Research – Internal Monitoring of Clinical Trials

1. Applicable to

Role	Responsibilities
District Director Quality, Strategy and Improvement (DDQSI)	It is the responsibility of the DDQSI to make sure research projects conducted at Central Coast LHD are well managed and delivered according to the relevant policies, guidelines and procedures. Research breaches/ or misconduct will be investigated and managed to assure that the rights and well-being of the human subjects are protected; the reported research data are accurate, complete and verifiable from source documents; and the conduct of the project is in compliance with the currently approved protocol/ amendment(s), Good Clinical Practice and the applicable regulatory requirements (for clinical trial).
Research Manager	It is the responsibility of the Research Manager to make sure authorised research projects are regularly monitored across the District on a risk basis. Any potential complaint/breach/misconduct is updated to DDQSI for further investigation/discussion/action. Feedback/concerns that are raised from a Research Governance Officer also need to be updated to the DDQSI accordingly.
Research Governance Officer	It is the responsibility of the Research Governance Officer to create a schedule for monitoring authorised research projects as delegated by the Research Manager. Any potential complaint/breach/misconduct is updated to the Research Manager for discussion. Feedback/concerns that are raised from a clinical trial team also need to be updated to the Research Manager accordingly.
All staff involved in Research	It's important to make sure research projects are authorised and conducted following the relevant research policies, guidelines, and procedures.

Contraindications	
Alerts	Applicable only to research projects which are conducted at Central Coast LHD. Responsibility for ensuring that research is reliably monitored lies with the institution under which the research is conducted, including Public Health Organisations (PHOs), via its research governance arrangements. CCLHD is ultimately responsible for ensuring the safety and welfare of research/ trial participants and their data, and ensuring that research is being

	conducted in compliance with applicable principles, guidelines and standards. Mechanisms for monitoring can include: a) Approvals from Human Research Ethics Committees (HREC) and Research Governance Offices (RGO); b) Reports from researchers; c) Reports from independent agencies, such as a Data and Safety Monitoring Board (DSMB); d) Review of safety event reports; e) Random inspections of research sites, data, project documentation or consent documentation; and f) Interviews with research project team or other forms of feedback from them. The frequency and type of monitoring should reflect the degree of risk to the research/ trial participants.

2. Purpose

The purpose of this SOP is to establish a standard procedure for the management of internal monitoring visits run by the Research Office which is to ensure research projects conducted at Central Coast LHD are well managed and delivered according to relevant policies, guidelines and procedures. Research complaints, breaches or misconduct are investigated and managed to ensure that the rights and well-being of the human subjects are protected; the reported research data are accurate, complete, and verifiable from source documents (where possible); and the conduct of the project follows the currently approved protocol/ amendment(s), Good Clinical Practice and applicable regulatory requirements.

This procedure relates to all CCLHD staff involved in research within Central Coast LHD.

3. Standard Operating Practice

1. The Institution, CCLHD	CCLHD is responsible for: • ensuring the integrity of their research programs, their researchers, and the individual projects • ensuring patient safety • management of resources • management of finances • conformance to contracts and agreements • compliance with policies (state, national and international requirements) • data security • secure record and sample keeping • management of complaints • management of (allegations of) research misconduct • management of intellectual property (IP) PHOs have the discretion to conduct on-site monitoring independently of HREC requests, including (but not limited to): • Monitor or inspection of research conduct • Monitor or inspection of data and sample storage and security • Interviews with (or other forms of feedback from) research team
2. CCLHD Researchers/ Investigators	Responsibilities necessary for CCLHD researchers involved in clinical and non-clinical research are to: • Ensure appropriate qualifications, skills and experience are held for the research being carried out, including up-to-date Good Clinical Practice (GCP) certification (for clinical trials and clinical research where consent is being obtained) • Declare any conflicts of interest (e.g., payments from other parties, IP/ commercial interests) • Ensure receipt of HREC approval and site-specific governance authorisation for research projects involving human participants prior to commencement of research • Provide regular reports/amendments to the relevant reviewing body during the project life cycle • Ensure the project is carried out according to the project protocol and all the associated documents • Actively communicate with the Research Office Additional responsibilities necessary for CCLHD investigators involved in clinical trials are to: • Maintain a list of any delegated duties with respect to the trial, and the persons and qualifications of those persons to whom the duties are assigned, such as delegation and

	signature log. • Possess a favourable HREC endorsement of the trial protocol, patient information and consent forms, recruitment procedures, consent form updates and any other information given to participants, prior to trial commencement • Provide regular trial reports to the HREC at least annually (more frequently if the HREC so desires) • Document any deviation from or violation of the approved protocol for reporting to the relevant HREC and sponsor (as per the SOPs) • Keep documentation of applications to the Clinical Trial Notification or approval (CTN or CTA) scheme (TGA): if site performs the online CTN submission or submits a CTA form, the original must be kept in the Trial Master File; if site is part of a multiple submission process, the TGA Acknowledgement form must be filed • Maintain accountability of the investigational product at the trial site/s • Ensure participants have made fully informed, written consent, with all trial procedures and risks fully explained • A copy of signed Participant Information Sheet and Consent Form must be given back to the trial participant to keep • Document the informed consent process and follow up visits in the process notes or relevant notes • Register clinical trials on the registry board
3. CCLHD Research Office	The CCLHD Research Office must ensure that clinical and non-clinical research is being conducted in accordance with institutional requirements, by: • Undertaking site specific assessments of research projects within the timeframe • Reviewing and processing amendments in a timely manner • Reviewing and processing required reports in a timely manner • Monitoring research projects on a risk basis Monitoring visits will be performed to ensure clinical trials and clinical research projects are in compliance with: • Good Clinical Practice guidelines (ICH-GCP) • The current version of the protocol • HREC approval and governance authorisation including participant consent documentation; data, sample and trial product storage; number of research participants; and commencement/ completion/ withdrawal dates • Conditions of site authorisation

4. Monitoring Process

Pre- Monitoring

- Schedule a date; time and place for the monitoring visit (also with Pharmacy for a drug trial)
- Send a monitoring confirmation email to PI and Trial Coordinator (Appendix A)
  - Attach CCLHD - Self-Assessment Monitoring Checklists for PIs (Appendix B)
  - Attach Research - Management of Clinical and Non-Clinical Data (Appendix C)
- Complete the CCLHD File Audit Checklist (Appendix D)
- Complete the CCLHD Research Office - Monitoring Checklist (Appendix E)
- Create a project folder in the monitoring schedule folder (save all the correspondence emails)

Day of Monitoring

- Print the CCLHD Clinical Trial Monitoring Tool (Appendix F)
- Conduct the monitoring visit independently
- Go through the monitoring findings and queries with trial coordinator +/- PI by the end of the monitoring visit
- Ask the trial coordinator +/- PI (if PI is available on the day) to sign and date the Clinical Trial Monitoring Tool
- Print the CCLHD Clinical Trial Monitoring Tool for CT Pharmacy (Appendix G), if it is a drug trial. Conduct this visit on the same or following day with the CT Pharmacist.

Follow up Monitoring

- Send monitoring follow up email
  - Outline the findings (with the action due date and responsible person)
  - Attach all the relevant documents
- Discuss with Research Manager if any concerns have been raised during the monitoring visit.

5. Definitions

Monitor	A systematic and independent examination of a research/ trial related activities and documents to determine whether the evaluated research/ trial related activities were conducted, and the data were recorded, analysed and accurately reported according to the protocol, sponsor's standard operating procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirement(s).

Clinical trial/ study	Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy. The terms clinical trial and clinical study are synonymous.
Clinical Trial Notification (CTN) Scheme	The CTN Scheme is a notification scheme to the TGA for clinical trials involving unapproved therapeutic goods. The requirement for a CTN is determined by the sponsor in consultation with the HREC that is reviewing the protocol and overseeing the clinical trial.
Clinical Trial Approval (CTA) Scheme	The CTA Scheme is an approval process by the TGA for clinical trials involving unapproved therapeutic goods. The requirement for a CTA is determined by the sponsor in consultation with the HREC that is reviewing the protocol and overseeing the clinical trial.
Compliance	Adherence to all the research/ trial-related requirements, Good Clinical Practice (GCP) requirements, and the applicable regulatory requirements.
Contract	A written, dated, and signed agreement between two or more involved parties that sets out any arrangements on delegation and distribution of tasks and obligations and, if appropriate, on financial matters. The protocol may serve as the basis of a contract.
Coordinating Principal Investigator (CPI)	An investigator assigned the responsibility for the coordination of investigators at different centres participating in a multi-centre trial. For single centre research, Coordinating Investigator and Principal Investigator are synonymous.
Data Safety Monitoring Board (DSMB)	A committee that reviews the accumulating data in a trial and recommends to the sponsor (either directly or indirectly) whether to continue, modify, or stop a trial for either safety or ethical reasons.
Documentation	All records, in any form (including, but not limited to, written, electronic, magnetic, and optical records, and scans, x-rays, and electrocardiograms) that describe or record the methods, conduct, and/or results of a trial, the factors affecting a trial, and the actions taken.
Good Clinical Practice (GCP)	Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting of clinical trials. Compliance with this standard provides public assurance that the rights, safety and well-being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible. These guidelines may be overridden by national legal requirements and the requirements of individual regulatory agencies as appropriate, to address matters relevant to local conditions or culture.
Health research	Health research means laboratory, pre-clinical and clinical research, and development in all its forms.

Human Research Ethics Committee (HREC)	A Human Research Ethics Committee (HREC) is responsible for reviewing research proposals involving human participants to ensure they are ethically acceptable and in accordance with relevant standards and guidelines.
Institution	Any public or private entity or medical facility where human research is conducted.
Intellectual property	Intellectual property is the legally recognised outcome of creative effort and economic investment in creative effort. It includes inventions, patents granted in respect of such inventions and applications for such patents; unpatented know-how, which comprise an invention or a way of doing something which is not public knowledge; confidential information and trade secrets; registered and unregistered designs and applications for registered designs; copyright; and all other rights resulting from intellectual activity in the scientific, industrial, literary or artistic fields.
Internal monitoring	An independent, objective assurance and consulting activity designed to add value and improve an organisation's operations. Internal monitoring helps an organisation accomplish its objectives by bringing a systematic, disciplined approach to evaluate and improve the effectiveness of risk management, control, and governance processes.
International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)	The ICH is an international body that defines a set of standards which governments can then transpose into regulations for clinical trials involving human subjects. The ICH brings together the regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of drug registration to ensure that safe, effective, and high quality medicines are developed and registered in the most resource-efficient manner.
Investigator's Brochure (IB)	A compilation of the clinical and nonclinical data on the investigational product(s) which is relevant to the study of the investigational product(s) in human subjects
Monitoring	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), Good Clinical Practice (GCP), and the applicable regulatory requirement(s).
Multi-centre trial	A clinical trial conducted according to a single protocol but at more than one site, and therefore, carried out by more than one investigator.
Non-clinical research	Research not performed on human subjects; in drug development, non-clinical studies are conducted, including animal studies, to determine drug availability (studies on pharmacokinetics), absorption, distribution, metabolism and elimination and preliminary studies that aim to investigate the candidate safety including genotoxicity, mutagenicity, safety pharmacology and general toxicology.
Principal Investigator (PI)	The individual who takes responsibility for the overall conduct, management, monitoring and reporting of research conduct at a site and submits the research project for site authorisation.

Protocol	A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents.
Public Health Organisation (PHO)	An Area Health Service or Local Health District (LHD), statutory health corporation, or affiliated health organisation in respect of their recognised services, under the Health Services Act 1997 (NSW).
Research	Investigation undertaken to gain or advance knowledge, understanding and insight. It does not include routine testing and routine analysis of materials, components or processes or the development of teaching materials and similar work.
Research data	Research data may include: (a) laboratory and field notebooks; (b) primary research data (including machine data in hardcopy or computer readable form); (c) databases; (d) clinical data, including clinical records; (e) questionnaires; (f) photographs; (g) audio-visual materials; (h) test responses
Research/ trial/ study product	The investigational pharmaceutical product/s being used in a clinical trial or non-clinical study.
Researcher	Any staff member engaged in research.
Research Governance Officer (RGO)	The individual appointed within the PHO who is responsible for the management of applications for site authorisation and oversight of authorised research projects.
Site Specific Assessment (SSA)	Public health organisations are required to undertake a site specific assessment (SSA) of each research project, thereby allowing the organisation to consider whether it has the capacity to conduct the research at that site. This SSA involves consideration of such matters as resources, staff, insurance and indemnity requirements etc.
Sponsor	The sponsor of a clinical trial is the company, institution or organisation, body or individual that takes overall responsibility for the conduct of the trial and usually initiates, organises and supports the clinical trial.
Standard Operating Procedures (SOPs)	Detailed, written instructions to achieve uniformity of the performance of a specific function.
Therapeutic Goods Administration (TGA)	The Therapeutic Goods Administration (TGA) is a division of the Australian Government Department of Health and Ageing and is responsible for regulating medicines and medical devices.

6. References

- Australian Code for the Responsible Conduct of Research (2018)
- Australian Code of Practice for the Care and Use of Animals for Scientific Purposes
- Australian/New Zealand Standard ISO 31000:2009 - Risk Management
- CCLHD Research Documentation Developed for External Presentation (PR2016_022)
- CCLHD Research Documentation Developed for External Publication (PR2016_023)
- CCLHD Research – Management of Clinical and Non-Clinical Data
- CCLHD Research and Clinical Trials - Financial Management procedure – PR2017_040
- CCLHD Research Code of Conduct.
- CCLHD Research – Responding to Allegations of Research Misconduct – PR2020_015
- Human Research Ethics Committees – Quality Improvement & Ethical Review: A Practice Guide
- Integrated addendum to ICH E6 (R1): Guideline for Good Clinical Practice E6 (R2) (November 2016)
- International Committee of Medical Journal Editors policy on clinical trial registration
- National Clinical Trials Governance Framework (2022)
- National Health and Medical Research Councils Values and Ethics: Guidelines for Ethical Conduct in Aboriginal and Torres Strait Islander Health Research (2003)
- National Mutual Acceptance Scheme
- National Statement on Ethical Conduct in Human Research (2007) – Updated 2018
- NHMRC: Authorship - A guide supporting the Australian Code for the Responsible Conduct of Research (2019)
- NHMRC: Ethical Considerations in Quality Assurance and Evaluation Activities (March 2014)
- NHMRC: Guide to managing and investigating potential breaches of the Australian Code for the Responsible Conduct of Research, 2018
- NHMRC: Reporting of Serious Breaches of Good Clinical Practice (GCP) or the Protocol for Trials Involving Therapeutic Goods (2018)
- NHMRC: Research Governance Handbook: Guidance for the national approach to single ethical review (2011)
- NHMRC Guidance: Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods (2016)
- NSW Health - Clinical Trial Research Agreements for Use in NSW Public Health Organisations - PD2011_028
- NSW Health - Research Governance in Public Health Organisations - GL2011_001
- NSW Health Guideline – Use of Human Tissue for Research
- Privacy Management Plan PD2015_036
- TGA's Australian Clinical Trial Handbook (November 2020)
- The Code of Practice for the exposure of Humans to Ionizing Radiation for Research Purposes
- NSW Health and Medical Research Mission and Strategic Review
- NSW Health Electronic Information Security Policy - PD2013_033
- NSW Health Guidance Document COVID-19 and Clinical Trials (NSW Health OHMR; 25 March 2020)
- NSW Health Guidelines - Research Governance in NSW Public Health Organisations - GL2011-001
- NSW Health - Clinical Trials Insurance and Indemnity Policy - PD2011_006

- NSW Health - Research – Authorisation to commence human research in NSW Public Health Organisations and Policy Directive - PD2010_056
- NSW Health Policy - Authorisation to commence human research in NSW Public Health Organisations - PD2010_056
- NSW Health Policy - Research - Model for Single Ethical & Scientific Review of Multi-Centre Research - PD2007_072
- NSW Health Policy Directive – Safety Monitoring and Reporting for Clinical Trials Conducted in NSW Public Health Organisations – PD2017_039
- NSW Operations Manual for Research Governance Officers, GL2010_015 (September 2010)
- NSW State Records 8.0.0 Research Management (GDA17)
- NSW State Records Act 1998
- NSW State Records General Retention and Disposal Authority – Public Health Services: Patient/Client Records (2011)

7. Related Resources and Appendices

Appendix A: Example of Monitoring Confirmation Email

Appendix B: CCLHD - Self-Assessment Monitoring Checklists for PIs

Appendix C: Research - Management of Clinical and Non-Clinical Data

Appendix D: CCLHD File Audit checklist

Appendix E: CCLHD Research Office - Monitoring Checklist

Appendix F: CCLHD Clinical Trial Monitoring Tool

Appendix G: CCLHD Monitoring Checklist for CT Pharmacy

8. Revision and Approval History

Date Approved	Revision No.	Name and position of Author and Approver	Next Review due
Oct 2018	1	Author: Dr Katherine Bolton, Research Governance Officer Approver: Amanda Jackson, Research Manager	Oct 2021
Apr 2023	2	Author: Yin Wang, Research Governance Officer Approver: Dr Katherine Bolton, Research Manager	Apr 2026

(Expand table as required)

Appendices

Appendix Number	Document Name	Document (pdf)
A	Example of Monitoring Confirmation Email	Appendix A - Example of Monitori
B	Self-Assessment Monitoring Checklist for PIs	Appendix B - CCLHD - Self-Assessı
C	Procedure - Management of Clinical and Non-Clinical Data	Appendix C - Research - Manager
D	CCLHD File Audit Checklist	Appendix D - CCLHD File Audit Ch
E	CCLHD Research Office - Monitoring Checklist	Appendix E - CCLHD Research Off
F	CCLHD Clinical Trial Monitoring Tool	Appendix F - CCLHD - Clinical Tria
G	CCLHD Clinical Trial Monitoring Tool for CT Pharmacy	Appendix G - CCLHD Monitoring '