



UNIVERSITY OF
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**University of Leicester and University Hospitals of Leicester NHS
Trust joint Research Support Office Standard Operating Procedures**

**University of Leicester (UoL) Research Governance Office
SOP S-1023 UoL**

**Investigator's Brochure (IB)/Summary of
Product Characteristics (SmPC)
Preparation, Review, Approval and Amendment for Research
Sponsored by the University of Leicester**

Version 3.2, Sept 2023

Office Base

Research Governance Office
University of Leicester
Academic Department, Ground Floor
Leicester General Hospital
Gwendolen Road
Leicester
LE5 4PW

Effective Date: October 2023

This SOP will be implemented in line with this document's effective date for all UoL Sponsored research still in set up. For active clinical research that is already in the recruitment phase (or further) at the time of implementation, this SOP must be implemented within 3 months of the effective date.

Please note the appendices associated with this SOP may be subject to interim changes. Please ensure that appendices are downloaded from the RGO webpages prior to use to ensure the latest version of the document is being used.

1.0 Introduction

This Standard Operating Procedure (SOP) describes the process to be adopted by a Chief Investigator when producing an Investigator's Brochure (IB) for a research study involving an Investigational Medicinal Product (IMP) to be used in either a new indication or as a new compound.

The outcome is that all research using IMPs has a comprehensive document detailing all known safety reference data and that this data is reviewed on at least an annual basis. Each IMP must have an IB.

2.0 Scope

This SOP applies to all research studies that are using, or intend to use, IMPs and that are sponsored by the University of Leicester (UoL).

3.0 Definition

An IB is part of the clinical trial authorisation (CTA) application. It documents all relevant information about the IMP, including chemical structure, non-clinical trials and clinical trials.

It should be prepared from all available information and evidence that supports the rationale for the proposed clinical trial and the safe use of the IMP within it. It should also detail which adverse reactions are expected and their frequency of occurrence, giving valuable safety information and guidance to the investigator(s) to use for assessing expectedness and determining the expedited reporting requirements of any suspected unexpected serious adverse reactions (SUSARs).

The IB is a key trial document required by the Competent Authority (CA) and the Research Ethics Committee (REC). It must be reviewed on at least an annual basis and updated if necessary.

3.1 When is a Full Investigator's Brochure Required?

3.1.1 When conducting an IMP study using a product that has not yet been granted a licensing authorisation (non- approved compound) a fully comprehensive IB is required. It is likely that this type of study will be categorised as Type C in accordance with the Medicines and Healthcare products Regulatory Agency (MHRA) Risk Based Assessment approach to IMP studies. However, this will be confirmed on a case-by-case basis at Sponsor Green Light Process risk assessment.

3.1.2 In cases where a licensed product is to be used outside of the licensed indication, or in a different subject population, it is not necessary to complete a full IB. A summary of relevant data that complements the existing Summary of Product Characteristics (SmPC) to support the use of the IMP in the study will be required instead. As Sponsor, UoL recommend that the summary is included within the protocol, and that a SmPC is appended to this document. It is likely that this type of study will be categorised as Type B in accordance with the MHRA Risk Based Assessment approach to IMP studies. However, this will be confirmed on a case-by-case basis at Sponsor Green Light Process risk assessment.

3.1.3 In cases where a licensed product is being used within the terms of its license an IB will not be required. The SmPC as published by the product manufacturer will be an appropriate document to use as Reference Safety Data for assessments of expectedness. It is likely that this type of study will be categorised as Type A in accordance with the MHRA Risk Based Assessment approach to IMP studies. However, this will be confirmed on a case-by-case basis at Sponsor Green Light Process risk assessment.

4.0 Preparation of the IB

The Chief Investigator is responsible for coordinating the production of the IB. It is recommended that input from other relevant personnel (i.e. pharmacy) is sought, and that all review comments are retained. It is important that where comments have been submitted but not incorporated, a record is kept along with a brief explanation as to why the suggested changes were not made.

The IB or SmPC forms part of the essential documents for an IMP study, and must be included within the documentation submitted to the Sponsor to be reviewed as part of the Sponsor review process. Where there is no evidence to show input during the preparation and production of an IB, a final review and sign off from the Clinical Trials Pharmacist will be required. This will be requested by the Research Governance Office.

The IB must not be forwarded to the Competent Authority (MHRA in the UK) or the REC prior to Sponsor sign off. The IB template is provided in Appendix 1.

4.1. Points to Consider when Preparing the Investigator's Brochure

The IB or equivalent document, e.g. SmPC for marketed products, must be used as the reference document for assessments of the expectedness of any adverse reaction that might occur during the clinical trial.

5.0 Review/Updates to the Investigator's Brochure

The IB or SmPC must be reviewed on at least an annual basis. The review and the decision to continue to use the existing version or to change the document must be documented using the UoL IB/SmPC review template (Appendix 2). This process must be completed irrespective of whether changes were necessary. It is expected that the Clinical Trials Pharmacist be involved in the review/revision process of the IB.

More frequent review/revision may be appropriate, but this will depend on the stage of development of the drug or the generation of relevant new information. However, in accordance with GCP, relevant new information may be so important that it should be communicated to all Investigators, and possibly to the REC and/or regulatory authority before an IB revision has taken place.

A copy of the revised IB must be sent to the Sponsor for final sign off before it is sent to all sites. The Sponsor will send to the Clinical Trials Pharmacist for review and sign off at every revision/review unless evidence of their involvement can be provided. The IB template requires signatures from the Chief Investigator, Clinical Trials Pharmacist and the Sponsor for each version.

It is the responsibility of the CI to ensure that all sites have most recent version of the IB once signed off by the Sponsor or the most recent version of the SmPC. It is expected that evidence be provided to show that the sites have received the latest version. An email trail will be acceptable evidence.

5.1 Submission of Revised Investigator's Brochures

Where an IB requires revision and not simply review, amendments will be made to the document, which requires both regulatory authority and REC approval. It is important to include the following information in the submission:

- how the risk/benefit assessment of the study has been affected
- how these changes impact the trial
- what alterations to the protocol are proposed to take account of these changes?

Where revisions alter benefit/risk assessment of the study, the revised IB must be submitted as a substantial amendment. Details on how to submit a substantial amendment can be found

in SOP S-1018 UoL. Where alterations to the protocol are required, it is advisable to submit all revised documents in one amendment.

5.2 Amendments Regarding Investigator's Brochure Safety Updates

The Reference Safety Information (RSI) for any IMPs involved in a clinical trial must stay consistent during each reporting period. At the end of the reporting period the Sponsor in collaboration with the Chief Investigator may assess the new safety information that has been generated and submit any proposed safety changes to the IB or RSI as a substantial amendment. This amendment should be supported by the Annual Safety Report/Development Safety Update Report and approved before the RSI is changed.

Changes to the RSI include the downgrading of reactions from unexpected to expected; until the amendment justifying the downgrading has been approved, the events must be treated as unexpected.

6.0 Responsibilities

Responsibility	Undertaken by	Activity
Sponsor	Head of Research Governance or delegate	Confirm an IB/SmPC is included within the Sponsor documentation submitted for review.
Sponsor	Head of Research Governance or delegate	Confirm with Pharmacy that a copy has been received to enable Pharmacy process to begin
Chief Investigator	Chief Investigator	Generate IB or provide copy of existing SmPC to the Sponsor as part of the Sponsor review documentation requirements.
Chief Investigator	Chief Investigator	Ensure that the annual review of IB/SmPC is undertaken, documented and distributed as required
Pharmacy	Clinical Trial Pharmacists	Ensure that an up to date IB is maintained in the Pharmacy file
Chief Investigator / Sponsor	Chief Investigator / Head of Research Governance or Delegate	Ensure revisions to IB are sent for relevant approvals to MHRA & REC.

7.0 Development and approval Record for this document

This table is used to track the development and approval of the document

Author	Job title	Reviewed by	Approved by	Date approved
Cat Taylor	Head of Research Governance	UoL Research Management and Operations Group (RSMOG)		28.09.2023

8.0 Review Record

This table is used to track the changes made on revised/reviewed versions.

Date	Issue Number	Reviewed By	Description Of Changes (If Any)
April 2015	2	RSMOG	Changes to logos, minor amendments to text and footer. Document retitled to include SPC in addition to IB. Addition of Loughborough University to front page.
Oct 2016	3	Diane Delahooke	Change of logo, addition of RSI review statement in Appendix 2.
Sept 2021	3.1	Cat Taylor	Administrative changes
September 2023	3.2	Cat Taylor	Administrative changes Minor updates to wording Removal of distribution record Appendix 1 – Formatting changes and minor administrative changes Appendix 2 – Administrative changes