Investigator’s Brochure

Introduction

The Investigator’s Brochure (IB) is given to clinicians, investigators, and other healthcare professionals involved in the conduct of clinical trials (for instance, the clinical trial coordinators and study nurses). The IB is a compilation of non-clinical and clinical data relevant to the study of the medicine in humans – it is the single most comprehensive document summarising the information on an investigational medicinal product.

Investigator’s Brochures are prepared by the sponsor, who also controls the distribution of the document. The IB for a clinical trial is submitted to national competent authorities (NCAs) for approval along with the Clinical Trial Application (CTA).

Why are Investigator’s Brochures important?

The IB provides the investigator and other staff with background information about the investigational medicinal product in order to help them work in line with the study protocol. It provides the clinician or potential investigator with the information they need to assess the appropriateness of a trial, including the benefit-risk ratio, in an independent and unbiased way.

The information in the IB also provides insight supporting the clinical management of study participants during the clinical trial, including information about doses, dose frequency, methods of administration, and safety monitoring procedures.

What is in an Investigator’s Brochure?

According to the legal framework for good clinical practice in clinical trials, the information in the IB should be ‘concise, simple, objective, balanced, and non-promotional’. This is particularly important to ensure that an investigator can understand the document and make an informed and unbiased benefit-risk assessment regarding the appropriateness of the trial.

The content of the IB should be approved by the researchers that generated the data, and it should be reviewed and updated at least once a year or upon receipt of significant new data.

The IB must include for each investigational medicinal product:

- Information on the sponsor’s name and the identity of the product (research number, generic and trade names).
- A confidentiality statement with instructions to treat the document as confidential and for the exclusive use of the investigator’s team, review boards, and ethics committees.
- A compilation of results gathered from non-clinical and clinical studies of the medicine.
- Background information on the properties and history of the investigational medicinal product.

Investigator’s Brochure: Table of Contents

An IB contains the following sections:

- Summary
    - Guidance for the investigator, highlights important information relevant to the development stage of the product.
- Introduction
    - Background information, basis for performing research, the chemical and generic name of the active substance (and trade name where applicable) in the investigational product, and the planned indication.
- Physical, chemical, and pharmaceutical properties and formulation
    - Relevant properties of the investigational product and excipients (inactive ingredients), including similarities to other known compounds; instructions for storage and handling of the product.
- Non-clinical studies
    - Summary results of pharmacology, toxicology, pharmacokinetic, and metabolism studies; explanations of methodology used, results, and relevance of findings; information about animal/laboratory studies and doses. This summary should also contain a discussion of the relevance of the findings to the compound and the possible unfavourable and unintended effects in humans.
- Effects in humans
    - Results of toxicology, pharmacokinetics, metabolism, safety, and efficacy studies, and where possible summaries of each clinical trial; information from previous market experience, including countries where the investigational product has or has not been approved.
- Summary of data and guidance for investigators
    - Overall discussion of non-clinical and clinical data to help anticipate adverse drug reactions (ADRs) or other problems in clinical trials.

How is the Investigator’s Brochure regulated?

Regulatory authorities (such as the European Medicines Agency (EMA) and national competent authorities (NCAs)) require an up-to-date IB for any medicine being studied. An IB is submitted to the regulatory authorities along with the Clinical Trial Application (CTA), and regulatory authorities also review any updates to the IB to ensure that it is accurate, complete, and impartial.

In some cases, for instance if the investigational product already has a marketing authorisation (MA) and its pharmacology is widely understood by medical practitioners, an extensive IB may not be necessary. In such cases, the Summary of Product Characteristics (SmPC) – or, where permitted by regulatory authorities, a package leaflet or labelling – may be used instead as an appropriate alternative to an IB. However, the substitute must provide current, comprehensive, and detailed information on all aspects of the investigational product that might be of importance to the investigator.

If a marketed product is being studied for a new use (a new indication), an IB specific to that new use should be prepared. When relevant new information is available, the investigators and Research Ethics Committees (RECs) should be told – where possible, before this new information is included in the revised IB.