UNIVERSITY OF LEICESTER, UNIVERSITY OF LOUGHBOROUGH
&
UNIVERSITY HOSPITALS OF LEICESTER NHS TRUST

JOINT RESEARCH SUPPORT OFFICE

STANDARD OPERATING PROCEDURES

University of Leicester (UoL) Research Governance Office
SOP S-1011 UoL

Version 6, November 2016

Site Initiation for Research Sponsored by University of Leicester

OFFICE BASE

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Effective Date: April 2017

1. Introduction

This Standard Operating Procedure (SOP) describes the procedures for initiation of:

- All Clinical Trials of Investigational Medicinal Product (CTIMP) research sponsored by the University of Leicester (UoL) that are either single or multisite investigator led trials.
- Any other research activity that is interventional and/or higher risk determined by the Sponsor Risk Assessment process as detailed in SOP S-1003 UoL.

An initiation visit must be performed where the Sponsor deems it necessary, prior to the Sponsor Green Light being confirmed.

The purpose of this SOP is to ensure that all required study authorisations and documentation are in place and that the protocol and relevant SOPs have been discussed with the Investigator and the study staff to ensure compliance with all statutory and applicable regulatory legislation. Initiation is integral to the quality control of a clinical trial and is designed to ensure quality of the study according to Sponsor requirements.

2. Scope

This SOP applies to all research using CTIMPs and any other research activity that is interventional and/or higher risk as determined by the sponsor.

3. Procedure.

The Initiation Visit must be undertaken prior to the Sponsor Green Light being given. Where appropriate, in the case of multi-centre studies, it may be possible to conduct the site initiation visit over the telephone by way of a telephone conference.

3.1 Preparing for the Initiation Visit

CTIMP Studies

The Sponsor or their Delegate must ensure that all approvals and regulatory documentation are in place/are in progress in order to open the study at site. This includes a favourable site specific assessment, and agreement that staff capacity is available to run the study at site.

Attendance is mandatory for the Chief Investigator (CI) and/or Principal Investigator(s) (PI), all key research staff working on the study and staff from departments that will be involved in the study, to participate in the initiation visit, and be available during the visit/teleconference where appropriate. It is recognised that more than one visit may be necessary to include ancillary departments such as pharmacy. Where the CI is not available, a 1:1 meeting to discuss the SIV should follow that conducted with the study team.

The Trials Monitor or designee will outline the requirements for the Site Initiation Visit in terms of attendance for the study team and in terms of time and resources. The Site Initiation Checklist will be provided prior to initiation which detailing the schedule of the visit and items to be reviewed / discussed (Appendix 1). This will also include the Pharmacy Checklist (Appendix 2) where pharmacy is involved.

Non CTIMPs

Where required by the Sponsor, initiation visits will be undertaken for non-CTIMP studies. Attendance is mandatory for the Chief Investigator at host/lead site and Principal Investigators at all other sites. All key research staff working on the study must also be in attendance along with staff from departments that will be involved e.g. pathology services. Other team members are actively encouraged to participate in the initiation visit and make themselves available where appropriate. Where the CI is not available, a 1:1 meeting to discuss the SIV should follow that conducted with the study team.

The trials monitor or Sponsor designee will outline the requirements for the Site Initiation Visit in terms of attendance for the study team and time and resources. A site initiation Check List will be provided prior to initiation detailing the schedule of the visit and items to be reviewed/discussed (Appendix 7). For non CTIMP studies only, the SIV can be delegated to the study team.

Non CTIMP Multicentre studies

For multicentre studies, where indicated by the Sponsor, it will be required that either an onsite or remote initiation visit be undertaken. Interim site review/s may be undertaken remotely. This will provide the Investigator's team and the Sponsor assurance of compliance with relevant legislation. All reports must be returned to the Sponsor, and will be reviewed in accordance with stated timelines. Requests for further clarification/ responses will be made by email. Once all issues are resolved, the site will be sent an email confirming closure of the report.

3.2 During the Site Initiation Visit

The Trials Monitor or their delegate will:

- Discuss the intended recruitment methods for the study. The current versions of the PIS/ICF will be reviewed and the monitor will discuss GCP compliant informed consent procedures with the Investigator and relevant personnel.

- Ensure that the CI/PI has completed the delegation of authority and signature log and will verify that all duties delegated by the CI/PI to other site staff have been documented. This is an on-going process to be completed throughout the study and will be reviewed on all monitoring visits as detailed in SOP S-1007 UoL.

- Verify that a signed and dated Curriculum Vitae (CV) has been provided by the CI/PI. In addition signed and dated CVs have been filed for other site staff listed on the delegation of authority and signature log.

- Verify that all identified study staff have been appropriately trained in GCP, the trial protocol and Standard Operating Procedures, verified by the completion and checking of the 'Read Log' (Appendix 3). It is expected that the Sponsor "Read Log" will be used unless specific research team reporting arrangements have been made in advance e.g. alternative electronic data capture (Q Pulse),

- All study staff attending the Initiation visit will sign the Site Initiation Visit Log (Appendix 4).

- Review with CI/PI and relevant staff, their understanding of the protocol, study procedures, investigational product, randomisation procedures, unblinding procedures and timelines.

- Confirm that the CI/PI has defined what will be considered as source data and that this has been accurately documented (Source Data Agreement Appendix 4 to SOP S-1007). In addition the monitor will discuss the CI/PI's responsibility to provide access to source data for monitoring and audit purposes.

- Clarify who will be responsible for CRF completion and clarify the procedure for entering data, as well as changes and corrections.

- Review the safety profile against the approved Reference Safety Information - Investigator Brochure (IB) or Summary of Product Characteristics (SPC) for the Investigational Medicinal Products (IMP) and verify that the most current documentation is filed and signed and dated.

- Review all IMP procedures including, but not limited to, receipt, storage, dispensing, accountability, return and destruction. Check the storage conditions for the IMP even if it has not been received at site at the time of the visit, in association with Pharmacy.

- Where appropriate, confirm that laboratory facilities and arrangements for the dispatch of samples to the laboratory are organised and that any specialised equipment that may be required, will be available throughout the period of the study, e.g. centrifuge, freezer, etc. Documentation relating to pathology processes and supplies should be stored in the Laboratory Manual.

- Confirm that procedures for allocation of participant numbers have been reviewed.

- Confirm that the site has all staff, facilities and equipment to perform the study.

- Verify that staff understand the requirements for safety reporting as per SOP S-1009 UoL. Ensure that the CI/PI has a procedure in place for the emergency unbinding for the study.

- Where appropriate, check that relevant personnel are registered for e-SUSAR.

- Ensure that the CI/PI is aware of their responsibility to communicate with the Ethics Committee and R&D departments and relevant Authorities on an on-going basis and provide the necessary reports to specified timelines i.e. Development Safety Update Report (DSUR) and Annual Progress Reports (APR).

- Check that the site has all staff, facilities and equipment to perform the study according to the study protocol and that all protocol specific procedures (including handling of any samples) have been explained.

- Ensure that the CI/PI is aware of their responsibility for the on-going maintenance of study documentation including correspondence in the Trial Master File/Investigator Site File as per SOP-S-1015 UoL. It is expected that the Trial Master File/Investigator Site File are inspection ready at all times.

- Ensure that the investigator is aware of the requirement to complete a Subject Screening Log (Appendix 5) /Subject Enrolment Log (Appendix 6) for all subjects participating in the study.

- Ensure that the Investigator is aware of their responsibility to ensure adequate cover during absences and of their obligation to have on-going oversight of the study.

3.3 Following the Initiation Visit

CTIMP Studies

The Trials Monitor or their Delegate will promptly submit a written report within 10 calendar days of the visit, recording any items outstanding or where clarification is required on the Site Initiation Outstanding Issues Report (Appendix 1 and 2 if pharmacy involved).

The CI/PI will be asked to review the report promptly and supply responses with regards to any issues that were highlighted at the initiation visit. The report will be signed by the Sponsor or their Delegate and the Investigator and the original will then be filed in the Trial Master File.

The Sponsor green light will not be given until the sponsor is satisfied that all issues raised at the initiation visit have been resolved.

The Sponsor or their Delegate will establish the next monitoring visit date and requirements with the CI/PI in line with the study specific Monitoring Plan. Monitoring is undertaken as per SOP S-1007 UoL Site management (Monitoring).

Non CTIMPs

The monitor or Sponsor designee will promptly submit a written report within 10 calendar days of the visit, recording any items outstanding or where clarification is required on the site initiation The CI/PI will be asked to review the report promptly and supply responses with regards to any issues that were highlighted at the initiation visit. The report will be signed by the monitor/designee and the Investigator and the original will then be filed in the Trial Master File with a copy retained for the Sponsor file.

The Sponsor green light will not be given until the Sponsor is satisfied that all issues raised at the Initiation visit have been resolved.

3.3 Multi-Site Initiation Visits

Multi-centre site initiation may be delegated to a clinical trials unit or agent of the Sponsor, the Chief Investigator or an appropriate member of the Research Team. A discussion about the most appropriate Initiation of sites i.e. Remote or site visit initiation will take place as part of the Risk Assessment Form completion.

In all cases, the relevant Site Initiation SOP and forms must be used and documented in the Trial Master File and Investigator Site File.

4. Non-Compliance

Site initiation is an important part of the process to ensure that all aspects of the study are clearly understood and appropriate personnel are fully appraised of their individual roles and responsibilities. UoL takes the responsibilities of Sponsor seriously, and it is important for the successful management of an IMP study that research teams are 'ready'. Failure to comply with this SOP will result in the Non-Compliance SOP-1016 being implemented at a CRITICAL finding. This may mean that the study is suspended before it's even started!

5. Responsibilities

	Responsibility	Undertaken by	Activity
1.	Sponsor or their delegate	Sponsor or their delegate	To ensure that all approvals and regulatory documents necessary for the study to commence at site are in place /in progress prior to the initiation visit occurring.
2.	Sponsor or their delegate & Chief Investigator	Sponsor or their delegate Chief Investigator.	To ensure that the CI/PI and all key Research staff involved in the study attend the Initiation Visit.
3.	Sponsor or their delegate	Trials Monitor or their delegate	To ensure all areas of the studies as detailed in the Study Initiation Visit Agenda are discussed with the CI/PI and Research team so that everyone is aware of their individual and collective responsibilities within the study.
4.	Sponsor or their delegate	Trials Monitor or their delegate	To ensure that all staff involved in the study have the necessary training/qualifications in place as detailed in Section 3 'during the site initiation visit' above.
5.	Sponsor or their delegate	Trials Monitor or their delegate	Submit a detailed written report within 10 days of the visit recording outstanding items and any clarification required.
6.	Sponsor or their delegate	Trials Monitor or their delegate	Review the Investigator's responses to the written report and ensure the report is signed by the Sponsor and Investigator and that the original is filed in the Trial Master File.
7.	Sponsor or their delegate	Trials Monitor or their delegate	Ensure all issues raised at the initiation visit have been resolved prior to study commencement at site.

This table is used to track the development and approval of the document and any changes made on revised / reviewed versions

6. Development and approval Record for this document

Author / Lead Officer:	Wendy Gamble
Job Title:	Research Governance Manager
Reviewed by:	UoL Research Management and Operations Group (RSMOG)
Approved by:	Professor Nigel Brunskill 
Date Approved	10/04/2017

7. Review Record

Date	Issue Number	Reviewed By	Description Of Changes (If Any)
Oct 2013	2	Wendy Gamble	Version 1 amended following review of Sponsor Processes

NB: Paper copies of this document may not be most recent version. The definitive version is held on the UoL College of Medicine, Biological Sciences and Psychology Website, Research Governance pages.

April 2014	3	Wendy Gamble	Version 2 amended to add in section on non-compliance
June 2015	4	Wendy Gamble	SIV checklist updated and introduction of separate pharmacy SIV checklist.
March 2016	5	Diane Delahooke	Review and update of SOP & appendices. Non CTIMP SIV checklist introduced.
Nov 2016	6	Diane Delahooke	Review for consistency against UHL SOP. RSI added.

8. Distribution Record

Date	Name	Department	Received

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