Research Ethics and Governance – Sponsor Responsibilities in Investigator Initiated Studies Procedure

TARGET AUDIENCE and SETTING

Principal Investigator when acting in the capacity of sponsor.

PURPOSE

A guide for Principal Investigators when acting as sponsor for investigator initiated or collaborative research studies.

DEFINITIONS and BACKGROUND

Investigator Initiated Clinical Trial:

An investigator Initiated 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.
- 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.

Sponsor:

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

Clinical Trial Notification Scheme (CTN):

A notification scheme whereby a sponsor of a clinical trial submits a notification to the Therapeutic Goods Administration (TGA) prior to commencing a clinical trial. All material relating to a proposed clinical trial, including the trial protocol is submitted directly to the Human Research Ethics Committee (HREC) by the researcher at the request of the sponsor. 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 TGA does not review any data relating the clinical trial. 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 Trial Exemption Scheme (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 obtained from an ethics committee and the institution at which the trial will be conducted.

PRECAUTIONS/CONTRAINDICATIONS

All researchers at Monash Health must conduct research in the manner indicated in the Human Research Policy and the Research Governance Procedure.

For Investigator Initiated Studies where the Institution is acting as the Sponsor, the Principal Investigator is responsible for carrying out Sponsor requirements such as submitting all documentation including safety and annual progress reports to HREC, the Institution (RGO – Research Governance Office) or TGA.

PROCEDURE

Prior to commencement of a clinical trial the sponsor must ensure that:

- A CTN or CTX is submitted to the TGA by making an appointment with Research Support Services for 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,
- Confirmation of endorsement from the relevant Human Research Ethics Committee(s) and notification of the approval etc. to the Therapeutic Goods Administration is obtained;
- 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, the trial protocol, and any Therapeutic Goods Administration requirements;
- Agreement is secured 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;
- A monitoring strategy is in place and submitted to HREC to include the type of monitoring, who is responsible for the monitoring and the frequency of monitoring;
- No omissions occur which might disentitle themselves, the Hospital or Human Research Ethics Committee, to such indemnity as could otherwise be available under the Medical Indemnity and Public Liability Policies;
- Appropriate insurance and indemnity for the trial and trial-related staff are provided, as well as measures for subject compensation for trial-related injury;
- The appropriate investigator(s) and institution(s) are selected to conduct and complete the trial according to Good Clinical Practice standards;
- The definitive, unambiguous allocation of trial-related duties and responsibilities to trial-related staff occurs and this is documented in the delegation log;
- 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;
- 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 policy;
- Provide a detailed study budget that demonstrates that there are sufficient resources to conduct the study;
- An a appropriate Good Clinical Practice (GCP) training course has been successfully completed by the Principal Investigator and all investigators participating in interventional studies as documented in the Good Clinical Practice Training procedure.

During the conduct of the clinical trial, the sponsor must ensure that:

- Trial design and appropriate analysis occurs;

- The delegation log for all investigators in the study is maintained and kept up to date by the Principal Investigator;
- Data handling, record keeping, and overall trial management occurs;
- All records relating to the study are maintained for a period of at least 15 years from the end of the trial (i.e. completion of data analysis) in the case of adults, and 25 years from the end of the trial in the case of paediatric participants.
- Medical expertise is on hand for trial-related medical queries or patient care;
- Investigational Products available to subjects free of charge;
- Appropriate urgent safety measures (with the investigator) are taken where necessary;
- Records of all adverse events reported by investigators are kept;
- Ongoing safety evaluation and Adverse Event /Adverse Drug Reaction reporting as outlined in the NHMRC "Safety monitoring and reporting in clinical trials involving therapeutic goods" (NHMRC 2016) guidelines;
- Appropriate manufacture, packaging, labelling/coding and distribution to trial sites of all investigational medicinal products occurs;
- Submission of an annual research progress report to Monash Health RGO and for multi-site studies where Monash Health is the HREC, an HREC annual research progress report.
- Compliance with Monitoring/Audit/Inspection requirements occurs; and
- Notification of any premature termination of the trial in question occurs in a timely manner; Submission of an annual research progress report to Monash Health RGO and for multi-site studies where Monash Health is the HREC, an HREC annual research progress report.

At the completion of the clinical trial the Sponsor must ensure that:

- Completion of the Clinical Study Report occurs and submission of a Final Report to Research Support Services by 30 April each year to cover the previous calendar year activities.

KEY STANDARDS, GUIDELINES OR LEGISLATION

Australian code for the responsible conduct of research (NHMRC, 2018),

National Statement on Ethical Conduct in Human Research (NHMRC 2018)

Safety monitoring and reporting in clinical trials involving therapeutic goods (NHMRC 2016)

International Council on Harmonisation Guidance for Good Clinical Practice E6(R2) (2016)

KEYWORDS

Clinical trial, human research, CTN, CTX, Principal Investigator; sponsor, GCP, TGA, HREC, RGO.

Document Governance	
Supporting Policy	Human Research (Strategic)
Executive Sponsor	Chief Medical Officer
Department Responsible	Research and Ethics
Document Author	Michael Kios, Research Governance Manager
Consumer Review Yes or No	No