**Guidance for GCP and Governance section staff**

**1. Categorise the study as a Medicines and Healthcare products Regulatory Agency (MHRA) regulated study.**

Staff should be cautious of any studies that involve any of the following in the protocol, as they may be MHRA regulated: 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 whether a study is MHRA-regulated. If it is still unclear the GCP Manager will send a scoping query to the MHRA by sending a copy of the protocol to the MHRA clinical trials helpline and retaining documented evidence to support the MHRA’s decision (i.e., the email from the MHRA and version of the protocol sent). The GCP Manager should keep the Chief Investigator (CI) informed of this decision-making process.

It may be necessary to confirm the status of the study with the MHRA at the grant stage to ensure that sufficient funds are costed and secured to support a successful MHRA regulated study.

The MHRA’s opinion whether a study is MHRA regulated is final. If the MHRA’s opinion is unforeseen it is the CI’s responsibility to comply with the applicable regulations of MHRA classification or revise their protocol so that it is no longer classified as a MHRA regulated study. The GCP Manager, on behalf of the sponsor, reserves the right to re-submit funding proposals and protocols for scoping review to the MHRA, including revisions to documents following the MHRA initial opinion including amendments once the study has started (see SOP 17a Amendments for sponsored studies - process for Joint Research Management Office (JRMO)).

**2. Kick-off meeting**

This meeting is mandated for all MHRA regulated studies .

The aims of the meeting are:

* To ensure all parties have a good and full understanding of the study and any vendors for the study.
* To ensure that the processes and actions needed prior to the sponsorship with conditions is flagged.
* To give the CI opportunity to fully describe the study and declare anything they have ‘forgotten’

The following attendees are mandated. The meeting must not be held without all being present:

* CI
* Trial coordinator ( or representative)
* Sponsor pharmacist
* GCP manager
* JRMO CT monitor
* Governance officer
* JRMO contract officer

Additional attendees can be invited if they are directly related to the study.

As general guidance:

* A 1hr 30 mins meeting slot should be allocated.
* The meeting must not be held until a valid submission has been received (This is ideally 2 weeks post submission, so any initial feedback has been sent )
* Minutes/notes and actions should be a documented and shared with all present and saved as part of study set up documentation.
* Use the Kick-off meeting agenda template (Appendix A)
* Review revised documents and the individual role set-up checklist (associated document 9). Work with the CI and team to ensure that a GCP compliant protocol has been achieved and a consensus is reached.
* Ensure that the CI is aware of study set-up SOPs including: SOP 45 Essential documentation and Trial Master File (TMF), SOP 46 Site selection, site initiation & site activation, SOP 47 Trial Committees, and associated documents so that relevant study documents are under development to avoid any delays with the ‘Sponsorship with conditions process.

Following the meeting, the CI is expected to work with the Costing and Contract Manager on their funding applications (See SOP 07 Costing & contracting). All funding milestones must be reviewed by the JRMO/GCP Managers before they are agreed with the funders (this is to ensure that they are realistic and feasible. The draft copy of the Health Research Authority (HRA) Schedule of Events and Statement of Activities templates should be discussed.

**3. For non-** **European Economic Area (EEA) sponsored MHRA Regulated Studies – decide whether Barts Health NHS Trust (Barts Health)/Queen Mary University of London (Queen Mary) agree to be the UK Legal Representative.**

Please note, at of the 31st December 2020 Barts Health and Queen Mary cannot be legal representatives in the EEA.

In all studies for which Barts Health or Queen Mary agrees to act as EU legal representative a contract will be put in place with the sponsor to detail the responsibilities Barts Health/Queen Mary have agreed to undertake on behalf of the sponsor. If the Sponsor Oversight Group (SOG) refuses to act as the UK Sponsor Rep the CI may appeal in accordance with the JRMO escalation process.

The GCP Manager will assess whether the research team needs to transfer the protocol onto the JRMO MHRA regulated study template protocol. The assessment will be based upon whether the existing protocol meets Queen Mary/Barts Health standards and UK and EU regulations.

**4. Discuss the assignment of the Chief Investigator.**

The following may be considered during the assignment of the CI: previous experience as a CI/PI on non-commercial or commercial MHRA regulated studies, multi-site/international studies (where relevant), experience on Research or Interventional studies, 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 GCP Manager and SOG will work with the research team or the Clinical Board/Institute to assess their experience and determine whether additional peer support, training or study management support is required.

If, however, there are concerns about an experienced CI’s previous non-compliant management of a MHRA regulated studies, the GCP Manager will escalate to the SOG who will decide on the suitability of the CI.

**5. International studies.**

Only Queen Mary can sponsor international research with a Queen Mary substantially employed CI. Barts Health, which has NHS’s Clinical Negligence Scheme for Trusts (CNST) indemnity, cannot cover non-NHS sites including international sites and therefore cannot sponsor international studies. The CI must be open and honest with the JRMO about their plans to open international sites at the onset.

The GCP manager to request a full justification for international studies. The selection of countries must be given prior to sponsorship approval. This will also include information about any clinical research organisation (CRO) that will be used to coordinate and secure international regulatory approvals and assigning a ‘National Coordinating Centre’ (NCC) for each country who is responsible for regulatory approvals and reporting.

For costing considerations for international studies see SOP 07 Costing and Contracts associated document 1 and for information that needs to be supplied to the JRMO for international site selection or additional sites, or additional countries see SOP 46 Site Activation.

**6. Undertake sponsorship review and risk assessment of the protocol and study, and feedback to the CI.**

Clinical trial application and protocol review

* The GCP Manager’s review should be done in parallel with the governance officer’s review.
* The GCP Manager must ensure that the clinical trial application and protocol complies with GCP standards, referring to the protocol guidance. Particular importance must be made to the pharmacovigilance procedures (see SOP 26a Pharmacovigilance and Safety Reporting for MHRA Regulated studies) and the end of trial definition/procedures (see SOP 18a Project closure: guidance for research staff of sponsored studies).
* Review patient related documents and the protocol and address any areas of concern with the research team. Send comments to the JRMO Governance Officer who will feed back to the CI.
* The GCP Manager should assess if additional expert advice or opinions are needed, prior to proceeding. For example, if blood products for a part of the protocol approval should be sought from the Barts Health NHS pathology. Other examples may include, but are not limited to, Imaging, Gene therapy advisor group and the medical physic department. Care should be taken to obtain approval at department level though the pre-determined departmental review process where possible.
* Perform risk assessment as per SOP 23 Risk Assessment.
* Ensure that the JRMO Governance Officer is aware of the GCP team’s items outstanding. N.B. to avoid delays, comments to the CI can be sent separately from the Governance Officer’s feedback. However, both the GCP manager and Governance Officer should read each other’s feedback to ensure that the feedback to the research team is consistent and to avoid multiple sets of comments.
* Ensure study has been added to EDGE and ReDA and sponsor oversight group meeting documents.

**7. Final MHRA Regulated study meeting.**

This meeting should occur before GCP agreement or Confirmation of sponsorship.

The following people must be invited to the meeting:

* CI
* Costing and contracts officer(s)
* GCP Manager(s)
* JRMO Monitor (as part of their study specific training – this includes studies for which they receive quarterly monitoring reports from external monitors),
* Assigned Governance officer
* Trial Coordinator/Trial Manager
* Trial Monitor (if monitored by person outside of the JRMO)
* Pharmacist
* Clinical physics expert (if a non-CE marked device)
* Other members of the JRMO/Study team are welcome to join the meeting.

The ‘Final Governance meeting report’ (see Associated Document 3) should be used as an agenda and 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 ‘Final Governance meeting report’ 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. Where necessary further meetings may be scheduled and must also be minuted.

Where appropriate ask the CI to bring the Trial Master File (TMF) as evidence that they are ready to start.

Ensure “CI and Sponsor agreement” is discussed and re-signed.

**Appendix A: Kick-off meeting agenda template**

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| --- | --- | --- |
| **Agenda Points** | **Suggested notes** | **Lead** |
| Introductions |  | GO/GCP Manager |
| Summary of status of study | * Valid submission received/Initial feedback sent | GO |
| CI briefly describe project | * GO to request the CI to prepare for this. It’s useful to hear summary of study and it is appropriate to ask for a’ lay ‘explanation so that it is understandable to all | CI |
| Confirm- GO officer ( consider items or information you may need for the Risks assessment) | * Sponsor- Who is the CI’s substantive employer? * CI confirmed to have capacity to run trial. * Chief Investigator’s Experience * Sites and nations and PICs? * NIHR portfolio status * Funding * Funding award agreement(s) * Funding letters for Portfolio Adoption process (stating amount and duration to cover project) * Protocol Peer review (See SOP 14 Peer Review) * Training requirements. | GO |
| Recruitment & participant population discussed, including feasibility of meeting targets | * Patient pathways * Conflicting studies * Reporting first patient consented * Reporting portfolio study figures monthly to the JRMO | GCP Manager |
| Documents | * Status of document set * Delegation of responsibilities * TMF set up | GCP Manager |
| IMP and IMP management discussion | To including but is not limited to:   * Phase of study, * Name IMPs, * CI confirm MHRA Risk category ( A,B,C) * CI assessment of risk the IMP, sourced? Importers/ Exporters/ Special handling procedures.- blinding, randomisation, * Sponsor pharmacists confirm they have reviewed and agree to protocol and MHAR application) | Sponsor Pharmacist |
| Vendors & Contracts | To including but is not limited to:   * Identify all Vendors, Service Providers, and Internal Queen Mary/Barts Health departments * Site agreements (are we providing any consumables? E.g., tissue kits, equipment, device / funding for collaborators / IMP to the sites)? * IMP supply agreement & technical agreement ( see Imp section) * Lab Service Level Agreement(s) * Material Transfer Agreement(s) – Any data or tissue being sent any location other research sites? * Statistician * International Agreements * Translators * Insurance – additional premiums required? | Contract Officer |
| Device/Equipment - | * Is there any equipment or device on loan or being gifted by from manufacturer? * Is it on the MIA (indemnifying the kit)? * Device Risk Assessment | GO |
| Data Management | * Database * Provider * Data management plan | GCP Manager |
| Pharmacovigilance | * Process, RSI, CI medical assessor role (NB delegates) * Pharmacovigilance agreements in place | GCP Manager |
| Monitoring arrangements | * Monitoring plan agreed | GCP Manager |
| Quality Assurance/Compliance/Study Specific SOPs | * Trial unit/group specific SOPs discussed and relation to JRMO QMS? | GCP Manager |
| AOB | * Feedback to discuss | GO |
| Close | * Summary and plan of action | GO |