Standard Operating Procedures (SOP) for:			
Site Selection, Site Initiation and Site Activation			
SOP Number:	**46**	Version Number:	**1.1**
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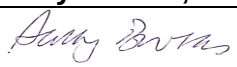
Signature:	
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Purpose and Objective:

This SOP outlines the minimum requirements for opening a site for a QMUL or BH sponsored study, and describes the procedure for the selection of suitable sites and for conducting site initiation and activation for trials.

This SOP is mandatory for all BH and QMUL sponsored CTIMPS.

For BH and QMUL sponsored non-CTIMP studies, this SOP should be used as best practice and implemented proportionately for all sponsored studies.

The purpose of this SOP is to ensure that:

- All essential documentation, approved protocol, SOPs, and required approvals are in place prior to the start of the trial at a site.
- All staff members at each site are aware of their responsibilities, the sponsor processes, and SOPs.
- The site team of CTIMPs has had GCP training which is current and documented.
- The 'delegation of tasks' log is completed before any trial related activities are performed, and that all individuals are authorized by the PI to undertake such tasks.
- The pharmacy (and / or individuals responsible for the IMP at site) is provided with notification to proceed with ordering IMP (if applicable), and that procedures for receipt, dispensing, destruction, and accountability are documented.
- To ensure that the site, sponsor, and coordination team contact details are up to date and correct, and that the site and pharmacy know how to contact the sponsor.

Scope:

This SOP covers the procedures that must be followed to ensure that a site is initiated prior to the screening and recruitment of any trial participant. It covers the procedures before initiation (including site selection), during the site initiation, and post-initiation to activate the site to begin the trial.

The CI is responsible for site selection, site initiation, and site activation in the Conditions of Sponsorship (in the delegation of responsibilities), by ensuring that all documentation is in an appropriate and secure location. It is recognised that this responsibility may be delegated to another member of the research team with sufficient knowledge and training. Therefore, for the purposes of this SOP, reference to the CI shall be deemed to also refer to the individual with delegated responsibilities for these activities.

This SOP is mandatory for all BH and QMUL sponsored CTIMPS.

For BH and QMUL sponsored non-CTIMP studies, this SOP should be used as best practice and implemented proportionately for all sponsored studies.

Abbreviations:	
AE	Adverse Events
ARSAC	Administration of Radioactive Substances Advisory Committee
BH	Barts Health NHS Trust
CA	Competent Authority
CI	Chief Investigator
CNST	Clinical Negligence Scheme for Trusts
CRF	Case Report Form
CRO	Clinical Research Organisation
CTIMP	Clinical Trial of an Investigational Medicinal Product
CV	Curriculum Vitae
e-CRF	Electronic Case Report Form
EU	European Union
EudraCT	European Clinical Trials Database
FCO	Foreign and Commonwealth Office
GCP	Good Clinical Practice
GP	General Practitioner
IB	Investigators Brochure
IMP	Investigational Medicinal Product
IRAS	Integrated Research Application System
ISF	Investigator Site File
JRMO	Joint Research Management Office
NCC	National Coordinating Centre
NHS	National Healthcare Service
NIMP	Non-IMP
Non-CTIMP	Clinical trial with no Investigational Medicinal Product
PI	Principal Investigator
PSF	Pharmacy Site File
QMUL	Queen Mary University of London
REC	Research Ethics Committee
SIV	Site Initiation Visit
SmPC	Summary of Product Characteristics
SOP	Standard Operating Procedure
SSI	Site Specific Information
TMF	Trial Master File
UK	United Kingdom

Definitions:

Site activation: The point at which the CI confirms the site can start the trial.

Relevant SOPs:

SOP 7 – Costing and Contracting.
SOP 11a – BH/QMUL Sponsorship of CTIMPs, ATMPs and Clinical Trials of Non-CE Marked Medicinal Devices – Process for Researchers
SOP 12 – BH / QMUL Sponsorship of non-CTIMPs
SOP 17a – Process for JRMO - Amendments for Sponsored Studies
SOP 26a – Pharmacovigilance and Safety reporting for Sponsored CTIMPs / ATMP
SOP 38a – Use of Computerized Equipment, Software and Systems in Clinical Research
SOP 45 – Essential Documentation including Trial Master Files and Files for All External Sites and Facilities

SOP Text:

Pre-Site Initiation:

	Responsibility:	Activity:
1.	CI	**Number of sites and location must be agreed as part of the Provisional Sponsorship Approval meeting.** The number of sites in the UK and abroad must be agreed with the sponsor (relevant GCP manager). The number of sites and locations are agreed as part of the Provisional Sponsorship Approval and in the Final CTIMP meeting. The sponsor reserves the right to cap the number of sites, depending on the level of resource and on-going compliance of the trial. For CTIMPs, once the study has received declaration of final sponsorship, any changes to the number of national or international sites must be agreed to by the sponsor *(SOP 17a - Amendments for Sponsored Studies*).
2.	CI	**CI to conduct a feasibility assessment of any prospective sites.** Careful site selection is the responsibility of the CI, who must ensure that study resources are directed to well-motivated, qualified sites with the potential to recruit eligible participants, generate high quality study data, and conduct the study within the regulations. Potential sites may be identified by contacting investigators who have previous experience in the therapeutic area, recommendations by colleagues, or via publications, professional groups, or research networks. Each PI must be qualified in education, training, and experience, which is evidenced in the form of a CV, and must be adequately resourced to properly conduct the study. Initial contact with a potential new site may be via an 'expression of interest' form. This is usually a brief document containing a short description of the trial, participant population, and expectation of site requirements. The CI will conduct a feasibility assessment of all potential sites (including the selection of Barts Health NHS Trust as a site). As a minimum, the following items must be assessed and documented: • Type of site (NHS or non-NHS) • Site's willingness to participate • Site's ability to complete all site specific procedures • PI training, experience, and availability • Staff resources, and the number of PI's active trials • Adequacy of facilities, equipment, and resources to conduct the study properly • Availability of potential eligible participants Details of any pre-initiation contact to assess site suitability should be documented and any issues raised must be addressed by the CI or delegate. Once information has been collected from the site, the CI should review and make a suitability decision. This process should be documented. If a feasibility assessment is deemed unnecessary, particularly if the site staff and facilities are already known to the CI or sponsor, the reason and decision for not performing a feasibility assessment must be documented in the TMF.

	Responsibility:	Activity:
		The above process should be repeated for the selection of all new sites, throughout the study's duration.
3.	CI	**CI to conduct due diligence in the selection of sites and countries to participate in the study, and provide the Sponsor with this information to enable the Sponsor to make an informed decision.** When considering taking a trial outside of the UK, the CI must discuss this in detail with the JRMO's GCP Managers and Contract Managers. The CI should consider the limitation of indemnification of international trials: BH, as an NHS Trust with Clinical Negligence Scheme for Trusts (CNST) indemnification, may only sponsor studies within the UK. QMUL as Sponsor may consider international studies but additional indemnification is required for each country, which must be costed and resourced by the CI (*SOP 7 – Costing and Contracting*). When research is to be conducted in countries within the EU, the CI should provide the GCP manager(s) with sufficient justification as to why additional countries are needed outside of the UK, how they will be funded (including covering additional insurance premium for each country), along with a short summary of each country's clinical management. It is the sponsor's requirement that the CI identifies a National Coordinating Centre (NCC) for each international site. The NCC(s) will be delegated regulatory and oversight responsibilities for their countries as part of the Sponsorship contracting process. Each country will be asked to comply with the EU directive, have contracts written under the jurisdiction of the Law of England and Wales, and agree to complete all the necessary submissions to their national research ethics committee and Competent Authorities on the sponsor's behalf. The CI should consider the resource and management implications and may consider contracting a Clinical Research Organisation (CRO) for the management of international studies. When research is to be conducted in countries outside of the EU, and in addition to the above, the CI and team must provide the GCP Managers with a short summary of the regulatory status of all countries, including differences to the EU Directive regulations and other regulations (for example, the Data Protection Act). The following additional information will need to be provided to the Sponsor when seeking approval for including non-EU countries in all studies (CTIMP and non-CTIMP): • Copies of the risk assessments made, including internal and any conducted by external organisations (e.g. CRO[s]). • If not covered in the risk assessment, provide a written account of the CI's and collaborators' experience of managing trials in these non-EU countries. • Any known issues of working in these countries and how they are managed or mitigated (e.g. additional administrative, regulatory or legal issues that are not relevant within the EU). • Confirmation that the sites selected are not within the areas that the Foreign and Commonwealth Office (FCO) currently advise against travel (see Foreign and Commonwealth Office website for details). • Confirmation that the Sponsor (or delegated organisation) is able to

	Responsibility:	Activity:
		freely audit the sites, given the FCO travel advice. • Confirmation of plans for shipment and distribution of the IMP, and the additional considerations for the transfer of samples, data (that will not be covered outside of the EU by the Data Protection Act), and supplies to and from the selected countries. This information must be sent to the Contracting and Costing Officer and GCP Manager.
4.	CI	**Once sites and countries are approved by the Sponsor, gain the necessary approvals at each site and country.** Once the additional UK sites are approved by the sponsor, and the study has already received final sponsorship approval and the green light to activate sites, the CI and study team may proceed with site approval by adding the sites to Part C of the IRAS form, and liaise with the JRMO about issuing site specific forms to the new sites. For international studies, once the country has been approved by the sponsor, and when the study has final sponsorship approval and the green light to activate sites, the CI may proceed to gain regulatory approvals in the new countries.
5.	CI	**Review the TMF to ensure that all essential documentation and contracts are in place prior to initiation.** Ensure that the Sponsor has received all the necessary documentation for the Sponsor Oversight File.
6.	CI	**Send Feasibility Questionnaires.** Request the completion of Site Feasibility Questionnaire(s) (if not already received), and Pharmacy Questionnaire(s). Send: • The Site Initiation Pack to the PI • Sponsor (JRMO) SOPs • Essential IMP documents for the Pharmacy Site File • Essential Documents for the Investigator Site File
7.	CI	**Request all site essential documentation from individual sites.** Request the following documents from each site: • Site R&D Approval / NHS Permission Letter / HRA Approval • Fully signed Clinical Trial Site Agreement • Copy of the PI's signed CV and GCP certificate • Completed delegation log • Completed site feasibility questionnaire • Completed site pharmacy questionnaire
8.	CI	**Check the all essential documentation is in the ISF.** Review the ISF against the TMF checklist to verify that the site has all the required essential documents on file. Highlight any missing documents from either file and arrange for them to be sent prior to site activation.

Site Initiation

	Responsibility:	Activity:
9.	CI	**Perform Site Initiation Visits (SIV) at each site, train site staff, resolve all issues, and complete reports.** All sites must undergo an SIV prior to the CI activating the site to start the trial (site activation). The SIV must be performed prior to the first subject being recruited at the site. This is mandatory for all CTIMPs. The aim of the SIV is to ensure that all sites and study staff are adequately aware of GCP, and trained in the protocol, study specific SOPs, source data and PI responsibilities before trial activities begin. SIVs must only be conducted after the trial has received the Final Declaration of Sponsorship. The SIV may be conducted prior to the Sponsor issuing the green light to activate sites. However, the CI should consider the SOPs of the sites (e.g. sites may require NHS Permission / HRA Approval to be issued before SIVs are booked). SIVs should be scheduled as close to Site Activation as logistically possible to ensure that training remains fresh in the mind of all site staff at the start of the trial. The PI, lead research staff (i.e. site research nurse[s]), and site pharmacist must be present during the SIV. The PI must be present during the SIV for all QMUL and BH sponsored CTIMPs. It is best practice to include the CI where possible in SIVs (if they are different to the PI). *Associated Document 1: Site Activation Checklist* and *Associated Document 4: Site Initiation Report*, or alternatives that have been agreed by the GCP Manager, should be used to conduct the meeting and document the visit in a report format. The person delegated by the CI to conduct the SIV should be thoroughly trained in the trial and protocol, including having a good understanding of all trial procedures, CRFs, expected AEs, unblinding procedures (for IMP and / or imaging as appropriate) and SOPs. This should be documented and reflected on the coordination delegation log (*SOP 45 – Essential Documentation Including TMFs and Files for all External Sites and Facilities*). During the visit the following should occur (as a minimum): • A meeting with the PI, pharmacy and key staff (i.e. monitor, site research nurse(s), trial coordinator), to discuss and review the protocol and all trial procedures. Pharmacy representatives can be met with separately. • A trial initiation presentation should be given to the PI and their research team and should cover, but is not limited to: ○ Delegation of responsibilities of the site; ○ Sponsor forms and logs of trial conduct; ○ Sponsor SOPs; ○ Informed consent and recruitment (the current versions of the PIS and ICF will be reviewed with the PI and relevant personnel); ○ Trial IMP, placebo, and NIMPs, including but not limited to receipt, storage conditions of the IMP (this should be checked even if the IMP has not been received at site at time of SIV), dispensing, accountability, return and destruction;

	Responsibility:	Activity:
		○ Monitoring plan and requirements, including access to source data; ○ Data management; ○ Ongoing maintenance of the ISF; ○ Biological samples (if applicable); ○ The requirements regarding the timeline and documentation of reviews of patient eligibility; ○ Description of the roles and responsibilities of a PI; ○ Study specific training logs; ○ Pharmacovigilance, safety reporting requirements, including pregnancy reporting and follow-up, and Urgent Safety Measures (*SOP 26a - Pharmacovigilance and Safety Reporting for Sponsored CTIMPs / ATMP*); ○ Amendments; ○ Sponsor contact details; ○ Discussion of Sponsor minimum clinical standards and compliance; ○ Details of what is expected at the site regarding study specific training; ○ End of Trial and archiving; ○ Procedure for PI cover during any absence. • The study team should be provided with the opportunity to ask questions. Any issues highlighted at the SIV which are not resolved during the visit need to be documented and followed-up before the site is activated. • A visit to (and meeting with) Pharmacy and / or any out of pharmacy storage areas. This visit must ensure that they are familiar with the IMP documentation and satisfied with the IMP management plan (and any other IMP related documents). Request details of the IMP storage arrangements and, where necessary, review IMP storage facility at the site. • A visit and review of any sample processing or storage areas. • An agreement of which documents and systems constitute "source data" and their location. This should be documented in the ISF (*SOP 45 – Essential Documentation Including TMFs and Files for all External Sites and Facilities*). • An assessment of local computerised systems (*SOP 38a - Use of Computerised Equipment, Software and Systems in Clinical Research*). • Training the team of study specific software, equipment, or devices, including the requirements for calibration and verification before the study starts, and maintenance once the study is open. The person delegated to perform the SIV must ensure that all trial staff attending the SIV will sign a Site Initiation Attendance log. A written report including actions and documents outstanding should be issued to the site within 2 weeks of the visit.

	Responsibility:	Activity:
10.	CI	**CI (or delegate) should follow *Associated Document 1: Site Level Feasibility Assessment Guidance* to activate the site.** Use *Associated Document 1* to create minimum site checks to be performed prior to the issuing of the site activation email. The site should not be activated until: • NHS/Site permission / HRA Approval / R&D approval is in place. • The Sponsor has received the signed site agreement. • The Sponsor has received a final signed copy of the SSI / HRA Capability and Capacity Assessment and Schedule of Events. • Any additional site approvals are in place at the site (e.g. ARSAC licence, clinical physics, imaging and pharmacy approval). • The delegation log has been completed and a copy retained by the coordinating team. • The research team's CV(s) and GCP training certificate(s) (within the last two years) are retained by the coordinating team. • All other essential documents have been collected by the coordinating centre. • SIV has been conducted, report sent, and all additional actions completed. • Test scans (if applicable; e.g. MRI), have been performed, and the quality and transfer has been deemed acceptable (*SOP 38a - Use of Computerised Equipment, Software and Systems in Clinical Research*). • Site has received e-CRF or CRF training, which should include clear guidelines as to when the CRF should be completed, how this is checked and monitored by the coordinating team and CI, and how problems are escalated. • IMP has been delivered to site.
11.	CI	**Complete Site Initiation Report along with actions and send to site.** If the SIV Report has been delegated to a person other than the CI, provide a copy of the initiation report to the CI to ensure that the report is an accurate reflection of the initiation visit. The original copy of the initiation report will be stored in the TMF. Resolve any actions that arose from the SIV. This may include the monitor providing copies of any documentation required by the CI to their TMF, or Sponsor Oversight file in the JRMO.
12.	CI	**Send an initiation follow-up letter to the pharmacy, outlining any outstanding actions.** It may also be necessary to send the initiation follow up letter to non-pharmacy individuals responsible for the IMP.
13.	CI	**File all site initiations/actions and correspondence in the TMF.**

Post-Site Initiation

	Responsibility:	Activity:
14.	CI	**Sites should be notified by email of their activation.** Once initiations are complete and follow up actions are addressed (if applicable), issue the site with a "Site Activation" email. Where possible, *Appendix A: Site Activation Email Template* should be used. This should be sent to the PI, pharmacy, monitor, and sponsor. The CI should be copied into this correspondence if this task has been delegated by them. The sponsor should be informed of the activation of each site by sending a copy of the email to: research.monitoring@bartshealth.nhs.uk. The site activation email is not an approval for all centres to commence recruitment, but is site specific. An individual site activation email must be sent.
15.	CI	**File all site activation correspondence in the TMF.** This will include a copy of the signed delegation log for each site which requires the PI to ensure that trial specific training is provided to the trial team (including new members as they join). See SOP 45 template for trial specific training.

Change Control

This section outlines changed from version 1.0 to version 1.1.

Section Changed	Summary and description of change
15	Addition of CI responsibility to ensure trial specific training logs are used
7 & 10	Details of required HRA Approval documents added
Associated Documents	Fourth associated document added: SIV Report Template Documents re-numbered

List of Appendices

	Document name
Appendix A	Site activation email template

List of Associated Documents

	Document name
Associated Document 1	Site Level Feasibility Assessment Guidance
Associated Document 2	Site Activation Checklist
Associated Document 3	SIV Presentation Template
Associated Document 4	Site Initiation Visit Report Template

The JRMO would like to acknowledge the Centre for Experimental Cancer Medicine for its templates that have been used and incorporated to create this SOP.

Appendix 1 Site Activation Email template

SUBJECT: (Insert trial acronym) Clinical Trial Opening Notification

Dear Study Team,

Trial name:
PI:
REC reference:
EudraCT:

The above trial is now open to recruitment at (Insert NHS Trust).

Current versions:
Protocol: (version and date)
IB / SmPC: (version and date)
Diary Card (where applicable):
CRFs: (version and date)
Patient Information Sheet: (version and date)
Consent sheet: (version and date)
GP letter: (version and date)
Pharmacy manual: (version and date)
If you require any additional information please contact (state name and contact details).

Kind regards

(Insert name)
(Insert job title)
(Insert contact details)

Flow Chart