# Clinical trials

## PURPOSE

This guideline provides recommendations regarding best practice for researchers initiating and conducting clinical trials in Metro South Health (MSH).

## OUTCOME

The intended outcome of this guideline is to provide guidance around Australia's clinical trials environment, which is complex, with various responsibilities resting with institutions, private organisations and companies, State or Territory Governments and the Commonwealth Government.

## SCOPE

This guideline applies to all MSH employees and collaborators who conduct human research within or in association with MSH, or through access to MSH participants, health records or data.

## GUIDELINE

**Key messages**

- MSH strongly recommends all researchers involved with clinical trials review the Australian Clinical Trials site prior to commencing.
- If a MSH clinician or a researcher is planning to conduct a clinical trial, it is important to consider:
    - mandatory completion of Good Clinical Practice (GCP) Training
    - informed consent processes
    - requirements to follow the sponsors' research protocol
    - safety data including the Investigator Brochure and Phase 1 results as appropriate.
- All clinical trials conducted in MSH must:
    - be submitted to a National Health and Medical Research Council (NHMRC) Certified Human Research Ethics Committee (HREC) for ethical clearance see Ethical & Scientific Review of Human Research Work Instruction (WIPR2023/TBA) and
    - follow the NHMRC Guidance: Safety monitoring and reporting in clinical trials involving therapeutic goods.
- The Clinical Research Facility is available for use by researchers, the community and industry partners.
- Review MSH work instruction WI2023-303 Metro South Health sponsorship of Clinical Trial Notification (CTN) scheme trials if requesting for MSH to act as sponsor.

- The National Health and Medical Research Council (NHMRC) states that clinical trials are research investigations in which people volunteer to test new treatments, interventions, or tests as a means to prevent, detect, treat or manage various diseases or medical conditions. Some investigations look at how people respond to a new intervention and what side effects might occur.
- This helps to determine if a new intervention works, if it is safe, and if it is better than the interventions that are already available. Clinical trials might also compare existing interventions, test new ways to use or combine existing interventions or observe how people respond to other factors that might affect their health (such as dietary changes).

## 1.0 CLINICAL TRIAL DEFINITION

- The World Health Organization (WHO) definition for a clinical trial is: ‘any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Clinical trial interventions include, but are not restricted to:
    - experimental drugs
    - cells and other biological products
    - vaccines
    - medical devices
    - surgical and other medical treatments and procedures
    - psychotherapeutic and behavioural therapies
    - health service changes
    - preventive care strategies and
    - educational interventions.
- Researchers may also conduct clinical trials to evaluate diagnostic or screening tests and new ways to detect and treat disease. Please see the Australian Clinical Trials site for more information.
- The search function on the Australian Clinical Trials Registry can be used to find trials in Australia and browse the listings of clinical trials websites and links for further information.

## 2.0 GOOD CLINICAL PRACTICE (GCP) TRAINING & RELEVANT GUIDELINES

### 2.1 GCP Training

- In accordance with MSH procedure PR2023-413 Research administration and compliance all researchers in MSH must have evidence of Transcelerate accredited GCP Training, research integrity training, appropriate clinical trial design, adequate resources, ethical clearance, SSA authorisation and compliance with the Research Policy Framework as a minimum.
- Good Clinical Practice (GCP) clearly outlines the responsibilities of a trial sponsor. The Therapeutic Goods Administration (TGA) discusses sponsor responsibilities in the Australian Clinical Trial

Handbook where they distinguish between the GCP definition of sponsor and the TGA's definition in the Therapeutic Goods Act.

- Researchers can complete MSH Good Clinical Practice (GCP) Training via MSHLearn.
    - GCP Certificates must be renewed every 3 years
    - All research team members performing clinical trial related tasks must complete the MSH GCP Training or a face-to-face GCP Training Session.
- Refer to MSH work instruction WI2023-287 Research integrity for more information on research integrity education.

### 2.2 Other training

- NHMRC have developed education modules related to clinical trials. Whether you are a researcher, in a research office or just wanting to find out more about how clinical trials are conducted, these modules use interactive learning, interviews with experts and knowledge reviews to provide an overview of the nature and importance of the clinical trials environment and approval process in Australia.
- Australian Clinical Trials Education Centre (A-CTEC) is a not-for-profit, Victorian developed, Australia-wide education centre, with a dedicated Learning Management System (LMS) hosting a suite of evidence-based, interactive clinical trials education opportunities suitable for a range of learning needs.

## 3.0 SPONSORS

- A sponsor will generally approach an institution, investigator or MSH division/department to conduct a clinical trial. MSH has oversight of any clinical trial related duties and functions carried out on its behalf, including clinical trial-related duties and functions that are subcontracted to another party.
- The trial sponsor is responsible for the initiation, management and financing (or arranging the financing) of the trial and carries the medico-legal responsibility associated with its conduct.
- Where MSH is to act as a CTN/CTA Sponsor, via the CTN Scheme – Notification/CTA Scheme – approval, for clinical trials of unapproved therapeutic goods (drugs, devices or biologicals), the Coordinating Principal Investigator/Principal Investigator (CPI/PI) and/or Sponsor Delegate must provide evidence that adequate management and processes are in place to support MSH in meeting its sponsor requirements for the conduct of the clinical trial, including in respect to trial monitoring. Please see the MSH work instruction WI2023-303 Metro South Health sponsorship of Clinical Trial Notification (CTN) scheme trials for more information.
    - Note: It is preferable for the CPI/PI to request for the external collaborating party to act as Sponsor in the first instance (i.e., University).

## 4.0 CLINICAL TRIAL DESIGN

- There are numerous considerations that should be made when planning a clinical trial—some of these are as follows:
    - What is the exact research question this clinical trial is intended to answer?
    - What is the primary outcome variable? Is this readily measured?

- Is it a direct measure of outcome or do you intend to rely on surrogate endpoints?
- Is the clinical trial design appropriate?
- Are participant numbers or event numbers sufficient to give adequate statistical power to detect a difference in treatments should one exist or demonstrate non-inferiority (i.e., can the clinical trial answer the proposed research question, or will the data be equivocal)?
    - This aspect of design represents a genuine ethical consideration undertaken by the Metro South Human Research Ethics Committee (MSHREC) and needs professional statistical consideration.
- Have you considered the ongoing treatment of clinical trial participants should they respond to the unapproved medical product under investigation? Building in a clinical trial extension provision into the original research project design not only fulfils GCP requirements but also can allow such treatment to continue without having to put together another clinical trial proposal after the initial clinical trial ceases. Of course, this is not the only way to provide ongoing treatment post-clinical trial but is a point to consider in the planning process.

## 5.0 QUALITY MANAGEMENT SYSTEMS

- Where the Sponsor Delegate requests for MSH to act as a sponsor for an investigator-initiated clinical trial (CTN Scheme), the following processes and systems **must be** established, documented, and provided as evidence as part of the ethical clearance and Site-Specific Assessment (SSA) authorisation processes.
- All other clinical trials may follow this process to ensure best practice.

### 5.1 Participant and staff numbers and resources

- Researchers should also consider participants and resourcing:
    - Are your clinical trial centre(s) likely to be able to provide an adequate number of participants for the clinical trial?
    - Should the clinical trial be extended to additional sites to ensure recruitment? (Dealing with this early on reduces the likelihood of additional TGA Clinical Trial Approval (CTA) or Clinical Trial Notification (CTN) scheme applications being required later. It also works towards adequate recruitment to satisfy statistical requirements).
- Implement adequate management, supervision systems and processes. Do you have adequate staffing, resourcing, facilities and oversight of the research protocol?
- Develop processes and systems that support MSH in meeting its sponsor requirements (as outlined under GCP principles) for the conduct of the clinical trial by:
    - Allocating necessary resources for the study, including funding, personnel, infrastructure, and equipment.
    - Ensuring that the study team has the expertise and resources required to conduct the research effectively and adhere to GCP guidelines.

- Ensuring that all study staff, including research coordinators and investigators, are appropriately trained and qualified to perform their roles (e.g., GCP Training, site specific Standard Operating Procedures [SOPs]).
- Document all implemented systems and processes (e.g., delegation log, training log etc.)

### 5.2 Documentation of investigational site qualifications and training records

- The clinical trial research teams must:
  - Maintain an up-to-date Curriculum Vitae (CV) and review as agreed with the sponsor.
  - Be qualified by education, training, and experience to assume responsibility for the proper conduct of the research project.
  - Meet all the qualifications specified by the applicable regulatory requirement(s). Current medical practitioner registration details and similar documentation should be referenced in the CV.
  - Maintain a list of appropriately qualified persons to whom the investigator has delegated significant research-related duties. The list is in the form of a Delegation Log and delegated duties should be captured and signed and dated by the investigator on a per person basis. The delegation log may be provided by the sponsor company but for investigator-initiated research project a separate site log should be developed.

### 5.3 Site Master File/electronic Trial Master File (eTMF)

- The Site Master File (SMF)/electronic Trial Master File (eTMF) for a clinical trial should contain all the essential documentation which complies with patient privacy and MSH data security requirements:
  - For commercially sponsored research projects, sponsoring companies will normally provide the site master file complete with tab separators for ease and consistency of filing.
  - For research projects conducted on behalf of smaller companies or for investigator-initiated research projects this may need to be provided by the Principal Investigator (or delegate).
- Note: Financial documentation such as the clinical trial agreement may be filed in a separate location to the site master file or as per sponsor request.
- GCP guidelines dictate which documents need to be included and categorised in the SMF/eTMF. For example:
  - Essential study documents: protocol, protocol amendments, investigator's brochure, procedures, and manuals, visit guidance, delegation log, etc.
  - Training documentation and materials: certificates, videos, supporting content, etc.
  - Safety documentation: safety letters, serious adverse event (SAE) reports, etc.
  - Ethics committee's documents: protocol amendments, approvals, communication, etc.
  - Audit or monitoring documents: onsite visit records, audit findings, etc.
  - Participant information: informed consent forms, visit guidance, brochures, recruitment materials, patient diaries, etc.
  - Site-specific documents: site CVs, training documentation etc.

- **Note**: site SOPs must be developed and accessible to the trial team however may be filed in a separate location to the site master file or as per Sponsor request.
- When performing sponsored clinical trials of pharmaceutical products, the site pharmacy will usually keep investigational product shipping, receipt, accountability and destruction documents. The site itself does not have to replicate these documents. However, the records must be made available to sponsors, monitors and auditors.

### 5.4 Clinical trial budget and funding documentation

- The MSH Clinical Trial Budget Tool Template should be used to identify all direct costs associated with the conduct of the clinical trial in its entirety including realistic “in-kind” costs.
    - If an internal resource is being used for monitoring (i.e., research staff from within MSH), consider costs associated in the overall clinical trial budget.
- All labour and non-labour costs including in-kind support must be identified and the budget must be reviewed by the relevant department Finance/Business Manager/s.

### 5.5 Legal requirements

- Some legal requirements to consider are:
    - Are adequate indemnity provisions in place for the clinical trial, including for the staff involved? Note that some indemnity cover does not include clinical trial related activities or the use of experimental treatments.
    - Do participant informed consent documents contain a full description of the requirements, risks and benefits of clinical trial participation, in plain English, such that participants can make an informed decision?
    - Are the investigational products correctly labelled and packaged according to the Pharmaceutical Inspection Convention Pharmaceutical Inspection Co-Operation Scheme?
    - Is the clinical trial to be conducted in accordance with legislative, regulatory and GCP requirements outlined in the Australian Clinical Trial Handbook: A simple, practical guide to the conduct of clinical trials to international standards of Good Clinical Practice (GCP) in the Australian context.

## 6.0 MONITORING AND DATA MANAGEMENT PLANS

- Researchers should consider who will be monitoring the clinical trial. If an external service provider is being used, ensure that the cost associated is included in the overall clinical trial budget.
- If an internal resource is being used (i.e., research staff from within MSH), costs associated must be included in the overall clinical trial budget – refer to MSH work instruction WI2023-305 Research monitoring for more information.
- Confirm arrangements for the development of a Research Monitoring Plan that is specific to the clinical trial being conducted. The study must be periodically monitored on site/remotely, before, during and after the study, and based on the study specific parameters such as nature, objective, purpose, design, complexity, blinding, size, and endpoints.

- The Data Management Plan describes the database design, data entry and data tracking guidelines, quality control measures, SAE reconciliation guidelines, discrepancy management, data transfer/extraction, and database locking guidelines.
- The Data and Safety Monitoring Board (DSMB) is an independent group of experts that advises the Sponsor. The members of the DSMB serve in an individual capacity and provide their expertise and recommendations. The primary responsibilities of the DSMB are to:
    - periodically review and evaluate the accumulated study data for participant safety, study conduct and progress, and, when appropriate, efficacy, and
    - make recommendations to the Sponsor concerning the continuation, modification, or termination of the trial.
- The DSMB considers study-specific data as well as relevant background knowledge about the disease, test agent, or patient population under study.

### 6.1 Monitoring

- The CPI/PI must provide access to all clinical trial documentation to the Research Monitor when requested and in accordance with the research monitoring plan and MSH work instruction WI2023-305 Research monitoring for more information. The Research Monitor may:
    - perform site initiation visits,
    - perform routine monitoring visits,
    - perform close-out visits,
    - assist sites with logistical/regulatory issues as needed, and/or
    - assist the PI and study team in the preparation for any potential governance/regulatory audit(s).
- The CPI/PI must ensure that the clinical trial is conducted and documented properly and in accordance/adherence with GCP guidelines, the HREC-approved protocol and reports serious incidents such as Adverse Drug Reaction (ADR), Adverse Event (AE) Serious Adverse Event (SAE) as required.

## 7.0 CLINICAL TRIAL RISK ASSESSMENT AND MANAGEMENT

- Risk assessment and management in clinical trials refers to the process of identifying, assessing, and mitigating the potential risks that may arise during the course of a clinical trial.
    - A sponsor organisation is exposed to potential risks in a number of areas, including but not limited to the following:
        - Financial
        - Legal ethical approval or contravention of pharmacovigilance requirements.
        - Reputation
- The CPI/PI is responsible for evaluating all risks to participants and the clinical trial data before the trial starts and developing a plan to control the risks to an acceptable level during protocol development.

- The process of clinical trial risk assessment when determining if MSH will act as Sponsor occurs during study submission as part of the ethical clearance and SSA authorisation process. The following documents must be utilised when undertaking the risk assessment process:
    - WI2023-292 Assessing and managing risk in research
    - Guideline for Good Clinical Practice ICH E6(R2)
    - TGA CTN scheme for approval for clinical trials of unapproved therapeutic goods (drugs, devices, or biologicals).

### 7.1 Complete a risk assessment specific to the clinical trial

- The CPI/PI completes an appropriate risk assessment of specific clinical trial risks which are related to protection of the rights, safety and well-being of clinical trial participants and the credibility of the clinical trial results.
- The scope of risks considered for a clinical trial should include but is not limited to:
    - Patient safety risks such as adverse reactions to the study drug or device and upholding inclusion/exclusion criteria
    - Protocol activities – complexity, time constraints, resource constraints etc.
    - The risk of the clinical trial intervention(s) relative to standard of care and the extent of knowledge about the intervention being tested.
    - Credibility of key data and documentation – i.e., data points are critical to the defined outcomes. How the data will be generated, collected, registered, and reported throughout the study.
    - Number of sites involved in the clinical trial and regulatory submissions such as HREC and RGO.
    - Established quality assurance systems like SOPs, laboratory guidelines/manuals, temperature monitoring of medication/biospecimen storage rooms, central monitoring etc.
    - For participants – physical, emotional, rights, privacy etc.
    - For researchers – experience, reputation, workload, capacity to receive funding etc.
    - For the institution – demand on/availability of resources, reputation, financial, capacity to receive funding etc.
- When performing a risk assessment, a combination of assessors should be involved where possible, including:
    - Persons with knowledge in the respective clinical indication and research field.
    - Persons with knowledge regarding the clinical procedures at the sites.
    - Pharmacist, radiologist, biochemist, statisticians, and other specialists when relevant.

### 1.2 Risk assessment and control

- After identifying the potential risks and critical processes/data before initiation of a clinical trial the CPI/PI must document a Research Risk Assessment and Management Plan which will be utilised by the Sponsor Delegate to:
    - Assess all identified risks against a Risk Impact Assessment Matrix in terms of the likelihood and severity/impact of the potential harm on participants (safety, rights, and well-being) and the reliability of the trial results.
    - Assess each risk individually using a risk matrix to assign the impact for the risk of low, medium, or high.
- The CPI/PI is responsible for managing risks for MSH and for clinical trial management. The goal of risk management is to ensure that the benefits of the clinical trial outweigh the potential risks to the study participants, while also maintaining the scientific integrity of the study.
    - **Note:** Where possible, risks should be eliminated. Where risk cannot be eliminated, protocols and supporting procedures should include methods to identify and manage risks and where required incidents should be reported through RiskMan/ CAMMS Risk Register.
- The Clinical Trial Risk Assessment should be reviewed periodically during conduct of clinical trials and when changes in risk are identified. This essential document should be version controlled and maintained in the eTMF.
- The risk-reduction activities identified during the risk assessment and risk management planning, should be incorporated into the protocol design, clinical monitoring plan, safety monitoring plans, trial-specific standard operating procedures/processes, and staff training.

## 8.0 CLINICAL TRIAL REGISTRATION

- Clinical trial registration is the process whereby key details about the design, conduct and administration of planned clinical trials are made available on a publicly accessible database known as a clinical trial registry. In Australia, registration must occur prospectively, that is before enrolment of the first participant. Prospective clinical trial registration is now widely accepted as an essential part of an overall strategy for improving research transparency.
- The Declaration of Helsinki, which is the cornerstone document guiding the ethical conduct of research in humans by physicians, now explicitly states that “every clinical trial must be registered in a publicly accessible database before recruitment of the first subject.” This approach is supported by the International Committee of Medical Journals Editors (ICMJE) which includes many of the world’s leading journals. In 2004, ICMJE declared that they would not consider a clinical trial for publication without evidence that it had been registered in a publicly accessible clinical trials registry prior to enrolment of the first participant. The World Health Organization (WHO) considers the registration of all interventional clinical trials to be “a scientific, ethical and moral responsibility”.
- In Australia, the Australian and New Zealand Clinical Trials Registry (ANZCTR) is one of the Primary Registries in the WHO Registry Network. To register a clinical trial, submit the details directly to Australian and New Zealand Clinical Trials Registry or an alternative ICMJE approved registry.

- Clinical trials registration is also important for participant recruitment. Registration allows people interested in participating in a clinical trial to search for relevant clinical trials on a single website. Registration also assists health professionals to identify relevant clinical trials for their patients.
- Researchers should register clinical trials as early as possible and ensure information such as contact details and clinical trial status is kept up to date. To assist people interested in participating in a clinical trial, language used in the general title and the lay summary should be brief, clear, written in plain English and easy to for a lay person to understand.

## 9.0 ETHICAL CLEARANCE—CLINICAL TRIALS REQUIREMENTS

- Clinical trials, due to the exposure of humans to as yet unproven treatments, pose additional risks and consequently have tighter controls and reporting requirements than some other research projects.
- For medicine and device research: Whether you are a researcher involved in a collaborative clinical trial project, a researcher involved in a commercially sponsored clinical trial, or a contract research organisation, you will need to develop an agreement between the parties involved in the research. Clinical trial advancement requires assured processes and understanding between the CPI/PI (lead) and participating sites. The primary focus is to achieve timely and efficient SSA authorisation for multi-centre clinical trials so that clinical trials can commence as soon as possible following HREC ethical clearance.
- Clinical trial specific ethical clearance requirements, in addition to standard submission requirements include:
    - brochures for patients
    - HREC only indemnities
    - certificate of insurance
    - investigators brochure
    - Radiation Safety Report—if clinical trial is using ionising radiation.

## 10.0 SSA AUTHORISATION—CLINICAL TRIALS REQUIREMENTS

- A parallel process of SSA authorisation is strongly recommended to ensure timely commencement of a clinical trial at MSH that has both ethical clearance and SSA authorisation.
- You may also need to arrange for indemnity for your research institution, research premises or ethics committee. Standard templates for clinical trial agreements and indemnities have been developed and should be used wherever possible in order to minimise the need for legal review.
- For clinical trials and post marketing research, the templates for contracts and indemnities are maintained by Medicines Australia. In addition to standard submission requirements include:
    - Medicines Australia Standard Indemnity
    - Certificate of Insurance
    - eCTN acknowledgement
    - Copies of GCP qualifications of research team

- Complete a Collaborative Research Group Clinical Trials Research Agreement (CRG CTRA) if required.
- The CPI/PI must receive SSA authorisation prior to commencement of the clinical trial.
- The CPI/PI is responsible for establishing a quality management system that ensures obtaining all applicable regulatory approvals efficiently and in a timely manner and that the eTMF is kept up to date including post-authorisation amendments and reports.

### 11.0 COMMERCIALLY SPONSORED CLINICAL TRIALS

- Following feasibility and site selection for a clinical trial there are specific tasks required of the sponsor/contract research organisation, and negotiation of additional assistance may be agreed for the clinical trial. As a sponsor/ contract research organisation, communication with clinical trial site personnel is essential to ascertain local site requirements for SSA authorisation.
- The SSA form, along with the supporting documents, is the vehicle for transferring all essential clinical trial documents from the principal investigator/clinical trial coordinator to the Metro South Research Governance Office (MSRGO).

## RESPONSIBILITIES

| Position | Responsibility | Audit criteria |
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| Sponsor | • The trial sponsor is responsible for the initiation, management and financing (or arranging the financing) of the trial and carries the medico-legal responsibility associated with its conduct.<br>• The Guideline for Good Clinical Practice (Section 5; pages 21-34) identifies the responsibilities of trial sponsors. The responsibilities detailed in the Guidelines are extensive. However, it is noted that "the methods used to assure and control the quality of the trial should be proportionate to the risks inherent in the trial and the importance of the information collected." (p.X) | N/A |
| Principal Investigator | • A Principal Investigator is responsible for the conduct of a study, ensuring that the study complies with GCP guidelines. | N/A |
| Coordinating Principal Investigator | • A Coordinating Principal Investigator (CPI) takes overall responsibility for the study and for the coordination across all sites is if a study is conducted at more than one study site. The Principal Investigator at each site will retain | N/A |

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| | responsibility for the conduct of the study at their site. | |
| Sponsor Delegate | • A nominated Sponsor Delegate within MSH who takes on responsibilities of the Sponsor. | N/A |

## DEFINITIONS

| Term | Definition |
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| Adverse drug reaction (ADR) | Adverse drug reactions concern noxious and unintended responses to a medicinal product. |
| 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 considered related to this medicinal product or not. |
| Clinical Trial<br>*(National Clinical Trials Governance Framework)* | A clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Clinical trials include but are not limited to:<br>• Surgical and medical treatments and procedures<br>• Experimental drugs<br>• Biological products<br>• Medical devices<br>• Health-related service changes<br>• Health-related preventative strategies<br>• Health-related educational interventions. |
| Collaborative Research Group Clinical Trials Research Agreement (CRG CTRA) | An agreement template that is to be used where a Hospital and Health Service (HHS) acts as and assumes all the responsibilities of a commercial sponsor. |
| Coordinating Principal Investigator (CPI)/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 CPI/PI. In this instance they may delegate tasks to other team members.<br>There are different terms used to distinguish the varying role of Investigators. If a study is conducted by a team of individuals at a study site, the Investigator is the responsible leader of the team and may be |

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| | called the Principal Investigator (PI). In this instance they may delegate tasks to other team members. |
| 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 participants are protected. |
| Investigator-initiated trial | A clinical trial that has the following characteristics:<br>• A pharmaceutical/device company is not acting as the sponsor for the purposes of the CTN application.<br>• A pharmaceutical/device company is not fully funding the conduct of the study, that is, making payment to the relevant hospital or investigator.<br>• The clinical trial addresses relevant clinical questions and not industry needs.<br>The CPI/PI or the Hospital/Institution is the primary author and custodian of the clinical trial protocol. |
| Quality Assurance (QA) | Covers all policies and systematic activities implemented within a quality system. QA ensures that data are recorded, analysed, and recoded in accordance with the protocol and GCP. The use of GCP guidelines ensures ethical and scientific quality standards for the design, conduct, recording, and reporting of HREC approved clinical trials that involve research participants. |
| Research Monitoring | ICH GCP defines monitoring as the act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, Standard Operating procedures (SOPs), GCP, and the applicable regulatory requirement(s). |
| Serious adverse event (SAE) | Any untoward medical occurrence that at any dose:<br>• Results in death<br>• Is life-threatening<br>(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).<br>• Requires inpatient hospitalisation or results in prolongation of existing hospitalisation;<br>• Results in persistent or significant disability/incapacity;<br>• Is a congenital anomaly/birth defect;<br>• Is a medically important event or reaction. |

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| Sponsor | The Sponsor is responsible for ensuring that the clinical trial is conducted in accordance with the protocol, GCP and applicable regulatory requirements. Specifically, MSH is the Sponsor for investigator-initiated clinical trials where MSH personnel has written the protocol, data is owned by MSH and/or is named on the CTN (as applicable). |
| Study Master File (SMF)/electronic Trial Master File (eTMF) | A Study Master File or an electronic trial master file (eTMF) is a technology solution designed to organise, collect, store, track, and archive required and essential study documents. The eTMF is an electronic version of the trial master file (TMF) that is now industry standard. Historically, the TMF was organised in paper form.<br>The eTMF is the collection of required documents associated with a single clinical trial that demonstrate the trial's compliant conduct and all associated activities for evaluation by regulators. Essential study documents include but are not limited to: complete and current training documentation and materials, delegation log, participant log, and safety documentation, PICF, Ethics, SSA, Audit or monitoring documents and participant information. |
| Study Procedure Manual (Manual of Procedures) | Is a handbook that details a study's conduct and operations as well as facilitates consistency in protocol implementation and data collection across study participants and sites. Essentially it operationalises the study protocol and describes each step of the study and how it is to be conducted. |

## RELATED AND SUPPORTING DOCUMENTS

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| **Legislation and other Authority** | **Legislation**<br>• *Hospital and Health Boards Act 2011* (Qld)<br>• *Information Privacy Act 2009* (Qld)<br>• *Privacy Act 1988* (Cth)<br>• *Public Health Act 2005* (Qld)<br>• *Statutory Bodies Financial Arrangements Act 1982* (Qld)<br>• *Therapeutic Goods Act 1989* (Cth)<br>**Regulations**<br>• *Hospital and Health Boards Regulation 2012* (Qld)<br>• *Information Privacy Regulation 2009* (Qld)<br>• *Therapeutic Goods (Medical Devices) Regulations 2002* (Cth)<br>**Health Service Directive**<br>• QH-HSD-035 Research Ethics and governance |
| **Standards** | • National Clinical Trials Governance Framework |

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| | • National Safety and Quality Health Service (NSQHS) Standards 2nd Ed.<br>  ○ Standard 1 – Clinical Governance<br>  ○ Standard 2 – Partnering with Consumers<br>• Australian Standard Medical and Surgical Equipment |
| **Supporting documents** | **Procedures**<br>• PR2023-411 Research excellence<br>• PR2023-412 Research support and management<br>• PR2023-413 Research administration and compliance<br>**Work instructions**<br>• WI2023-287 Research integrity<br>• WI2023-288 Research quality management systems<br>• WI2023-299 Data and privacy<br>• WI2023-290 Research authorship, peer review and publication<br>• WI2023-291 Research complaints and misconduct<br>• WI2023-292 Assessing and managing risk in research<br>• WI2023-299 Ethical and scientific review of research<br>• WI2023-301 Site specific assessment of research<br>• WI2023-297 Gift cards (for use as research incentives)<br>• WI2023-299 Ethical and scientific review of research<br>• WI2023-300 Exemptions from research review<br>• WI2023-301 Site specific assessment of research<br>• WI2023-302 Research contracts and study execution<br>• WI2023-303 Metro South Health sponsorship of Clinical Trial Notification (CTN) scheme trials<br>• WI2023-304 PowerTrials - ieMR research support module<br>• WI2023-305 Research monitoring<br>• WI2023-306 Post approval – research amendments, reporting and closure<br>**Guidelines**<br>• GL2023-99 Planning a research project<br>• GL2023-100 Research Participant Information and Consent Form (PICF)<br>• GL2023-101 Research contract clauses<br>• GL2023-102 Use of electronic signatures in research contracts<br>**Supporting resources – external**<br>• Australian Clinical Trials Education Centre (A-CTEC) - Melbourne Academic Centre for Health (machaustralia.org) |

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| | • Australian Clinical Trials (NHMRC)<br>• Clinical Trial Approval (CTA) Scheme<br>• Clinical Trial Notification (CTN) Scheme<br>• Guidance for Good Clinical Practice – ICH GCP (Annotated by TGA)<br>• Queensland Clinical Trials Coordination Unit (QCTCU)<br>• Queensland Clinical Trials Portal<br>• Safety monitoring and reporting in clinical trials involving therapeutic goods<br>• The National Statement on Ethical Conduct in Human Research<br>• TGA Clinical Trials Handbook<br>• NHMRC Safety monitoring and reporting in clinical trials involving therapeutic goods<br>• NHMRC Data Safety Monitoring Boards<br>• VCCC Alliance Sponsorship Risk Assessment and Management |

## HUMAN RIGHTS ACT 2019

Metro South Hospital and Health Service is committed to respecting, protecting, and promoting human rights. Under the *Human Rights Act 2019*, Metro South Health has an obligation to act and make decisions in a way that is compatible with human rights and, when making a decision, to give proper consideration to human rights. When making a decision about research, decision-makers must comply with that obligation. Further information about the *Human Rights Act 2019* is available at: https://www.forgov.qld.gov.au/humanrights.

## GUIDELINE DETAILS

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| **Document Author** | Manager, Research Development, Metro South Research |

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## REVIEW HISTORY

| Version | Approval date | Effective from | Authority | Comment |
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| 1.0 | 15/01/2021 | 15/01/2021 | Executive Director, Metro South Research | New document. |
| 2.0 | 7/12/2023 | 13/12/2023 | Chief People, Engagement and Research Officer | Update to links and references. |