St George's University Hospitals NHS
NHS Foundation Trust

Standard Operating Procedure (SOP)

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Signature of Authorisor			

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They may print off this document for training and reference purposes.

Standard Operating Procedure (SOP)
Applying to the MHRA for Clinical Trials Authorisation

SOP Chronology

SOP Version Number:	Reason for Change:	Author:
V1.0	Original Version.	Lisa Clutterbuck
V2.0	Updated with new Trust Logo and Foundation Trust and some links to MHRA website, change of title from CRGM to HRG	Nadia Azzouzi
V3.0	Updated with new MHRA process and JREO SOP format	Debs Rolfe

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1. Background

The EU Directive 2001/20/EC definition of a clinical trial is:

"...any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more investigational medicinal product(s), and/or to identify any adverse reactions to one or more investigational medicinal product(s) and/or to study absorption, distribution, metabolism and excretion of one or more investigational medicinal product(s) with the object of ascertaining its (their) safety and/or efficacy".

Any research that fulfils the definition of a clinical trial, as described above requires a Clinical Trial Authorisation (CTA) from the Competent Authority in the Member State in which research is being carried out. The Competent Authority in the United Kingdom (UK) is the MHRA, the Medicines and Healthcare products Regulatory Agency.

A CTA will only be issued by the Competent Authority if it has no objections to the research proposal. The EU Directive has been transposed into UK law as the Medicines for Human Use (Clinical Trials) Regulations 2004 and subsequent amendments.

2. Joint Research and Enterprise Office (JREO) Policy

All JREO SOPs will be produced and approved in accordance with the JREO SOP on SOPs and must be used in conjunction with local NHS Trust and St George's policies and procedures.

The JREO acts as the representative of both St George's University of London (SGUL) and St George's University Hospitals NHS Foundation Trust (SGHFT). St George's will be the official name used on all SOPs to represent both institutions acting as Sponsor.

3. Scope

This SOP outlines the role of the JREO and the Chief Investigator when applying to the MHRA for a Clinical Trial Authorisation (CTA) for CTIMP studies, sponsored by St George's.

4. Definitions

For general research management related acronyms used in this SOP refer to "General Research Definitions" working practice document JREOWPD0020

5. Responsibilities

This SOP is to be followed by the JREO Governance and Approvals team: Head of Research Governance & Delivery (HRGD), the Regulatory Assurance Manager (RAM), and Regulatory Support Officers (RSOs).

It is the responsibility of the HRGD to ensure that the SOP is updated and audited where necessary.

It is the responsibility of the Chief Investigator (CI) to ensure that the completed documentation is submitted through the Integrated System Application System (IRAS) and respond to subsequent requests from the JREO and/or the MHRA. The responsibility of the submission to MHRA via the Common European Submission Portal (CESP) is delegated to the RAM as Sponsor contact, unless delegated to a 3rd party as part of an external study management agreement.

It is the responsibility of the assigned member of the Research Governance Team (RGT) to ensure review of all relevant documents in accordance with this SOP prior to submission of the Clinical Trial application to the MHRA.

6. Procedure

6.1 Investigator Procedure

a) The Chief Investigator must inform the HRGD and/or the RAM that they wish to conduct a CTIMP sponsored by St George's and thus intitiate the Sponsorship in Principle process. The CI should refer to JREOSOP0003 Sponsorship in Principle.

b) On notification from the RAM that the Clinical Trial application to the MHRA should be started, the Investigator and/or delegated research team member must apply for a EudraCT number. The EudraCT number can be applied for following the link: https://eudract.ema.europa.eu

c) The email containing the EudraCT reference number assigned must be forwarded to the RAM upon request

d) The Chief Investigator must supply the relevant documentation required for submission to the MHRA to the RAM and/or HRGD upon request. Within the IRAS system (transfer the MHRA Medicines (EudraCT application form) by supplying the email contact details of the RAM within the system) this will allow the RAM to cross-check and authorise the application via electronic signature.

e) Upon receipt back of the signed IRAS forms ensure all other authorisation signatures are in place and then assign the whole project within IRAS to the RAM

f) The Investigator must ALSO supply the following documentation (a valid MHRA application) to the RAM for review:

- A covering letter
- MHRA medicines EudraCT application form authorised
- Protocol
- Investigator's Brochure (IB) or document replacing the IB
- IMPD (Investigational Medicinal Product Dossier)/simplified IMPD
- A non-investigational medicinal product dossier (if required)
- Scientific Advice (if available)
- EMA Decision (A copy of the EMA's Decision on the decision of the Paediatric Investigation Plan and the opinion of the Paediatric Committee if applicable)
- The Content of the labelling of the IMP (or justification if absent)
- Manufacturer's authorisation or Importer's authorisation plus QP declaration on GMP for each manufacturing site if the product is manufactured outside of the EU
- PIS and consent forms (MHRA like these for information purposes only)

The Clinical Trial Application can be downloaded either from IRAS or from the EudraCT website. Once complete, the Clinical Trial Application should be saved as an XML file.

Each document must be provided as one file and have a cut and paste functionality.

It is the Investigator's and/or delegated research team member's responsibility to supply further documentation and/or information to the HRGD and/or RAM upon request.

6.2 JREO Procedure

a) On receipt of notification to the RAM and/or HRGD of a CTIMP from an Investigator, the RAM must initiate the Sponsorship in Principle process with the Investigator (JREOSOP0003).

b) The RAM must advise the Investigator and/or delegated research team member on the process of applying to the MHRA for a Clinical Trial Authorisation (CTA). Details can be found on the MHRA website:
https://www.gov.uk/guidance/clinical-trials-for-medicines-apply-for-authorisation-in-the-uk
The definitive list is detailed above in 6.1 f).

c) On submission of the valid documentation to the RAM, the RAM should review for completeness and compliance with UK clinical trial regulations. The RAM should review the application within 5 days before responding to the Investigator with any queries, clarifications, amendments or requests for further information.

d) The RAM will confirm with the Lead Research Pharmacist prior knowledge and input into the CT application..

e) Once satisfied that all documentation is in place, the RAM will request initiation of IRAS authorisation and sign the Clinical Trial Application as the named Sponsor representative

f) The RAM will complete the MHRA submission in accordance with JREOWPD0004 MHRA submission format

g) The RAM will receive an initial upload acknowledgment via CESP if the application is valid.

h) The MHRA will confirm validation and receipt of the application within 5 working days. The RAM must retain all receipts and correspondence within the study specific e-folders and physical files. If the application is invalid, the RAM will be asked to provide the missing information.

The initial assessment by the MHRA will be conducted within 30 days which begins on valid receipt of an application. The RAM will be sent a letter informing them of one of the following outcomes:

1. Acceptance of the request for a clinical trial authorisation

2. Acceptance of the request for a clinical trial authorisation subject to conditions

3. Grounds for non-acceptance of the request for a clinical trial authorisation

If the outcome of the request is 2, the RAM will need to work with the investigator to ensure conditions are met. All evidence must be retained in the site file and may be required to be sent together with the MHRA conditional approval to the HRA assessor to facilitate HRA approval

If the outcome of the assessment is 3, the RAM will need to work with the Investigator to amend or add to the information provided to the MHRA within 14 days.

j) All correspondence with the MHRA should be filed accordingly by the RAM and/or HRGD in the electronic and paper Sponsor File according to the JREO CTIMP Index JREODOC0066)

k)The CI must be supplied with all MHRA correspondence, to be filed in the TMF

l) The MHRA CTA must be sent to the nominated HRA assessor by the RAM/HRGD to facilitate HRA approval

7. References

- MHRA (Medicines and Healthcare products Regulatory Agency)
- www.gov.uk/mhra
- EudraCT – https://eudract.ema.europa.eu
- IRAS (Integrated Research Application System) - www.myresearchproject.org.uk

8. Appendices

None associated with this SOP