Post approval – research amendments, reporting and closure

PURPOSE

This work instruction describes the processes for activities which may occur post ethical clearance and Site-Specific Assessment (SSA) authorisation such as amendments, reporting and closure in Metro South Health (MSH).

OUTCOME

The intended outcome of this work instruction is to:

- Outline processes for post approval activities to ensure research continues to be conducted in an ethical and scientifically robust manner by upholding principles outlined within the PL2023-92 Research Policy.
- Provide guidance on the completion of the HREC/RGO Annual Progress/Final Report (Attachment 1).

This work instruction outlines processes described in MSH procedure PR2023-413 Research administration and compliance and upholds principles outlined within the Research Administration and Compliance Handbook.

SCOPE

This procedure 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.

WORK INSTRUCTION

1. STEP 1: AMENDMENTS TO RESEARCH PROJECTS

- Amendments to a research project which may affect the ongoing ethical and scientific acceptability of the research project or the suitability of the research at the MSH site must be submitted for review to Metro South Research. Amendments may include but are not limited to:
    - Change to the research protocol.
    - Change to the Participant Information and Consent Form (PICF).
    - Change to participant recruitment such as the use of advertising documents.
    - Site specific changes.
    - Change to Principal Investigator/Coordinating Principal Investigator (PI/CPI) and change in research personnel involved in the research project/s.
    - Changes to staffing levels or number of sites.
    - Research budget updates or changes that affect finance, costing or resourcing.

- Inclusion of external institution investigator or team member belongs to a non-Queensland Health institution, University etc.
- Updated insurance certificates.
- Variations to research contracts/agreements including changes to the legal name of the third (3rd) party entity.
- Changes to the Clinical Trial Approval (CTA) or Clinical Trial Notification Form (CTN).
- Pathology/Radiology/Pharmacy costing changes.
- Change to the investigator brochure because of safety/ toxicity reports either relating to the current indication or associated indication that materially changes study equipoise considerations.
- Change in sponsor or addition of an external institution.
- Change to the risk rating at identified in the Research risk assessment and management plan – refer to MSH work instruction WI2023-292 Assessing and managing risk in research.
- Any other matters which may impact on the conduct of the research project in MSH.

- An administrative amendment is defined as changes to the details of research that have no significant implications for participants or for the conduct, management or scientific value of the research project. For example:
  - Correction of typographical errors in the protocol or other research project documentation.
  - Amended contact details for the sponsor or research project staff.
  - Appointment of new or change of support staff contact.

1.1 Amendment fees

- All non-administrative amendments to previously approved sponsored research protocols that are submitted to the Metro South Human Research Ethics Committee (MSHREC) for review attract a fee.
- Refer to MSH procedure PR2023-413 Research administration and compliance for more information.

1.2 Ethics amendments

- Amendments for the MSHREC must be submitted through the Ethical Review Manager (ERM) applications as a sub-form to the HREA.
- The following details must be included:
  - A brief description of the changes.
  - The rationale for the changes.
  - Any ethical and scientific implications for the ongoing conduct of the research project.
  - Any regulatory changes to the status of the investigational medicine or device, if applicable.
  - Amended study documents with updated version control (tracked changes and clean versions).
- Refer to MSH work instruction WI2023-299 Ethical and scientific review of research for more information.

1.3 SSA amendments

- Amendments that may have a bearing on site specific documentation, financial arrangements or have legal implications (e.g., amendments to contracts) must be submitted to the Metro South Research Governance Office (MSRGO) along with a copy of the Human Research Ethics Committee (HREC) approval letter.
- All SSA amendments are created in ERM as a sub-form to the SSA.
- Amendments for MSRGO review require completion of the relevant section of the applicable Research Contracts Approval and Study Execution Form (RCASE Form).
    - Refer to MSH work instruction WI2023-302 Research contracts and study execution for more information.
- The RCASE Form in this case acts as a cover letter, it must be filled out with:
    - A brief description of the changes.
    - The rationale for the changes.
    - Any implications for the ongoing conduct of the research project.
- For research projects that have not been approved by the Metro South Human Research Ethics Committee (MSHREC), submit the HREC approval of the amendment along with any updated site-specific changes on the RCASE Form.
- Upon submission of an amendment, the MSRGO will perform a formal review of requirements and relay information, via the SSA in ERM, of any outstanding requirements.
- The PI/CPI must sign for contractual and *Public Health Act* changes, and the coordinator/associate investigators are able to sign on behalf the PI/CPI for all other amendments.
- Further assessment/more information may be required by the MSRGO.
- PI/CPI will be formally advised by the MSRGO when the research project amendments have been approved via ERM.
- Refer to MSH work instruction WI2023-301 Site specific assessment of research for more information.

1.3 PowerTrials amendments

- It is mandatory to maintain the PowerTrials record in the ieMR for studies that involve patient consent.
- Refer to MSH work instruction WI2023-304 PowerTrials - ieMR research support module for more information regarding managing amendments and enrolment of patients.

1.4 Version control and track changes

- As part of the ethics and SSA amendment process it is vital for research project documentation to be submitted with version control and track changes.
- See Attachment 2: Track Change Guide for more information.

2. STEP 2: SERIOUS ADVERSE EVENT (SAE)/SUSPECTED UNEXPECTED SERIOUS ADVERSE REACTION (SUSAR) REPORT

- Researchers must report serious adverse events (SAE) and suspected unexpected serious adverse reactions (SUSAR) to the sponsor.

- The Sponsor is responsible for ensuring that the research project is conducted in accordance with the research protocol, GCP and applicable regulatory requirements.

- MSH conforms to the National Health and Medical Research Council (NHMRC) Position Statement: Monitoring and Reporting of Safety for Clinical Trials.

2.1 MSHREC review

- MSHREC will review:
  - Safety reports if appropriate and necessity is provided by the researcher.
  - Research protocol violations (not deviations).
- The Executive Summary of safety information produced for international regulators, such as a Development Safety Update Report (DSUR), may serve as the annual safety report sent to HRECs (a full DSUR is not required). Otherwise, a DSUR does not need to be submitted for review if there has been no change to the risk-benefit ratio and thus no ethical implications to the conduct of the study at sites under MSHREC clearance.
  - See the NHMRC Guidance: Safety monitoring and reporting in clinical trials involving therapeutic goods for more information.
- Where MSH is the nominated Sponsor of a study, the Sponsor must follow the recommendations in the NHMRC Guidance. Refer to MSH work instruction WI2023-303 Metro South Health sponsorship of Clinical Trial Notification (CTN) scheme trials for more information regarding sponsor responsibilities and monitoring plans.

2.2 MSRGO review

- The MSRGO no longer requires submission of amendments, which do not have an impact on ongoing site acceptability (see note below).
- Documentation not required:
  - Site specific PICFs
  - *Dear Investigator Letters (DIL)
  - *Independent Data Monitoring Committee (IDMC) outcome letters where study can continue as planned
  - Suspected Unexpected Serious Adverse Reactions (SUSAR) notifications
  - Serious Adverse Event (SAE) notifications
  - Data Safety Update Reports (DSUR)
  - Safety reports (including line listings)
  - *Protocol deviations
  - Research protocols/protocol amendments
  - Investigator brochures/investigator brochure amendments
  - Synopsis
  - Case Study

- Curriculum Vitae

- Note: Items marked with an Asterix (*) are also not required by the MSHREC unless they have a bearing on the ongoing ethical and scientific validity of a study.
    - Note: This is not applicable to research projects being conducted under the TeleTrials Model at this time.

3. STEP 3: ANNUAL PROGRESS REPORTING

- The PI/CPI and research teams are required to submit a HREC/RGO Annual Progress/Final Report for each research project on 30 April each year that the project is active and will permit ongoing ethical clearance until such time as a Final Report is submitted.
- Complete details of research activity using the HREC/RGO Annual Progress Report/Final Report uploading as a supporting document in ERM.
    - Annual progress reports are not required for studies that were approved as exempt.
    - Where the MSHREC is the approving HREC, there is no requirement to submit an annual progress report to the MSRGO (i.e., there is no need to establish an SSA or submit an annual progress report under the SSA), however if the approving HREC is not the MSHREC then the report will need to be submitted to those RGOs as per their procedures.
- Refer to Attachment 3: Quick Guide – Submitting an Annual Progress Report.
- Contact MSH-Ethics@health.qld.gov.au for further information if required.

4. STEP 4: GRANT FUNDED RESEARCH

4.1 Metro South Health Research Support Scheme (MSH RSS)

- Recipients of MSH RSS research grants, with HREC approval from the MSHREC, are required to provide an annual progress report to the MSHREC via ERM by 30 April each year.
- If the recipients have HREC approval external to MSHREC, then an annual progress report is required to be submitted via the SSA for the Metro South site.
- MSH RSS Conditions of Award state funding may be withdrawn in circumstances where unsatisfactory progress is determined by the MSH Research Grants Committee.
- Final reports are due by 30 April in the year following the funding end date and will be requested via a notification from the MSH SmartyGrants account. The final report will be completed online by the grant recipient through SmartyGrants.

4.2 External research grant

- Progress, final and financial reports are required by most funding bodies as part of the conditions of the research grant/award.
- Reporting requirements will be scheduled in the relevant funding agreement. It is recommended the grant recipient diarises reporting deadlines.
- Continued funding of the research project and the eligibility to compete for future funding is often reliant on their completion.

- Clinicians and researchers are encouraged to contact the coordinating body for the research grant for more information about reporting requirements.

4.3 Post-award management of research grants budgets and Internal Order Numbers (ION)

- PI/CPI and/or research project contacts must meet with their respective business/finance manager at least quarterly to monitor their research cost centre expenditure.
- It is advisable to meet in May of each year applicable to allow effective planning for the new financial year if appropriate.
- Appropriate oversite of a research grant budget will facilitate timely and accurate financial reporting to the funding body.

5. STEP 5: SUSPENSION OR TERMINATION OF A RESEARCH PROJECT

- From time-to-time a research project may be suspended with approval from the MSHREC.
- If a decision is made by the PI/CPI to either suspend or cease a research project (prior to the expected date of completion) a completed HREC/RGO Annual Progress/Final Report must be forwarded to the MSHREC Office and MSRGO via ERM.
- To enable a suspension the PI/CPI must formally write to the MSHREC Chair regarding the circumstances surrounding the suspension.
- The formal letter should also include an indication of when the research project is likely to continue again.

6. STEP 6: COMPLETION OF STUDY

- Upon completion of the research on the expected completion date, a completed HREC/RGO Annual Progress/Final Report notifying of closure must be forwarded to the MSHREC Office via ERM following the same requirements as Annual Progress Reports specifically noting the study is closed and when it was closed.
- Final reports are not required for studies that were approved as exempt.
- Where the MSHREC is the approving HREC, there is no requirement to submit a final report to the MSRGO (i.e., there is no need to establish an SSA or submit a final report under the SSA), however if the approving HREC is not the MSHREC then the report will need to be submitted to those Research Governance Offices as per their procedures.

RESPONSIBILITIES

Position	Responsibility	Audit criteria
Executive Management Team	Ensure collaborative, harmonised, clear and detailed publicly available policies and procedures are in place for the ethical and scientific review of all MSH research.	N/A

Principal Investigator (PI)/ Coordinating Principal Investigator (CPI) - responsible officer	Ultimately responsible for all elements of the research project—from initial application, amendments and final reports.	N/A

DEFINITIONS

Term	Definition
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 *(National Clinical Trials Governance Framework definition)*	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: • Surgical and medical treatments and procedures • Experimental drugs • Biological products • Medical devices • Health-related service changes • Health-related preventative strategies • 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.
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 subjects are protected.
Principal Investigator (PI)/Coordinating Principal Investigator (CPI)	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.
Serious adverse event (SAE)	Any untoward medical occurrence that at any dose:

	• results in death • is life-threatening (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). • Requires inpatient hospitalisation or results in prolongation of existing hospitalisation. • Results in persistent or significant disability/incapacity. • Is a congenital anomaly/birth defect. • Is a medically important event or reaction.
Sponsor	An individual, company, institution, or organisation which takes responsibility for the initiation, management, and/or financing of a clinical trial'. Note the term Sponsor is relevant to all research – not just commercially sponsored research (e.g. grant-funded, or unfunded research may be sponsored by the university or hospital that is the administering institution).
Ethical Review Manager (ERM)	Web based content manager supported by the Office of the Director General via Office of Research Innovation, Queensland Health.

RELATED AND SUPPORTING DOCUMENTS

Legislation and other Authority	**Legislation (as updated and replaced from time to time)** • *Australian Research Council Act 2001* (Cth) • *Hospital and Health Boards Act 2011* (Qld) • *Financial Accountability Act 2009* (Qld) • *National Health and Medical Research Council Act 1992* (Cth) • *Public Health Act 2005* (Qld) • *Public Sector Ethics Act 1994* (Qld) • *Research Involving Human Embryos Act 2002* (Cth) • *Therapeutic Goods Act 1989* (Cth) **Regulations** • *Financial Accountability Regulation 2009* (Qld) • *Financial and Performance Management Standard 2009* (Qld) • *Hospital and Health Boards Regulation 2012* (Qld) • *Public Health Regulation 2018* (Qld) • *Therapeutic Goods (Medical Devices) Regulations 2002* (Cth) • *Therapeutic Goods Regulations 1990* (Cth)

	Other authority • National Statement on Ethical Conduct in Human Research (2023) • Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice ICH E6(R2) • ICH Quality Guidelines • ISO 9001:2015 Quality management systems - Requirements **Department of Health** • Health Service Directive: Research Ethics and Governance Directive QH-HSD-035:2023 • Research Management Policy QH-POL-013:2022 • Research Management Standard QH-IMP-013:1:2022

Standards	• National Clinical Trials Governance Framework
	• National Safety and Quality Health Service (NSQHS) Standards 2nd Ed.
	  ○ Standard 1 – Clinical Governance
	  ○ Standard 2 – Partnering with Consumers

Supporting documents	**Procedures** • PR2023-411 Research excellence • PR2023-412 Research support and management • PR2023-413 Research administration and compliance **Work instructions** • WI2023-299 Ethical and scientific review of research • WI2023-300 Exemptions from research review • WI2023-302 Research contracts and study execution • WI2023-303 Metro South Health sponsorship of Clinical Trial Notification (CTN) scheme trials • WI2023-304 PowerTrials - ieMR research support module • WI2023-305 Research monitoring • WI2023-306 Post approval – research amendments, reporting and closure **Guidelines** • GL2023-99 Planning a research project • GL2023-100 Research Participant Information and Consent Form (PICF) • GL2023-101 Research contract clauses • GL2023-102 Use of electronic signatures in research contracts • GL2021-77 Clinical trials • GL2023-103 TeleTrials **Attachments** • Attachment 1: HREC/RGO annual progress/final report

	• Attachment 2: Track change guide • Attachment 3: Quick guide – submitting an annual progress report

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.

WORK INSTRUCTION DETAILS

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