Western Health

STANDARD OPERATING PROCEDURE

Sponsor Obligations for Investigator Initiated Trials

Standard Operating Procedure

Western Health

SOP reference	011
Version:	3.0 dated June 2019
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Approved by	Mr Bill Karanatsios, Research Program Director
Signature and date	

Amendment History

VERSION	DATE	AMENDMENT DETAILS
2.0	04 Dec 2015	
3.0	June 2019	Updated to align with MACH SOPs

1. AIM

To define Sponsor Responsibilities in the conduct of Investigator driven studies.

2. SCOPE

All phases of clinical investigational for medical products, medical devices and diagnostics.

3. APPLICABILITY

Where Western Health (WH) is acting in the capacity of sponsor.

4. PROCEDURE

4.1. Sponsor Responsibilities

The sponsor for an investigator initiated trial may be an individual (e.g. the investigator or department head), a company (e.g. a not-for-profit) an organisation (e.g. a charity) or an institution (e.g. a public hospital). Each institution will have its own policy regarding the sponsorship role. For all Investigator Initiated Studies where Western Health (WH) is the Lead site WH assumes the role of Sponsor.

The sponsor must:

STEP	ACTION
4.1.1	Ensure that any clinical trial involving a drug or device not approved for marketing in Australia (or approved for an indication other than that proposed in the clinical trial) and for which there is no commercial sponsorship is duly notified to the insurer.
4.1.2	Ensure that Quality Assurance and Quality Control systems are in place to ensure trials are conducted; data is gathered, and subsequently reported, in compliance with Good Clinical Practice (GCP), the trial protocol, and any Therapeutic Goods Administration (TGA) requirements.
4.1.3	Secure agreement from all involved parties to ensure direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by domestic and foreign regulatory authorities
4.1.4	Ensure that no omissions occur which might disentitle themselves, the Institute or Human Research Ethics Committee (HREC), to such indemnity as could otherwise be available under the Medical Indemnity and Public Liability Policies.
4.1.5	Select appropriate investigator(s) and institution(s) to conduct and complete the trial according to GCP standards.
4.1.6	Allocate definitive, unambiguous allocation of trial-related duties and responsibilities to trial-related staff.
4.1.7	Have in place appropriate insurance and provide an indemnity for the trial and trial-related staff, as well as measures for participant compensation for trial-related

	injury.
4.1.8	Ensure the confirmation of ethical approval from the relevant HREC(s), authorisation form from the Institution Research Governance Office (RGO) and notification of the approval etc. to the TGA.
4.1.9	Ensure that funding arrangements are declared in the protocol submissions to warrant that the clinical trial retains its "investigator initiated" status under the Victorian Managed Insurance Authority (VMIA) policy.
4.1.10	Ensure that appropriate medical expertise is on hand for trial-related medical queries or patient care.
4.1.11	Utilise qualified individuals throughout all stages of the trial process to help inform the trial design and data analysis.
4.1.12	Should provide appropriate resources and supervision to administer data handling, record keeping, and overall trial management.
4.1.13	Maintain all records relating to the study for a period of at least 15 years from the end of the Trial (i.e. study closeout) in the case of adults and at least 25 years from the end of the trial (i.e. study closeout) in the case of children.
4.1.14	Ensure that agreements made with the investigator/institution and any other parties involved with the clinical trial, are in writing, as part of the protocol or in a separate agreement.
4.1.15	Ensure that Investigational Products are available to participants free of charge.
4.1.16	Maintain a system for the disposition of unused investigational product and for the documentation of this disposition.
4.1.17	Take appropriate urgent safety measures (with investigator) where necessary.
4.1.18	Keep records of all adverse events (AEs) reported by investigators.
4.1.19	Ensure appropriate manufacture, packaging, labelling/coding and distribution to trial sites of all investigational medicinal products.
4.1.20	Provide ongoing safety evaluation, updates and Significant Safety Issues (SSIs) and Suspected Unexpected Serious Adverse Reaction (SUSAR) reporting to participating sites, the HREC and relevant regulatory authorities as required
4.1.21	Ensure adherence to and compliance with Monitoring/Audit/Inspection requirements.
4.1.22	Act on any non-compliance with the protocol, Standard Operating Procedures (SOPs), GCP and /or any applicable regulatory requirements.

4.1.23	Promptly notify all sites, the HREC and relevant regulatory authorities of any premature termination or suspension of the trial in question.
4.1.24	For multisite trials the sponsor must ensure that: **4.1.24.1** all sites comply with the protocol and the relevant regulatory authority(ies) requirements **4.1.24.2** all sites obtain ethical approval for the conduct of the trial **4.1.24.3** all sites are aware of their roles and responsibilities in the conduct of the trial **4.1.24.4** facilitates communication between investigators **4.1.24.5** ensure that the trial will not be conducted (when engaging foreign jurisdictions) in lesser terms than the terms expressed in the National Statement on Ethical Conduct in Human Research 2007.

5. GLOSSARY

Adverse event (AE)

Any untoward medical occurrence in a patient administered a medicinal product and which does not necessarily have to have a causal relationship with this treatment. An adverse event can therefore be any unfavourable and unintended sign (for example, an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to this medicinal product.

Associate Investigator

Any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions (e.g., associates, residents, research fellows). Also referred to as "Sub-Investigator".

Clinical Trials Agreement (CTA)

An agreement governing the safety and efficacy of outside collaborators, proprietary biologics or pharmaceutical compounds in clinical studies.

European Union (EU)

A politico-economic union of European countries

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.

Principal Investigator (PI)

An individual responsible for the conduct of a clinical trial at a trial site ensuring 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. In this instance they may delegate tasks to other team members.

Investigator initiated trial

A clinical trial that has the following characteristics:

- A pharmaceutical/device company is not acting as the sponsor for the purposes of the CTN application.
- A pharmaceutical/device company is not fully funding the conduct of the study, that is, making payment to the relevant hospital or investigator.
- The clinical trial addresses relevant clinical questions and not industry needs.
- The principal investigator or the Hospital/Institution is the primary author and custodian of the clinical trial protocol.

Investigational Product

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

Medical Indemnity

Is a form of professional **indemnity** insurance cover defined by Australian legislation – the Medical Indemnity (Prudential Supervision and Product Standards) Act 2003

Monitoring

The act of overseeing the progress of a clinical trial and ensuring that it is conducted, recorded, and reported in accordance with the protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirement(s).

Research Governance Office (RGO)

Site/institutional office that are accountable for the research activities conducted at their site to ensure that research is conducted according to established ethical principles, guidelines for responsible research conduct, relevant legislation and regulations and institutional policy.

Significant Safety Issue (SSI)

A safety issue that could adversely affect the safety of participants or materially impact on the continues ethical acceptability or conduct of the trial.

Serious adverse event (SAE)

Any untoward medical occurrence that at any dose:

- Results in death.
- Is life-threatening.

(NOTE: The term "life-threatening" in the definition of "serious" refers to an event/reaction in which the patient was at risk of death at the time of the event/reaction; it does not refer to an event/ reaction which hypothetically might have caused death if it were more severe).

- Requires inpatient hospitalisation or results in prolongation of existing hospitalisation.
- Results in persistent or significant disability/incapacity.
- Is a congenital anomaly/birth defect.
- Is a medically important event or reaction.

Source Document

Original documents (where the data was first recorded), data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, participants' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, participant files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial).

Sponsor

An individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial.

Suspected Unexpected Serious Adverse Reaction (SUSAR)

An adverse reaction that is both serious and unexpected

Therapeutic Goods Administration (TGA)

Australia's regulatory agency for medical drugs and devices.

Urgent Safety Measure (USM)

A measure required to be taken in order to eliminate an immediate hazard to a participant's health or safety. *Note: This type of significant safety issue can be instigated by either the investigator or sponsor and can be implemented before seeking approval from HREC's or institutions.*

Victorian Managed Insurance Authority (VMIA)

Victorian Insurance and Risk management statutory authority

6. REFERENCES

1. Based on VMIA GCP SOP No.011 Version:1.0 Dated 17 September 2007
2. Based on MACH GCP SOP No.011 Version 1.0
3. Note for guidance on Good Clinical Practice (CPMP/ICH/135/96) annotated with TGA comments DSEB, July 2000, section 5.
4. Standard Operating Procedures for Clinical Investigators, World Health Organisation, version 1.1.
5. EU Clinical Trials Directive, Sponsorship responsibilities in publicly funded trials, Medicines for Human Use (Clinical Trials) Regulations 2004, section 5.
6. Australian Clinical Trial Handbook – Guidance on conducting clinical trials in Australia using 'unapproved' therapeutic goods version 2.2 (October 2016)
7. Clinical Trials - Insurance and Risk Management Guidelines Dec 2018
8. NHMRC Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods (2016)
9. The National Statement on Ethical Conduct in Human Research (2007 and updates)

7. AUTHORS/CONTRIBUTORS

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8. PRIMARY PERSON/DEPARTMENT RESPONSBLE FOR DOCUMENT

Western Health Office for Research