Standard Operating Procedure for:			
Barts Health NHS Trust/Queen Mary University of London sponsorship of MHRA-regulated studies: Process for JRMO staff			
SOP Number:	**11b**	Version Number:	**9.0**
Effective Date:	**5th November 2021**		**5th November 2023**

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Background:

When Barts Health NHS Trust (Barts Health) or Queen Mary University of London (Queen Mary) agree to sponsor a Medicines and Healthcare products Regulatory Agency (MHRA)-regulated trial i.e., a clinical trial of an investigational medicinal product (CTIMP) or an advanced therapy investigational medicinal product (ATIMP) they are accepting considerable legal and regulatory responsibilities and organisational risks.

ICH GCP E6 R2 defines 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 being supplied to the regulators for their consideration.
- Defining roles and responsibilities for the duration of the trial.

- Monitoring and audit.
- 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.
- Study oversight.
- Guidance for academic supervisors.
- Providing on-going quality assurance.

The Medicines for Human Use (Clinical Trials) Regulations 2004 requires insurance or indemnity for liabilities of the sponsor and investigator.

Purpose:

The purpose of this standard operating procedure (SOP) is to outline the actions and steps undertaken by the Joint Research Management Office (JRMO) before granting sponsorship with conditions and confirmation of sponsorship for MHRA-regulated studies.

This SOP is written:

a. To ensure that Barts Health/Queen Mary JRMO staff are aware of the processes for issuing sponsorship, authorising the Integrated Research Application System (IRAS) form as sponsor for regulated studies, and the documentation necessary for sponsorship review.
b. To ensure all Barts Health or Queen Mary sponsored CTIMPs have a formal sponsorship agreement in place to comply with the legal requirements of the Medicines for Human Use [Clinical Trials] 2004 Statutory Instrument, 1031 and all subsequent amendments, the UK policy for health and social care research, 2017 and Good Clinical Practice (GCP).
c. To ensure that all Barts Health or Queen Mary sponsored ATIMPs have a formal sponsorship agreement in place to comply with the legal requirements of the EC regulation 1394/2007 on advanced therapy medicinal products and amending Regulation (EC) No 726/2004 in addition to the legal requirements of MHRA-regulated studies.
d. To outline the process undertaken for Barts Health or Queen Mary to agree to act as legal representative of a MHRA-regulated study on behalf of a sponsor who is based outside of the UK.

Scope:

This SOP applies to all staff in the JRMO, in particular the costing and contract team, research governance and performance team and the GCP and compliance team, who work on Barts Health/Queen Mary sponsored MHRA-regulated studies

It describes the JRMO procedure, in response to receiving a formal sponsorship request from a Chief Investigator (CI), for granting sponsorship including the review process and sponsorship confirmation.

For sponsorship of MHRA-regulated Clinical Investigations, please refer to *SOP 9 Sponsorship of Clinical Investigations and other MHRA-regulated Medical Device Studies*

Abbreviations:

AcoRD	Attributing the costs of health and social care research
APR	Annual Progress report
ATIMP	Advanced Therapy Investigational Medicinal Products
Barts Health	Barts Health NHS Trust
CI	Chief Investigator

CNST	Clinical Negligence Scheme for Trusts
CTIMP	Clinical Trial of an Investigational Medicinal Product
DPA	Data Protection Act
DPIA	Data Protection Impact Assessment
DSUR	Development Safety Update Report
GCP	Good Clinical Practice
HRA	Health Research Authority
IG	Information Governance
IMP	Investigational Medicinal Product
IRAS	Integrated Research Application System
JRMO	Joint Research Management Office
MHRA	Medicines and Healthcare products Regulatory Agency
NIHR	National Institute for Health Research
OID	Organisation Information Document
PI	Principal Investigator
QC	Quality Control
Queen Mary	Queen Mary University of London
REC	Research Ethics Committee
ReDA	Research Database Application
RM	Research Management
SOG	Sponsor Oversight Group
SOP	Standard Operating Procedure

Definitions:

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

- CI:
  - in relation to a clinical trial conducted at a single trial site, the investigator for that site, or
  - 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:
  - 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 professionals:
  - Doctor
  - Dentist
  - Nurse
  - Pharmacist

For Barts Health and Queen Mary *single site* sponsored regulated studies the CI should be the site's Principal Investigator (PI).

Relevant SOPs:
• SOP 7 Costing and contracts • SOP 9 Sponsorship of Clinical Investigations and other MHRA-regulated Medical Device Studies • SOP 10 Confirmation of Capacity and Capability • SOP 19 Annual Progress Report • SOP 21 Sponsorship, management, and oversight of international-only research: MHRA Regulated studies and interventional research • SOP 23 Risk assessment • SOP 27 JRMO Internal Filing Process • SOP 42a IMP management – Barts Health/Queen Mary sponsored studies

SOP Text:		
	Responsibility	**Activity**
		Early Engagement
1.	Governance Team	**Governance Team will guide researchers and offer their support in development, design and set up of their study.** The level or type of support and guidance will depend on what type of study and experience of the researcher. Ensure that the researcher is aware of the use of appropriate protocol template (*SOP 11a Associated Document 2*) the submission checklist (*SOP 11a Associated Document 3*) and local process.
2.	Costing and Contracts Officer	**Whilst costing the study, inform the GCP and Governance Manager of all potential MHRA-regulated studies** Consult with the allocated GCP and Governance Manager to ensure that appropriate study costs are included (*SOP 7 Costing and contracting*).
3.	Assigned Research Management (RM) and Governance Officer	**Assess study with regards to regulatory categorisation acting as legal representative and inclusion of any international sites.** Categorise the study. Assess and agree with the CI whether or not the study falls under the scope of the UK regulations. For non-UK sponsored regulated studies Work with the investigator to determine whether Barts Health/Queen Mary are to be the UK legal representative**.** **Seek advice from the GCP team, as necessary.** Studies with international sites. If the MHRA-regulated study is to have international research sites please see *SOP 21 Sponsorship, management, and oversight of international-only research: MHRA Regulated studies and interventional research* for further details.

		The GCP and Governance Manager must approve the study expanding internationally and, as sponsor representative, reserves the right to refuse expansion. Appeals to the JRMO's decision may be made to the Sponsor Oversight Group (SOG). For guidance refer to *Associated Document 1 Guidance for GCP and Governance section*.
4.	GCP and Governance Manager or Assigned RM and Governance Officer	**Upon receipt of funding, consider holding an Early Engagement meeting.** Consider an Early Engagement meeting with the CI, Governance team, GCP representative and Costing and Contracts Officer (*Associated Document 2 Early engagement meeting - clarification tool*). The purpose of this meeting is to discuss the planned study, all the management support functions, governance issues, potential study costs (the HRA Schedule of Events and Organisation Information Document (OID) templates can also be discussed), and supply of the Investigational Medicinal Product (IMP) for the trial.
5.	GCP and Governance Manager	**Assess the assignment of the CI.** If the CI has not previously worked as a CI on a Barts Health or Queen Mary sponsored MHRA-regulated study, it may be necessary to discuss their proposal to be the CI with the SOG. For MHRA regulated studies sponsored by Barts Health or Queen Mary, the CI must have a substantive contract with the sponsor (Barts Health or Queen Mary accordingly). The CI must be medically qualified in the therapeutic area and be able to prescribe the IMP. If any of these are not the case the matter will be escalated to SOG to make a decision on assignment of CI
Confirmation of Sponsorship		
6.	Assigned RM and Governance Officer (Governance Team Leader may assume this role if allocated the study)	**Upon receipt of a sponsorship submission, assess whether the sponsorship application pack is valid using the valid submission checklist (*SOP 11a Associated document 2*) and register the study accordingly on EDGE using the relevant attributes and workflows as per EDGE Manual. Proceed with sponsorship review.** Respond to researcher as soon as possible (maximum 5 working days) upon receiving the submission. The response should confirm receipt of a valid submission or reject the submission due to mandatory documents being missing (*Associated Document 3 Valid submission email* and *Associated Document 4 Invalid submission email*). Use of the flowchart when responding to the researcher is recommended. Provide the research team with guidance and signpost additional support if needed.

		The date of sponsorship submission is the date the JRMO receives a complete valid submission application. The JRMO's clock will not start until a valid submission is received. The JRMO RM and Governance Officer's review is the primary sponsorship review and includes the protocol, IRAS form, IMP labels and all documents that are submitted to the Research Ethics Committee (REC), HRA and the MHRA for approval. Ensure the relevant sponsor pharmacist and other support department(s) are aware of the study and have access to all up-to-date documentation. Approval should be given in accordance with *SOP 42a IMP Management – Barts Health/*Queen Mary *sponsored studies.* Information governance (IG) requires completion of a pre-screening questionnaire (See SOP 16a AD 2 for full details and procedure). This will determine whether a full Data Protection Impact Assessment (DPIA) form must be completed. Where the DPIA form is required, confirmation of the assessment will be required from the IG team prior to sponsorship with conditions being granted. Any concerns about the application should be brought to the attention of the Research Governance Team Leader and raised with the relevant Barts Health/Queen Mary expert i.e., IG, HTA representative, IT.
7.	GCP and Governance Manager	**Undertake sponsorship review and risk assessment of the protocol and study.** Follow *SOP 23* and perform risk assessment. Review all study documentation in tandem with the assigned RM and Governance Officer. Send all comments to the assigned RM and Governance Officer who will feed back to the researcher. Ensure study has been added to Research Database Application (ReDA). Allocate a JRMO Clinical Trial Monitor to the study. Invite the CI to forthcoming CI training and ensure that the research team are aware of the approvals process i.e., how it differs from non-MHRA regulated studies.
8.	Assigned RM and Governance Officer	**Collate the feedback from the RM and Governance Officer and GCP and Governance Manager's review. Feedback to the researcher.** The assigned RM and Governance Officer collates the comments provided by the GCP and Governance Manager with their own comments. The comments are to be combined and fed back to the researcher as a single response to the submission.
9.	GCP & Governance Manager/Assigned RM and Governance Officer	**Organise, host, and document the Kick-off meeting. *(Associated document 5*)** The purpose of the kick-off meeting is to ensure that the key stakeholders from the JRMO and the CI's team are aware of the: • key information about the study.

		• requirements for sponsorship to be issued. • contracts and agreements that need to be put in place. • actions that must be completed once the study has been submitted for regulatory approval. It is mandatory for the CI to attend the Kick-off meeting and it is recommended that the Study Coordinator or Trial Manager attends as well. From the JRMO, the GCP and Governance Manager, RM and Governance Officer and Costings and Contracts Officer must be present. The JRMO Clinical Trial Monitor assigned to the study should attend the meeting where possible. For meeting guidance see *Associated Document 5: Governance team sponsorship review*
10.	Costings and Contracts Officer	**Attend the Kick-off meeting and then inform the GCP and Governance Manager and RM and Governance Officer once primary contracts have been executed.** The Contracts and Costings Officer is responsible for creating the contract checklist. (See *SOP 7 Costings and Contracts Associated Document 1 JRMO Contract Checklist*) During the Kick-off meeting, complete the contract checklist and ensure that all required contracts are identified. Send a draft to the CI for confirmation that all contracts have been identified, save the contract checklist in the indemnity folder once it has been agreed with the CI and inform the RM&G officers and GCP manager that the first stage of the checklist is completed. Once the primary funding contract has been executed, inform the GCP and Governance Manager and RM and Governance Officer. For guidance see *SOP 7 Costing and Contracting (Associated Document 1: Costing and contract checklist*).
11.	Costing and Contracts Officer	**Confirm costings.** Ensure that each activity in the HRA application has been correctly allocated according to the National Institute for Health Research (NIHR) guidelines (i.e., Attributing the costs of health and social care research (AcoRD)) as either: • Service cost • Research cost • Service support • Treatment • Excess Treatment

		Once satisfied inform the RM and Governance Officer that the process is completed and send them a copy of the agreed documentation.
12.	GCP and Governance Manager	**Complete "GCP checklist part 1" (*Associated document 6*) and advise CI of the next steps.** When the GCP and Governance Manager's checklist is complete inform the RM and Governance Officer that the GCP team are ready to issue sponsorship with conditions. Where possible include the JRMO Clinical Trials Monitor in any meetings about the study to share information.
13.	Assigned RM and Governance Officer	**Prepare to issue sponsorship with conditions.** Ensure all feedback and requests have been actioned. Liaise with GCP and Governance Manager to obtain agreement to proceed in writing. Complete the 'governance team sponsorship review' form (see *Associated Document 5*) for the study file and enter the initial details into the EDGE database. All correspondence and governance decisions (including in meetings and by phone) must be documented and saved in the study file (*See SOP 27 Internal Filing Process*). If medicinal products are being used, ensure pharmacy have reviewed the study and confirmation of their approval is in place from the authorised Clinical Trials Pharmacist. Approval should be given according to *SOP 42a IMP Management-Barts Health/Queen Mary sponsored studies*. When satisfied, ask the Governance Team Leader to Quality Control (QC) the study sponsor file.
14.	Governance Team Leader (or delegated Governance team member)	**MHRA-regulated trials - QC cross-check.** Undertake an in-depth QC check of the documentation and approvals. Once satisfied sign the 'Governance team sponsorship review' form as evidence of the sponsor's QC check. This must be performed by someone other than the RM and Governance Officer who undertook the sponsorship review, to ensure that a 'fresh pair of eyes' reviews before confirmation of sponsorship.
15.	Assigned RM and Governance Officer	**Issue 'Sponsorship with conditions' letter_**(*see Associated Document 7a/b & 8*). Do this only following receipt of a written 'go-ahead' email from a GCP and Governance Manager. This should be issued as a PDF. Review study file and send (PDF) letters out to CI and study team contact (if applicable) as appropriate. Ensure study team is aware that any changes or reply to comments from external bodies should be submitted to the Governance section pre- submission.

Once REC/MHRA approval is received		
16.	GCP and Governance Manager	**Schedule and hold the Final Governance meeting.** Once informed by the RM & Governance office that REC and MHRA approvals have been received, the GCP and Governance Manager should schedule and hold the final Governance meeting. The purpose of the final Governance meeting is for the sponsor to identify all outstanding items before the GCP and Governance Manager can issue sponsorship with conditions. This meeting can occur before or after Governance agreement is issued by the RM and 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. The 'final governance meeting report' (*Associated Document 9*) should be used as an agenda and circulated before the meeting so that the CI and team can prepare. Any actions or items outstanding identified in the meeting should be followed up to resolution. Ensure the Sponsor-CI agreement is discussed and re-signed. (*See associated documents 10a and 10b*)
17.	Costing and Contracts Officer	**Finalise the Contracts Checklist.** Following the Final Governance meeting the 'costing and contracts checklist' should be finalised and sent to the CI for signature (see *SOP 7 - Costing and contracting*). The JRMO RM and Governance Officer cannot issue Confirmation of sponsorship until the 'costing and contracts checklist' has been signed by the CI and returned to the Costing and Contracts Manager Inform the GCP and Governance Manager and RM and Governance Officer in writing once the 'costing and contracts checklist' is complete. Ensure all checklists and contracts are saved electronically in (EDGE) and any wet ink signature copies filed within the sponsor oversight files.
20.	GCP and governance manager	**Send GCP managers agreement to proceed. .** Once all actions for Final Governance meeting have been completed , and the GCP managers Checklist part 2 (*Associated Document 6*) completed send an email confirming GCP managers agreement to Assign a Governance Officer.
Issuing Confirmation of Sponsorship		
21.	Assigned RM and Governance Officer	**Upon receipt of all approvals and documentation and receipt of GCP managers agreement to proceed issue confirmation of sponsorship (*Associated Document 11*)**

		Once MHRA, HRA and REC approvals are received (including documented evidence that their conditions of approval have been met) the RM and Governance Officer can proceed to issue confirmation of sponsorship once: • All approvals and associate documents submitted to HRA, REC and MHRA have been received (signed and final version) as listed in the HRA and REC approvals. This includes a signed protocol. • Check that MHRA, HRA and REC conditions are met. • Ensure that these documents are saved in the Sponsor Oversight File, in the study specific electronic folder and EDGE. • Sponsor pharmacy final approval (*see SOP 42a IMP management-Barts Health/*Queen Mary *sponsored studies*). • 'Costing and contracts checklist' have been received from the Contract Manager and saved in the sponsor file. • Fully complete the 'governance team sponsorship review' form (*Associated Document 5*) in the study file**.** • GCP manager has sent GCP manager agreement to proceed Issue Confirmation of Sponsorship when evidence that all actions are completed has been received and filed
22.	Assigned RM and Governance Officer	**Filing and Activation** Update EDGE, indemnity folder, print and save hardcopy. Pass study file to appropriate GCP team staff member to ensure Sponsor oversight file set up is completed.
23.	JRMO Monitor	**Set up sponsor oversight file, schedule first monitoring visit, according to monitoring plan, set annual report reminders on ReDA.** • File Confirmation of sponsorship • Create a ReDA record for the study • Ensure that all annual report reminders are set before they are due, update ReDA with Development Safety Update Report (DSUR), Annual Progress Report (APR) and end of trial reminders (for date on IRAS from). (See SOP 19 Annual Progress Report) • Add study to Monitoring tracker and complete with relevant reminders • Ensure EDGE MHRA dossier attribute is up to date • Obtain relevant documents for the sponsor oversight file from the RM and Governance Officer, and set-up and store the file in the GCP team's sponsor files cupboard.

Site approval		
24.	JRMO RM and Governance officer	**Ensure SOP 10 (Confirmation of Capacity and Capability) is followed for local site approval.**

Change control

This section outlines changes from version **8.0** to version **9.0**

Section changed	Summary and description of changes
All	Changes to responsibilities
All	Removal of Quality Control checks post HRA approval
All	Removal of flow chart

List of appendices

There are no appendices for this SOP.

List of associated documents

Document ref.	Document name
Associated document 1	Guidance for the GCP and Governance section
Associated document 2	Early engagement meeting - clarification tool
Associated document 3	Valid submission email (not a public document)
Associated document 4	Invalid submission email (not a public document)
Associated document 5	Governance team sponsorship review (not a public document)
Associated document 6	GCP Manager set-up checklist
Associated document 7a	Barts Health regulated trial sponsorship with conditions letter (not a public document)
Associated document 7b	Queen Mary regulated trial sponsorship with conditions letter (not a public document)
Associated document 8	Sponsorship with conditions email template (not a public document)
Associated document 9	Final governance meeting report
Associated document 10a	Barts Health Sponsor-CI agreement (CI) (not a public document)
Associated document 10b	Queen Mary Sponsor-CI agreement (CI) (not a public document)
Associated document 11	Sponsor confirmation of sponsorship email template (not a public document)