RDSOP25 Sourcing Investigational Medicinal Products (IMPs) for Clinical Trials of an Investigational Medicinal Product (CTIMP’s).

Greater Manchester Mental Health NHS Foundation Trust
Title of Standard Operating Procedure: RDSOP25 Sourcing Investigational Medicinal Products (IMPs) for Clinical Trials of an Investigational Medicinal Product (CTIMP’s).

Document Summary: This standard operating procedure (SOP) describes the processes for sourcing IMP and states the documentation that must be reviewed during this process.

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R & I Pharmacist

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 & I SOPs

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<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>
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<tr>
<td>Review of SOP content</td>
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<td>Review by Author, redraft, submission to R &amp; I Operational Group</td>
<td>Minutes of R &amp; I Operational Group</td>
<td>Head of R &amp; I Office</td>
<td>Research &amp; Innovation Committee</td>
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1. Introduction

All clinical trials of an investigational medicinal product (CTIMP’s) must adhere to The Medicines for Human Use (Clinical Trials) Regulations 2004 and subsequent amendments. These Regulations state that CTIMP’s must be authorised by the Medicines Healthcare products Regulatory Agency and conducted according to Good Clinical Practice (GCP) and Good Manufacturing Practice (GMP).

Sourcing of Investigational Medicinal Products (IMPs) must comply with the principles of GCP and GMP and the over-arching Clinical Trials Regulations.

Greater Manchester Mental Health NHS Foundation Trust (GMMH) does not hold a Manufacturer’s Authorisation for IMP (MIA(IMP)). Therefore IMP manufacturing cannot occur on Trust premises.

2. Purpose

This standard operating procedure (SOP) describes the processes for sourcing IMP and states the documentation that must be reviewed during this process.

3. Roles and Responsibilities

3.1 Duties within the organisation

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

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 or local Principal Investigator to ensure up-to-date SOPs are filed in the Investigator Site File and are available to research staff, and to inform the Research Support Co-ordinator of the names of all research staff involved on a study so that copies of SOPs can be distributed appropriately.

It is the responsibility of the study Chief Investigator or Principal Investigator to designate if the SOPs of another organisation are to be followed for a study. For example those of a Clinical Research Network or commercial sponsor. If there is significant conflict between the external SOP and the Trust R & I SOP it is the responsibility of the CI or PI to resolve these with the Research Office prior to starting the study.
4. Procedure

4.1 Sourcing IMP

- The R & I Pharmacist must check with the investigator to see whether the R & I Pharmacist is to source the IMP – active and/or placebo.

- Where a pharmaceutical company is supplying a licensed product (drug and formulation) for a CTIMP, the R & I Pharmacist will enquire if the company can supply placebo IMP.

- If the company cannot supply placebo IMP, the R & I Pharmacist must contact companies with a Manufacturer’s Authorisation for IMP (MIA(IMP)) to see if they can supply matching placebo. The R & I Pharmacist must try to obtain quotes (for the manufacture of placebo IMP, including Qualified Person (QP(IMP)) release) from different companies. The quote(s) must be discussed with the investigator to ensure sufficient funding is available. A copy of the quote to be used should be given to the investigator and the original copy filed in the R & I CTIMP file.

- Depending on what is required, companies such as Aptuit, Brecon Pharmaceuticals, Catalent, DHP pharma, Penn or Piramal Healthcare Ltd could be approached for manufacturing purposes/clinical trials supplies. Units at Guy’s and St Thomas’ NHS Foundation Trust, Royal Free Hampstead NHS Trust or University College London Hospitals NHS Foundation Trust may be able to provide certain manufacturing services. The R & I Pharmacist must obtain quotes for manufacturing costs (including QP(IMP) release) and these must be discussed with the investigator to ensure there are sufficient funds.

- If the R & I Pharmacist is to source an unlicensed drug or formulation or get a licensed product repackaged, the R & I Pharmacist must ensure these are manufactured in a licensed production unit, authorised by the Medicines and Healthcare products Regulatory Agency (MHRA), in accordance with Good Manufacturing Practice (GMP(IMP)) and labelled as described in Annexe 13. (The labels could also include space for the date of dispensing and participant’s initials or full name to be added).

- The R & I Pharmacist must ensure the company/unit has a licence (MIA(IMP)) to carry out the particular manufacturing function being
requested (for example if the company/unit is to encapsulate IMP, then the licence must state that the company/unit is authorised by the MHRA to do this). Licences can be checked via the MHRA internet site.

- Where IMP (active or placebo) is to be sourced from a licensed production unit, a technical agreement must be set up with the company. If a technical agreement has not been started or finalised, the R & I Pharmacist will ask to see the company’s ‘template’ technical agreement before going on to agree a final version. The R & I Pharmacist must ask for a copy of the finalised technical agreement so it can be filed in the R & I CTIMP file.

- The manufactured IMP must be released for use by a QP (IMP), following testing for that particular CTIMP, according the requirements stated in the MHRA clinical trial application and authorisation. The IMP will be released with a QP release document that must state the batch has been made according to GMP and the product specification file. This paperwork must be signed by a QP listed on the manufacturer’s licence.

- The R & I Pharmacist must check the IMP supplier is listed in the clinical trial authorisation application form (any changes to this would require a substantial amendment).

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<tr>
<th>Status of IMP (active or placebo)</th>
<th>QP(IMP) Release Required</th>
<th>Import QP(IMP) Required</th>
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<tbody>
<tr>
<td>Licensed in the United Kingdom (UK) (Product (IMP) remains in original packaging)</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>UK Licence but Unlicensed Indication (IMP remains in original packaging and is prepared and administered according to the summary of product characteristics/manufacturer’s information)</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Unlicensed but Manufactured in the UK</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Licensed/Unlicensed outside the European Union (EU) (Check on the European Medicines Agency (EMA))</td>
<td>Yes</td>
<td>Yes</td>
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Table 1 – Summary of QP(IMP) Release/Import Documentation Required
If the product to be used as IMP is a licensed drug with a marketing authorisation being dispensed in its licensed packaging, a certificate of analysis or QP release is not required, even if the drug is being used for an unlicensed indication.

Where QP(IMP) release documentation is required, it is required for each batch of IMP (not necessarily every delivery of IMP). QP(IMP) release documentation is essential if the source is non-EU.

Written evidence is required to support any changes of storage conditions of IMP or expiry dates and the information should state why the change was necessary and that changes have been approved by the QP(IMP).

An import QP(IMP) licence and QP(IMP) release documentation are required if the product is sourced from a non-EU country that does not have a MRA in place.

If a product is obtained through a licensed importer, evidence would be needed that the importer had a licence to import the product (an import QP(IMP) licence would be needed). Technically, it would be a QP who would import the product, therefore the QP would need to be named on the import licence.

For products sourced from non-EU countries with a MRA in place, the product would need QP recertification in the UK (have QP(IMP) release documentation), but not need import QP(IMP) documentation.

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<tr>
<th>internet site to see which countries have a mutual recognition agreement (MRA).</th>
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<tr>
<td>Manufacturing Process Required (and product sourced within the EU or from a country with a MRA)</td>
<td>Yes</td>
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<tr>
<td>Manufactured before May 2004</td>
<td>No</td>
</tr>
</tbody>
</table>
5. References and Bibliography

Statutory Instrument 2004/1031: The Medicines for Human Use (Clinical Trials)

Statutory Instrument 2006/1928: The Medicines for Human Use (Clinical Trials)
Amendment Regulations 2006.