Standard Operating Procedures (SOP) for:			
BH/QMUL Sponsorship of CTIMPs, ATMPs and Clinical Trials of non-CE marked Medicinal Devices – Process for Researchers			
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Author:	**R. Fay, Research Governance & GCP Manager**
Reviewer:	**K. Mahiouz, Clinical Trials Facilitator**
Reviewer:	**E. Clough, R&D Governance Operations Manager**

Authorisation:	
Name / Position	**Sally Burtles Director of Research Services & Business Development**
Signature	
Date	**7/4/16**

Background

When Bart's Health NHS Trust (BH) or Queen Mary University of London (QMUL) agrees to Sponsor a Clinical Trial of a Medicinal Product (CTIMP), Advanced Therapy Medicinal Products (ATMPs), or Clinical Trials of a non-CE marked Medical Devices they are accepting considerable legal and regulatory responsibilities and organizational risks.
For Clinical Trials of Investigational Medicinal Products (CTIMPs), the European Commission Directive 2001/20/EC define the Sponsor as: An individual, company, institution or organisation which takes responsibility for the initiation, management and/or financing of a clinical trial.

The Health Research Authority (HRA) sets out guidance on the expectations of Sponsors. This includes that Sponsors should satisfy themselves that the trial meets the relevant standards and that arrangements are put and kept in place for management; appropriate peer review; all supporting information is supplied to the regulators for their consideration; defined roles and responsibilities for the duration of the trial; monitoring and audit; a risk assessment processes; public and participant involvement in the trial; ensuring the training and suitability of the research team; public registration of the trial; dissemination of the results; project oversight; guidance for academic supervisors and providing on-going quality assurance.

NB: HRA processes are being introduced in April 2016, admin aspects of this SOP may change rapidly. Please see HRA website for guidance.

The EU Directive requires insurance or indemnity for liabilities of the Sponsor and investigator.

Purpose and Objective:

The purpose of this standard operating procedure is to outline the review and development activities undertaken by the Chief Investigator, or staff they delegate responsibilities to, in order to request Bart's Health NHS Trust (BH) or Queen Mary University of London (QMUL) to grant Sponsorship of a CTIMP, ATMP or Clinical Trial of a non-CE marked Medical Devices. (Please note the JRMO process for granting Sponsorship is outlined in SOP 11b).

This SOP is written:

a. To ensure that BH/QMUL research staff are aware of the processes for obtaining Sponsorship of a CTIMP, medicinal devices and ATMPs and the documentation that they need to supply to the JRMO so that Sponsorship review can be undertaken. To ensure all BH or QMUL Sponsored CTIMPs have a formal Sponsorship agreement in place to comply with the legal requirements of the EU Directive on Clinical Trials and all UK Legislation (Medicines for Human Use [Clinical Trials] 2004 Statutory Instrument,1031 and all amendments), the Research Governance Framework for Health & Social Care 2005, and Good Clinical Practice (GCP).
b. To ensure that all BH or QMUL Sponsored Clinical Trials that involve non-CE marked medical device

trials have a formal Sponsorship agreement in place that comply with the legal requirements of the Medical Devices Regulations 2002 (Statutory Instrument 2002/618) which came into force on 13 June 2002 and implement the provisions of the Medical Devices Directive 93/42/EEC, Active Implantable Medical Devices Directive 90/385/EEC and In Vitro Diagnostic Medical Devices Directive 98/79/EEC.

c. To outline the process undertaken for BH or QMUL to agree to act as EU Legal Representative of a CTIMP on behalf of a Sponsor who is based outside of the European Economic Area (EEA).

Scope:

This SOP applies to all requests for BH/QMUL to Sponsor CTIMPs, Advanced Therapy Medicinal Products (ATMPs), Clinical Trials of non-CE marked Medical Devices that are required to notify MHRA before they start and all BH and QMUL staff working on any activity that falls under them. For the purpose of this SOP 'CTIMPs' means all regulated clinical trials including: CTIMPs, ATMP and Clinical Trials of non-CE marked devices.

Abbreviations:

BH	Barts Health NHS Trust
JRMO	Joint Research Management Office
QMUL	Queen Mary University of London
CTIMP	Clinical Trial of a Medicinal Product
ATMP	Advanced Therapy Medicinal Products

Definitions *(if needed)*

Chief Investigator: The UK Statutory Instrument 2004/1031 defines who can act as a Chief Investigator:

"chief investigator" means—
(a) in relation to a clinical trial conducted at a single trial site, the investigator for that site, or
(b) in relation to a clinical trial conducted at more than one trial site, the authorised health professional, whether or not he is an investigator at any particular site, who takes primary responsibility for the conduct of the trial;

"investigator" means, in relation to a clinical trial, the authorised health professional responsible for the conduct of that trial at a trial site, and if the trial is conducted by a team of authorised health professionals at a trial site, the investigator is the leader responsible for that team;

The Statutory Instrument distinguishes between 'authorised' health professional and health 'care' professional.

Authorised health professional is defined as:
(a) Doctor
(b) Dentist
(c) Nurse
(d) Pharmacist

Health care professional is defined as
(a) Doctor
(b) Dentist
(c) Nurse
(d) Pharmacist
(e) a person registered in a register of ophthalmic opticians maintained under section 7 of the Opticians Act 1989
(f) a person registered in a register established and maintained under article 5 of Health Professions Order 2001
(g) a registered osteopath as defined by section 41 of the Osteopaths Act 1993, or
(h) a registered chiropractor as defined by section 43 of the Chiropractors Act 1994

Therefore, using the definition of 'authorised' health professional, only those professions listed (a) to (d) may act as a Chief Investigator (or a Principal or co-investigator).

For BH and QMUL *single site* sponsored CTIMPs the Chief Investigator should be the Bart's Health NHS Trust site's Principal Investigator.

Relevant SOPs

This SOP is closely linked with:

SOP 1 Research project application
SOP 7 Costing and Contracting for BH & QMUL Sponsored CTIMPs
SOP 10 JRMO internal filing process
SOP 11a BH-QMUL sponsorship - Process for Researchers
SOP 13a Governance Permissions Sponsored
SOP 14 Peer Review
SOP 17c Process for Researchers - Amendments for Sponsored studies
SOP 18a Project closure: guidance for research staff of Sponsored studies
SOP 23 Risk Assessment
SOP 38a Use of Computerized Equipment in a research projects
SOP 38b Trial Data Management Systems
SOP 40 Vendor assessment
SOP 42a IMP Management -BH/QMUL Sponsored studies
SOP 45 Essential documentation and Trial Master File (TMF)
SOP 46 Site selection, site initiation and site activation

SOP Text

	Responsibility	Activity
1.	Chief Investigator (CI)	**Work with JRMO to obtain an accurate cost for the trial** The CI is responsible for ensuring that CTIMPs are accurately and realistically costed in the formative stages to ensure that it has adequate funding to be deliverable, successful and compliant. It is the CI's responsibility to ensure that a CTIMP is adequately resourced. Funding should include, but is not limited to, trial management and coordination, monitoring, establishing, maintaining and running a GCP compliant database, IMP (pharmacy/distribution/excess treatment) costs, site's supplies & equipment, imaging costs staff and participant travel, MHRA fees including amendment fees, external contractors i.e. labs, sample, handling and storage costs, all subcontractors and outsourced facilitates, Contract Research Office (CRO), statisticians (see SOP 7, associated document 2 JRMO Contract Checklist and SOP 1 for Costing question with prompts). The Chief Investigator should discuss the proposed CTIMP with the JRMO GCP Managers as early as possible, i.e. at the funding application stage so that advice on the resources required in a funding application can be included. The JRMO cannot guarantee the approval of any provisional Sponsorship application for CTIMPs that are considered to have insufficient funds to support the trial design or its management. The JRMO may ask the CI to seek further funding or to reduce the scope of the trial design to meet the secured budget. Contacting the JRMO and GCP team at the early stage can prevent unnecessary delays in the set-up process. Before agreeing to any milestones with funders, the CI should discuss their feasibility with the GCP Manager. This is to avoid agreeing to milestones such as deadlines for REC approval, first patient recruited or for reporting results that may not be realistic or take into consideration the regulatory and site approval timelines or protocol design. It is anticipated by the JRMO that the majority of CTIMPs will be managed by a Clinical Trials Unit (CTU) or established research centre at BH or QMUL. As such the CTU or a research centre will need to be involved as early as possible to ensure that their costs

		are captured in the funding application. Where this is not the case the CI must be able to demonstrate to the JRMO that they have adequate trial management support, i.e. a dedicated Trial Manager, and previous experience as a Chief Investigator to deliver the trial compliantly. This is one aspect of the JRMO Risk Assessment of the CTIMP study. The CI should consult with the funder as to whether they will specify the use of a particular CTU, in which case the CI may need to cost for this additional funding in the award application.
2.	Chief Investigator (CI)	**Categorise the trial as a CTIMP** If there is any ambiguity as to whether a trial is a CTIMP or a non-CTIMP, the CI must discuss this with the JRMO GCP Manager. The CI should consider if the trial uses any of the following: drugs; vitamins; nutritional supplements; food supplement; devices that deliver drugs e.g. stents; probiotics; or imaging tracers. Please refer to the MHRA website for guidance on determining a CTIMP. If it is still unclear the JRMO will send a scoping query to the MHRA by sending a copy of the protocol to the MHRA clinical trials helpline, retaining documented evidence to support the MHRA's decision (i.e. the email from the MHRA and version of the protocol sent). It may be necessary to confirm the status of the trial with the MHRA at the grant stage to ensure that sufficient funds are secured to support a successful CTIMP. The MHRA's opinion as to whether a trial is a CTIMP is final. If the MHRA's opinion is unforeseen it is the CI's responsibility to comply with the applicable regulations of a CTIMP classification or to revise the protocol or grant proposal so that it is no longer classified as a CTIMP. The JRMO, as Sponsor, reserves the right to re/submit a funding proposal or protocols for scoping review with the MHRA, including following revisions to the proposal or amendments to the protocol (see SOP 17a - Amendments for Sponsored studies - process for JRMO).
3.	Chief Investigator (CI)	**Write the Protocol using the Sponsor approved template.** The CI must write a protocol using the current version of the JRMO CTIMP Protocol Template. This is available on the JRMO website or from the GCP Managers and JRMO Governance team. Special attention should be given to ensuring that no template wording or guidance remains in the submitted protocol, and that it is consistent, accurate and proof read before it is submitted to the JRMO. All protocol writing guidance must be taken into consideration. The JRMO is not responsible for the scientific development of the protocol but will ensure it is compliant with GCP, MHRA, HRA and other regulatory requirements and guidance. If the JRMO receives a protocol that is not on the JRMO's approved template they will ask the CI to transfer to the approved template before issuing Provisional Sponsorship approval.
4.	Chief Investigator (CI)	**Once funding is secured, send protocol to JRMO and meet with GCP Manager and Costing and Contract Manager. Attend CTIMP Support Meeting with the JRMO** The CI should send a copy of the protocol to the GCP Manager and Costing and Contract Manager for review. It may be necessary at this stage to hold a CTIMP Support Meeting. This initial meeting with the CI is to discuss all the support functions, governance issues, potential study costs, supply of the IMP/manufacturer of the device for the trial. Following the meeting the CI is expected to work with the Costing and Contract Manager on their funding applications (see SOP 07 – Costing & Contracts).
5.	Proposed UK/EU Chief Investigator (CI)	**For non-EEA Sponsored CTIMPs – formally request the JRMO to be the UK Legal Representative** When QMUL or BH are requested to act as UK Legal Representative of a CTIMP whose main Sponsor is based outside of the European Economic Area (EEA) the

		JRMO's Sponsor Oversight Group will need to agree in principle to act as UK Legal Representative. Send a copy of the protocol to the GCP Manager and Contracts Manager and arrange a meeting with them. The GCP Manager will liaise with the Sponsor Oversight Group and report back to the CI/UK Investigator. In all trials for which BH or QMUL agree to act as EU legal representative a contract will be put in place with the external Sponsor to detail the responsibilities BH or QMUL have agreed to undertake. If the JRMO declines to act as UK Sponsor Representative the CI may appeal to the Sponsor Oversight Group in accordance with the JRMO escalation policy. The GCP Manager will assess whether it will be a condition of becoming a UK Legal Representative to ask the research team to transfer the protocol on to the JRMO CTIMP protocol template. The assessment will be based upon whether the version received meets QMUL or BH standards and UK and EU regulations. Once the JRMO have agreed to act as Legal Representative, the process follows as per the rest of this SOP.
6.	Chief Investigator (CI)	**Allocate an independent named statistician to the study (not the CI).** For trials within the remit of this SOP a named statistician must be allocated to the trial for the duration of the trial. The statistician must be suitably qualified and experienced in the type and phase of the trial, which will be evident from their CV. It is not acceptable for the CI to act as the statistician. The statistician's role is to give independent and expert advice on the trial at the design phase during the study i.e. should there be any amendments that may impact on the statistics or data integrity and during the final analysis of the results. It may be necessary to contract an external statistician or put in place a work order but this will be established during the contract meetings with the JRMO (see SOP 07 – Costing & Contracts).
7.	Chief Investigator (CI)	**Discuss the assignment of a new Chief Investigator with the JRMO.** If the CI has not previously worked on a BH or QMUL Sponsored CTIMP, discuss with the GCP Manager their proposal of becoming the CI. For trials Sponsored by QMUL or BH, the CI must have a substantive contract with the Sponsor (BH or QM accordingly). The CI must be medically qualified in the therapeutic area and be able to prescribe the IMP. This is so that the Sponsor can delegate to the CI the role of pharmacovigilance medical assessor. The following experience may be considered by the Sponsor Oversight Group: previous experience as a CI/PI on non-commercial or commercial CTIMPs, multi-site/international trials (where relevant), experience on non-CTIMP trials, previous GCP and regulatory compliance, previous experience of working on MHRA inspected trials, previous experience of safety assessments/pharmacovigilance. The CI does not necessarily have to be the grant holder but it is expected that the CI is centrally involved in the protocol writing and development. For new CIs the JRMO will work with the research team, Clinical Academic Group (CAG) or Institute to assess their experience and determine whether additional peer support, training or trial management support is required.
8.	Chief Investigator (CI)	**Arrange Peer Review and Institute/CAG Review of the protocol** Send the protocol for comprehensive and independent peer review. The peer review of the research proposal by a funder is not sufficient for a CTIMP; the protocol must also be reviewed by individuals who are independent of the research team and are experts in the field relevant to the therapeutic area. The peer review includes, but is not limited to, whether the protocol is scientifically sound, understandable, comprehensive, consistent and compliant with the regulations. Full peer review guidance is found in SOP 14 – Peer Review). It is the CI's responsibility to address and evidence that all peer reviewers' comments have been addressed before submitting the study to the JRMO for provisional approval.
9.	Chief Investigator (CI)	**Site Feasibility Assessment** It is the CI's responsibility to undertake a site feasibility assessment (see SOP 46 - Site selection, site initiation and site activation) at the early stage in the study design to

		ensure that the trial design and protocol are practicable. A protocol may be scientifically valid but a feasibility assessment will consider whether it is logistically possible at all/each site. The JRMO therefore, requires that this is undertaken and the protocol adapted to include feedback from sites and collaborators before it is approved by the Sponsor and regulators. <u>If the CTIMP is to have international research sites.</u> Only QMUL can Sponsor international research with a QMUL substantially employed CI. BH, with NHS's CNST indemnity cannot Sponsor international studies. The CI must be open and honest with the JRMO about their plans to open internationally at the beginning of the CTIMP. A full justification for international trials and the selection of countries must be given prior to Sponsorship approval. This will also include information about any Contract Research Organisation (CRO) that will be used to coordinate and secure international regulatory approvals (see SOP 6 – Vendor Assessments). A National Coordinating Centre (NCC) will be required in each country to oversee on-going national regulatory compliance. See SOP 46 Site selection, site initiation and site activation) for information that needs to be supplied to the JRMO for international site selection or additional internal countries. The GCP Manager must approve the trial expanding internationally and, as Sponsor, reserves the right to refuse expansion. Appeals to the JRMO's decision may be made to the Sponsor Oversight Group as per the JRMO's escalation policy.
10.	Chief Investigator (CI)	**Coordinate approvals of the protocol from support departments** At this design stage, the CI should seek out the support department's review and input into the protocol. The support department's risk assessments and feedback should be included in the protocol development and their costs included in funding requests These might include the following support departments (depending on the trial design): • Imaging, Clinical Radiation Expert (CRE), Medical Physics Expert (MPE) and laboratories. • Clinical Trials Pharmacist approval (see SOP 42a - IMP management for Sponsored CTIMPs) • Clinical Physics' risk assessment • Medical photography
11.	Chief Investigator (CI)	**With the Costing and Costing Manager, begin the contract negotiations with external parties** Ensure that all contracts and agreements are reviewed by the JRMO Costing and Contracts team. Where QM Innovation (QMI) or the Business Development Unit (BDU) staff have been involved in the contract negotiations, the CI must ensure that the JRMO are kept informed, as QMI or BDU's input may be required during the (mandatory) Costing and Contract meetings. Certain contracts may be expected to be in place prior to REC and MHRA submission e.g. non-disclosure agreements with the IMP supply company/device manufacturer if the company's confidential information is required for REC or MHRA submissions. Contracts must only be signed by QMUL or BH authorised signatories (see SOP 7 – Costing and Contracts). The CI must disclose all conflicts of interest that may exist when professional judgment concerning the patients' welfare or the validity of research may be influenced by a secondary interest. It may arise for a CI when they have a financial interest that may influence, or be perceived to potentially influence, probably without their knowing, their interpretation of their results or those of others. Such interests may be financial gain or vested interest, i.e. shares in the IMP or device supplier, or receipt of funds from a third party with interests in the research output e.g. a commercially funded research associate post or personal relationship with the third party. It is of particular importance to disclose any CI conflict of interest as they are delegated the role of Sponsor's pharmacovigilance medical assessor, where independent judgement is paramount to patient safety. As Sponsors, the JRMO must be made explicitly aware of any competing interests that

		the CI or members of their team may have. In the interest of transparency the CI must disclose all conflicts of interest in the protocol and in the IRAS forms.
Provisional Sponsorship Approval		
12.	Chief Investigator (CI) or delegate	**Submit a valid Sponsorship application pack to the JRMO and register the trial on public databases.** **The trial team must not apply to HRA/REC or competent Authority (MHRA in the UK) for approvals until the Sponsor has granted permission to do so.** Once funding has been secured, and once all the relevant actions above have been addressed, submit a valid submission pack to JRMO via research.submission@bartshealth.nhs.uk. Use the JRMO submission checklist (see this SOP 11a associated document 1) to ensure the pack is considered 'valid' by the JRMO. This submission should include all documents that will be reviewed by the Health Research Authority (HRA), Research Ethics Committee (REC), Confidentiality Advisory Group (CAG) and MHRA or other regulatory body. The CTIMP Conditions of Sponsorship will be supplied by the GCP Manager, as it will be trial specific. All documentation needed by HRA/REC and MHRA application must be submitted in parallel so that the JRMO can review the consistency across all documents. Failure to send all documents together in one pack to the JRMO may cause a delay in the Sponsorship review and approval process. If the study is eligible for adoption on the NIHR portfolio, the portfolio adoption form (PAF) must be submitted via IRAS. It is mandatory that all BH and QMUL Sponsored studies that are eligible, are submitted for NIHR portfolio adoption. For guidance on eligibility and submission see the NIHR website. It is the CI's responsibility to obtain a EudraCT number, and the ClinicalTrials.gov registration or the ISRCTRN number. Guidance is found on ClinicalTrials.gov website and EudractCT website.
13.	Chief Investigator (CI) or delegate	**Upon receipt of the GCP Manager's and JRMO Governance Officer's feedback, revise documents and feedback clarifications to the JRMO.** Upon receipt of the JRMOs comments on your documents, provide clarification and/or revised comments and send tracked-changed documents back to the Governance Officer and GCP Manager. Ensure that all documents are returned and that all queries raised by the JRMO have been clarified, as failure to do so may delay Provisional Sponsorship approval. The JRMO will endeavour to give you one set of comments, however for practical reasons it may be necessary to provide them as two set of comments. The JRMO welcomes meetings to discuss areas of concern with the research team.
14.	Chief Investigator (CI) and research team	**Attend the Kick-off Meeting with the JRMO** The JRMO will invite the CI and coordination team to attend the Kick-off meeting. The purpose of the meeting is to identify all necessary contracts so that the negotiations can begin whilst the regulatory approval applications are in progress. The HRA Schedule of Events and Statement of Activities required for HRA approval will be reviewed to ensure that they include all activities in the protocol and all costs have been identified (see HRA website for details). It is recommended that the Trial Coordinator/Manager attends this meeting. It is mandatory for the CI to attend the Kick-off meeting. The Conditions of sponsorship (see Associated Documents 3) will be discussed and ideally signed during this meeting.
15.	Chief Investigator (CI) or	**Request Sponsor authorisation on the IRAS REC form. Submit to regulators and inform JRMO of all correspondence with the regulators, including amendments.** Once the letter of provisional Sponsorship approval has been received by the CI, the CI

	delegate	must request Sponsor Representative authorisation of the IRAS form sponsorsrep@bartshealth.nhs.uk via the IRAS authorisation tab. Guidance on requesting signature authorisation can be found on the IRAS website. The CI or their team should email their assigned JRMO Governance Officer once this is complete so that they can coordinate the approvals (as IRAS does not send alerts with each new request). N.B. Any changes to the IRAS form, other than adding the REC number, will invalidate the authorisation Sponsor and Chief Investigator signatures on the IRAS form. Therefore, only request Sponsor authorisation when the IRAS forms has been finalised to avoid repeat signature requests. It is the team's responsibility to submit to the HRA, NIHR portfolio adoption, REC and MHRA according to current guidelines (see MHRA and HRA websites for guidance) and to track the trial's approval progress. The CI or delegate should submit the REC and MHRA applications in parallel to avoid delays. It is the CI's responsibility to ensure all fees are paid as per current MHRA guidelines (please see MHRA website for details). Once submitted to REC and the MHRA, send copies of the final versions of the documents to the JRMO Governance Officer and all acknowledgement letters or correspondence from the regulators for the Sponsor file. This may include making amendments to approved documents (see SOP 17c - Amendments for sponsored studies - Process for researchers). Please note that any changes made to trial documentation after provisional approval **must be** approved by the JRMO GCP manager prior to submission. This includes responses to REC and the regulators.
16.	Chief Investigator (CI)	**Whilst the application is with regulators, begin trial specific management set-up including preparation of SOPs, database and facilitate contract negotiations** Following the submission to the regulators the CI and research team should continue with setting-up the trial including: • Setting up the trial master file (TMF) and investigator site file (ISF). See SOP 45 - Essential documentation and Trial Master File (TMF). • Designing the CRF. This needs to be reviewed and approved by the CI and statistician (see SOP 38a and b Trial data management systems). • Commencing database design and validation and any associated computer programs (SOP 38 - Trial data management systems) • Send a copy of the protocol to the trial database/computer programmer to ensure the CRF matches the protocol. • Drafting of study specific SOPs (e.g. randomisation, unblinding SOPs, IMP management plan for multi-site studies). • Progressing contract negotiations. • Preparing the Site Initiation training, see SOP 46 - Site selection, site initiation and site activation for a template PowerPoint. • Preparing trial committee charters, see SOP 47 - Trial Committees for guidance and template charters. • Preparing the monitoring plan with the GCP Manager. See SOP - 28 Monitoring for template monitoring plan. • Recruiting/assigning trial specific research posts i.e. research nurse/trial coordinators. • Attending the REC meeting to answer any questions raised by the committee so that their decision can be made during the meeting.
Signing the IRAS R&D Form N.B – Final Declaration, R&D Sign-off and the Final CTIMP meeting proceed in parallel (see flowchart at end of this document)		

17.	Chief Investigator (CI) or delegate	**Send REC, MHRA and HRA approvals to the JRMO. Continue with NHS set-up.** Send the JRMO Governance Officer all approvals from the regulators and evidence that the conditions of their approvals have been met. If the regulators request amendments to the documents send revised documents to the GCP Manager for approval prior to resubmission to the regulator. This is to ensure that the Sponsor has oversight of the changes that may impact upon the conditions of Sponsorship and indemnity before they are approved by the regulators.
Final Declaration of Sponsorship N.B – Final Declaration, and Final CTIMP Meeting proceed in parallel (see flowchart at end of this documents). For guidance on gaining NHS Confirmation of Capacity and Capability at sites please see the IRAS website and for Bart's see SOP 13a - Governance permissions for sponsored studies).		
18.	Chief Investigator (CI) and Research team	**Prepare for and attend the Final CTIMP meeting with the JRMO.** Once the REC and MHRA approval have been sent to the JRMO, the GCP Manager will schedule the 'Final CTIMP meeting'. This will also be the second contract meeting, with the Costing and Contract Manager. The purpose of the 'Final CTIMP meeting' is for the Sponsor to identify all items outstanding, including contracts, before the GCP Manager can issue the 'green light' to activate the sites. This meeting can occur before or after the Final Declaration of Sponsorship is issued by the JRMO Governance Officer but must be after the REC and MHRA have approved the study. The CI must be present for the meeting to take place. Other members of the JRMO or trial team are welcome to join the meeting e.g. research nurse, data manager, and statistician as part of trial specific training, clinical physics expert (if a non-CE marked device). The CI and study team must prepare for the meeting. The 'green light' checklist/Final CTIMP meeting (see Associated Document 4) should be used as an agenda and will be circulated before the meeting so that the CI and team can prepare. At the meeting an attendance sheet must be completed and saved in the Sponsor file. Following the meeting the 'green light' checklist/Final CTIMP meeting report (see associated document 4) must be completed by the GCP Manager and distributed to the study team. Any actions or items outstanding identified in the meeting should be emailed to the CI and followed up to resolution. The CI should bring the TMF as evidence that the essential documents are in place to start, or demonstrate to the GCP Manager that they have existing TMF SOPs/systems in place that comply with SOP 45 - Essential documentation and Trial Master File (TMF).
19.	Chief Investigator (CI)	**Sign the Costing and Contract Checklist and complete all items outstanding in the Final CTIMP meeting report.** Following the Final CTIMP meeting, the GCP Manager will send the 'green light' Checklist and Final meeting report (see Associated Document 4). It is the CI's responsibility to complete all actions identified in this report and send evidence to the GCP Manager. Once all contracts are fully executed, the Costing and Contract Manager will send the CI the 'Contracts Checklist.' This must be signed and returned to the JRMO before Final Declaration of Sponsorship is given. A condition of issuing Final Declaration of Sponsorship is that CI has signed the completed Contracts Checklist (see Associated document 2). The Conditions of Sponsorship (see Associated Documents 3) will be discussed and ideally re-signed during this meeting.
20.	Chief Investigator (CI)	**Upon receipt of Final Declaration of Sponsorship complete site NHS Confirmation of Capacity and Capability for each site.** Upon receipt of Final Declaration of Sponsorship, progress to preparing to activate research sites (see SOP 46 - Site selection, site initiation and site activation). This SOP

		applies to all sites including BH or QMUL. Research teams must note that the NHS Confirmation of Capacity and Capability does NOT give permission to begin recruiting to the trial. **The CI must receive the Sponsor's 'green light' to activate sites email (see below) and NHS Confirmation of Capacity and Capability before recruiting any patients/subjects.** Invite the JRMO GCP Manager and JRMO monitor to the first (London based) site initiation visit, who will attend where possible as part of their trial oversight training.
21.	Chief Investigator (CI)	**Receive the 'green light' to activate sites from the GCP Manager.** Upon completion of all Greenlight checks and Final Declaration of Sponsorship, the GCP Manager will send the CI an email giving them the 'green light' to activate sites. Neither the CI nor any site may begin recruitment until this is received in writing from the GCP Manager.
22.	Chief Investigator (CI)	**Activate sites as per SOP 46.** Formal green light must be given in writing to the sites in order to commence recruitment**.**

FLOW CHART
Sponsorship Process of BH/QMUL Sponsored CTIMPs
FOR RESEARCHERS

Costing the CTIMP

CI – Ensure the CTIMP has been costed by the JRMO before applying to the funder. See SOP 7 Costing and Contracts.

CI - secure adequate funding for the scope of the CTIMP.

CI – liaise/meet with the GCP Manager and JRMO Costing and Contract Manager.

CI - Draft protocol using JRMO CTIMP protocol template (see copy on JRMO website).

Prepare documents required for Sponsorship Review

CI or delegate - Arrange for peer and CAG/Institute Review of the protocol. Seek support department review i.e. pharmacy and radiation/imaging. Include feedback in protocol.

CI or delegate – Undertake a feasibility assessment of the protocol at the research sites. Include feedback from sites in the protocol (see SOP 46 - Site selection, site initiation and site activation).

Provisional Sponsorship Submission

CI or delegate - Complete JRMO submission documents (see associated document 1 JRMO Submission checklist) and submit to research.submission@bartshealth.nhs.uk – receive acknowledgement of receipt by JRMO.

CI or Delegate - Respond to the JRMO's feedback.

Submit final documents and request Sponsor authorisation on IRAS forms sponsorsrep@bartshealth.nhs.uk
(Process cont'd on the next page)

CI - Attend Kick-off meeting with JRMO.

Receive Provisional Sponsorship Approval

Obtain MHRA and REC approval

CI or delegate - submit application documents to HRA/REC and MHRA.
Send any correspondence to the JRMO, attend REC meeting and send GCP manager revisions to documents for sponsor approval.

CI or delegate - Whilst waiting for regulation approvals begin:
- Identify where ARSAC licences are required at sites
- Database - see SOP 38 for guidance
- Write Trial Specific SOPs
- Recruitment of key staff in place
- Work with Costing and Contract Manager re. Site Contracts

CI or delegate - Upon receipt of MHRA, HRA and REC approvals send these to the JRMO along with all revised documents and evidence that conditions of approval have been met

Request Final Sponsorship Declaration R&D form authorisation

CI or delegate - work with the JRMO Governance Officer to **Receive your Final Declaration of Sponsorship**

Continue with the site set-up

CI and team - attend second Final CTIMP meeting with JRMO (these meetings usually merged to save time).

CI - Sign Contract Checklist send to contract Manager (see associated document 2)
CI or delegate - Complete all items identified in the Final CTIMP meeting report and send to GCP Manager

CI - receive letter of 'green light' to activate sites from the GCP Manager

Receive the 'Green light' – Activate sites

PI at each site - get NHS Confirmation of Capacity and Capability, including contracts, ARSAC licences, support department approvals i.e. pharmacy imaging, clinical physics, department/CAG approval

CI – Once notified of NHS Confirmation of Capacity and Capability, Perform Site Initiation Visits.

Begin research site activation by informing PI(s) they can start recruiting (see SOP 46 Site selection, site initiation and site activation)

Change Control

This is a new SOP.

List of Associated Documents *(these are standalone documents)*

Associated Document 1	JRMO Document Submission checklist
Associated Document 2	JRMO Contract Checklist
Associated Document 3a	BH Conditions of Sponsorship (CI) (not a public document)
Associated Document 3b	QMUL Conditions of Sponsorship (CI) (not a public document)
Associated Document 3c	BH Conditions of Sponsorship (CI & CTU) (not a public document)
Associated Document 3d	QMUL Conditions of Sponsorship (CI & CTU) (not a public document)
Associated Document 4	Final CTIMP Meeting Report