# Supply and Labelling of Investigational Medicinal Products (IMPs) for Clinical Trials

<table>
<thead>
<tr>
<th>Version</th>
<th>1.2</th>
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<tr>
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<td>26 March 2012</td>
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<tr>
<td>Author:</td>
<td>Claire Daffern, QA Manager</td>
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<tr>
<td>Approved by:</td>
<td>Dr Sarah Duggan, CTU Manager</td>
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## Revision Chronology:

<table>
<thead>
<tr>
<th>Revision</th>
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<th>Reason for change</th>
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<tbody>
<tr>
<td>Version 1.2</td>
<td>26 March 2012</td>
<td>Format change to comply with SOP 1</td>
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<td>Version 1.1</td>
<td>26 March 2010</td>
<td>Addition of details regarding transfer of IMP(s) between sites (section 3.3.4).</td>
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<td>Version 1.0</td>
<td>26 March 2008</td>
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Supply and Labelling of Investigational Medicinal Products (IMPs) for Clinical Trials

1. Purpose
This Standard Operating Procedure (SOP) describes the management process for the supply of Investigational Medicinal Product(s) (IMPs) and how IMP(s) must be labelled according to the requirements of the Medicines for Human Use (Clinical Trials) Regulations 2004 and EU Directive 2003/94/EC.

This SOP focuses on IMP activities that staff within Warwick Medical School and investigational sites may undertake and therefore is not an exhaustive SOP to cover all aspects concerning IMPs in clinical trials.

2. Background
All clinical trials of IMPs are legally required to comply with International Conference on Harmonisation Good Clinical Practice (ICH GCP) guidelines, the Medicines for Human Use (Clinical Trials) Regulations 2004 and associated amendments.

Part 6 of the Medicines for Human Use (Clinical Trials) Regulations 2004 details the requirements for the manufacture and importation of IMPs. The regulations require that IMPs used in clinical trials are manufactured to Good Manufacturing Practice (GMP) standards and that GCP is adhered to.

ICH GCP sections 5.12 (Information on Investigational Products); 5.13 (Manufacturing, Packaging, Labelling and Coding of Investigational Products) and 5.14 (Supplying and Handling Investigational Products) explain the Sponsors responsibilities regarding IMPs.

Manufacturing and packaging will be the responsibility of the IMP supply company involved in the trial and should be detailed in contractual agreements.

The IMP supply company is responsible for conducting final checks before the release of an IMP. This should be done by the Qualified Person (QP) to ensure that each batch has been manufactured to GMP standards and all checks and documentation is in place prior to dispatch.

3. Procedure
3.1. Who?
The Chief Investigator (CI) has overall responsibility for the management, storage, use and accountability of IMP(s) as detailed in section 4.6 of ICH GCP entitled “Investigational Products”. Responsibility may be delegated to other suitably qualified members of the trial team e.g. Trial Coordinator, Pharmacist.
3.2. When?
The IMP supply and labelling requirements should be determined at the earliest possible stage of the trial design process as the costs need to be included in the grant application.

The MHRA must approve the labels before the trial can start.

3.3. How?
The CI should determine the supply, labelling requirements, storage conditions and dispensing procedures for all IMPs in the trial. It is good practice to involve a pharmacist and the IMP supplier in these decisions.

3.3.1 IMP supply
IMP(s) may be obtained directly from a pharmaceutical company, a specialist clinical trial supplier or from standard NHS stock depending on the design of the trial.

Trial sites should not be supplied with any IMP(s) until all required documentation has been obtained (e.g. Approvals in place from the main Research Ethics Committee, the MHRA (if applicable), the NHS Trust’s R&D offices, and the signed contract between the sponsor and the site).

Each site should be properly informed about their responsibilities. This will usually take place during the site initiation with the pharmacy department and should include:

- Purpose of the trial
- Explanation of responsibilities
- Codes e.g. for participant randomisation or unblinding
- Description of the IMP and any handling or safety issues
- Source of the products to be used
- Labelling requirements
- Name and contact details of the investigators and of others involved in the management or administration of the trial
- Documentation for retention in the pharmacy

3.3.2 Labelling
The requirements for labelling IMP(s) for clinical trials are covered by the Medicines for Human Use (Clinical Trials) Regulations 2004 and EU Directive 91/356. An example label should be sent to the MHRA with the Clinical Trials Authorisation (CTA) application. This sample should include the text of the labelling to be used and be provided in a format representative in terms of size of the label to be used. The labelling requirements for IMP(s) used within and outside of its marketing authorisation (MA) are detailed below.

In placebo controlled or blinded trials it is necessary to present all supplies in consistent packaging with consistent labelling to maintain blinding.
3.3.2.1 IMP used within its marketing authorisation
For an IMP used within its MA, the product can be labelled in accordance with the requirements for a dispensed medicine. However, to be consistent with other countries, it is recommended that IMPs are labelled following the guidelines in Annex 13 of Good Manufacturing Practice (GMP). In practice, this means adding the name of the investigator, trial specific code (e.g. EudraCT number) and trial subject code to the label already in place for the product.

Example of label:

```
Trial (EudraCT number)
Investigator: Dr xxxxxx
Product name, form and strength

Directions (as specified by the prescriber)
Patient name & subject code                  Date of Supply:
Name and address of hospital/primary care supplier

Keep out of reach of children
Any additional cautionary label (as recommended by the BNF)
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N.B. The cautionary label “Keep out of reach of children” is a legal requirement on all UK dispensed medicines. Further information is available in Appendix 9 of the British National formulary (BNF).

The quantity of dosage forms (tablets, capsules etc.) is generally also added for dispensed medication. For reconstituted drugs, an expiry/use-by date is also required.

3.3.2.2 IMP used outside its marketing authorisation
Labelling requirements of IMPs used outside their MA are stated in Annex 13 of the European Union’s GMP regulations as follows:

<table>
<thead>
<tr>
<th>Annex 13 labelling requirements</th>
<th>Comment</th>
</tr>
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<tbody>
<tr>
<td>(a) Name and address of sponsor or investigator (the main contact for information on the product, clinical trial and emergency unblinding)</td>
<td>Paragraph 27 of Annex 13 allows that the address and telephone number of the main contact for information need not appear on the label if the subject has been given a leaflet or card which provides this detail and has been instructed to keep this in their possession at all times.</td>
</tr>
<tr>
<td>(b) Pharmaceutical dosage form, route of administration, quantity of dosage units.</td>
<td>This information would be included on the label of the marketed product itself</td>
</tr>
<tr>
<td>(c) the batch and/or code number to identify the contents and packaging operation</td>
<td>This information would be included on the label of the marketed product itself</td>
</tr>
<tr>
<td>(d) a trial reference code allowing identification of the trial, site, investigator and sponsor if not given</td>
<td>The trial reference code could be the EudraCT number; the site could be identified by the normal hospital</td>
</tr>
</tbody>
</table>
Elsewhere

- the trial subject identification number/treatment number and if relevant the visit number
- the name of the investigator (if not included in (a) or (d))
- directions for use (reference may be made to a leaflet or other explanatory document intended for the trial subject or person administering the product)
- “For clinical trial use only” or similar wording
- period of use (use-by date, expiry date or re-test date as applicable), in month/year format and in manner that avoids any ambiguity
- “Keep out of reach of children” except when the product is for use in trials where the product is not taken home by participants

Example of label:

<table>
<thead>
<tr>
<th>For Clinical Trials Use Only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial (EudraCT number)</td>
</tr>
<tr>
<td>For use in trial (give directions for use as stated in patient information leaflet for the trial)</td>
</tr>
<tr>
<td>Investigator: Dr xxxxx</td>
</tr>
<tr>
<td>Sponsor: xxxxxx</td>
</tr>
<tr>
<td>Product name, form and strength</td>
</tr>
<tr>
<td>Directions (as specified by the prescriber)</td>
</tr>
<tr>
<td>Patient name and subject code Date of Supply</td>
</tr>
<tr>
<td>Name and address of hospital/primary care supplier</td>
</tr>
<tr>
<td>Keep out of reach of children</td>
</tr>
<tr>
<td>Any additional cautionary label (as recommended by the BNF)</td>
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</tbody>
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3.3.3 Drug accountability

Each site must maintain records to document shipment, receipt, handling, return and disposal/destruction of used and unused IMP(s). However, for drugs already having an MA which are supplied via the site pharmacy, detailing shipment, receipt and return is not applicable.

Drug accountability logs should be kept for each trial to detail:

- Name of site and Principal Investigator
- Subject identification code
- Date dispensed
If local practices are in place for drug accountability these should be utilised.

Ideally, all IMP(s) should be stored and dispensed by pharmacy. According to ICH GCP, if appropriate, IMP(s) may be stored in a locked cupboard in other areas e.g. clinics or ward areas as determined by the sponsor and documented in the protocol.

The agreed process for the destruction of unused IMP(s) at the end of a trial should be documented.

### 3.3.4 Transfer of IMP(s) between research sites

Once an IMP has been delivered to a site it should not subsequently be transferred to another site without first being returned to the clinical trial supply company for inspection and further QP release. The packs would then be available for delivery to another site. Documentation (quantity, locations, dates, method of transfer) on the IMP transferred should be maintained.

As there would be costs involved in any drug pack transfer, this should only be done if there were no other options to ensure supplies are available at a particular site.

**List of Abbreviations**

- CI: Chief Investigator
- CTA: Clinical Trial Authorisation
- ICH: International Conference on Harmonisation
- IMP: Investigational Medicinal Product
- GCP: Good Clinical Practice
- GMP: Good Manufacturing Practice
- MA: Marketing Authorisation
- MHRA: Medicines and Healthcare products Regulatory Agency
- QP: Qualified Person
- SOP: Standard Operating Procedure