Title of Standard Operating Procedure: RD SOP 32 Gaining MHRA Approval

Document Summary: To describe the procedure for preparing and approving Trust R & I SOPs within the Trust, and also the procedure for review and archiving of these SOPs

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Target Audience: Trust-wide, Research Community, Internal and External Researchers

Consultation: R & I Office, research community and R & I Committee members

Approval Committee: R & I Committee

Cross Reference Document(s): Research Approval Policy
All Trust R & I SOPs

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<table>
<thead>
<tr>
<th>Minimum Monitoring Requirement</th>
<th>Frequency</th>
<th>Process for monitoring</th>
<th>Evidence</th>
<th>Responsible Individual(s)</th>
<th>Response Committee(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review of SOP content</td>
<td>Annually</td>
<td>Review by Author, redraft, submission to R &amp; I Operational Group</td>
<td>Minutes of R &amp; I Operationa l Group</td>
<td>Head of R &amp; I Office</td>
<td>Research &amp; Innovation Committee</td>
</tr>
</tbody>
</table>

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Contents

1. Introduction ................................................................. 3
2. Purpose ........................................................................... 3
3. Roles and Responsibilities ............................................... 3
3.1 Duties within the organisation ....................................... 3
3.2 Specific to this SOP ..................................................... 3
4. Procedure ................................................................. 4
4.1 Definitions ..................................................................... 4
4.2 Obtaining a EudraCT number ......................................... 4
4.3 Complete the application form ........................................ 4
4.4 Documents required for Submissions ............................... 5
4.5 MHRA review ........................................................... 5
4.6 Outcomes from MHRA review ........................................ 6
4.7 Post MHRA Approval ................................................... 6
5. Equality Impact Assessment ............................................. 6
6. Consultation, Approval and Ratification Process ................. 7
6.1 Consultation and Communication with Stakeholders ............ 7
6.2 SOP Approval Process ................................................. 7
7. Dissemination and Implementation ................................... 7
7.1 Dissemination ........................................................... 7
7.2 Implementation of Procedural Documents ....................... 7
8. Review, Monitoring Compliance and the Effectiveness of Procedural Documents ........................................ 8
8.1 Process for Monitoring Compliance and Effectiveness ........... 8
8.2 Standards and Key Performance Indicators ‘KPIs’ .................. 8
9. References and Bibliography ............................................ 9
10. Associated Trust Documents ........................................... 10

Appendix 1 – Gaining MHRA Approval Flowchart .................... 11
1. Introduction

Clinical trial authorisation (CTA) is required for any clinical trial of an investigational medicinal product (CTIMP) to be conducted in the UK. This is obtained from the competent authority – the MHRA.

2. Purpose

The purpose of this SOP is to outline the process of gaining MHRA approval for studies classified as CTIMP’s (Clinical Trial of an Investigational Medicinal Product).

3. Roles and Responsibilities

3.1 Duties within the organisation

It is the responsibility of the Research Office to make Trust R & I SOPs available to all research active staff working on Trust premises.

It is the responsibility of the study Chief Investigator (CI) or local Principal Investigator (PI) to ensure that up-to-date copies of Trust R & I SOPs are available to research staff.

It is the responsibility of the study Chief Investigator (CI) or local Principal Investigator (PI) to distribute study-specific SOPs to appropriate members of the research team and to ensure that up-to-date copies are filed in the Investigator Site file and are available to research staff.

It is the personal responsibility of all staff to follow Trust procedural documents.

3.2 Specific to this SOP

Gaining MHRA approval as detailed in this SOP is the responsibility of the Sponsor (as defined below), although this can be delegated, for example to a Clinical Trials Unit (CTU).

4. Procedure

According to the European Clinical Trials Directive (2001/20/EC), clinical trials of investigational medicinal products (CTIMP’s) in human subjects require authorisation by the competent authority (MHRA in the UK) in addition to a favourable opinion by a REC/HRA.
4.1 Definitions

Clinical Trial of Investigational Medicinal Product (CTIMP) - any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamics effects of one or more investigational medicinal product(s), and/or to identify any adverse reactions to one or more investigational medicinal products(s) and/or to study absorption, distribution, metabolism and excretion of one or more investigational product(s) with the object of ascertaining its (their) safety and/or efficacy.

Sponsor - Individual, organisation or group taking on responsibility for securing the arrangements to initiate, manage and finance a study. I.e. GMMH may take on the role of sponsor following agreement from the R & I Committee.

4.2 Obtaining a EudraCT number

Before submitting a Clinical Trial Application, a EudraCT Number must be obtained. EudraCT is a database of all International clinical trials of medicinal products. The EudraCT number will be a unique reference for each trial. The number must be included on the clinical trial authorisation application to the MHRA and all other documentation related to the trial.

A EudraCT number can be applied for at: https://eudract.ema.europa.eu/

4.3 Complete the application form

The Clinical Trial Application form is accessed through the Integrated Research application System (IRAS) http://www.myresearchproject.org.uk. The R & I office will provide guidance on the completion of the application form and the submission process; this can also be found on the IRAS website.

It is strongly recommended that the applicant reads the available guidance on the application process that can be found at: https://www.gov.uk/guidance/clinical-trials-for-medicines-apply-for-authorisation-in-the-uk

For GMMH Sponsored CTIMP’s the CI is responsible for ensuring that all documentation is submitted to R & I prior to submission to the MHRA. This should be after the application for sponsorship and funding/costing assessment by GMMH.

4.4 Documents required for submission

Applications are submitted to the MHRA through the Common European Submission Portal (CESP; see section 9). An application to the MHRA should include the
following (see MHRA website for details on how the documents should be formatted and submitted):

A covering letter including EudraCT number, Trial identification code, Title of trial (all in the heading) and details of any special considerations such as patient populations or phase 1 studies.

A protocol (see RD SOP35 Writing a protocol and consent documentation)

An Investigator Brochure or Summary of Product Characteristics

Content of the labelling of the IMP (in compliance with Good Manufacturing Practice and Annex 13 – see section 9)

Qualified Person declaration

A summary of scientific advice

For details of the application fee see the MHRA website. This may not be applicable for studies that come under the Notification Scheme.

A copy of all documents should be filed on Q-Pulse (the Trial Master File) by the R & I Office.

**4.5 MHRA Review**

Valid Clinical Trial Applications are assessed within 30 days of the receipt.

MHRA must provide a response within a total of 60 days from receipt of the original application (except for trials involving medicinal products for gene therapy, somatic cell therapy or medicinal products containing genetically modified organisms where the timeframe is 90 days). If further information is requested this should be sent to the MHRA within 14 days of the request so not to affect the 60 day timeline. All correspondence will be sent to the person named in Section C of the Clinical Trial Application form (i.e. the Chief Investigator (CI) or Sponsor’s representative) and should be filed on Q-Pulse (the Trial Master File) by the R & I Office.

**4.6 Outcomes from MHRA Review**

Following assessment of the valid application a letter will be sent informing the Sponsor of:

Acceptance of the request for a clinical trial authorisation OR

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

Grounds for non-acceptance of the request for a clinical trial authorisation.
4.7 Post MHRA Approval

The CI is responsible for ensuring that a copy of the MHRA approval letter is forwarded to the R & I office.

All subsequent amendments must be reviewed to see if they require MHRA approval.

The CI is responsible for forwarding copies of any MHRA approval letters relating to substantial amendments to R & I.

The CI is responsible for ensuring that any reports sent to the MHRA are also forwarded to the R & I Office.

5 Equality Impact Assessment

This SOP has been equality impact assessed by the author using the Trust’s Equality Impact Assessment (EQIA), which has been submitted to the Equality and Diversity Department for ‘Service Equality Team Sign Off’.

No significant issues in relation to equality, diversity, gender, colour, race or religion are identified as raising a concern

6 Consultation, Approval and Ratification

6.1 Consultation and Communication with Stakeholders

All Trust R & I SOPs are written by a member of the Research Office staff with relevant expertise and experience. Additional advice is sought from members of the research community within the Trust, including the Research & Innovation Operational Group, R & I Committee, or external advisors, as necessary.

6.2 SOP Approval Process

All SOPs must be sent to the R & I Manager in order to start the SOP approval process.

All Trust R & I SOPs are subject to approval by the R & I Committee. The SOP will then be sent to the Trust Management Board for ratification.
7 Dissemination and Implementation

7.1 Dissemination

When approved, this SOP will be made available through Q-Pulse. Q-Pulse will publish approved SOPs to the Trust Research Office website. The Trust intranet will contain a link to direct staff to the approved SOPs on the external website. Only the current version will be available.

All researchers listed on the Research Office ‘active researcher’ mailing list will be notified by email when an updated version of an SOP is available.

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All researchers listed on the Research Office ‘active researcher’ mailing list will be notified by email when an updated version of an SOP is available.

7.2 Implementation of Procedural Documents

Support and advice on the implementation of this SOP can be obtained via the Research Office.

3. Review, Monitoring Compliance with the Effectiveness of Procedural documents

8.1 Process for Monitoring Compliance and Effectiveness

Review will be undertaken by the Research Office Management. Compliance with the Trust R & I SOPs by researchers will be monitored via the Trust’s Research Governance Monitoring Programme where appropriate.

SOP contents will be reviewed against any changes to the applicable guidelines and regulations and taking into account any feedback received from researchers or via the Monitoring Programme.

Review and monitoring will be conducted based on an initial risk assessment of the project. This process may change based on results of any monitoring visit.

The outcome of the review – and any resulting amendments - will be reported to the R & I Committee.
8.2 Standards and Key Performance indicators ‘KPI’s’

This SOP will be available on the Trust website and via Q-Pulse.
This SOP must be reviewed at least every two years or when there are significant changes to the document.

9 References and Bibliography

Terms of Reference for the GMMH R & I Committee

Is it a Clinical Trial of a Medicinal Product? Algorithm:


See IRAS ‘Guidance on preparing an application to MHRA Medicines for a Clinical Trial Authorisation using IRAS’

https://www.hra.nhs.uk/about-us/committees-and-services/integrated-research-application- system/


UK Policy Framework for Health and Social Care Research v3.3 07/11/17  

A EudraCT number can be applied for at: https://eudract.ema.europa.eu/

For information on submissions to the MHRA via the Common European Submission Portal (CESP) see Clinical trials for medicines: apply for authorisation in the UK: 
https://www.gov.uk/guidance/clinical-trials-for-medicines-apply-for-authorisation-in-the-uk

Appropriate websites for up to date requirements at the time of application: 
www.hra.nhs.uk
9 Associated Trust Documents

Research Approval Policy
RDSOP03 Definition and delegation of investigator responsibilities for CTIMP’s
RDSOP8a Pharmacovigilance for Trust-Sponsored MHRA-regulated Clinical Trials
RDSOP9 Serious breaches of GCP or the clinical trial protocol
RDSOP10 IMP Management and accountability
RDSOP11 Research Governance Monitoring (onsite inc. CTIMP’s)
RDSOP13 Contracts Management
RDSOP14 Trust Sponsorship of Research
RDSOP15 Writing a GCP compliant protocol- CTIMP’s
RDSOP19 Financial Management of a Clinical Trial
RDSOP20 End of Study Notification
RDSOP21 Retention of data, off site archiving and destroying documents
RDSOP22 Confirmation of C & C for CTIMP’s
RDSOP24 Sourcing Pharmacy Services from Pharmacy Providers
RDSOP25 Sourcing Investigational Medicinal Products (IMPs) for Clinical Trials of an Investigational Medicinal Product (CTIMP’s)
RDSOP26 Using Non-Investigational Medicinal Products (NIMP’s) in Clinical Trials of an Investigational Medicinal Product (CTIMP’s)
RDSOP27 Implementing a Drug Recall for IMP/NIMP
RDSOP28 Randomization and Unblinding for CTIMP’s
RDSOP31 Study close out
RD SOP33 R & I Committee Safety Oversight
RDSOP34 Development safety update reporting
1. Appendix 1 – Gaining MHRA Approval Flowchart

- Obtain Trust Sponsorship
- Obtain EudraCT Number from EudraCT website
- Complete MHRA application form in IRAS (www.MHRA.gov.uk)
- Save completed documentation including IRAS form in PDF format onto a disk along with a covering letter and relevant documentation as per section 4.4
- MHRA provides initial response within 30 days of receipt of a valid application
- CTA Approved
- Grounds for non acceptance & requests further information
- Submit further information within
- MHRA provides response within 60 days of receipt of original application
- CTA Approved
- CTA Approved
- CTA Not Approved
- Submit New Application