**Sponsor to Chief Investigator (CI) Sponsorship Agreement (Medicines and Healthcare products Regulatory Agency (MHRA) Regulated Studies)**

**Including Conditions of Sponsorship and Delegation of Duties**

**Study title:**

**IRAS Number:**

**CI:**

**Barts Health NHS Trust [Barts Health]** will act as a Sponsor, as defined by theUK Policy Framework for Health and Social Care Research (2017) and the UK Medicines for Human Use (Clinical Trials) Regulations (2004) and all subsequent amendments for the above listed study.

The Governance Operations Manager is delegated by Barts Health to act as sponsor representative on behalf of the organisation. The Joint Research Management Office (JRMO) Governance team is responsible for conduct of sponsor responsibilities except where delegated to the CI and team.

Sponsorship of this study is granted on the condition that the CI adheres to the conditions described below. Failure to comply with any of these conditions will be escalated, where appropriate, and non-compliance may lead to study suspension and/or withdrawal of sponsorship.

The CI and all members of the research team must comply with all current regulations applicable to the performance of the study, including, but not limited to, the UK Policy Framework for Health and Social Care Research (2017), the World Medical Association Declaration of Helsinki (1996), the UK Medicines for Human Use (Clinical Trials) Regulations (2004) and subsequent amendments, Good Clinical Practice Guidelines, the Human Tissue Act (2004) and the General Data Protection Regulations(GDPR) Data Protection Act 2018 (DPA).

Any requests from the sponsor for further information on the study are to be responded to promptly by the CI or delegated point of contact.

Sponsorship will not be activated, and therefore the study must not start, until: -

1. The Sponsor to CI Sponsorship Agreement has been fully signed by the CI and the sponsor’s representative.
2. CI and Co-ordinating team members have attended a JRMO Good Clinical Practice (GCP) course and the CI has attended the JRMO led CI workshop session within 2 years of sponsorship with conditions.
3. The MHRA “notice of acceptance letter” has been obtained, received by the sponsor and any remarks on that “notice of acceptance letter” have been addressed and accepted in writing by the MHRA (if applicable) or the MHRA notification scheme acknowledgement letter has been received and the MHRA has not raised an objection within 14 days of issuing the letter.
4. A “Favourable ethical opinion” from an appropriately constituted research ethics committee (REC) has been granted, received by the sponsor and, where applicable, ‘the conditions of favourable opinion’ have been met and sent to REC.
5. A Health Research Authority (HRA) approval letter has been issued and received by the sponsor.
6. On an individual site basis, “Confirmation of Capacity and Capability” has been obtained from research sites.
7. Confirmation of Sponsorship and to activate sites has been obtained from the JRMO.

Additionally, during the study the CI must ensure that:-

1. Compliance
   1. The clinical trial is conducted in accordance with the protocol.
   2. All correspondence and communication with HRA, REC, MHRA or other regulatory bodies is copied in full to the JRMO as sponsor.
   3. All amendments are notified to and approval by the JRMO prior to submission to the REC, MHRA or HRA. Once applicable approval is received, the CI must ensure that all sites are informed of the amendment and local approval/acknowledgment of each amendment is sought as appropriate.
   4. Participants give written informed consent to participate in the study, using the version of the consent form and patient information sheet that have received a favourable opinion by the REC. All e-consenting systems must be compliant with JRMO SOP 38a on Computer systems, fully validated and agreed by JRMO Governance team prior to use.
   5. The JRMO is notified of any major staff changes to the co-ordinating team. The delegation log is kept up to date at all times.
   6. Appropriate contracts containing delegation of responsibilities are in place between third party sub-contractors and the sponsor before their work begins. The CI will notify the JRMO of all external parties, vendors or suppliers, and any changes in these.
   7. Sponsor approval is received for any Principal Investigator (PI), site or country selected to participate in the study, prior to formally involving them in the study.
   8. A Trial Master File (TMF) is created containing all essential documents appropriate for the study in accordance with JRMO Standard Operating Procedure (SOP) 45. This must be made available for monitoring, audit or inspection as required.
   9. All deviations to protocol , GCP and relevant regulations are reported to the sponsor as per SOP 31 Non-Compliance.
2. Data Integrity
   1. All relevant clinical trial data are accurately transcribed from source documents (where applicable) to a case report form (CRF) and to a database.
   2. All site CRFs are completed in full, and that they are signed and dated by the site PI or delegate.
   3. Sites are aware of their responsibilities to create and maintain accurate source data on all aspects of the study, this includes any electronic health data(e-HR). All site e-HR systems used to collect data must be appropriately validated and compliant with MHRA guidance.
   4. Data is generated, recorded, handled, stored and reported accurately, securely and in accordance with the protocol, sponsor’s SOP 38 series, GDPR DPA 2018 and GCP.
   5. Any database used is approved by the JRMO and suitably validated in accordance with the protocol, sponsor’s SOP 38 series, GDPR DPA 2018 and GCP.
3. Reporting
   1. The JRMO is notified of each site activation date (notification timing as per the studies monitoring plan).
   2. The JRMO is notified of the date of the first signed consent form at each site (notification timing as per the studies monitoring plan).
   3. Sponsor is informed immediately of any urgent safety measures taken to protect participants enrolled in the study. A written notice is sent to the MHRA, REC and sponsor within 3 days.
   4. Annual Progress Reports (APRs) are sent to the sponsor, allowing ample time for review (at least one week) in order to be submitted to the REC within 30 days of the anniversary of REC approval.
   5. Development safety update reports (DSURs) are sent to the sponsor, allowing ample time for review (at least one week) in order to be submitted to the REC and MHRA within 60 days on the anniversary of MHRA approval.
4. Safety
   1. Sites record all adverse events (AEs) in the patient’s notes (electronic or paper as appropriate) and CRF.
   2. Serious adverse events (SAEs) and suspected unexpected serious adverse reactions (SUSARs) relating to clinical trials of drugs or devices are reported to the sponsor (or delegate) within 24 hours of learning of the event.
   3. CI is the sponsor’s medical advisor for this study and is responsible for assessing every SAE and SUSAR and all the related issues on behalf of the sponsor as per SOP 26a. CI must ensure a delegated alternative medical advisor is clearly documented where CI cover is needed.
   4. CI is responsible for ensuring SUSARs are reported to REC within the required timeframes.
   5. All investigators at all sites are informed of any SUSARs occurring in relation to the investigational medicinal products (IMPs) that have occurred in this study.
   6. Potential serious breaches of GCP and the protocol are reported to the sponsor within 24 hours of the CI becoming aware of the breach.
5. Monitoring /Audits/Inspections
   1. All study documentation and staff involved in the study are available for monitoring/audit/inspection if requested by the MHRA or the sponsor.
   2. Monitoring arrangements outlined in the protocol, study SOP or manual and sponsor’s SOPs are adhered to .
6. Study Closure
   1. The JRMO is notified of the end date of the study and any extension or early termination of the study.
   2. An “end of trial (EoT) notification” is sent to the REC and MHRA once approved by the sponsor, within 90 days of the conclusion date, or within 15 days if the study is terminated early.
   3. Submit an end of clinical trial report to the sponsor for review prior to final submission to MHRA and REC within one year of the ‘EoT notification’
   4. Ensure all public databases are fully updated with the result in a timely manner
   5. TMF and all coordinating documents relating to the study are archived with the Trust’s Corporate Records archiving facility for a minimum of 25 years and in accordance with the JRMO archiving policy.
   6. All sites are adequately resourced to archive as per Sponsor’s SOP 20 (Archiving).
   7. The JRMO are notified of any outputs of the research such as guidelines, publications, presentation, changes in service delivery etc. prior to external submission or presentation. This includes declaration of any intellectual property stemming from the research.
   8. In the event that research misconduct or data integrity concerns have been raised, the JRMO, as sponsor, in discussion with senior management of the affected organisation, reserves the right to review, request a hold on publication submission or to refuse permission to publish.
7. Funding
   1. The CI must ensure all elements of the study are adequately funded, including ensuring adequate staffing and site costs. Any shortfall or overspend is the responsibility of the Cis Department or Institute. This applies to any subsequent amendments and extension to the study.

**Delegation of Duties**

**JRMO acting as Sponsor on behalf of Barts Health, delegates the responsibilities below to the CI.**

*This table will be reviewed and finalised on a per study basis. This is a template and the below table has been completed as a guide only.*

*This form is to be used only upon agreement with the GCP manager when a recognised CTU or group is being delegated duties directly by the sponsor.*

*Once the table is complete, remove this highlighted text.*

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| **DUTIES** | **CHIEF INVESTIGATOR** | **CTU ( insert name)** | **SPONSOR** |
| Obtaining regulatory approvals following review and approval by the JRMO governance team | X |  |  |
| All interactions and consultation with the MHRA and other regulatory bodies following consultation with the JRMO Governance team. | X |  |  |
| Requesting and maintaining regulatory approvals | X |  |  |
| Requesting and maintaining sponsor approval during the life cycle of the study | X |  |  |
| Creating and submitting all amendments following review and approval by JRMO governance team |  | X |  |
| Using new vendors or subcontractors (central or site specific) following review and approval by JRMO governance team |  | X |  |
| Country, site and PI selection. | X |  | Sponsor retains the right to veto any country, site or PI. |
| Generating study-specific risk assessment as per SOP 23 (Risk assessment) |  |  | X |
| Providing insurance / indemnity for study |  |  | X |
| Creating and submitting APRs to REC and distributing to sites, within 30 days of end of the reporting period following review by sponsor |  | X |  |
| Final review and submission of APRs to REC and distributing to sites, within 30 days of end of the reporting period following review by sponsor | X |  |  |
| Creating and submitting development safety update reports (DSURs) to sponsor for approval |  | X |  |
| Final review and submitting DSURs to MHRA. | X |  |  |
| Distributing DSURs to sites, within 60 days of end of the reporting period |  | X |  |
| Creating the EoT notifications within 90 days of the end of trial definition, or within 15 day if early termination occurs. Submitting EoT notifications following review by sponsor |  | X |  |
| Creating and submitting the clinical study report within one year of end of trial notification, following review by sponsor. | X |  |  |
| Compliance |  |  |  |
| Reporting and follow up of all suspected potential serious breaches of GCP and / or the protocol to Sponsor within 24 hours of becoming aware of the breach. This should include management of issues in liaison with sponsor ensuring corrective and preventive action (CAPA) is conducted in full. | X | X |  |
| Ensuring that all study activities are conducted within the remit of the patient consent provided. |  | X |  |
| Ensuring that all participants give full informed consent in writing. |  | X |  |
| Ensuring the co-ordinating team delegation log is completed and up to date at all times. |  | X |  |
| Ensuring appropriate SOPs are produced and followed and the relevant sponsor’s SOPs are complied with. |  | X |  |
| Ensuring that PIs are informed of the requirement to re-consent, when appropriate. |  | X |  |
| Resolving clinical queries from participating sites / National Coordinating Centres | X |  |  |
| Ensuring that 24 hour unblinding (or MHRA approved risk adapted system) is available for all blinded studies. |  | X |  |
| Performing monitoring as per monitoring plan. |  | X |  |
| Ensuring compliance with any conditions within any contracts associated with the study. This will include but is not limited to funding agreements and IMP suppliers. |  | X |  |
| Medical Advisor |  |  |  |
| Undertaking initial and on-going safety evaluation of the IMPs. This should be documented and include any potential actions and conclusions reached. | X |  |  |
| Undertaking medical review of all serious adverse events, including their severity, causality, relatedness and expectedness. | X |  |  |
| Ensuring there is a provision for 24 hour medical advice (or MHRA approved risk adapted system) for all sites as trial medical representative. | X |  |  |
| IMP |  |  |  |
| Overseeing the supply of study medication and comparators including distribution of study medication to sites. | X |  |  |
| Conducting on-going and final drug accountability. | X |  |  |
| Labelling/coding of study medication. | X |  |  |
| Authorisation of destruction of unused drugs. |  |  | X |
| Ensuring sponsor pharmacy representative is informed of all changes, issues or concerns. |  | X |  |
| Study Documentation |  |  |  |
| Establishing and maintaining the TMF following sponsor procedures, following sponsor SOP 45 Essential Documentation including TMF |  | X |  |
| Generating and updating study documentation for the duration of the study (i.e. study protocol, patient documents etc.). |  | X |  |
| Ensuring document control procedures are in place and maintained for the duration of the study, including version control logs of all regulatory approved documents. |  | X |  |
| Creating, distributing and implementing study-specific SOPs |  | X |  |
| Translating study documents / localised documents such as the protocol, Patient Information Sheet, Consent Form and GP Letter.  The protocol will either (1) be certified by a legal representative or accredited translator for correct translation, or (2) be back translated by an independent person. Copies of documents and evidence of work to be filed in the local TMF |  | X |  |
| Preparing and distributing Investigator Site File/s and study documents to participating sites. |  | X |  |
| Tracking and managing patient recruitment / randomisation, ensuring site and central enrolment log is up to date. |  | X |  |
| Ensuring expedited written notice of any urgent safety measures taken to protect participants enrolled in the study are sent to the MHRA REC and sponsor within 3 days of learning of the event. | X |  |  |
| Ensuring all trial management documents relating to the study are archived with the Trust’s Corporate Records archiving facility for a minimum of 25 years. |  | X |  |
| Ensuring all site documents are archived at all sites for a minimum of 25 years. |  | X |  |
| Trial Committees |  |  |  |
| Setting up (including creation of committee terms of reference or charter), planning and coordination of trial committees (including Trial Management Groups, Trial Steering Committees and Data Monitoring Committees as appropriate) and ensuring committees meet in accordance with study protocol. |  | X |  |
| Ensuring that sponsor is notified of all committee meetings and are given minutes when they are finalised. |  | X |  |
| Samples |  |  |  |
| Managing bio-specimen kit preparation, where applicable. Ensuring appropriate documented procedures and quality control checks are in place. |  | X |  |
| Managing the collection, storage and processing of samples. |  | X |  |
| Overseeing sample analysis and reporting. Ensuring appropriate documented procedures and quality control checks are in place |  | X |  |
| Ensuring appropriate disposal or transfer of samples prior to the end of the trial notification. This should be conducted as per protocol and participant consent. |  | X |  |
| Pharmacovigilance |  |  |  |
| Ensuring systems are in place to allow expedited reporting of SAE reports from participating sites to JRMO within 24 hours of learning of the event. |  | X |  |
| Acting as liaison between sponsor and site regarding pharmacovigilance queries. |  | X |  |
| Ensuring expedited reporting of SUSARs to competent authorities within UK. |  |  | X |
| Ensuring expedited reporting of SUSARs to competent authorities outside UK (where applicable). |  | X |  |
| Ensuring expedited reporting of SUSARs to REC within and outside UK. |  | X |  |
| Dissemination of SUSARs to participating sites. |  | X |  |
| Data |  |  |  |
| Design and creation of CRFs, ensuring their compliance to the protocol and regulatory application. |  | X |  |
| Final review and sign-off of CRFs | X |  |  |
| Database design, validation and maintenance. |  | X |  |
| Final approval and sign-off of database | X | X |  |
| Data capture, integrity and management (including data cleaning, issuing of queries and resolving of data queries). |  | X |  |
| Ensuring that all generated data is recorded, handled, stored and reported accurately, securely and in accordance with the protocol, the GDPR DPA 2018. |  | X |  |
| Ensuring database lock occurs prior to any analysis. |  | X |  |
| Statistical analysis. |  | X |  |
| Generation and submission of final clinical study summary report to sponsor (for review) and final submission to MHRA and REC. | X |  |  |
| The CI will endeavour to publish the results of the study and as a minimum ensure that they are on a public website | X |  |  |
| Uploading the results of the study on to a public website within one year of end of trial notification. |  | X |  |
| Informing the JRMO of planned publications/ presentations etc. as early as possible and prior to publication. | X |  |  |

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| **At sponsorship:** | | |
| **Study title:** | | IRAS Number: |
| Chief Investigator:  **I have read and understood the above conditions and delegated duties and agree to adhere to these responsibilities and duties for the Study stated above.**  Print name  Signature: Date: | | |
|  |  |  |
| On behalf of CTU :  **I have read and understood the above conditions and delegated duties and agree to adhere to these responsibilities and duties for the Study stated above.**  Print name  Role:  Signature: Date: | | |
|  |  |  |
| On Behalf of Sponsor:  **I have reviewed, discussed and agree the delegation of duties outlined in this agreement.**  Print name  Signature: Date: | | |

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| --- | --- | --- |
| **At sponsorship with conditions:** | | |
| **Study title:** | | IRAS Number: |
| Chief Investigator:  **I have read and understood the above conditions and delegated duties and agree to adhere to these responsibilities and duties for the Study stated above.**  Print name  Signature: Date: | | |
|  |  |  |
| On behalf of CTU :  **I have read and understood the above conditions and delegated duties and agree to adhere to these responsibilities and duties for the Study stated above.**  Print name  Role:  Signature: Date: | | |
|  |  |  |
| On Behalf of Sponsor:  **I have reviewed, discussed and agree the delegation of duties outlined in this agreement.**  Print name  Signature: Date: | | |