RDSOP26 Using Non-Investigational Medicinal Products (NIMPs) for Clinical Trials of an Investigational Medicinal Products (CTIMPs).

Greater Manchester Mental Health NHS Foundation Trust
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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>
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<td>Minutes of R &amp; I Operational Group</td>
<td>Head of R &amp; I Office</td>
<td>Research &amp; Innovation Committee</td>
</tr>
</tbody>
</table>
# Contents

1. Introduction ........................................................................................................... 3  
2. Purpose .................................................................................................................. 4  
3. Roles and Responsibilities ...................................................................................... 4  
3.1 Duties within the organisation ............................................................................ 4  
4. Procedure .............................................................................................................. 4  
4.1 NIMP’s being used for Non-Trust Sponsored CTIMP’s ....................................... 4  
4.2 NIMP’s being used for Trust Sponsored CTIMP’s .............................................. 5  
5. References and Bibliography .................................................................................. 6

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Page 2 of 6
RDSOP26 Using Non- Investigational Medicinal Products (NIMP’s) for Clinical Trials of an Investigational Medicinal Products (CTIMP’s)

1. Introduction

All clinical trials of an investigational medicinal product (CTIMPs) must adhere to The Medicines for Human Use (Clinical Trials) Regulations 2004 and subsequent amendments.

The dispensing processes for investigational medicinal products (IMPs) must comply with the principles of Good Clinical Practice (GCP) and Good Manufacturing Practice (GMP) and the over-arching Clinical Trials Regulations, as well as conform to The Medicines Act 1968.

The same level of quality and safety should be ensured for non-investigational medicinal products (NIMP’s) as for the IMPs used in CTIMPs.

Non-Investigational Medicinal Products (NIMP’s) “fall under general medicines legislation and GMP rather than the Clinical Trials Regulations. In this way, NIMP’s that are authorised medicinal products are governed by the requirements of Directive 2001/83/EC, including Title IV, which contains the GMP requirements”. [Medicines and Healthcare products Regulatory, 2012].

The following describes what a NIMP is, according to guidance from the European Commission;

NIMP’s are medicinal products that fall within Article 3(3) of Directive 2001/83/EC, while not falling within the definition of IMP as defined in Article 2(d) of Directive 2001/20/EC.

For instance, some clinical trial protocols require the use of medicinal products such as concomitant or rescue/escape medication for preventive, diagnostic or therapeutic reasons and/or to ensure that adequate medical care is provided for the subject. They may also be used in accordance with the protocol to induce a physiological response.

Medicinal products that do not have a marketing authorisation, but are prepared in accordance with a magistral formula, i.e. prepared in a pharmacy in accordance with a medical prescription for an individual patient, and medicinal products prepared in a pharmacy in accordance with the prescriptions of a pharmacopoeia and intended to be supplied directly to the patients served by the pharmacy in question, i.e. officinal formula, as referred to in Article 3(1) and (2) of Directive 2001/83/EC may also be an NIMP.”

NIMP’s can be categorised as:

- rescue medication
- challenge agents
- medicinal products used to assess end-points in the CTIMP
- oncomitant medicinal products systematically prescribed to the clinical trial participants
- background treatment
2. Purpose

This procedure outlines instructions for using NIMP’s in CTIMP’s.

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.

It is the personal responsibility of all staff to follow Trust (or the designated alternative organisations) procedural documents.

The Research & Innovation Office is responsible for managing Trust R & I SOPs including their approval, dissemination and archiving. All Trust R & I SOPs must be made available via Q-Pulse and published on the Trust website.

4. Procedure

4.1 NIMP’s being used for Non-Trust Sponsored CTIMP’s

- Check the CTIMP protocol and, if available, the clinical trial application documents submitted to the Medicines and Healthcare products Regulatory Agency (MHRA) to see if any NIMPs are included in the trial.
If there is any doubt, ask the sponsor to clarify in an email whether NIMP’s are being used (a copy of this email should be filed in GMMH’s trial-specific electronic R & I file and the site pharmacy file for the trial).

If NIMP’s could be used in the trial, check the sponsor is providing them. If the sponsor is requesting site pharmacies source the NIMP(s), ask the sponsor to approve the products to be used, via email used (a copy of this email should be filed in GMMH’s trial-specific electronic R & I file and the site pharmacy file for the trial).

Check with the sponsor whether they need any information recording by pharmacy staff when a NIMP is dispensed. If so, use sponsor-approved documentation, such as a NIMP accountability log, or follow the sponsor’s instructions for recording which participants received which NIMP (with an evaluation of compliance where necessary or as per sponsor’s instructions).

Report any adverse events or reactions related to NIMP’s in line with the protocol and/or sponsor’s instructions.

For any NIMP recalls, follow the sponsor’s instructions.

4.2 NIMP’s being used for Trust Sponsored CTIMP’s

If NIMP’s are to be used within a Trust sponsored CTIMP, ensure the NIMP’s are included in the protocol and in the clinical trial application to the Medicines and Healthcare products Regulatory Agency (MHRA).

If there is any doubt whether a medicine is a NIMP, contact the MHRA clinical trials helpline for advice and ask the MHRA if they could put their decision in writing/an email.

Refer to the European Commission guidance on the “simplified documentation requirements for NIMP’s in the application dossier” for details about what NIMP-related documents should be submitted to the MHRA at the time of applying for a clinical trial authorisation. This guidance can be accessed via the following link:


Where possible, use a NIMP with a United Kingdom marketing authorisation or which is an authorised medicinal product in any other member state of the European Union.
RDSOP26 Using Non-Investigational Medicinal Products (NIMP’s) for Clinical Trials of an Investigational Medicinal Products (CTIMP’s)

- If the NIMP does not have a marketing authorisation in the European Union, the Trust and/or R & I Pharmacist should ensure the NIMP is of an appropriate quality for the purposes of the CTIMP and that the principles of GMP have been taken into account to safeguard clinical trial participants.

- Decide whether Greater Manchester Mental Health NHS Foundation Trust (GMMH) is sourcing and supplying the NIMP(s) to be used in a particular trial or if the site pharmacies are going to be asked to do this.

- If site pharmacies are sourcing the NIMP(s), GMMH must oversee this process and authorise the products to be used. GMMH and/or the R & I Pharmacist must ensure all the necessary NIMP-related documentation is in place before any NIMP is dispensed at the site.

- Ensure the trial-specific prescription has space to prescribe NIMP(s).

- Design a NIMP accountability log for use within the trial and implement a system to ensure there is a record of which participant received which NIMP and that there is a log of the batch number and expiry date of the product dispensed.

- Where an evaluation of participant compliance with NIMP(s) is necessary, this should be recorded on the case report form (CRF).

- Ensure there are procedures in place for reporting adverse events or reactions related to NIMP’s (for example if the adverse reaction has been associated with an interaction between IMP and NIMP, or the reaction could be due to either the IMP or NIMP). Adverse events and reactions related to NIMP’s should be reported in the same way as they are to be reported for the IMP(s).

- Ensure there are procedures in place for recalling NIMP.

5. References and Bibliography


