Clinical Trial Governance Procedure

Section 1 - Purpose and Scope

Purpose

(1) The University of Queensland (UQ or the University) expects research to be conducted responsibly, ethically, and with integrity. This Procedure describes the necessary governance processes related to legislation, regulations, guidelines, policies, procedures and good practice arrangements mandatory for clinical trials undertaken under the auspices of the University.

(2) This Procedure should be read in conjunction with the:

a. Responsible Research Management Framework Policy;
b. Human Research Ethics Procedure; and
c. National Statement on Ethical Conduct in Human Research (National Statement).

In addition, when applicable, please refer to the:

d. Australian Clinical Trial Handbook;
e. AIATSIS Code of Ethics for Aboriginal and Torres Strait Islander Research; and
f. Working with Children Policy.

(3) All University staff, title holders and students are required to conduct themselves in a manner consistent with the Responsible Research Management Framework Policy, Australian Code for the Responsible Conduct of Research, the National Statement, and the standards set out in the relevant UQ code or charters:

a. Staff and title holders: Staff Code of Conduct Policy
b. Students: Student Code of Conduct Policy
c. Higher degree by research (HDR) candidates: Higher Degree by Research Candidate Charter.

Context

(4) A clinical trial is defined as any study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes, including biomedical and/or behavioural outcomes.

(5) In this Procedure, clinical trials involving therapeutic goods or products as defined by the Therapeutic Goods Administration (TGA) are termed Investigational Medicinal Products (IMP) or Investigational Medicinal Devices (IMD). Clinical trials investigating health related interventions not involving investigational medicinal products or devices are termed Non-IMP/D trials.

(6) UQ staff, title holders and students conducting clinical trials are referred to as ‘investigators’ throughout this Procedure.

Scope

(7) This Procedure applies to all investigators conducting or assisting with the conduct of clinical trials when:

a. acting in their University capacity, and
b. UQ is the sponsor or a site for a clinical trial.

(8) This Procedure does not apply to investigators when acting outside their University employment, enrolment, or affiliation (refer to Consultancy, Secondary Employment and Internal Work Policy and Consultancy Procedure).

(9) Conducting clinical trials interstate and/or in international jurisdictions may present additional considerations related to key controls, including insurance, legal and regulatory requirements. Investigators are responsible for familiarising themselves with the relevant jurisdictional requirements, and if required, must seek specialist legal and governance advice prior to engaging with sites that are located overseas.

Section 2 - Process and Key Controls

(10) To be ethically acceptable, human research must comply with the National Statement and demonstrate the values of research merit and integrity, justice, beneficence and respect.

(11) All clinical trials should be conducted in accordance with the principles of the ICH Guideline for Good Clinical Practice, section 2.

(12) All researchers undertaking clinical trials should have a current certificate in Good Clinical Practice.

Section 3 - Key Requirements

Requirement (section of this Procedure)	IMP clinical trial	IMD clinical trial	Non-IMP/D clinical trial
Protocol and associated essential documentation (clauses 13-16)	Required	Required	Required
Risk assessment and management plan (clauses 17-21)	Required	Required	Required
Ethical approval (clauses 22-25)	Required	Required	Required
Clinical trial registration (clauses 26-27)	Required	Required	Required
Insurance cover (clauses 28-35)	Required	Required	Required
Indemnity and compensation arrangements (clauses 36-37)	Required	Required	Required
Contracts and agreements (clauses 38-42)	Required	Required	Required
Identification of trial sponsor (clauses 43-45)	Required	Required	Not required
Site-specific assessment (clauses 46-48)	If applicable	If applicable	If applicable
Clinical Trial Notification (CTN) or Clinical Trial Approval (CTA) (clauses 49-51)	Required	Required	Not required
Progress reporting (clauses 52-53)	Required	Required	Required
Safety monitoring and reporting (clause 76)	Required	Required	Not required
Reporting of Serious Breaches of GCP or the Protocol (clauses 79-81)	Required	Required	Not required
ICH Guideline for GCP (annotated by the TGA)	Required	Not required	Not required

Requirement (section of this Procedure)	IMP clinical trial	IMD clinical trial	Non-IMP/D clinical trial
Medical devices ISO 14155:2020 (UQ login required)	Not required	Required	Not required
Therapeutic Goods Act 1989	Required	Required	Not required

Part A - Prior to Conducting a Clinical Trial – Start-up

Protocol and Associated Essential Documentation

(13) The Protocol for a clinical trial describes the objectives, design, methodology, statistical considerations and organisation of the trial. It plays a key role in planning, conduct, interpretation, oversight, and external review by detailing the plans from ethics approval to dissemination of results.

(14) UQ investigators must use the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist.

(15) The Protocol must be developed in conjunction with a risk assessment and management plan (clauses 17 to 21 of this Procedure).

(16) The investigator must maintain the Protocol and/or approved documentation. The maintenance includes ongoing monitoring, and necessary amendments, seeking appropriate approvals for any changes.

Risk Assessment and Management Plan

(17) Investigators must assess and manage the risks associated with a clinical trial to protect all stakeholders and to increase the likelihood of achieving the objectives of the trial.

(18) The investigator of the clinical trial must complete the UQ Clinical Trial Risk Assessment and Management Plan Template (RAMP), consistent with the Enterprise Risk Management Framework Policy.

(19) The appropriate signatory in accordance with the identified managed risk level (MRL) rating and the oversight/reporting level in the Risk Action Table of the Risk Matrix, must approve the RAMP.

(20) The approved RAMP must be submitted to the Research Ethics and Integrity (REI) unit as part of the ethics approval or ratification (see clauses 22 to 25 of this Procedure).

(21) The investigator must maintain the effectiveness of the RAMP for the duration of the clinical trial. The maintenance includes ongoing monitoring and necessary amendments, seeking appropriate approvals for any changes.

Ethics Approval

(22) Clinical trials must undergo ethical and scientific review, approval, and monitoring by a National Health and Medical Research Council (NHMRC) certified Human Research Ethics Committee (HREC) and/or other ethical review bodies, such as the Australian Institute of Aboriginal and Torres Strait Islander Studies (AIATSIS) HREC.

(23) UQ HREC will provide the ethical review for a clinical trial conducted at a UQ site. Ethics approval must be sought in accordance with the Human Research Ethics Procedure.

(24) Clinical trials conducted at a hospital site must seek ethical approval from the designated hospital HREC. If multiple sites are involved, the National Mutual Acceptance scheme may be accessed if available; otherwise separate ethical approvals must be sought from each site.

(25) All external HREC approvals require ratification by UQ. All approved amendments and reports must be submitted

to REI.

Clinical Trial Registration

(26) All clinical trials must be registered on a publicly accessible approved database, prior to participant recruitment. This is a requirement of the National Statement, the Code, and the International Committee of Medical Journals Editors.

(27) The investigator is responsible for ensuring the registration is completed and for maintaining the relevance of the registration information.

Insurance Cover

(28) UQ and its subsidiaries have cover for liability associated with a clinical trial conducted by them or on their behalf where:

a. a research subject suffers a bodily injury; and
b. the injury arises directly from a clinical trial covered by the policy.

provided they are acting:

c. within the scope of their duties in connection with the clinical trial; and
d. within the terms of any Protocol (including informed written consent requirements); and
e. in accordance with all relevant policies, procedures, legal and regulatory requirements.

(29) University insurance coverage automatically applies to trials unless excluded from cover or requiring prior declaration to approve cover as outlined under clauses 30 to 35.

Insurance Declaration and Notification

(30) To ensure appropriate coverage, all clinical trials must be declared or notified to UQ's insurer by Insurance Services. Appropriate insurance and compensation arrangements must be included in Participant Information Sheets.

Declaration

(31) The following clinical trials must be declared and accepted by the University's insurer before the commencement of the trial:

a. involving participants aged two years and below;
b. pregnancy-related; and
c. those being undertaken overseas (non-Australian trials), where local insurance cover is required.

(32) The UQ investigator, or delegate, must submit an Insurance for Human Research Studies – Declaration for Approval to REI.

(33) REI is responsible for the review and endorsement of the declaration, and submission to Insurance Services.

Notification

(34) For all other clinical trials (except excluded trials) the Insurance for Human Research Studies – Notification must be completed after ethics approval to ensure no prejudice to insurance cover.

Indemnity and Compensation Arrangements

(35) Commercially sponsored clinical trials where the involvement of UQ is limited to either:

a. ethical review by its HREC, or
b. the provision of premises for the conduct of the trial,

will require the clinical trial sponsor to provide indemnification. The sponsor must provide evidence of indemnity through use of the Medicines Australia Indemnity Form.

(36) Clinical trials conducted under the sponsorship of a Collaborative or Cooperative Research Group (CRG) agreement do not require indemnity.

Contracts and Agreements

(37) All clinical trials require a contract if a third party is to:

a. participate in the conduct of;
b. provide financial support for; or
c. provide products for use in, the clinical trial.

(38) The Research Office, and potentially Legal Services (Research), must be involved from the outset to help establish the appropriate contracts between UQ and other entities. Contracts must be undertaken in accordance with the Administration of Research Funding - Applications, Grants and Contract Research Policy. The details specific to the clinical trial project including funding, budget, resulting intellectual property, and data or material transfer requirements must be documented in the agreement.

(39) The contracts and agreements between trial sponsors and third parties must ensure all roles and responsibilities are clearly defined.

(40) Clinical trials spanning one or more hospital, or another institution, require a Clinical Trial Research Agreement (CTRA). UQ recommends use of the Medicines Australia Clinical Trial Research Agreement templates.

(41) All agreements, and any subsequent amendments, must be authorised in accordance with the Schedule of Contract Delegations and Sub-delegations before trial commencement.

Identification of a Sponsor

(42) A formal sponsor is required for the use of 'unapproved' therapeutic goods (IMP or IMD) in a clinical trial conducted under the CTN/CTA schemes.

(43) The sponsor must be an Australian entity who will assume responsibility for the scientific, ethical, regulatory and legal aspects of the trial.

(44) UQ can assume the sponsorship role for a UQ Investigator-Initiated Trial (IIT) or as part of an academic and/or non-commercial Collaborative or Cooperative Research Group (CRG).

Site of Clinical Trial

(45) A Site-Specific Assessment (SSA) must be submitted to the relevant hospital research governance office if one or more of the proposed clinical trial sites are located within a hospital. Each hospital site will require an SSA application (unless it is part of a Single Hospital Health Service SSA application process). The site Principal Investigator (different to the UQ investigator) is responsible for submitting the SSA and all associated documentation. SSA requirements and

guidance is managed by the hospital site.

(46) Any amendments to the HREC approved protocol or associated documentation requires acknowledgment or approval from the relevant hospital research governance office.

(47) A formal SSA application is not required when UQ is the clinical trial site. REI approves UQ as the site as part of the UQ ratification process.

Clinical Trial Notification (CTN) or Clinical Trial Approval (CTA)

(48) The sponsor of a clinical trial involving an 'unapproved' IMP or IMD must notify the TGA prior to the commencement of the trial through a Clinical Trial Notification (CTN) or Clinical Trial Approval (CTA).

(49) The clinical trial investigator, or delegate, must complete and submit a CTN data capture form to REI along with the Protocol and proof of HREC approval(s).

(50) REI, representing the University as the clinical trial sponsor, will submit the CTN or CTA to the TGA.

Part B - Conducting a Clinical Trial

(51) The clinical trial must be conducted in accordance with its Protocol and the requirements and conditions of any approvals, contracts, and relevant regulations and legislation including:

a. Annual progress reports to HREC and funding bodies as required;
b. Safety and Adverse Event reporting;
c. Administration of research funding in accordance with appropriate policies and agreements.

(52) The ongoing efficacy of the clinical trial documentation must be monitored throughout the trial with necessary amendments, variations approved by the relevant bodies.

Part C - Closing, Terminating or Halting a Clinical Trial

Closing

(53) Closing a clinical trial will require:

a. submission of results (including negative, inconclusive, or positive results) to the registry where the clinical trial was registered;
b. notification to all approval bodies;
c. notification and meeting reporting requirements of any funding bodies;
d. notification to applicable stakeholders as per CTRA/agreements;
e. dissemination of clinical trial results by publication;
f. trial results being shared with participants in accordance with the trial Protocol; and
g. research data and information to be managed in accordance with the Protocol, the Research Data Management Policy and national and international privacy and data regulations.

Early Termination or Halt

(54) A clinical trial may be required to terminate or temporarily halt if:

a. significant safety issues have arisen, or urgent safety measures are required;
b. there are or have been substantial deviations from the trial Protocol;

c. unforeseen factors are impacting trial resources or delivery;
d. HREC and/or other regulatory approvals are withdrawn;
e. adverse events of unexpected type, severity, or frequency are encountered; or
f. as the trial progresses, the continuation of the trial would disadvantage some of the participants as determined by the investigators or others monitoring the trial.

(55) Notification of urgent safety measures, early termination or halt must be provided to investigators, TGA approving authorities and relevant institutional delegates within the specified timelines in the NHMRC Guidance - Safety Monitoring and Reporting in Clinical Trials involving Therapeutic Goods.

Section 4 - Roles, Responsibilities and Accountabilities

The University of Queensland as Sponsor

Relevant for Clinical Trials of IMP and IMD

(56) Acting as the clinical trial sponsor carries specific roles and responsibilities in accordance with Section 5 of ICH Guideline for Good Clinical Practice.

(57) UQ as sponsor can delegate any or all of its clinical trial-related duties and functions, including safety reporting, to a third party, provided the sponsor retains oversight and audit arrangements. The ultimate responsibility for the quality and integrity cannot be delegated.

Investigators

(58) The roles and responsibilities of investigators involved in IMP or IMD clinical trials are set out in Section 4 of the ICH Guideline for Good Clinical Practice.

(59) The investigator's responsibilities include:

a. ensuring adequate financial and other resources are available to conduct the clinical trial;
b. overseeing the conduct of the clinical trial in accordance with the applicable Protocol;
c. taking appropriate steps to ensure compliance with all legislative, regulatory, policy and other requirements applicable to a particular clinical trial, including any requirements of the HREC;
d. monitoring and updating the risk management plan throughout the clinical trial project to ensure the effectiveness of risk mitigations and completeness of identified risks;
e. maintaining records, including relevant fully executed agreements;
f. monitoring the conduct of investigators and others undertaking activities within the clinical trial;
g. meeting all safety monitoring and reporting responsibilities in accordance with the NHMRC Guidance - Safety Monitoring and Reporting in Clinical Trials involving Therapeutic Goods; and
h. submission of results (including negative, inconclusive, or positive results) to the registry where the clinical trial was registered.

Human Research Ethics Committee (HREC)

(60) The primary role of the HREC is to protect the welfare and rights of participants in research and review research proposals involving human participants to ensure that they are ethically acceptable and in accordance with relevant standards and guidelines. The HREC has the ability to withdraw ethics approval for a trial.

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(61) HRECs are also responsible for:

a. ensuring that the conduct of all research approved by the HREC is monitored following the provisions set out in the National Statement and the trial Protocol;
b. monitoring the continued benefit-risk ratio of the trial, in particular, whether any safety reports received impact on the continued ethical acceptability of the trial;
c. approving any monitoring and reporting arrangements; and
d. meeting all safety monitoring and reporting responsibilities.

Research Ethics and Integrity

(62) Research Ethics and Integrity (REI) is responsible for:

a. providing guidance, on ethical and governance requirements relating to clinical trials;
b. the receipt of an approved RAMP ahead of referring the project to a UQ HREC/ratification;
c. assessing research governance criteria during the ethics review process and, when completing TGA notification (if applicable);
d. maintaining online information on sponsor and investigator responsibilities;
e. submitting CTN/CTA and any amendments to the TGA;
f. maintaining a register of IMP and IMD clinical trials; and
g. maintaining a record of safety reporting.

Authorised Delegate

(63) The authorised delegate, in accordance with the Schedule of Contract Delegations and Sub-delegations, is responsible for the approval of the commencement of the clinical trial at UQ.

(64) The following documents are included in the agreement signatory process:

a. Trial protocol.
b. HREC approval/ratification and conditions (as applicable).
c. RAMP.
d. UQ insurance confirmation.
e. CTN acknowledgment or CTA approval (if applicable).
f. Site-specific assessment (if applicable).

Research Office

(65) The Research Office is responsible for:

a. identifying a suitable template contract, in partnership with external parties such as hospital sites, CROs, local sponsors, or local representatives in foreign jurisdictions;
b. reviewing and providing advice on completion of the schedule details;
c. liaising with Legal Services (Research) as required, e.g., if special conditions need to be drafted, or third party agreements need full legal review; and
d. arranging for sign-off by the relevant authorised delegate.

Approver and Overseer of Risk Assessment and Management Plan

(66) The University Line Manager of the clinical trial principal investigator is responsible for the initial review of the

RAMP. The level of approval and oversight may require escalation, dependent on the overall assessed managed risk level and risk matrix, refer to clauses 17 to 21 of this Procedure.

Section 5 - Monitoring, Review and Assurance

(67) The Deputy Vice-Chancellor (Research and Innovation) is responsible for the development, compliance monitoring, and review of this Procedure.

Section 6 - Recording and Reporting

Record Keeping

(68) Recording and reporting for the clinical trial begins upon authorisation of the trial and continues through all phases, including closure and dissemination of results.

(69) UQ investigators must maintain records in accordance with the Information Governance and Management Framework and Research Data Management Policy. The coordinating principal investigator must meet all reporting and publication requirements of the approving HRECs, funding bodies and regulatory agencies.

Specific for IMP and IMD Clinical Trials

(70) To be GCP compliant, a risk-based monitoring plan should be developed to describe the proposed monitoring strategy, responsibilities of all the parties involved, methods and rationale.

(71) The RAMP, Protocol and when required, a separate monitoring plan, will outline the requirements.

(72) The TGA may conduct a regulatory inspection of a clinical trial where necessary on safety grounds or stop a trial where that action is in the public's interest.

(73) There are specific requirements for essential documentation as outlined in Section 8 of the Guideline for Good Clinical Practice and Section 7.4 of ISO 14155 for IMD.

(74) Essential documents are those, which individually and collectively permit evaluation of the conduct of a trial, and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, sponsor and monitor with the standards of GCP with all applicable regulatory requirements.

Safety Reporting

(75) To address the collection, verification and reporting of adverse events and Adverse Reactions that occur in clinical trials involving IMPs and IMDs under CTN/CTA schemes, UQ follows the NHMRC Guidance - Safety Monitoring and Reporting in Clinical Trials involving Therapeutic Goods in combination with the safety reporting outlined in the approved protocol and, including event notification as defined by Insurance Services if there is a potential clinical trial claim.

Reporting of Significant Safety Issues

(76) The investigator, their delegate, or the sponsor may have to take immediate urgent safety measures to protect participants or investigators in the event of significant safety issues.

(77) Urgent safety measures can be instigated by either the investigator or sponsor and can be implemented before seeking approval from HRECs or institutions.

Reporting Serious Breaches of Good Clinical Practice

(78) A serious breach of Good Clinical Practice or the Protocol must be reported. The breach may affect the safety and rights of clinical trial participants, and/or the clinical trial results.

(79) Serious breaches must be reported per the Reporting of Serious Breaches of Good Clinical Practice (ICH-GCP) or the Protocol for Trials Involving Therapeutic Goods.

(80) Depending upon the breach category, it may need to be reported to the funder and require further consideration following the University's Research Conduct Policy and Procedures.

Section 7 - Appendix

Definitions

Term	Definition
Adverse Event	any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in participants, whether or not related to the investigational medicinal product/intervention.
Adverse Reaction	any untoward and unintended response to an investigational medicinal product/ intervention related to any dose administered.
Investigator-initiated Trials (IIT)	are clinical studies initiated and managed by non-pharmaceutical company researchers, like individual investigators, institutions, collaborative groups or cooperative groups.
Investigational Medicinal Device (IMD)	medical device being assessed for safety or performance in a clinical investigation. This includes medical devices already on the market, that are being evaluated for new intended uses, new populations, new materials or design changes.
Investigational Medicinal Product (IMP)	A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorisation when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, a new patient group or when used to gain further information about an approved use. Note - This definition includes biologicals used as investigational medicinal products.
Protocol	is a document that describes the background, rationale, objectives, design, methodology, statistical considerations, and organisation of a clinical research project.
Research	the concept of research is broad and includes the creation of new knowledge and/or the use of existing knowledge in a new and creative way so as to generate new concepts, methodologies, inventions and understandings. This could include synthesis and analysis of previous research to the extent that it is new and creative.
Staff	continuing, fixed-term, and research (contingent funded) and casual staff members.
Student	a person enrolled as a student at the University or undertaking courses or programs at the University.
Title Holders	visiting academics, academic title holders, industry fellows, emeritus professors, adjunct and honorary title holders, and conjoint appointments.

Status and Details

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