.19.3 Noclor will ensure reported incidents are sufficiently addressed, and closed, cross referenced where necessary (i.e where the incident is also a participant specific adverse event requiring reporting within the trial) or further investigated /escalated if a possible serious breach has been identified refer to 4.27. 4.19.4 The CI/PI should file trial specific incident reports (and related correspondence) in the S/TMF and ISF.	
4.20	**Medical Oversight (Clinical Trials)** 4.20.1 The PI is responsible for the medical care/decisions of the participants enrolled on the trial and should be closely involved in their management 4.20.2 The PI should be able to demonstrate (evidence on file) complete oversight of the trial for the duration of the trial (even if responsibilities are delegated out). 4.20.3 The medical review of any participant assessments by qualified physicians (as delegated by the PI and as they appear on the delegation log) should be clearly documented in medical records and CRFs (i.e evidence that they have been reviewed with a date and signature of medical reviewer). 4.20.4 Any clinically significant events should be recorded, reported and monitored as required for the medical event (and for the trial).	Principal Investigator (PI)

4.21	**Medical Records (Flagging)** 4.21.1 Once a participant has consented to take part in a research study their medical records should be flagged up to indicate their involvement. The rationale for flagging up medical records is: ▪ to ensure treating health professionals are aware of a patient's involvement in a research study ▪ that health professionals have access to study information that might be relevant to a patient's medical care (the participant consent form and associated patient information sheet should be filed in the medical records) ▪ research teams are notified of hospital admissions or adverse events in study patients ▪ the medical notes for research participants are retained for a specified period following the end of the study 4.21.2 Noclor (where acting on sponsor behalf) do not instruct sites on what systems should be used locally to flag up medical notes. Individual NHS Trusts should have their own workable policy. Advice should be sought from the local Information Governance Department if in doubt. 4.21.3 Site study staff should check (at visit) to ensure the medical notes have been flagged appropriately. For CTIMPs this check will be included in the trial specific monitor plan. 4.21.4 All case notes should be checked for accuracy of retention dates prior to study archiving at site.	Principal Investigator (PI)
4.22	**Monitoring** Monitoring is designed to verify the quality and safety of a study and ensure that it is conducted, recorded and reported according to the protocol (and any conditions of approval or subsequent amendments), sponsor procedures, GCP and the applicable regulatory requirements. Monitors should be familiar (trained) in the protocol and all other applicable documents, procedures and the relevant regulatory requirements and delegated responsibilities by the CI (unless the sponsor is monitoring or has outsourced monitoring activities for a specific trial). **4.22.1 Clinical trials** **4.22.1.1 Monitor Plans** 4.22.1.1.1 Clinical Trials will be monitored according to a trial-specific monitor plan. Refer to Risk Assessment SOP Noclor/Spon/S03/0X. 4.22.1.1.2 The monitor plan will detail the programme of checks that will be carried out locally at participating sites (self -checks) and at site (monitor site visits) and remotely /centrally by the	Chief Investigator (CI)

trial co-ordinating team (trial monitor/manager).

4.22.1.1.3 In addition for CTIMPs, the monitor plan will detail what monitor checks are required/completed by sponsor (or delegated party). *Non-CTIMP clinical trials have central monitor checks conducted by sponsor; the details of these checks are documented outside of the monitor plan.*

4.22.1.1.4 Source Data Verification (SDV) - the monitor plan will specify the level of SDV that will be carried out at site monitor visits. The source data location log should have been agreed/completed at site initiation. Refer to Site Initiation and Activation Noclor/Spon/S05/0X

4.22.1.1.5 The monitoring plan as relevant to participating sites (i.e what will be required of them during the trial) should be communicated at site initiation. Refer to Site Initiation and Activation Noclor/Spon/S05/0X

4.22.1.2 Monitor Report Templates

4.22.1.2.1 The monitor plan should provide details of the monitor report templates that will be used for the trial.

4.22.1.2.2 For CTIMPs, the monitor report templates must be reviewed and approved by the Noclor Sponsor Representative (revision may be required to ensure the templates capture all the compliance checks required by sponsor as detailed in the monitor plan).

4.22.1.3 Procedures for site monitor visits

4.22.1.3.1 Prior to a site monitor visit the trial monitor should :

- contact the site and request specific time /date that the PI and other key members of trial staff are available
- state which documentation/files will need to be made available /will be collected and which departments will be visited
- send a letter/email to confirm details of monitor visit
- prepare for the visit (e.g refer to the monitor plan, review previous monitor visit reports/outstanding actions, data query logs, SAE reports etc)

4.22.1.3.2 During a site monitor visit the trial monitor should :

- ensure the objectives of the visit are met (as outlined in the trial monitor plan for that visit)
- collect any documents/data (as specified in the monitor plan)
- ensure that any inconsistencies /errors on CRFs detected at site monitoring are corrected during the visit where possible by authorised study site personnel as documented on the Delegation of Authority & Signature Log and data query /clarification forms are updated as

relevant

- ensure the Site Initiation and Monitor Log Noclor/Spon/T09/0X is completed by all those involved in the monitor visit.

4.22.1.3.3 After a site monitor visit, the trial monitor should:

- follow up in writing via letter or email to the PI and appropriate staff highlighting action items (or any areas of concern)
- make a record of any telephone calls (i.e keep a telephone log/record sheet for sites that should be filed in the TMF site file with monitor reports /correspondence etc)
- ensure any reports of protocol violations /non-compliance are reported to the Noclor Sponsor Representative according to Protocol Deviations, Non-Compliance and Serious Breaches (Clinical Trials) Noclor/Spon/S10/0X
- complete a monitor visit report (template as relevant to monitor visit and as detailed in the monitor plan). This report should be sent to the Trial Manager/CI for review and approval
- send a signed copy of the monitor report to the PI (for attention and action and for filing in the ISF) and send a copy to Noclor Sponsor Representative within 15 calendar days of the visit

4.22.1.4 All actions identified at monitor visits should be closed by the date specified in the monitor visit report.

4.22.1.4.1 Ongoing unresolved actions should be reviewed by the CI/ trial oversight committee's (as unresolved issues at sites maybe identify trends for training or inform revision to the protocol/procedures).

4.22.1.5 All documentation relating to monitoring activities performed during the trial must be documented and retained in the relevant sections of the S/TMF (site files) and available for audit /inspection by sponsor at any time.

4.22.2 Other Research

4.22.2.1 Any study specific monitoring plans will be reviewed/agreed as part of the risk assessment process and should be worked to as outlined/agreed. Refer to Risk Assessment Noclor/Spon/S03/0X

4.22.2.2 The Noclor Sponsor Representative will carry out central monitor checks according to Noclor sponsor oversight procedures

	4.22.2.3 All documentation relating to monitoring activities performed during the trial must be documented and retained in the relevant sections of the S/TMF (site files).	
4.23	**Notifying GPs** 4.23.1 GPs should be informed of participant involvement if this has been consented to at the outset (with GP letter approved by REC) 4.23.2 Evidence that a GP letter has been sent should be retained for monitoring and audit purposes (e.g a copy of signed /dated letter filed in the medical notes).	Principal Investigators (PIs)
4.24	**Oversight Committees** The study management and oversight arrangements should be defined in the protocol. 4.24.1 Copies of any terms of reference/charters (as relevant to the study oversight committees established), meeting agendas, papers and minutes should be filed in the S/TMF. 4.24.2 For clinical trials, copies of all meeting minutes (recommendations to sponsor from TSC/IDMC as appropriate) should be sent to the Noclor Sponsor Representative in a timely manner. 4.24.3 Where an Independent Data Monitoring Committee (IDMC) is reviewing blinded data, a file note detailing the location of the IDMC confidential minutes should be placed in the TMF until the study is prepared for archive at this point the IDMC minutes will be filed in place of the file note.	Chief Investigator (CI)
4.25	**Participant Confidentiality** 4.25.1 According to ICH GCP, it is the Investigator's responsibility that records identifying the subject are kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published the subject's identity will remain confidential. 4.25.2 During study initiation (where applicable) the responsibilities of the Investigator with regards to subject confidentiality should be discussed with the entire site study team, to ensure that everyone is fully aware of the importance of maintaining subject confidentiality. 4.25.3 Breaches in confidentiality 4.25.3.1 For clinical trials breaches in confidentiality should be reported as non-compliance according to Protocol Deviations, Non-Compliance and Serious Breaches (Clinical Trials)	Principal Investigators (PIs)

	Noclor/Spon/S10/0X and in line with local Trust incident reporting procedures (refer to 4.14) 4.25.3.2 For all other research breaches in confidentiality should be reported as incident (refer to 4.14)	
4.26	**Protocol Deviations** Protocol deviations are unintended non-serious departures from the approved protocol 4.26.1 For clinical trials protocol deviations should be recorded according to Protocol Deviations, Non-Compliance and Serious Breaches (Clinical Trials) Noclor/Spon/S10/0X 4.26.2 For all other research, a record of any protocol deviations should be maintained on a deviation log by the participating sites in the ISFs (where relevant) and centrally by the CI in the SMF. The CI should continually monitor protocol deviations to establish whether an amendment to the protocol or further training is required to prevent escalation into more serious violations or breaches (see 4.27).	Chief Investigator (CI) /Principal Investigators (PIs)
4.27	**Protocol Violations, Non-Compliance to Protocol/ GCP and Serious Breaches** A protocol violation or non-compliance is a deviation from the protocol/GCP/study/sponsor procedures that is not approved by the sponsor/REC/MHRA prior to its implementation and that could potentially /or has impacted on the subjects' safety or compromised the integrity of study data 4.27.1 For clinical trials, , protocol violations and non-compliance to Protocol /GCP should be reported in accordance with SOP Protocol Deviations, Non-Compliance and Serious Breaches (Clinical Trials) Noclor/Spon/S10/0X 4.27.2 For all other research, protocol violations and non-compliance to Protocol /GCP should be reported within 24 hours of becoming aware of the event to the Noclor Sponsor Representative by completing and submitting the Non-Compliance Report Form Noclor/Spon/T05/0X (available to download from the Noclor website https://www.noclor.nhs.uk/document-library). 4.27.2.1 The form should be emailed to sponsor.noclor@nhs.net and copied to CI for urgent attention referring in the subject of the email as 'Non-Compliance Report' 4.27.2.2 The Noclor Sponsor Representative will make a judgment on whether the reported violation / non-compliance is 'serious' and requires further reporting [note : although SOP Deviations, Non-Compliance and Serious Breaches (Clinical	Chief Investigator (CI) /Principal Investigators (PIs)

	Trials) Noclor/Spon/S10/0X specifically relates to clinical trials, Section 6 of this SOP will apply to all other research where the sponsor deems a serious breach has occurred]	
4.28	**Randomisation** 4.28.1 The responsibilities and procedures for the production, dissemination and location of the randomisation schedule (electronic and paper versions) should be documented the S/TMF. This document should be sent to the Noclor Sponsor Representative for review (prior to any dissemination of the schedule). Refer to Study Set-Up and Approval Noclor/Spon/S04/0X 4.28.2 Where third parties are involved in either the creation of, dissemination of or receipt of the randomisation schedule then the relevant contracts must have been fully executed prior to these activities. 4.28.3 For double blind trials where the study team are to retain blindness, the master randomisation schedule/ records should be retained separately (under the care of the person delegated responsible as per 4.28.1) to the rest of the trial documentation until the end of trial when they should be placed in the S/TMF. A file note should be placed on file to detail the location of the master randomisation schedule until the end of the trial. 4.28.4 An audit trail should be evident on file to support/track the dissemination and location of the randomisation schedule.	Chief Investigator (CI)
4.29	**Reporting Requirements** The various bodies involved in the funding, regulation, sponsorship and approval of health research have specific reporting requirements that must be complied with. The nature and timing of the reports required will depend on the study type. **4.29.1 Annual Progress Reports-Research Ethics Committee (REC).** 4.29.1.1 Applicable to all research with a favourable ethics opinion 4.29.1.2 Report due on the anniversary of the REC approval (not the date the study commenced). 4.29.1.3 To be submitted within 30 days of the anniversary (unless the study has officially declared ended before this anniversary). 4.29.1.4 Progress report should be prepared and submitted by the CI using the appropriate template. 4.29.1.5 Reports should be disseminated to Noclor Sponsor Representative and Principal Investigators. **4.29.2 Development Safety Update Reports (DSURs)** 4.29.2.1 Applicable to CTIMPs	Chief Investigator (CI)

	4.29.2.2 DSUR due on the year anniversary of the Clinical Trial Authorisation (CTA) 4.29.2.3 DSUR prepared and submitted in accordance with DSUR SOP (PV 003) **4.29.3 Funder Reports** 4.29.3.1 As stipulated in the terms and conditions of the grant 4.29.3.2 Noclor Sponsor Representative to be sent copy of report **4.29.4 Recruitment Updates** 4.29.4.1 For clinical trials, the Noclor Sponsor Representative should be sent monthly recruitment updates (recruitment figures should be provided by site by month) 4.29.4.2 For NIHR portfolio studies, accrual data should be uploaded monthly as instructed by NIHR	
4.30	**Risk Management** Risk management is the responsibility of all parties involved and is a continuous process. Refer to Risk Assessment (Sponsored Research) Noclor/Spon/S03/0X.	Chief Investigator (CI)/Noclor Sponsor Representative
4.31	**Safety Reporting (Clinical Trials)** **4.31.1 CTIMPs** 4.31.1.1 Safety reporting procedures must be detailed in the trial protocol and supporting documentation. 4.31.1.2 Pharmacovigilance (PV) responsibilities of the sponsor are outsourced to a third party (referred to as the PV responsible person/party). 4.31.1.3 Noclor adopt the third party PV SOPs. The SOPs implemented (PV 001 and PV 002) are generic for CTIMPs sponsored by a Noclor Partner NHS Trust. 4.31.1.4 Each specific CTIMP will have an agreed schedule of work under the main service level agreement with the PV responsible party. 4.31.1.5 Each CTIMP will have PV Study Specific (PVSS) details agreed and documented during study set-up (once the schedule is fully executed). These PV details will include the safety reporting contact details (dedicated email and fax line) and any additional/specific reporting requirements for the trial. 4.31.1.6 The CI will sign confirmation of training in the (adopted) PV SOPs and the PVSS. 4.31.1.7 The PV database and file will be transferred to the CI at the end of trial by the PV responsible person/party (*during the trial a file note in the TMF should provide the location of PV information)	Chief Investigator (CI)

	4.31.2 Non-CTIMP Clinical Trials 4.31.2.1 All Serious Adverse Events (SAEs) should be reported to the Noclor Sponsor Representative at sponsor.noclor@nhs.net sponsor within 24 hours according to protocol/ study specific safety reporting SOPs and templates as agreed during Study Set-Up and Approval Noclor/Spon/S04/0X 4.31.2.2 SAEs judged as related and unexpected should be reported by the CI to main REC within 15 calendar days of being made first aware using NRES template. The Noclor Sponsor Representative should be copied in. 4.31.2.3 All SAE reports and related correspondence should be filed in the S/TMF	
4.32	**Sponsor SOPs** **4.32.1 Clinical Trials** 4.32.1.1 Specific sponsor SOPs are mandated for clinical trials (both CTIMPs and non-CTIMPs) 4.32.1.2 The sponsor SOPs will be distributed to the CI as appropriate (distribution will be controlled by the Noclor Sponsor Representative) 4.32.1.3 The sponsor SOPs that are mandated should be added to the Document Inventory Log Noclor/Spon/T07/0X 4.32.1.4 The CI will be required to sign off (esign) 'Confirmation of Training' in the SOPs they have been sent 4.32.1.5 The CI is responsible for ensuring that members of his/her team are appropriately trained according to their delegated roles and responsibilities and that the relevant SOP training logs are completed and filed in the S/TMF 4.32.1.6 Any deviations from sponsor SOPs 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). 4.32.1.6.1 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. 4.32.1.6.2 A copy of the completed and signed form should be filed with the SOP in the S/TMF. 4.32.1.7 The CI is responsible for retaining and archiving copies of Sponsor SOPs (and the associated training records) that have been worked to for the duration of a trial in the S/TMF **4.32.2 For all other research** 4.32.2.1 Noclor will not control the distribution of sponsor SOPs for use in non-clinical trial research studies in the same way as detailed in 4.34. Clinical Trials.	Chief Investigator (CI)

	4.32.2.2 The CI is responsible for checking that he/she is working to current versions of relevant sponsor SOPs. 4.32.2.2.1 Current versions of Sponsor SOPs and templates will be accessible on the Noclor website (in the training and resources section) 4.32.2.2.2 Noclor will notify CIs of new or revised SOPs through the website alerts, newsletter updates etc	
4.33	**Statistical Analysis** 4.33.1 The finalised plan for statistical analysis (whether it is within the protocol or a separate Statistical Analysis Plan) should be followed. 4.33.2 The CI is responsible for ensuring that the statistical analysis plan (where this is a separate document to the protocol) remains consistent with the version of the protocol, any changes should be version controlled and retained in the S/TMF. 4.33.3 The processes for provision of interim datasets for analysis and reporting as per the requirements of the statistical analysis plan should be detailed in the data management plan (refer to 4.10) 4.33.4 All outputs of statistical analysis must be appropriately version controlled (tables, figures etc) to ensure that the resulting reports are accurate.	Chief Investigator (CI)
4.34	**Study Procedures** The CI is responsible for consistency checking across all essential study documents (including trial specific SOPs or procedures manuals) to ensure that information is consistent and accurate and strictly version controlled.	Chief Investigator (CI)
4.35	**Temporary Halts/Suspensions (Clinical Trials)** Refer to Temporary Halt (Clinical Trials) Noclor/Spon/S09/0X	Chief Investigator (CI)
4.36	**Unblinding (Code Break)** 4.36.1 Procedures for unblinding (i.e how to unblind, who can unblind and what details are recorded where regarding unblind) should be detailed in either the protocol or in separate trial specific procedures document (such as a procedures manual or SOP). 4.36.2 The system for out-of-hours contact and emergency unblinding at site should be tested periodically to ensure that it works as intended. Any tests should be documented in the ISF.	Chief Investigator (CI)/Principal Investigator's (PIs)
4.37	**Urgent Safety Measures (Clinical Trials)** Refer to Urgent Safety Measures (Clinical Trials) Noclor/Spon/S08/0X	Chief Investigator (CI)/Principal Investigator's (PIs)

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

7. Associated Documents

Document Reference ID	Document Type	Document Title
Noclor/Spon/S02/0X	SOP	Sponsorship Request and Declaration
Noclor/Spon/S03/0X	SOP	Risk Assessment (Sponsored Research)
Noclor/Spon/S04/0X	SOP	Study Set-Up and Approval (Sponsored Research)
Noclor/Spon/S05/0X	SOP	Site Initiation and Activation (Clinical Trials)
Noclor/Spon/S07/0X	SOP	Amendments (Sponsored Research)
Noclor/Spon/S08/0X	SOP	Urgent Safety Measures (Clinical Trials)
Noclor/Spon/S09/0X	SOP	Temporary Halts (Clinical Trials)
Noclor/Spon/S10/0X	SOP	Protocol Deviations, Non-Compliance and Serious Breaches (Clinical Trials)
Noclor/Spon/S11/0X	SOP	End of Study Notification, Close-Out and Reporting (Sponsored Research)
Noclor/Spon/S12/0X	SOP	Archive (Sponsored Research)
Noclor/Spon/T02/0X	Template	TMF Index
Noclor/Spon/T02a/0X	Template	TMF Sponsor Lead Site File Index

Noclor/Spon/T02b/0X	Template	TMF Site File Index
Noclor/Spon/T03/0X	Template	ISF Index
Noclor/Spon/T05/0X	Template	Non-Compliance Report Form
Noclor/Spon/T06/0X	Template	Amendment Log
Noclor/Spon/T07/0X	Template	Document Inventory Log
Noclor/Spon/T08/0X	Template	Site Initiation Report (Clinical Trials)
Noclor/Spon/T09/0X	Template	Site Initiation and Monitor Log
Noclor/Inter/T12/0X	Template	SOP Deviation Form

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.

Copies of 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.

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.