

SOP-QA-14 V5

Title: SmPC, Investigator Brochure and IMP Dossier

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Document History

Version	Description of update	Date Effective
3	Reformatted	1-4-17
4	Abbreviations added at 4 Appendix 1 replaced with reference to MHRA Inspectorate Blogs	1-8-20
5	Inclusion of Combined trials of IMP/investigational device at 1.2 Reference to Clinical Trial Pharmacist at 1.3, removal of duplication at 3.1 additional reference added at 5	9-8-23

1. Scope

- 1.1 This document applies to all researchers participating in research projects involving a Medicinal Product (MP) sponsored or co-sponsored by UoA and/or NHSG. It also applies to all UoA and NHSG staff supporting such research activities.
- 1.2 Medicinal Product research projects include:
- Clinical Trials of Investigational Medicinal Product (CTIMPs) falling under the Medicines for Human Use (Clinical Trials) Regulations 2004 as amended, or equivalent legislation out with the United Kingdom.
 - Combined trials of Investigational Medicinal Product and an investigational device.
 - Clinical Trials of Medicinal Product which do not fall under the above regulations.
- 1.3 SmPC/SPC (Summary of Product Characteristics), IB (Investigator Brochure) and IMPD (Investigational Medicinal Product Dossier) are termed 'regulatory documents'. The regulatory documentation, specifically the SmPC/SPC and IB, shall contain the Reference Safety Information (RSI) which will be used in the assessment of any adverse reactions (see SOP-QA-22 – Adverse Events in CTIMPs).


In the context of this SOP, regulatory documentation includes:

- **SmPC/SPC** - This is the document approved as part of the marketing authorisation of a medicine; containing the definitive description of the product both in terms of its chemical, pharmacological and pharmaceutical properties and the clinical use to which it can be put, etc. SmPCs are available on www.medicines.org.uk.
- **IB** - This is a compilation of the clinical and non clinical data on the investigational medicinal product(s) which is relevant to the study of the product(s) in human subjects; it should support the rationale for the proposed clinical trial and the safe use of the product(s).
- **IMPD** - This gives information on the quality of any IMP (including placebo), including summaries of information related to the quality, manufacture and control of the IMP.
- **sIMPD** - A simplified version of the IMPD. The Sponsor and/or Manufacturer will provide guidance as to whether an IMPD or sIMPD is required.

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Guidance as to which regulatory documents are required for specific research projects can be found in section 3.1 (table 1). The Clinical Trials Pharmacist will advise on medicinal products used in research (see SOP-QA-15 - Management of Medicinal Products used in research) and other documentation that may be required.

- 1.4  The expectation is that research projects which use:
- 1) **Licensed medications** will use the manufacturers SmPC/SPC and an IB is not required.
 - 2) **Unlicensed medication** is likely to require an IB and a sIMPD or an IMPD. The Sponsor will provide guidance on this.
 - 3) **Placebo** will require a sIMPD or IMPD for the placebo. The manufacturer or Sponsor will provide guidance on this.

2. Responsibilities

Chief Investigator (CI) Delegated by Sponsor to prepare and update regulatory documents.

 The CI may delegate duties to appropriately qualified and experienced research team members or an appropriate third party (eg MP or placebo manufacture). Any such delegation shall be documented in the site delegation log, co-sponsorship agreement or third party agreement (see SOP-QA-16 – Selection and management of third parties).

3. Procedure

Research project documentation and approvals

3.1 For guidance on the regulatory documents required for different types of research project, see table 1.

Table 1



Type of Research Project	Regulatory documents required
CTIMP using a licensed product	<ul style="list-style-type: none"> • An SmPC/SPC is required for the licensed product • If there is a placebo, Sponsor will provide guidance as to whether an sIMPD or IMPD is required
CTIMP using an unlicensed product	<ul style="list-style-type: none"> • An IB will be required for the unlicensed product • Sponsor will provide guidance as to whether an sIMPD or IMPD is required for the unlicensed product • If there is a placebo, Sponsor will provide guidance as to whether an sIMPD or IMPD is required
Non-CTIMP using a licensed product	<ul style="list-style-type: none"> • An SmPC/SPC is required for the licensed product • If there is a placebo, Sponsor will provide guidance in relation to the requirement for an sIMPD or IMPD
Non-CTIMP using an unlicensed product	<ul style="list-style-type: none"> • The Sponsor shall provide guidance as to which regulatory documents are appropriate

3.2 The CI, or delegate, shall prepare the appropriate regulatory documents which shall be submitted (along with all other required Sponsor documents) to the Research Governance Team (RGT) for review **before** sponsorship is approved and approvals are sought (see SOP-QA-4 - Applying for sponsorship).


3.3 The Sponsor shall review the regulatory documents, with guidance from the Clinical Trials Pharmacist (see SOP-QA-15 - Management of Medicinal Products used in research), and request any required changes before agreeing sponsorship for the research project.

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- 3.4 **After** Sponsor approval, the CI shall submit all required documentation to the Research Ethics Committee (REC), Research & Development (R&D) and the Medicines and Healthcare products Regulatory Agency (MHRA) (if applicable) for approval.
- 3.5  The CI shall send the Sponsor copies of any correspondence from REC or MHRA in which they request changes to the regulatory documents.
- 3.6  The CI shall also forward the amended regulatory documents for Sponsor review **before** they are resubmitted to the REC or MHRA. The Sponsor shall review the amended regulatory documents and request any required changes before confirming ongoing sponsorship.


Research project start-up

- 3.7 The CI, or delegate, shall provide copies of the approval letters and the approved regulatory documents to all relevant parties (eg Sponsor, manufacturer, third parties, Clinical Trials Pharmacies, Co-Investigators, R&D departments). For further information see SOP-QA-6 – Study start-up.
- 3.8  The CI or delegate shall ensure copies of approval letter and approved regulatory documents are filed in the Trial Master File (TMF) (see SOP-QA-7 - Trial Master File).

Annual review of regulatory documents

- 3.9 The CI, or delegate, shall review all regulatory documents at least annually. For research projects which have MHRA approval this should be done at the time of Development Safety Update Review (DSUR) preparation (see SOP-QA-21 – APRs and DSURs). If no updates are required, this should be recorded in the DSUR.
 If updates are required, this is likely to constitute a substantial amendment (see 3.11).
- 3.10 For research projects which do not require MHRA approval this should be done at the time of Annual Progress Report (APR) preparation. If no updates are required, this should be documented in the TMF using a file note or log as appropriate.
 If updates are required, this is likely to constitute a substantial amendment (see 3.11).
- 3.11 When updates to regulatory documents are required, the updated versions should be submitted for Sponsor review and approval prior to submitting them to the REC, MHRA and R&D if appropriate (see SOP-QA-19 – Amendments).

Extraordinary review of regulatory documents

- 3.12  If the research team becomes aware of any new and important information regarding the MP, consideration should be given to updating the regulatory documents out with the annual review cycle. In such cases, guidance should be sought from the RGT.

4. Abbreviations and definitions

APR	Annual Progress Report
CI	Chief Investigator
CTIMP	Clinical Trial of an Investigational Medicinal Product
DSUR	Development Safety Update Report
IB	Investigator Brochure
IMPD	Investigational Medicinal Product Dossier
MHRA	Medicines and Healthcare products Regulatory Agency
MP	Medicinal Product
R&D	Research & Development (NHS)

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REC	Research Ethics Committee
RGT	Research Governance Team
RSI	Reference Safety Information
sIMPD	Simplified Investigational Medicinal Product Dossier
SmPC/SPC	Summary of Product Characteristics
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File

The EU Directive 2001/20/EC (Clinical Trials Directive) defines a medicinal product as:

*'A pharmaceutical form of an **active substance or placebo** being tested or used as a reference in a clinical trial, including products already with a marketing authorisation but used or assembled (formulated or packaged) in a way different from the authorised form, or when used for an unauthorised indication, or when used to gain further information about the authorised form.'*

5. Related documentation and references

SOP-QA-4	Applying for sponsorship
SOP-QA-6	Study start-up
SOP-QA-7	Trial Master File
SOP-QA-15	Management of Medicinal Products used in research projects
SOP-QA-16	Selection and management of third parties
SOP-QA-19	Amendments
SOP-QA-21	APRs and DSURs
SOP-QA-22	Adverse Events in CTIMPs
TMP-QA-6	Investigator Brochure Template

[MHRA Inspectorate Blog – Reference Safety Information for Clinical Trials](#)

[MHRA Inspectorate Blog – Reference Safety Information II](#)

[Reference Safety Information \(RSI\) for Clinical Trials- Part III - MHRA Inspectorate \(blog.gov.uk\)](#)

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