South Eastern Health and Social Care Trust

Standard Operating Procedure
(SOP)
Research and Development Office

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1. INTRODUCTION

The Investigator's Brochure (IB) is a compilation of the clinical and nonclinical data on the investigational product(s) that are relevant to the study of the product(s) in human subjects. Its purpose is to provide the investigators and others involved in the trial with the information to facilitate their understanding of the rationale for, and their compliance with, many key features of the protocol, such as the dose, dose frequency/interval, methods of administration and safety monitoring procedures. The IB also provides insight to support the clinical management of the study subjects during the course of the clinical trial. The information should be presented in a concise, simple, objective, balanced, and non-promotional form that enables a clinician, or potential investigator, to understand it and make his/her own unbiased risk-benefit assessment of the appropriateness of the proposed trial. For this reason, a medically qualified person should generally participate in the editing of an IB, but the contents of the IB should be approved by the disciplines that generated the described data.

This guideline delineates the minimum information that should be included in an IB and provides suggestions for its layout. It is expected that the type and extent of information available will vary with the stage of development of the investigational product. If the investigational product is marketed and its pharmacology is widely understood by medical practitioners, an extensive IB may not be necessary. Where permitted by regulatory authorities, a basic product information brochure, package leaflet, or labelling may be an appropriate alternative, provided that it includes current, comprehensive, and detailed information on all aspects of the investigational product that might be of importance to the investigator. Once an investigational product has a marketing approval the IB is superseded by the Summary of Product Characteristics (SmPC). The approved summary of product characteristics (SmPC) may be used in place of an investigator brochure (IB) if the Investigational Medicinal Product (IMP) is authorised in any EU Member State and is used according to the terms of the marketing authorisation. If the conditions of use in the clinical trial differ from those authorised, the SmPC should be supplemented with a summary of relevant clinical and non-clinical data that support the use of the IMP in the clinical trial.

The IB should be reviewed at least annually and revised as necessary. More frequent revision may be appropriate depending on the stage of development and the generation of relevant new information. However, in accordance with Good Clinical Practice, relevant new information may be so important that it should be communicated to the investigators, and possibly to the Research Ethics Committees (RECs) and/or regulatory authorities before it is included in a revised IB.

Generally, the sponsor is responsible for ensuring that an up-to-date IB is made available to the investigator(s) and the investigators are responsible for providing the up-to-date IB to the responsible RECs. In the case of an investigator led trial, the sponsor-investigator should determine whether a brochure is available from the commercial manufacturer. If the investigational product is provided by the sponsor-investigator, then he or she should provide the necessary information to the trial personnel. In cases where preparation of a formal IB is impractical, the sponsor-investigator should provide, as a substitute, an expanded background information

section in the trial protocol that contains the minimum current information described in this guideline.

2. OBJECTIVE

This objective of this SOP is to describe when an IB is required, the minimum content required and when to update the IB.

3. SCOPE

This SOP applies to all Clinical Trials of IMPs (CTIMPs) that are sponsored or co-sponsored by the SEHSCT.

4. PROCEDURE

4.1 General Considerations

The IB should include:

4.1.1 Title Page

This should provide the sponsor's name, the identity of each investigational product (i.e., research number, chemical or approved generic name, and trade name(s) where legally permissible and desired by the sponsor). An edition number, release date and a reference to the number and date of the edition it supersedes, be provided. An example is given in Appendix 1.

4.1.2 Confidentiality Statement

The sponsor may wish to include a statement instructing the investigator/recipients to treat the IB as a confidential document for the sole information and use of the investigator's team and the IRB/IEC.

4.2 Contents of the Investigator Brochure

An example of the Contents of an Investigator Brochure is given in Appendix 2, however at the time of production of an IB the European Commission - Detailed guidance on the request to the competent authorities for authorisation of a clinical trial on a medicinal product for human use, the notification of substantial amendments and the declaration of the end of the trial (CT-1) (2010/C 82/01) and current MHRA requirements and guidance should be followed.

As sponsor the Research Office will assess the suitability of the Investigator Brochure.

For most Trust sponsored trials a Summary of Product Characteristics will be used, not an Investigator Brochure. If an SmPC is not available then as sponsor the Trust will require the CI to generate a suitable IB.

4.3 IB UPDATES

The IB for each IMP will be updated and validated at least once a year. If no changes or updates are required or available, a statement signed by the CI stating this fact will be inserted into the front of the dossier and version and edition control updated.

Annual updates to the investigator's brochure which alter the benefit:risk assessment of the trial should be submitted as substantial amendments to the MHRA and the main REC. The following information should be provided in the submission:

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

Annual updates to the investigator's brochure which do not alter the benefit:risk assessment of the trial should not be submitted to the MHRA or main REC as substantial amendments.

If an SmPC is being used then it must be checked regularly to confirm if updates are available and assess the impact of the update to the trial.

4.4 IB TRACKING

Investigator Brochures are controlled documents and as such, their circulation must be tracked and receipted to ensure that all Investigators and recipients are in possession of the latest and most up to date version.

5. REGULATIONS, GUIDELINES, REFERENCES, SOP LINKS etc.

The Medicines for Human Use (Clinical Trials) Regulations 2004
http://www.uk-legislation.hmso.gov.uk/si/si2004/20041031.htm

The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006
http://www.opsi.gov.uk/si/si2006/20061928.htm

European Commission Detailed guidance on the request to the competent authorities for authorisation of a clinical trial on a medicinal product for human use, the notification of substantial amendments and the declaration of the end of the trial (CT-1) (2010/C 82/01)

6. APPENDICES

6.1 Template Title Page

6.2 Template Table of Contents

6.1 Template Title Page

TITLE PAGE (Example)

SPONSOR'S NAME

Product:

Research Number:

Name(s): Chemical, Generic (if approved)

Trade Name(s) (if legally permissible and desired by the sponsor)

INVESTIGATOR'S BROCHURE

Edition Number:
Release Date:

Replaces Previous Edition Number:
Date:

6.2 Template Table of Contents

TABLE OF CONTENTS OF INVESTIGATOR'S BROCHURE (Example)

- Confidentiality Statement (optional)
- Signature Page (optional)

1 Table of Contents

2 Summary

3 Introduction

4 Physical, Chemical, and Pharmaceutical Properties and Formulation

5 Nonclinical Studies
5.1 Nonclinical Pharmacology
5.2 Pharmacokinetics and Product Metabolism in Animals
5.3 Toxicology

6 Effects in Humans
6.1 Pharmacokinetics and Product Metabolism in Humans
6.2 Safety and Efficacy
6.3 Marketing Experience

7 Summary of Data and Guidance for the Investigator

NB: References on
1. Publications
2. Reports
These references should be found at the end of each chapter
Appendices (if any)