

MELBOURNE HEALTH		OFFICE FOR RESEARCH	
		STANDARD OPERATING PROCEDURE: SOP010	
		Investigator Responsibilities	
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1. AIM

To define Investigators' responsibilities and to provide instruction when performing clinical study(ies) under applicable regulatory requirements.

2. SCOPE

All phases of clinical investigation of medicinal products, medical devices, therapeutic interventions and diagnostics.

3. APPLICABILITY

Principal Investigator, Sub-Investigator, research coordinators and other staff delegated trial-related activities by the Principal Investigator.

4. PROCEDURE

Investigator Responsibilities

The investigator(s):

- Should ensure that clinical studies are carried out according to International Conference on Harmonisation (ICH), regulatory authorities requirements and any other local requirements.
- Should have written evidence of ICH GCP training. Melbourne Health Maintain current certified GCP training if involved in clinical trials at Melbourne Health or where specified by the Office for Research for particular researchers/projects. To meet OfR requirements the GCP training must be recognised by the certification process that TranCelerate Biopharma INC has implemented to recognise GCP training courses that contain material meeting the minimum criteria agreed to by its member organizations (pharma companies). For details of the criteria refer to http://www.transceleratebiopharmainc.com/wp-content/uploads/2013/10/TransCelerate-GCP-Training-Minimum-Criteria-in-Operating-Principles_0.pdf
- Should have an understanding that when a trial is sponsored by an agency/pharmaceutical company, they may be requested to follow their

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procedures in order to comply with company obligations. Agreement between all parties should be discussed before initiating the trial.

- Should ensure that they are appropriately qualified to conduct the trial.
- The investigator is responsible for supervising any individual or party to whom the investigator delegates trial-related duties and functions conducted at the trial site.
- If the investigator/institution retains the services of any individual or party to perform trial-related duties and functions, the investigator/institution should ensure this individual or party is qualified to perform those trial-related duties and functions and should implement procedures to ensure the integrity of the trial-related duties and functions performed and any data generated
- Should inform the subject's primary physician about the subject's participation in the trial if the subject has a primary physician and if the subject agrees to the primary physician being informed.

Note: Although a subject is not obliged to give his/her reason(s) for withdrawing prematurely from a trial, the investigator should make a reasonable effort to ascertain the reason(s), while fully respecting the subject's rights.

- Must declare any conflicts of interest, payments etc. from other parties.
- Must maintain a list of any delegated duties with respect to the trial, and the persons and qualifications of those persons to whom the duties are assigned.
- Should be able to demonstrate that adequate subject recruitment is likely to be possible, with necessary time available to conduct the study to GCP requirements, and with adequate facilities and trial staff.
- Must provide medical care to trial participants that is necessary as a result of any adverse events experienced during or following the trial that are related to the trial, and must be responsible for all trial-related medical decisions
- Must possess, prior to trial commencement, a favourable HREC endorsement of trial protocol, patient information and consent documents, recruitment procedures, consent form updates and any other information given to subjects.
- Must present all trial related documents to the HREC for review including the Investigator's Brochure as well as updates.
- Must ensure that the trial is conducted according to the approved protocol.
- Must document any deviation from the protocol for later review.
- Minor protocol deviations that do not compromise or impinge in any way on the patient's safety do not need to be reported to the HREC.

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- Must ensure that no deviation from the protocol occurs without HREC endorsement, unless it is required to prevent imminent harm to participants. If the protocol deviation results in the creation of a “separate and distinct” therapeutic good as defined in section 16 of the Therapeutic Goods Act 1989, a new notification is required for CTN or CTX trials.
- Should ensure CTN notification is completed, or in the case of CTX a new “notification of intent to conduct clinical trial” form, for any new trial site subsequently added to a study.

Note: If MH is the CTN sponsor, contact the Office for Research to make an appointment for the submission of electronic CTN forms notifications.

- Must ensure accountability of the investigational product at the trial site(s).
- Must ensure that subjects have made fully informed, written consent, with all trial procedures and risks adequately explained and that the principles and essential elements of Informed consent are upheld and included in the information document;
- Should be thoroughly familiar with the appropriate use of the investigational product(s), as described in the protocol, in the current Investigator's Brochure, in the product information and in other information sources provided by the sponsor.
- Should ensure that all persons assisting with the trial are adequately informed about the protocol, the investigational product(s), and their trial-related duties and functions.
- Should submit written summaries of the trial status to the HREC annually, or more frequently, if requested by the HREC.
- Should provide written reports to the sponsor, the HREC and, where applicable, the institution promptly on any changes significantly affecting the conduct of the trial, and/or increasing the risk to subjects.
- Should comply with the applicable regulatory requirement(s) related to the reporting of unexpected serious adverse drug reactions to the regulatory authority(ies) and the HREC.
- Should promptly inform the trial subjects if the trial is prematurely terminated or suspended for any reason as well as the institution and should assure appropriate therapy and follow-up for the subjects, and where required by the applicable regulatory requirement(s), inform the regulatory authority(ies).

Note: if the investigator terminates or suspends a trial without prior agreement of the sponsor, they should inform the institution where applicable, and the investigator/institution should promptly inform the sponsor and the HREC, and

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provide the sponsor and the HREC a detailed written explanation of the termination or suspension.

- Should, upon completion of the trial, where applicable, inform the institution; the investigator/institution should provide the HREC with a summary of the trial's outcome, and the regulatory authority(ies) with any reports required.

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.

Clinical Trials Notification (CTN)

A notification scheme whereby all material relating to the proposed trial, including the trial protocol is submitted directly to the HREC by the researcher at the request of the sponsor. The TGA does not review any data relating to the clinical trial.

The HREC is responsible for assessing the scientific validity of the trial design, the safety and efficacy of the medicine or device and the ethical acceptability of the trial process, and for approval of the trial protocol.

The institution or organisation at which the trial will be conducted, referred to as the 'Approving Authority', gives the final approval for the conduct of the trial at the site, having due regard to advice from the HREC.

CTN trials cannot commence until the trial has been notified to the TGA and the appropriate notification fee paid.

Clinical Trials Exemption (CTX)

An approval process whereby a sponsor submits an application to conduct clinical trials to the TGA for evaluation and comment.

A TGA Delegate decides whether or not to object to the proposed Usage Guidelines for the product. If an objection is raised, trials may not proceed until the objection has been addressed to the Delegate's satisfaction.

If no objection is raised, the sponsor may conduct any number of clinical trials under the CTX application without further assessment by the TGA, provided use of the product in the trials falls within the original approved Usage Guidelines. Each trial conducted must be notified to the TGA.

A sponsor cannot commence a CTX trial until written advice has been received from the TGA regarding the application and approval for the conduct of the trial has been

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obtained from an ethics committee and the institution at which the trial will be conducted. There are two forms, each reflecting these separate processes (Parts), that must be submitted to TGA by the sponsor.

Part 1 constitutes the formal CTX application. It must be completed by the sponsor of the trial and submitted to TGA with data for evaluation.

Part 2 is used to notify the commencement of each new trial conducted under the CTX as well as new sites in ongoing CTX trials. The Part 2 form must be submitted within 28 days of the commencement of supply of goods under the CTX. There is no fee for notification of trials under the CTX scheme.

Delegate

A person delegated specific but appropriate tasks in relation to the conduct of a clinical trial.

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 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.

Sub Investigator

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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).

6. REFERENCES

1. Note for guidance on Good Clinical Practice (CPMP/ICH/135/96) annotated with TGA comments DSEB, July 2000, sections 4.
2. Standard Operating Procedures for Clinical Investigators, World Health Organisation, version 1.1.
3. The Australian Clinical Trial Handbook, Therapeutic Goods Administration, March 2006.
4. Access to Unapproved Therapeutic Goods, Clinical Trials in Australia, Therapeutic Goods Administration, October 2004

7. APPENDICES

Appendix 1: SOP Change Log

DOCUMENT END

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APPENDIX 1: SOP CHANGE LOG

<i>Version No.</i>	<i>Reason for Issue</i>
1	First issue
2	Up date GCP training information in Section 4
3	Clarify requirement for notification of protocol deviations
4	<p>Update template and information including:</p> <ul style="list-style-type: none"> • Maintain current certified GCP training if involved in clinical trials at Melbourne Health or where specified by the Office for Research for particular researchers/projects. To meet OfR requirements the GCP training must be recognised by the certification process that TranCelerate Biopharma INC has implemented to recognise GCP training courses that contain material meeting the minimum criteria agreed to by its member organizations (pharma companies). For details of the criteria refer to http://www.transceleratebiopharmainc.com/wp-content/uploads/2013/10/TransCelerate-GCP-Training-Minimum-Criteria-in-Operating-Principles_0.pdf • Note: If MH is the CTN sponsor, contact the Office for Research to make an appointment for the submission of electronic CTN forms notifications' • The investigator is responsible for supervising any individual or party to whom the investigator delegates trial-related duties and functions conducted at the trial site. • If the investigator/institution retains the services of any individual or party to perform trial-related duties and functions, the investigator/institution should ensure this individual or party is qualified to perform those trial-related duties and functions and should implement procedures to ensure the integrity of the trial-related duties and functions performed and any data generated.

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