# STU-SOP-TM-010 – Standard Operating Procedure on Summary of Product Characteristics, Investigator Brochure and Investigational Medicinal Products Dossier

## 1. Purpose and Definitions

This Standard Operating Procedure (SOP) describes the requirements for an Investigator Brochure, Investigational Medicinal Product Dossier or the use of a Summary of Product Characteristics for a Clinical Trial of Investigational Medicinal Product (CTIMP) or non CTIMPs using licensed or un-licensed medicinal products.

| Definitions | |
|---|---|
| **Medicinal Product (MP)** | Any substance or combination of substances presented as having properties for treating or preventing disease in human beings<br>**OR**<br>any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.<br><br>Medicinal products can be human, animal, vegetable or chemical in origin. A substance may come under both parts of the definition; however, it need only fall under either part of the definition to be classified as a MP. |
| **Summary of Product Characteristics (SmPC)** | Provided by the marketing authorisation holder of a licensed medicine. It contains the definitive description of the product's chemical, pharmacological and pharmaceutical properties, details clinical use and is updated as new information becomes available. All current SmPCs for UK licensed medicines are listed on the electronic Medicines Compendium (eMC) – see references for link. |
| **Investigator Brochure (IB)** | Compilation of the clinical and non-clinical data on any Investigational Medicinal Product (IMP) which is relevant to the study of the IMP in human participants. It details the rational and safe use of the product in a CTIMP. |
| **Reference Safety Information** | The RSI is the list of medical events defining all expected reactions for any medicinal product administered in a research project. The RSI is a defined section of the IB/SmPC not the entire document. |
| **Investigational Medicinal Product Dossier (IMPD)** | Provided information on the quality of the IMP (including placebo) and includes details on the manufacture and handling of the IMP. |
| **Simplified Investigational Medicinal Product Dossier (sIMPD)** | Simplified version of the IMPD which may be a SmPC when a licensed product is used. The Sponsor will usually provide guidance on whether an IMPD or sIMPD is appropriate. |

## 2. Background

All CTIMPs under the UK and EU clinical trials regulations are required by law to demonstrate the rationale for the safe use of an Investigational Medicinal Product (IMP). CTIMPs with sites in Northern Ireland must be compliant with EU regulations.

A clinical trial involving a MP not falling under the above regulations must document the rationale for the safe use of a MP by summarising information within 'regulatory documents' – i.e. an IB, IMPD or the use of an existing SmPC if a licensed drug.

A SmPC will usually replace an IB if a medicinal product is authorised for use in the UK and EU and is used in accordance with the marketing authorisation.

If a medicinal product is used outside the marketing authorisation (making it an IMP), supplementary information that supports the use of the IMP and details the RSI will be required. This may be a separate IB document or detailed within the protocol.

An IMPD is required for each CTIMP application. However, this may be a sIMPD in the form of the SmPC for a UK or EU authorised product. The same IB/IMPD may be used by one sponsor for multiple research projects. Summary guidelines on IMPs are detailed in ICH GCP (see references).

## 3. Roles and Responsibilities

The **Sponsor** is responsible for reviewing and agreeing the regulatory documents required for all research projects involving a medicinal product.

The **Chief Investigator** (CI) or delegate is responsible for ensuring the required regulatory documents are reviewed on an annual basis and disseminating the documents to the research team.

**Swansea Trials Unit** (STU) is responsible for overseeing that regulatory documents comply with applicable legislation and guidance.

The **Trial Manager** (TM) or delegate is responsible for ensuring the regulatory documents are available in the Trial Master File (TMF), reviewed during the life cycle of the research project and for keeping a log of reviews and revisions.

**External use of SOP**: this SOP and Associated Documents (AD) may be used for research projects not adopted by STU where Swansea University (SU) staff and associated NHS organisations require guidance. In such instances, oversight responsibility for any associated tasks will not be the responsibility of STU.

## 4. Procedure

### 4.1 Required Regulatory Documents, Approvals and Amendments

Sponsors will usually determine the regulatory documents required with guidance from a manufacturer and/or clinical trials pharmacist and agree any required changes before agreeing to sponsor the research project.

Table 1 provides general guidance on the regulatory documents potentially required for CTIMPs and other research projects. The Sponsor shall provide guidance as to which regulatory documents are appropriate.

For instances when an IB is required the available template (STU-AD-TMP-040) or sponsor equivalent should be used.

**Table 1**

| Type of Research Project | Regulatory documents required | | | |
|---|---|---|---|---|
| | SmPC | IB | IMPD | sIMPD |
| CTIMP using a licensed product | ✓ | | | |
| CTIMP using an unlicensed product | | (✓) | (✓) | (✓) |
| Non-CTIMP using a licensed product | ✓ | | | |
| Non-CTIMP using an unlicensed product | (✓) | (✓) | (✓) | (✓) |
| Placebo | | | (✓) | (✓) |

() indicates combination of documents may be required.

The CI, or delegate, shall prepare the appropriate regulatory documents and submit them as required for sponsor assessment.

Following Sponsor assessment, the CI shall submit all required documentation as part of a Clinical Trial Authorisation (CTA) submission to the relevant competent authority (Medicines and Healthcare products Regulatory Agency (MHRA) in the UK) to obtain the required approvals.

For a CTIMP in the UK, there is a single application for both Clinical Trial Authorisation (CTA) and Research Ethics Committee (REC) opinion. Local R&D permissions are obtained via capacity and capability (C&C) assessments. For non-regulated MP projects MHRA authorisation is not required. These processes are described in dedicated SOPs.

The Sponsor must review any revision to regulatory documents to endorse continuing sponsor approval. The CI must obtain Sponsor agreement before submission to the required authorities.

### 4.2 Research project set-up

The Trial Master File, Investigator Site Files and projects stakeholder files e.g. site pharmacy, vendors will contain copies of required regulatory documents and approval letters.

### 4.3 Annual Review of Regulatory Documents

The CI shall ensure that all regulatory documents are reviewed at least annually. For CTIMPs this should be completed at the time of the annual Development Safety Update Report (DSUR). See STU-SOP-TM-007 APR-DSUR for further information.

Updates/changes to the regulatory documents will usually constitute a substantial amendment and should be submitted for Sponsor authorisation prior to seeking the required approvals (see 5.1). When no update is required to the regulatory documents, this should be recorded in the DSUR or project review log.

**4.4 Extraordinary Review of Regulatory Documents**

Should the CI become aware of any new and important information regarding the medicinal product, consideration should be given to updating the regulatory documents outside the annual review cycle. The sponsor must be kept informed.

Regardless of any update, the RSI in place at the beginning of an annual reporting period remains the reference for expectedness assessments for the DSUR report i.e. a report cannot be submitted early and assessments are based on the approved RSI only.

RSI updates must be submitted with the annual DSUR, listing significant changes and indicating the date the new RSI was implemented.

**4.5 Reference Safety Information**

The RSI must be clearly identified as part of the IB/SmPC and/or protocol in the initial application for a CTA. Reactions to be excluded from expedited reporting must be identified within the current approved version of protocol.

When the RSI has been approved by a regulatory body it can only be changed following a substantial amendment. Implementation of the new RSI must follow approval.

For international CTIMPs there may be differing RSIs in use. In such instances the CI needs to ensure that all relevant UK SARs/SUSARs are assessed against the UK approved RSI.

Changes to an existing SmPC not affecting the RSI need not be sent to the approving regulatory body(s). All such decisions should be recorded as part of a revised risk assessment and held in the TMF.

Changes to previous RSI does not allow the downgrade of previously reviewed SUSARs, similar new events may be classed as expected.

## 5. References

- Health Research Authority website (HRA) - http://www.hra.nhs.uk/
- Medicine and Healthcare products Regulatory Agency website (MHRA) - https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency/services-information
- UK policy framework for health and social care research (2017) - https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/
- UK Medicine for Human Use (Clinical Trials) Regulations 2004 - http://www.legislation.gov.uk/uksi/2004/1031/contents/made
- Electronic Medicines Compendium - www.medicines.org.uk
- Clinical Trials Toolkit - http://www.ct-toolkit.ac.uk/routemap/trial-supplies/
- Community code relating to medicinal products or human use Directive 2001/83/EC -Microsoft

Word - Human Code.doc (europa.eu)

- International Council for Harmonisation (ICH) http://www.ich.org/products/guidelines.html

It is assumed that by referencing the principal regulations that all subsequent amendments are included in this citation.

## 6. Associated Documents

| Number | Title | Location |
|---|---|---|
| STU-AD-TMP-040 | Investigator Brochure Template | Q-Pulse |

## 7. Abbreviations

| List of Abbreviations | |
|---|---|
| **CI** | Chief Investigator |
| **CTA** | Clinical Trials Authorisation |
| **CTIMP** | Clinical Trial of an Investigational Medicinal Product |
| **DSUR** | Development Safety Update Report |
| **eMC** | Electronic Medicines Compendium |
| **EU** | European Union |
| **HRA** | Health Research Authority |
| **ICH GCP** | International Council for Harmonisation Good Clinical Practice |
| **IB** | Investigator Brochure |
| **IMP** | Investigational Medicinal Product |
| **IMPD** | Investigational Medicinal Product Dossier |
| **ISF** | Investigator Site File |
| **MHRA** | Medicines and Healthcare products Regulatory Agency |
| **REC** | Research Ethics Committee |
| **RSI** | Reference Safety Information |
| **sIMPD** | Simplified Investigational Medicinal Product Dossier |
| **SmPC** | Summary of Product Characteristics (also termed SPC) |
| **SOP** | Standard Operating Procedure |
| **SB UHB** | Swansea Bay University Health Board |
| **STU** | Swansea Trials Unit |
| **SU** | Swansea University |
| **TM** | Trial Manager |
| **TMF** | Trial Master File |

## 8. Appendices

**Appendix 1: Document History**

| **Version No:** | 3 | **Effective Date:** | 20-Jun-24 |
|---|---|---|---|
| **Description of changes:** | Update to template v5<br>Update to procedures | | |

## Appendix 2: Flowchart for Required Regulatory Documents