

Medicines Australia Principles on Conduct of Clinical Trials and Communication of Clinical Trial Results

Preamble

Medicines Australia represents research-based pharmaceutical, biotechnology and contract research companies. Our members discover, develop, manufacture and market new medicines and vaccines to help people to live longer and healthier lives.

The development of new therapies to treat and prevent diseases and improve quality of life is a long and complex process. A critical part of that process is the conduct of clinical trials, the study of a pharmaceutical product in humans (trial participants). Clinical trials involve the assessment of both potential benefits and risks to the participants and to society at large. Investigational clinical trials are conducted to answer specific questions and some aspects of the therapeutic profile (benefits and risks) of the product(s) tested may not be fully known without study in humans. In sponsoring and conducting clinical trials, Medicines Australia members place great importance on respecting and protecting the safety of trial participants.

Principles for the conduct of clinical trials are set forth in internationally recognised documents, such as the Declaration of Helsinki and the International Conference on Harmonisation Note for Guidance on Good Clinical Practice (ICH GCP). The principles of these and similar reference standards are translated into legal requirements through laws and regulations enforced by national authorities such as the Therapeutic Goods Administration and the Australian Health Ethics Committee. Medicines Australia members have always been committed, and remain committed, to sponsoring clinical trials that fully comply with all legal and regulatory requirements.

Many different entities and individuals contribute to the safe and appropriate conduct of clinical trials, including not only sponsoring companies but also clinical research organisations, regulatory agencies; clinical trial site staff, medical professionals who serve as clinical investigators; pharmacists; hospitals and other institutions where research is conducted; and Human Research Ethics Committees (HRECs).

Medicines Australia has published these voluntary principles to clarify our members' relationships with other individuals and entities involved in clinical trials. The key issues addressed here are:

- Protecting Trial Participants;
- Conduct of Clinical Trials;
- Ensuring Objectivity in Clinical Trials; and
- Disclosure of Clinical Trial Results.

These principles reinforce the commitment of our members to the safety of trial participants. They provide guidance to address issues that bear on this commitment in the context of clinical trials that enrol trial participants and are designed, conducted and sponsored by member companies.

Commitment to Protecting Trial Participants

Medicines Australia members conduct clinical trials in a manner that upholds the primary importance of protecting the safety and respecting the rights of trial participants. Our members' interactions with trial participants, as well as with clinical investigators and the other persons and entities involved in clinical trials, recognise this fundamental principle and reinforce the precautions established to protect trial participants.

Our members have adopted the "*Guidelines for Compensation for Injury Resulting from Participation in a Company-sponsored Clinical Trial*" published by Medicines Australia. Clinical trials conducted by our members are conducted subject to these Guidelines.

Conduct of Clinical Trials

Medicines Australia members conduct clinical trials in accordance with applicable laws and regulations, as well as locally recognised Good Clinical Practice. When conducting or participating in clinical trials our members follow the ICH GCP guidelines.

Clinical Trial Design

Medicines Australia members conduct clinical trials based on scientifically designed protocols that balance potential risk to the trial participant with the possible benefit to the participant and to society. Scientific, ethical and clinical judgments must guide and support the design of the clinical trial, particularly those aspects directly affecting the trial participants such as inclusion/exclusion criteria, endpoints, and choice of control, including active and/or placebo comparator.

Selection of Investigators

Investigators are selected based on qualifications, training, research or clinical expertise in relevant fields, the potential to recruit trial participants and ability to conduct clinical trials in accordance with good clinical practices and applicable legal requirements.

Training of Investigators

Investigators and their staff are trained on the clinical trial protocol, pharmaceutical product, procedural issues associated with the conduct of the particular clinical trial, and their key responsibilities as investigators under the ICH GCP guidelines.

Human Research Ethics Committee (HREC) Review

Prior to commencement, each clinical trial is reviewed by one or more HRECs that have independent decision-making authority.

- The HREC has the responsibility to protect trial participants and is responsible for monitoring the conduct of clinical trials.
- The HREC is provided relevant information from prior trials, the clinical trial protocol, and any materials developed to inform potential participants about the proposed trial.
- The HREC may disapprove, require changes, or approve the clinical trial protocol
- The HREC can ask any question of the sponsor and will not approve a clinical trial protocol unless satisfied with the answers.
- The HREC must give written approval before any participants are enrolled at the institution or other trial site for which it has responsibility.
- The HREC will recommend to the Approving Authority at the institution or proposed trial site whether the trial should be conducted. The HREC may also be the Approving Authority for a particular trial site.

Informed Consent

Our members require that clinical investigators obtain and document informed consent, freely given and without coercion, from all potential trial participants.

- Potential trial participants are to be adequately informed about potential benefits and risks, the possibility that they may receive a placebo treatment, alternative procedures or treatments, nature and duration of the clinical trial, and provided the opportunity to ask questions about the trial and receive answers from a qualified health care professional.
- Clinical investigators are encouraged to disclose to potential trial participants during the informed consent process that the investigator and/or the institution is receiving payment for the conduct of the clinical trial.
- In those cases where trial participants—for reasons such as age, illness, or injury—are incapable of giving their consent, the informed consent of a legally acceptable representative is required.
- Because participation in a clinical trial is voluntary, all trial participants have the right to withdraw from continued participation in the clinical trial, at any time, without penalty or loss of benefits, including medical treatment, to which they are otherwise entitled.

Clinical Trial Monitoring

Clinical trials are monitored using appropriately trained and qualified individuals. The sponsor will have procedures for these individuals to report on the progress of the trial.

- These individuals verify compliance with good clinical practices, including (but not limited to) adherence to the clinical trial protocol, the informed consent process, enrolment of appropriate trial participants, and the accuracy and complete recording of clinical trial data.
- If a sponsor learns that a clinical investigator is significantly deficient in any area, it will either work with the investigator to obtain compliance or discontinue the investigator's participation in the trial, and notify the relevant authorities as required.

Privacy and Confidentiality of Medical Information

Sponsors respect the privacy of trial participants and safeguard the confidentiality of their medical information in accordance with all applicable laws and regulations. While access to confidential medical records may at times be necessary to verify clinical information, no information that identifies individual participants is retained by Sponsors.

Quality Assurance

Procedures are followed to ensure that trials are conducted in accordance with good clinical practices and that data are generated, documented and reported accurately and in compliance with all applicable requirements.

Ongoing Safety Monitoring

All safety issues are tracked and monitored in order to better understand the safety profile of the product under trial. Significant new safety information will be shared promptly with the clinical investigators, any Data and Safety Monitoring Board / Committee (DSMB) or equivalent, and the HREC and reported to regulatory authorities in accordance with applicable law. Sponsors require that the clinical investigators ensure that trial participants are made aware of this new information.

Ensuring Objectivity in Clinical Trials

Medicines Australia members respect the independence of the individuals and entities involved in the clinical trial process, so that they can exercise their judgement for the purpose of protecting trial participants and to ensure an objective and balanced interpretation of trial results. In any sponsored clinical trial the Investigator is ultimately responsible for all decisions affecting the safety of trial participants. Members' contracts and interactions with them will not interfere with this independence.

Independent Review and Safety Monitoring

In certain trials, the participants, investigators and the sponsor may each be blinded to the treatment each participant receives to avoid the introduction of bias into the trial. In such cases, monitoring of interim trial results and of new information from external sources by a DSMB may be appropriate to protect the welfare of the trial participants. If a DSMB is established, its members should have varied expertise, including relevant fields of medicine, statistics, and bioethics. Sponsors help establish, and also respect, the independence of DSMBs.

- Clinical investigators participating in a clinical trial of a pharmaceutical product should not serve on a DSMB that is monitoring that trial. It is also not appropriate for such an investigator to serve on DSMBs monitoring other trials with the same product if knowledge accessed through the DSMB membership may influence his or her objectivity.
- A voting member of a DSMB should not have significant financial interests or other conflicts of interest that would preclude objective determinations. Employees of the sponsor may not serve as members of the DSMB, but may otherwise assist the DSMB in its evaluation of clinical trial data.

Payment to Clinical Trial Participants

Clinical trial participants provide a valuable service to society. They take time out of their daily lives and sometimes incur expenses associated with their participation in clinical trials. When payments are made to trial participants:

- Any proposed payment should be reviewed and approved by an independent HREC.

- Payments should be based on the trial participants' time and/or reimbursement for reasonable expenses incurred during their participation in a clinical trial, such as parking, travel, and lodging expenses.
- The nature and amount of compensation or any other benefit should be consistent with the principle of voluntary informed consent.

Payment to Clinical Investigators

Payment to clinical investigators or their institutions should be reasonable and based on work performed by the investigator and the investigator's staff, not on any other considerations.

- A written contract or budgetary agreement should be in place, specifying the nature of the trial services to be provided and the basis for payment for those services.
- Payments or compensation of any sort should not be tied to the outcome of clinical trials.
- Clinical investigators or their immediate family should not have a direct ownership interest in the specific pharmaceutical product being studied.
- Clinical investigators and institutions should not be compensated in company shares or share options for work performed on individual clinical trials.
- When enrolment is particularly challenging, reasonable additional payments may be made to compensate the clinical investigator or institution for time and effort spent on extra recruiting efforts to enrol appropriate trial participants.
- When clinical investigators and their staff are required to travel to meetings in conjunction with a clinical trial, they may be compensated for their time and offered reimbursement for reasonable travel, lodging, and meal expenses. The venue and circumstances should be appropriate for the purpose of the meeting.

Public Disclosure of Clinical Trial Results

Availability of clinical trial results in a timely manner is often critical to communicate important new information to the medical profession, patients and the public. Medicines Australia members design and conduct clinical trials in an ethical and scientifically rigorous manner to determine the benefits, risks, and value of pharmaceutical products. As sponsors, our members are responsible for receipt and verification of data from all trial sites for the clinical trials they conduct. Our members ensure the accuracy and integrity of the entire trial database.

Communication of Trial Results

Clinical trials may involve already marketed products and/or investigational products. Medicines Australia members commit to timely communication of meaningful results of controlled clinical trials of marketed products or investigational products, regardless of outcome. Communication includes publication of a paper in a peer-reviewed medical journal, abstract submission with a poster or oral presentation at a scientific meeting, or making results public by some other means.

In all cases, the trial results should be reported in an objective, accurate, balanced and complete manner, with a discussion of the strengths and limitations of the trial.

Authorship

Consistent with the International Committee of Medical Journal Editors and major journal guidelines for authorship, anyone who provides substantial contributions into the conception or design of a trial, or data acquisition, or data analysis and interpretation; and writing or revising of the manuscript; and has final approval of the version to be published should receive appropriate recognition as an author or contributor when the manuscript is published. Conversely, individuals who do not contribute in this manner do not warrant authorship.

- Companies sometimes employ staff to help analyse and interpret data, and to produce manuscripts and presentations. Such personnel must act in conjunction with the investigator-author. Their contributions should be recognised appropriately in resulting publications — either as a named author, a contributor, or in acknowledgments depending on their level of contribution.
- All authors whether from within a sponsoring company or external, will be given the relevant statistical tables, figures, and reports needed to support the planned publication.

Related Publications

For a multi-site clinical trial, analyses based on single-site data usually have significant statistical limitations, and frequently do not provide meaningful information for health care professionals or patients and therefore may not be supported by sponsors. Such reports should not precede, and should always reference, the primary presentation or paper of the entire trial.

Investigator Access to Data and Review of Results

As owners of the trial database, and in accordance with relevant privacy legislation, sponsors have discretion to determine who will have access to the database. Generally, trial databases are only made available to regulatory authorities. Individual investigators in multi-site clinical trials will have their own trial participants' data, and will be provided the randomisation code after conclusion of the trial. Sponsors will make a summary of the trial results available to the investigators. In addition any investigator who participated in the conduct of a multi-site clinical trial will be able to review relevant statistical tables, figures, and reports for the entire trial.

Clinical Trial Participant Communication

Investigators are encouraged to communicate a summary of the trial results, as appropriate, to their clinical trial participants after conclusion of the trial.

Sponsor Review

Sponsors have the right to review any manuscripts, presentations, or abstracts that originate from our trials or that utilise our data before they are submitted for publication or other means of communication. Sponsors commit to respond in a timely manner, and not suppress or veto publications or other appropriate means of communication (in rare cases it may be necessary to delay publication and/or communication for a short time to protect intellectual property). Where differences of opinion or interpretation of data exist, the parties should try to resolve them through appropriate scientific debate.

Provision of Clinical Trial Protocol for Journal Review

If requested by a medical journal when reviewing a submitted manuscript for publication, the clinical trial sponsor will provide a synopsis of the clinical trial protocol and/or pre-specified plan for data analysis with the understanding that such documents are confidential and should be returned to the sponsor.

1 Modelled on the PhRMA Principles On Conduct Of Clinical Trials And Communication Of Clinical Trial Results.

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