SOP Title: Investigator's Brochure Content, Design, Amendments, Filing & Distribution

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Author Signature:  **Date:** 10 October 2017
The author is signing to confirm the technical content of this document

Institution name: Melbourne Children's

Reviewed and Approved by:
These signatures confirm the reviewers agree with the technical content of the document and that this document is approved for implementation at the Melbourne Children's Campus.

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Signature:  **Date:** 9 November 2017

This document is effective from the date of the last approval signature and will be reviewed in two years.

Document History

Revision	Modified by	Change No.	Description of Change
1.0	[Author]	N/A	New Issue

1. AIM

To describe the procedures related to investigator's brochure content, design, amendments, filing and distribution for MCRI developed products used in clinical trials of Investigational Medicinal Products (IMPs) and Investigational Medical Devices (IMDs) sponsored by MCRI.

2. SCOPE

This SOP:

- Relates to MCRI-developed products that do not have a Therapeutic Goods Administration (TGA) Marketing Authorisation and are used as IMPs/IMDs in trials sponsored by MCRI
- Does not apply where another organisation is responsible for creating and maintaining the IB.
- Is applicable to all phases of clinical investigation of IMPs/IMDs

The Coordinating Principal Investigator (CPI) / Principal Investigator (PI) must assume the role of Sponsor with regards to the responsibility for creating and maintaining the IB for any Investigator-initiated trial (IIT) involving MCRI-developed products that do not have a Marketing Authorisation. In this document, this role is termed the Sponsor-Investigator.

3. APPLICABILITY

The Sponsor-Investigator and any qualified member of the research team at Melbourne Children's who have been delegated trial-related activities involving the content, design, amendments, filing and distribution of the Investigator's Brochure.

4. BACKGROUND

The Investigator's Brochure (IB) is a compilation of the clinical and non-clinical data on the investigational product(s) that are relevant to the study of the product(s) in human subjects.

Its purpose is to provide Investigators and study team 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.
- Safety information that acts as a reference against which the expectedness of an adverse reaction is determined.
- Insight to support the clinical management of the study subjects during the course of the clinical trial.

The Investigator must provide the HREC with a current copy of the Investigator's Brochure at the time of ethics submission.

5. PROCEDURE

5.1 Content of the Investigator's Brochure

The Sponsor-Investigator/delegate is responsible for creating and maintaining the IB in accordance with this SOP.

The specific content of an IB will vary depending on whether the subject of investigation is a medicinal product or device. For guidance on the content and design of the IB, refer to the Note for guidance on Good Clinical Practice (CPMP/ICH/135/96) annotated with TGA comments DSEB, July 2000.

The use of an IB template is recommended to facilitate the inclusion of all the required elements as per ICH GCP. CRDO recommends the Niche.org IB template available at the following link: http://www.niche.org.uk/resource_centre.html

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.

5.2 Finalisation of the Investigator's Brochure

The Sponsor-Investigator is responsible for reviewing the IB to ensure:

- It includes the required sections
- It lists the expected side effects

5.3 Filing and Distribution of the Investigator's Brochure

The Sponsor-Investigator/delegate is responsible for filing the IB in the Trial Master File (TMF) and distributing the approved IB to applicable parties, such as Investigators at participating sites and to the HREC.

5.4 Updates to the Investigator's Brochure

The Sponsor-Investigator is responsible for ensuring the IB is reviewed at least annually. More frequent revision may be appropriate depending on the stage of development and the generation of relevant new information. The Sponsor-Investigator/delegate is responsible for making revisions to the document and must approve the updates before releasing the new version.

New versions of the IB must contain a revision history indicating the changes that were made to the document.

The Sponsor-Investigator/delegate is responsible for filing the revised IB in the TMF and distributing the newly approved version to applicable parties including Investigators at participating sites and to the HREC.

6. GLOSSARY

Clinical Research Development Office (CRDO)

The Clinical Research Development Office (CRDO) provides education and training to facilitate and increase capacity for clinical and public health research across the Melbourne Children's campus. This includes the development and implementation of Standard Operating Procedures and templates to enable researchers to conduct high quality research.

Good Clinical Practice (GCP)

A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

Human Research Ethics Committee (HREC)

A body which reviews research proposals involving human participants to ensure that they are ethically acceptable and in accordance with relevant standards and guidelines. The National Statement requires that all research proposals involving human participants be reviewed and approved by an HREC and sets out the requirements for the composition of an HREC.

International Conference on Harmonisation (ICH)

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use is a joint initiative involving both regulators and research-based industry focusing on the technical requirements for medicinal products containing new drugs.

Investigator

An individual responsible for the conduct of a clinical trial at a trial site and ensures that it complies with GCP guidelines.

- If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the Principal Investigator (PI). In this instance they may delegate tasks to other team members.
- If a trial is conducted at more than one trial site, there will be a PI taking overall responsibility for the trial will be known as the Coordinating or Chief Principal Investigator (CPI).

Where the PI or CPI takes on responsibilities of the Sponsor, this role is termed the Sponsor-Investigator. Sponsor-Investigator.

Investigator's Brochure (IB)

A compilation of the clinical and non-clinical data on the investigational product(s) that are relevant to the study of the product(s) in human subjects.

Investigational Medical Device

Medical device being assessed for safety or performance in a clinical investigation. This includes medical devices already on the market that are being evaluated for new intended uses, new populations, new materials or design changes.

Investigational Medicinal Product

A pharmaceutical from of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, a new patient group or when used to gain further information about an approved use.

Melbourne Children's

This term is used to encompass all staff from The Royal Children's Hospital, Murdoch Children's Research Institute and Department of Paediatrics University of Melbourne who initiate or carry out research under one or more of these institutional affiliations.

Protocol

A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial.

Standard Operating Procedure (SOP)

Detailed, written instructions to achieve uniformity of the performance of a specific function.

Sponsor-Investigator

Sponsor-Investigator is a term used for investigator-initiated studies. It is an individual who is responsible for both the initiation and conduct of a study. The term does not include any person other than an individual. This person will be:

- the Principal Investigator for single-site investigator-initiated studies
- the Coordinating Principal Investigator for multi-centre investigator-initiated studies

Sub/Associate Investigator

Any individual member of the clinical trial team designated and supervised by the Principal investigator at a trial site to perform trial-related procedures and/or to make important trial-related decisions (e.g., associates, residents, research fellows, clinical research coordinators. The P.I. will designate who will be nominated as Sub/Associate Investigators for that site.

7. REFERENCES

Note for guidance on Good Clinical Practice (CPMP/ICH/135/96) annotated with TGA comments DSEB, July 2000.

Integrated Addendum to ICH E6 (R1): Guideline for Good Clinical Practice E6 (R2), dated 9 November 2016

NHMRC National Statement on Ethical Conduct in Human Research, 2007 (and all updates)

NHMRC Safety monitoring and reporting in clinical trials involving therapeutic goods, November 2016

END OF STANDARD OPERATING PROCEDURE