

4 - INVESTIGATORS

Coordinating Principal Investigator and
Principal Investigator

Non-Commercial
Clinical Trials

1. Roles and Responsibilities of the Coordinating Principal Investigator when conducting Non-Commercial Clinical Trials

The coordinating principal investigator is;

- a) In relation to a clinical trial conducted at a single trial site, the investigator¹ for that site; or
- b) In relation to a clinical trial conducted at more than one trial site, the health professional, whether or not he or she is an investigator at any particular site, who takes primary responsibility for the conduct of the trial.

The coordinating principal investigator (CPI) has responsibility for submitting the trial for scientific and ethical review and any ongoing communication with the reviewing HREC or their institutional research governance office. For international trials, a CPI must be identified who will take responsibility for the study within Australia.

For non-commercial trials, the overall responsibility for initiating and managing the trial, lies with the sponsor. However, as the person responsible for leading the team of researchers undertaking the design, conduct and reporting of the trial, the CPI should have oversight of all activities, even when they are delegated to third parties such as clinical trial units or coordinating centres. The typical role of a coordinating principal investigator is outlined below.

- Ensure that the trial is based on a thorough review of scientific literature including whether any relevant systematic review exists.
- Ensure that sufficient safety and efficacy data from nonclinical studies and/or clinical trials are available to support human exposure by the route, at the dosages, for the duration, and in the trial population to be studied.
- Secure funding and/or confirm sufficient resources are available to conduct the trial.
- Confirm proposals are good value for money, feasible and scientifically sound by submitting them for independent review.
- Ensure that a trial sponsor has been identified and this entity has agreed to perform the role of sponsor for the trial.
- Undertake/oversee the design of the trial with support from all relevant specialist staff (e.g. statistician, research methodologist or trial coordinating centre/unit).
- Ensure a trial risk assessment has been carried out and proportionate trial management and monitoring plans are in place.
- Develop/endorse a protocol that is compliant with international standards including the [SPIRIT Statement](#).
- Develop/endorse an appropriate strategy for independent trial oversight (e.g. Trial Management Group, Trial Steering Committee, and Data Safety Monitoring Board).
- Ensure appropriate mechanisms for ongoing safety monitoring are in place (i.e. that are commensurate to the risks and complexities of the trial).
- Oversee the preparation of the budget and the management of the budget for the conduct of the trial.
- Ensure that research practices reflect current professional (ethical, legal and good practice) standards for research, including the declaration of conflicts of interest.
- Where applicable, ensure that arrangements are in place for trial supplies and that all requirements for therapeutic goods supplies are met (e.g. manufacture/packaging/labelling).
- Confirm that each member of the trial team is aware of, and accepts their trial-related duties.

¹ For most clinical trials, the Coordinating Principal Investigator (CPI) is usually also the Principal Investigator (PI) at their site so takes on both sets of responsibilities outlined in this document

- Ensure all other relevant trial documentation are developed (e.g. Participant Information and Consent Form, Case Report Form).
- Oversee the set-up of a clinical trial database and the development of a data management plan² and procedures to ensure the collection and analysis of high quality, accurate data.
- Register the trial on a publically accessible database such as the [Australian New Zealand Clinical Trials Registry \(ANZCTR\)](#) before the first participant is recruited.
- Facilitate communication between the trial sponsor and Human Research Ethics Committee (HREC), and where applicable, the Therapeutic Goods Administration in accordance with national guidance and jurisdictional policy.
- For multicentre trials, ensure collaboration and communication with participating sites in accordance with national guidance and jurisdictional policy.
- For multicentre trials, ensure each participating site is not opened until all regulatory and governance requirements have been met.
- Ensure that any amendments are approved/authorised in accordance with jurisdictional policy, legislation and national standards
- Oversee the set-up and maintenance of a Trial Master File.
- For trials involving therapeutic goods, develop/obtain an investigator's brochure (or product information) and ensure that the Reference Safety Information used to identify unexpected adverse reactions or unanticipated adverse device effects, is clearly defined.
- Ensure that the investigator's brochure/product information is reviewed/updated annually.
- Ensure annual progress reports incorporating information from all sites involved in the trial (if multi-centre) are produced and sent to the HREC and if required, all participating sites.
- Ensure that reports on the progress and outcomes of the trial, required by the sponsors, funders, or others with a legitimate interest, are produced on time and to an acceptable standard.
- If the author of a publication, adopt the role of guarantor on published outputs.
- Notify review bodies that the trial has ended and publish a summary of trial results within jurisdictional and funder's timelines.
- Ensure where applicable, a [CONSORT](#) compliant full trial report is produced and made publically available when produced.
- Ensure that trial findings are opened to critical review through the accepted scientific and professional channels and wherever possible, arrange to make findings and data accessible following expert review.
- Fulfil commitments to trial participants, such as providing information about the outcome(s) of the trial.
- Ensure all trial data (including the Trial Master File) and materials, are archived appropriately and retrievable for audit purposes.

2. Roles and Responsibilities of the Principal Investigator when conducting Clinical Trials

The principal investigator (PI) is the person responsible, individually or a leader of the researchers at a site, for the conduct of a trial at that site. In a single centre trial, the principal investigator may also be the coordinating principal investigator.

The principal investigator should give priority at all times to the dignity, rights, safety and wellbeing of participants. For trials involving therapeutic goods, a full set of good clinical practice responsibilities are outlined Section 4 of ICH GCP (drugs) and Section 9 of ISO 14155 (medical devices). It is

² This may be incorporated into the protocol for simple trial.

recommended that where applicable, these responsibilities³ are applied to all clinical trials as they provide a framework for trial conduct that will help protect the right, safety and well-being of trial participants and the reliability and robustness of trial data.

Principal investigators must either personally conduct or personally supervise their trials and should maintain oversight of any functions delegated to their trial team⁴. Some of the key responsibilities of the principal investigator are outlined below.

Overview of responsibilities sourced from the Good Clinical Practice Guidelines (ICH GCP) for trials involving investigational medicinal products (IMDs)

- Be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial.
- Be thoroughly familiar with the appropriate use of the IMP(s).
- Maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.
- Be aware of, and comply with, Good Clinical Practice (GCP) and applicable regulatory requirements.
- Ensure that a feasibility assessment has taken place to ensure that the site has adequate resources to conduct the trial (time, personnel and facilities) and be able to demonstrate (e.g., based on retrospective data) a potential to recruit the required number of suitable participants within the agreed recruitment period.
- Ensure adequate medical care for all trial participants.
- Conduct the trial in compliance with the protocol.
- Where appropriate, assign some or all duties for IMP accountability at the trial site(s) to an appropriate pharmacist or another appropriate individual.
- Ensure IMP is stored accordance with applicable good manufacturing practice (GMP) and used in accordance with the approved protocol.
- Where applicable, ensure the correct use of the IMP is explained to trial participants.
- Ensure that the randomisation code is broken only in accordance with the protocol.
- Maintain records of the delivery to the trial site, inventory, use by each participant, and the return to the sponsor or alternative disposition of unused IMP(s).
- Obtain and document informed consent in compliance with the applicable regulatory requirement(s) and GCP.
- Ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor
- Submit progress reports and final reports to the institution
- Maintain the trial documents as specified in Essential Documents for the Conduct of a Clinical Trial (Section 8 of ICH GCP) and take measures to prevent accidental or early destruction of these documents.
- Report Serious Adverse Events (SAEs) immediately (within 24 hours) to the sponsor except for those SAEs that the protocol or other document identifies as not needing immediate reporting.
- Make a reasonable effort to ascertain the reason(s) for early withdrawal of a participant from the trial, while fully respecting the participant's rights.
- Promptly inform the trial participants of any premature termination of the trial and assure appropriate therapy and follow-up.

³ Although some of the responsibilities outlined in these documents are specific to trials involving therapeutic goods, the majority can be applied to all clinical trials.

⁴ FDA Guidance: Investigator Responsibilities: Protecting the Rights, Safety, and Welfare of Study Subjects

Overview of responsibilities sourced from the Good Clinical Practice Guidelines (ISO 14155 2011) for trials involving investigational medical devices (IMDs)

- Be qualified by education, training and experience to assume responsibility for the proper conduct of the clinical investigation.
- Be experienced in the field of application and trained in the use of the IMD under consideration.
- Conduct the trial in accordance with ISO 14155 (2011) and the Clinical Investigation Plan (CIP).
- Demonstrate that the site has the proposed number of eligible participants needed within the agreed recruitment period, and adequate facilities for the foreseen duration of the clinical investigation.
- Ensure compliance with the applicable regulatory requirements and ethical principles for the process of obtaining informed consent.
- Document and explain any deviation from the approved CIP that occur during the course of the clinical investigation.
- Provide adequate medical care to a participant during and after a participant's involvement in a clinical investigation in the case of adverse events.
- Provide the participant with the necessary instructions on proper use, handling, storage and return of the IMD, when it is used or operated by the participant.
- Provide the participant with well-defined procedures for possible emergency situations related to the clinical investigation, and make the necessary arrangements for emergency treatment, including decoding procedures for blinded/masked clinical investigations.
- Report to the sponsor without unjustified delay, all serious adverse events and device deficiencies that could have led to a serious adverse device effect.
- Make all reasonable efforts to ascertain the reason(s) for a participant's early withdrawal from the clinical investigation while fully respecting the participant's rights.
- Supervise the use of the IMD and the disposal of the IMD in accordance with sponsor requirements upon completion or termination of a clinical investigation.

Additional responsibilities for all clinical trials

- Ensure the trial is conducted in accordance with Australian legislation and guidance.
- Adhere to any requirements specified by the institution where the trial is conducted (*the institution*), including any relevant research policies and procedures.
- Ensure all support departments are provided with an accurate breakdown of trial requirements (e.g. tests/assessments/visits) so that they can determine their capacity and capability to support the trial based on an understanding of the resources that are required, over and above standard care.
- Secure research authorisation from *the institution* before commencing the trial.
- Ensure amendments to the trial protocol/clinical investigation plan are authorised by *the institution*⁵ before being implemented (unless deviation from the protocol is necessary to protect a participant from an immediate hazard).
- Provide all required reports to *the institution* in accordance with local, jurisdictional and national requirements.
- Report safety information in accordance with the NHMRC Guidance for Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods.

⁵ Amendments should be approved by the HREC before they are submitted to the institution for assessment and local authorisation.