CLINICAL TRIALS - INVESTIGATOR'S BROCHURE

PROCEDURE ©

DOCUMENT SUMMARY/KEY POINTS

- The purpose of this procedure is to ensure that Investigator's Brochures (IB) developed or used by SCHN Investigators for clinical trials comply with NSW Health, SCHN and regulatory requirements.
- This procedure must be followed by all personnel involved in the conduct of clinical trials.

Approved by:	SCHN Policy, Procedure and Guideline Committee	
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Team Leader:	Clinical Research Manager	**Area/Dept**: Kids Research

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CHANGE SUMMARY

- Not applicable – New Sydney Children's Hospitals Network Procedure.

READ ACKNOWLEDGEMENT

- Read/Acknowledge Only – Personnel involved in the conduct of clinical trials.

TABLE OF CONTENTS

This document reflects what is currently regarded as safe practice. However, as in any clinical situation, there may be factors which cannot be covered by a single set of guidelines. This document does not replace the need for the application of clinical judgement to each individual presentation.

Purpose/Scope

The purpose of this procedure is to ensure that Investigator's Brochures (IB) developed or used by SCHN Investigators for clinical trials comply with NSW Health, SCHN and regulatory requirements. This procedure must be followed by all personnel involved in the conduct of clinical trials.

It is acknowledged that the content of the IB will vary depending on whether the investigational agent is a medicinal product, a device or other therapeutic intervention. The descriptions provided below reference the use of a medicinal product, in the case of a device or other therapeutic intervention there may be additional considerations and/or terminology applicable.

Background

An Investigator's Brochure (IB) is a document that provides objective information about the quality, safety and effectiveness of an unapproved Investigational Product (IP), through summarising the relevant clinical and non-clinical data.

The information in the IB provides the Investigator with an understanding of the rationale for protocol requirements such as the IP dose, dose frequency, mode of administration, as well as any safety monitoring procedures. The IB also provides insight to support the clinical management of participants, such as the investigation of adverse events that may occur during the course of their involvement in a clinical trial.

Procedure

Development

The IB is usually prepared and maintained by the manufacturer of the IP. In many instances the manufacturer will be a commercial entity who is also acting as the Sponsor for the clinical trial, and as such, is responsible for approval of the IB.

In the case of investigator-initiated or cooperative group trials of unapproved IP, such as IP developed by SCHN, the responsibility for preparation and maintenance of the IB will be held by the Coordinator Principal Investigator (CPI) in consultation with the Trial Management Committee (TMC).

The type and extent of information covered in the IB will vary according to the stage of development for the IP. However, at a minimum, IBs must include the information outlined in Section 7 of the TGA Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95). The use of the standard 'Table of Contents' template (Section 7.5) is recommended to ensure adherence with regulatory requirements.

For clinical trials involving advanced therapeutics, additional considerations, as outlined in the European Commission Guidelines on Good Clinical Practice specific to Advanced Therapy Medicinal Products, must also be addressed.

For approved (marketed) products, the Product Information (PI) may be deemed suitable for use in lieu of an IB, provided that it includes current, comprehensive and detailed information on all aspects of relevance to the proposed use of the IP. If the marketed product is being evaluated for a new indication and does not meet the former requirements, then an IB specific to that use should be prepared. The current PI for approved products can be accessed via the TGA's Australian Register of Therapeutic Goods (ARTG).

Implementation

As per the TGA Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) Section 4.1.2, the Investigator is required to be thoroughly familiar with the appropriate use of the IP, as described in the current Protocol and IB (or equivalent).

The Investigator/Institution must ensure that the responsible HREC has provided approval for the IB or equivalent information about the IP, prior to the commencement of the clinical trial.

The frequency with which revisions to the IB are required will be dependent on the stage of development for the IP and the nature of new data that is generated. However, it is recommended that IBs are reviewed at least annually.

The revised IB must be given a new version number and date and a history of changes provided (either in the IB or as a separate summary of changes document). If no revisions are necessary, the Sponsor/CPI should ensure that a Note to File (NTF) or equivalent (e.g. Statement of Validity) is prepared to denote that the review was undertaken and no revisions were warranted.

Regardless of the frequency with which the IB is revised, any new, significant information about the IP that may have an impact on the continued ethical acceptability of the clinical trial or indicate the need for amendments to the protocol, must be communicated to Investigators, the HREC and regulatory authorities (as applicable) as soon as possible.

The Investigator must also ensure that they obtain acknowledgement from the HREC for receipt of the updated IB; and any amendments to the protocol or other documentation implemented in response to new, significant information about the IP.

The Investigator also must not implement any deviation from, or changes to, the protocol (e.g. as a result of new, significant information about the IP or for other reasons) without agreement by the Sponsor and documented approval from the responsible HREC/RGO. The only exception to this being where a deviation is necessary to eliminate an immediate hazard(s) to participants, or when the change(s) involves only logistical or administrative aspects of the trial.

Abbreviations and Definitions

ARTG	Australian Register of Therapeutic Goods
CMI	Consumer Medicine Information
CPI	Coordinating Principal Investigator
GCP	Good Clinical Practice
HREC	Human Research Ethics Committee
IB	Investigator's Brochure
ICH	International Conference on Harmonisation
IP	Investigational Product
ISO	International Organization for Standardization
NHMRC	National Health and Medical Research Council
NSW	New South Wales
NTF	Note To File
PD	Policy Directive
PI	Product Information
RGO	Research Governance Office
SCHN	Sydney Children's Hospitals Network
TGA	Therapeutic Goods Administration
TMC	Trial Management Committee

Related Documents

1. European Commission - Guidelines on Good Clinical Practice specific to Advanced Therapy Medicinal Products - https://ec.europa.eu/health/system/files/2019-10/atmp_guidelines_en_0.pdf
2. ISO 14155:2020 – Clinical Investigation of medical devices for human subjects – Good clinical practices - https://www.iso.org/obp/ui/#iso:std:71690:en
3. NHMRC (2016) – Guidance - Safety Monitoring and Reporting in clinical trials involving therapeutic goods - https://www.nhmrc.gov.au/about-us/publications/safety-monitoring-and-reporting-clinical-trials-involving-therapeutic-goods
4. NHMRC - National Statement on Ethical Conduct in Human Research (2007) - Updated 2018 - https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018
5. NHMRC – Reporting of Serious Breaches of Good Clinical Practice (GCP) or the Protocol for Trial Involving Therapeutic Goods – https://www.nhmrc.gov.au/about-us/publications/safety-monitoring-and-reporting-clinical-trials-involving-therapeutic-goods#block-views-block-file-attachments-content-block-1
6. NSW Health PD2017-039 – Safety Monitoring and Reporting for Clinical Trials Conducted in NSW Public Health Organisations - https://www1.health.nsw.gov.au/pds/Pages/doc.aspx?dn=PD2017_039
7. SCHN Policy – Clinical Research [DRAFT]
8. SCHN Policy – Sponsorship [DRAFT]
9. SCHN Policy 2015-9060 – Research – Authorisation of Proposals to Conduct Research on Humans - http://webapps.schn.health.nsw.gov.au/epolicy/policy/3604
10. SCHN Policy 2012-9029 – Research – Ethical and Scientific Review of Human Research - http://webapps.schn.health.nsw.gov.au/epolicy/policy/2683
11. SCHN Procedure 2019-145 – Clinical Research - Record Keeping - http://webapps.schn.health.nsw.gov.au/epolicy/policy/4661
12. SCHN Procedure - Clinical Trials – Protocol [DRAFT]
13. TGA – Australian Register of Therapeutic Goods - https://www.tga.gov.au/australian-register-therapeutic-goods
14. TGA - Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) - https://www.tga.gov.au/sites/default/files/ich13595an.pdf
15. TGA - Note for Guidance on Clinical Safety Data Management: Definitions and Standards for Expedited Reporting (CPMP/ICH/377/95) - https://www.tga.gov.au/publication/note-guidance-clinical-safety-data-management-definitions-and-standards-expedited-reporting