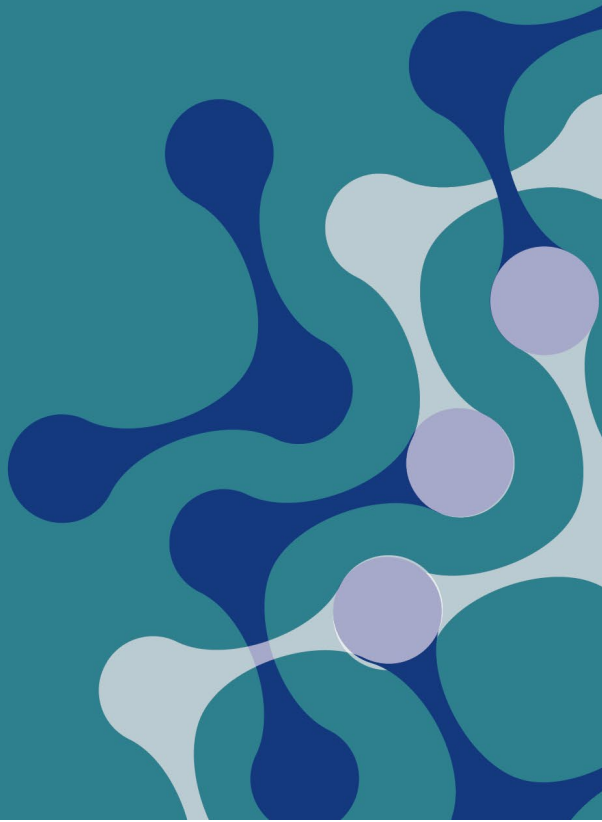
Office for Health and Medical Research

NSW Clinical Trials Quality Recognition Scheme

Site Application Guide

2025



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Quality Recognition Scheme Goal

Ensure high quality operational conduct of clinical trials

Vision: NSW is a centre of excellence that provides a high quality and efficient environment to conduct clinical trials with the aim of improving health outcomes for NSW residents.

The **guiding principles** that underpin this scheme are:

- Ensuring that clinical trials conducted in NSW are as safe as possible for all people participating in, and delivering the trials
- Ensuring alignment with best practice internationally and nationally for operational conduct
- Strengthening the capability in NSW to be a centre of excellence for early phase trials
- Ensuring continuous quality improvement to ensure the health system is responsive to new scientific and technological advances, and research methodologies.

Introduction

The NSW Clinical Trials Quality Recognition Scheme (QRS) is an Office for Health and Medical Research (OHMR) initiative to assess the quality conduct of clinical trial units in NSW. The QRS originates from the Early Phase Clinical Trial (EPCT) Framework for NSW which was endorsed by the sector and approved by the Chief Health Officer in 2017. The Framework addresses a government priority, identified in the Strategic Review of Health and Medical Research (2012), to develop phase I clinical trial capability in NSW. This Framework is one component of a broader suite of initiatives to build capacity to make NSW a centre of excellence for all clinical trials.

Quality management in clinical trials is increasingly recognised as significant for reducing risk and ensuring participant safety. Clinical trial units with robust quality management practice can conduct more efficient, reliable, and successful clinical trials, ultimately leading to better participant outcomes[1].The QRS's marking criteria emphasises quality management practice across the key standards.

The QRS serves as a gap analysis for sites and supports best practice delivery of clinical trial services. It will recognise sites that meet quality criteria and guide those working towards it, enhancing capability and building capacity in the clinical trial sector. The QRS aims to create a supportive environment for trial activity in NSW.

Purpose

This document is a guide for sites wishing to apply for quality recognition under the QRS. It describes the QRS requirements, the application procedure, and the review process.

Rationale

OHMR developed the QRS to ensure clinical trials have high standards of research practice, trial quality and a focus on participant safety. The QRS is modelled on the UK's Medicines and Healthcare

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[1] A Alghabban et al. 2021 '*Clinical Quality Management System (CQMS): A Framework for Operational Excellence and Compliance with God Clinical Practice (GCP)',* Journal for Clinical Studies. Clinical-Quality-Management-System-CQMS.pdf

Products Regulatory Agency Phase I accreditation scheme of early phase sites, acknowledging that early phase trials carry the greatest clinical uncertainty. However, it aims to make sure that all clinical trials are as safe as possible and of high quality, to strengthen public confidence in clinical trial conduct in NSW.

The QRS will recognise sites meeting the quality criteria and provide guidance to sites working towards the criteria. This recognition will be valid for 3 years, unless significant changes at site warrant review. The QRS criteria for quality align with Standard 1 of The National Clinical Trials Governance Framework, including:

- Governance, leadership & culture
- Patient safety and quality improvement systems
- Clinical performance & effectiveness
- Safe environment for the delivery of care.

Scope

The QRS scope covers site operations, facilities, and staff skills and experience. It will not address the conduct of individual trials.

Trial units must demonstrate that they meet regulatory Good Clinical Practice with robust procedures that set the highest safety and quality standards in the conduct of clinical trials. Safety processes for avoiding harm to trial participants, including the ability to handle emergencies should be clear and in operation. Sites should maintain data quality, through processes that demonstrate adherence to trial protocols and assessment of the appropriateness of a study's design. Sites should also be able to accurately assess their own facilities, resources, and expertise to safely deliver clinical trials relative to risk associated with the trial design.

Assumption: Trial units must comply with the requirements of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) GCP (with TGA annotation) and/or ISO 14155, the Australian Clinical Trial Handbook and the National Statement on Ethical Conduct in Human Research, as a pre-requisite for applying for the QRS. The standards listed herein supplement ICH GCP and ISO 14155 requirements by providing additional guidance for the implementation of certain ICH GCP requirements with focus on risk management and quality procedures for operations.

Note: The QRS focuses on a facility's infrastructure to conduct clinical trials and does not review individual clinical trial conduct. As such, a recognition under the scheme does not validate or endorse a site for GCP or ISO 14155 compliance.

The assessment of these standards does not reflect the full scope and does not replace the need for a standard regulatory GCP inspection or Sponsor audit. QRS recognition is not intended to indicate that the pre-requisite compliance has been validated or endorsed. If any anomalies/concerns are observed during the assessment, that are outside of the QRS scope, the site is responsible for notification to the ethics committee and/or research governance office as required.

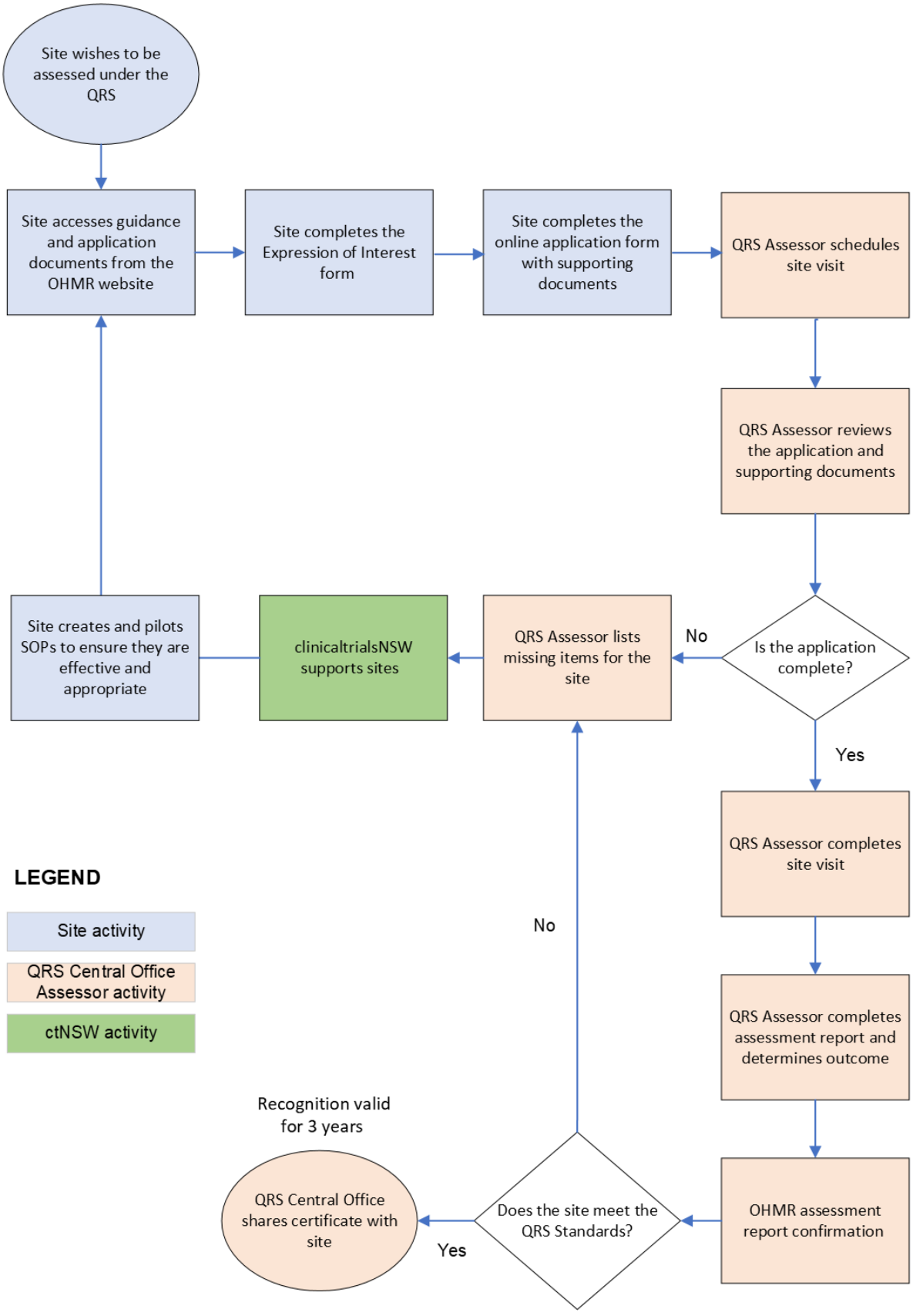
Eligibility criteria

To be assessed under the QRS, a site:

- must be based in NSW
- may operate in public or private health service organisations
- must have demonstrated experience in conducting clinical trials (for full QRS recognition)
- can demonstrate GCP compliance, with no unresolved critical or major findings from previous GCP audits or regulatory inspections

- have current and active control documents such as Standard Operating Procedures (SOPs), policies, and relevant associated documents.

Quality Recognition Scheme Process



Quality Recognition Scheme Standards

The QRS assesses five standards to review a sites suitability to conduct high quality and safe clinical trials.

- Adequate **medical and clinical governance oversight** at site level
- Efficient and effective system to ensure **quality**
- **Risk assessment and management** procedures in place, demonstrating that the site continuously verifies and assesses all aspects of a trial conduct
- Appropriate **research team** expertise for clinical trials
- Adequate **infrastructure** and resources to conduct clinical trials and **appropriately respond to medical emergencies**

OHMR has defined and summarised the expectations for quality management of clinical trials under the QRS in the "High Level Assessment Standards."

Understanding and meeting the standards

- A clinical trial site demonstrates that it meets the necessary quality and safety standards under the QRS through two components that will be reviewed by QRS assessors:
- Submitting a complete application form
- Participating in an on site assessment.

The QRS Application Form

- The application form, hereafter 'the form', aims to allow parts of the QRS review to be conducted offsite. This 'desktop' review is performed by a QRS Assessor. The Assessor will review the content in the application form as well as supplemental evidence such as:
- Standard Operating Procedures (SOPs)
- Work Instructions (WIs) and other Associated Documents
- Plans
- Checklists
- Meeting related documents such as agenda and minute examples and templates
- Training logs
- Other relevant templates
- The form is an opportunity to demonstrate the site's routine operational processes and ongoing practices that provide a robust and safe infrastructure to conduct clinical trials. Supplemental documents are uploaded in the form, and document names and sections can be referenced in subsequent sections of the form to prevent repeated uploads. If the site does not have a formal document detailing a process, please describe the process in the free-text boxes provided.
- **Submissions** are made using an online application form hosted in REDCap**.**

Please note: the application form intentionally deviates from the chronology of the QRS standards to keep operationally linked information together and increase the ease of form completion.

Return code

You can click "Save & Return Later" to complete the form over more than one session. When you exit the form, you will receive an email with a personalised link and return code. Please refer to this email to return to your application.

Please contact the QRS Central Office on MOH-QRS@health.nsw.gov.au if you are unable to return to your application.

Completing the form

When completing the application form please:

- Avoid using acronyms without providing the full term the first time it is used. E.g., “early phase clinical trials (EPCT)”.
- Throughout modules 1 – 4, you will be asked for information that addresses a particular issue. If you have a SOP that addresses the requested information, please note the SOP title in the free text field and, if relevant, the specific section of the SOP. You will be able to upload a copy of the SOP in Module 5. **You are not expected to copy and paste information from an SOP into the form.**
- When providing required documents, **do not upload any** trial specific documents or contracts that contain confidential or restricted information. Please provide templates only. If a standard template is not available, ensure the document is redacted prior to upload.

Site assessment visit

- Once the application form and supporting document review is complete, the QRS Assessor will schedule a site assessment visit at the trial location. Site visits will generally be scheduled for a minimum full day. Through an audit process, the site assessment visit allows a trial site to demonstrate how their facilities and systems support the safe and appropriate management of clinical trial activities. Please see Appendix B for a sample agenda with requisite attendees.
- OHMR will provide an agenda for the day to allow sites to prepare for the visit.

Application Form Module 1: Site Description & Clinical Trial Experience

Framework Criteria:

Module 1 provides assessors with background information about the site's clinical trial experience and capabilities. It addresses:

- Criteria 5.1 - Adequate infrastructure and resources to conduct clinical trials.

Table 1: Module 1 contents – Site Description and Clinical Trial Experience

Module Section	Context
Site description	• Please provide OHMR with a named site contact for ongoing correspondence.
	• Define the type of site applying for QRS review. For example, site is an NSW public hospital. This will support an assessor to broadly understand the scope of practice at site.
	The hours of operation can guide the site assessment date and facilitate convenient communication between the site and OHMR.
Clinical trial experience	• The number of trials at a trial site will broadly indicate the size of the unit, its operations, and its overall trial experience.
	• Therapeutic area, clinical trial intervention experience, and the types of clinical trials conducted at site provide greater insight into the breadth of activity at site.
Staff resources	• The available staff resources indicate the unit's capacity to conduct trials and manage the research workload.
	• **Research Nurses:** please use the 'research nurse' field to describe registered nurses that are working on trials in a nursing capacity. If the unit has registered nurses employed as study coordinators, that is, they were not hired in a nursing capacity, please include them as 'study coordinators.' However, where a registered nurse has been employed to conduct **both** study coordination and nursing duties, please include them as 'research nurses.' • This will support the assessor to determine the training and qualification requirements
	• **Visiting Researchers and Casual Staff:** the assessor will consider the expertise, and the appropriateness of training and supervision provided to visiting, contract, and casual staff.
Site facilities	• Describes the locations where clinical trial activities are performed to orient the assessor for the onsite visit. It also allows the assessor to determine whether the site has the infrastructure to conduct clinical trials safely. • Includes equipment used in clinical trials, pharmacy facilities, and biospecimen management and laboratory details. A site floorplan is requested. This should include location of key safety equipment e.g. call bells, emergency trolleys

Application Form Module 2: Medical Supervision & Emergency Management

Framework Criteria:

Module 2 demonstrates to assessors that sites that sites have established and documented procedures in place to manage medical emergencies. It addresses:

- Criteria 5.2 - Adequate and appropriate site facilities to appropriately respond to medical emergencies
- Criteria 5.3 – Appropriately trained trial site and other on the floor personnel
- Criteria 5.4 – 24-hours medical cover
- Criteria 5.5 – Availability of Emergency and/or intensive care unit in a reasonable proximity or equivalent 24-hour emergency provision
- Criteria 5.6 – Provision for emergency transfer and treatment.

Table 2: Module 2 contents – Medical Supervision & Emergency Management

Module Section	Context
24-hour medical supervision	Demonstrates the site's procedures to ensure patient safety is maintained and prioritised for all clinical trials. Procedures should be line with trial risk.
	Provides insight into site's risk-based staff rostering strategies to ensure immediate/on-call medical response (as appropriate to the trial activities) during usual working hours and out-of-hours.
Facility readiness in emergency	Will demonstrate that all areas routinely accessed by trial participants are reviewed for safety, have necessary procedures, and appropriate equipment to manage patient safety.
	Emergency Trolley/Bag (if applicable): Demonstrates to assessors that the emergency trolley is accessible and is stocked and maintained in accordance with the ANZCOR Resuscitation Council guidelines. Site must also follow any organisational process and checks.
Clinical Emergency Response System: Protocol or Plan	• Demonstrates staff are appropriately trained to recognise and respond to a participant whose condition is deteriorating. This section allows the assessor to determine that site staff are trained and qualified to handle medical emergencies.
Intensive emergency care provision & transfer	• Clinical trial units must have established contingency plans to ensure patients receive intensive and/or emergent care as required. This section demonstrates a site's ability to provide safe intensive emergency care on site and as needed rapid transfer of study participants from clinical trial units to Emergency Departments/Intensive Care Units.
Emergency response readiness and testing	Discusses the site's practices for ensuring site staff are appropriately trained to manage medical emergencies (Basic Life Saving, Advanced

	Life Saving or other requirements). This section will examine the site's mock scenarios and actual emergency experience.

Application Form Module 3: Research Team

Framework Criteria:

Module 3 demonstrates to assessors that sites have an appropriately organised and trained site team. It addresses:

- Criteria 1.1 – Clinical/Medical governance accountability at sites including clear lines of responsibilities for Investigators and other medical personnel
- Criteria 1.2 – Head of Site (HoS) oversight and involvement in risk assessment and management of clinical trials
- Criteria 4 – Appropriate research team experience and qualification for conducting trials

Table 3: Module 3 contents – Research Team

Module Section	Context
Site Management / Governance accountable persons	• The QRS requires personnel working on clinical trials to be appropriately trained and qualified. A short-form or Transcelerate curriculum vitae (CV) does not provide relevant professional training and experience for assessment. **Please upload long-form CVs and appropriate training logs for specific staff members.** Please submit an organisational chart of the clinical trial unit.
Position descriptions (PDs)	Please upload the relevant PD for the named role. The job title within the PD does not have to match the position listed in the application form.
CVs	Assessors will review CVs for education, qualifications, certifications, and experience gained through relevant employment. While it is not required to include an exhaustive list of publications or presentations, a short summary or overview would be appropriate.
Medical indemnity	Describes additional risk mitigation strategies that may have been implemented by the site. Please describe any strategies or note if standard facility/trial practices are used.
Training and staff resourcing	Demonstrates that personnel are adequately trained, and appropriate resources are available to conduct clinical trials safely.
Delegating tasks	Demonstrates to assessors that all clinical trial related tasks are formally delegated to ensure ongoing trial oversight is maintained. Please see the 'Completing the form' section of this guide for guidance on uploading documents.

Application Form Module 4: Quality & Risk Management

Framework Criteria:

Module 4 demonstrates to assessors that sites have efficient and effective processes to ensure quality is maintained and risk is mitigated. It addresses:

- Criteria 2 – Demonstrate efficient and effective systems and processes to ensure quality
- Criteria 3 – Risk assessment and management procedures in place demonstrating that the site (independently of the sponsor and the Ethics Committee) continuously verifies and assesses all aspects of the EPCT.

Table 4: Module 4 contents – Quality and risk management

Module Section	Context
Responsible person	Please name the person(s) responsible for managing SOPs at the site. This refers to the 'Document Controller' who ensures SOPs are current and active.
SOP Management	This section describes the site's process to ensure SOP(s) are current and distributed to staff. It also describes the quality steps to ensure that old versions are removed from circulation.
Quality Monitoring & Corrective Action/Preventative Acton (CAPA)	Demonstrates the site has robust processes to identify, report, and respond to process or protocol non-compliances. Assessors will ensure these processes are designed to correct and prevent future breaches, as well as report non-compliances to the proper authority.
Audit and Inspection	The site's audit and inspection history demonstrate that a site effectively and proactively addresses findings and implements strategies to minimise the likelihood that they will occur again. To be eligible to be assessed under the QRS, a site **must have no unresolved critical or major audit/inspection findings.**
Risk Management Procedures	Please use this section to describe how the site manages risk for clinical trials and formally documents these practices. Include any specific risk procedures used for trials that may require higher level of risk consideration i.e. early phase clinical trials.
	Risk Management Plan (RMP) or equivalent: the QRS acknowledges that a singular document may not be used to document a trial's risk. Please include all the site's processes as needed. If this information is included across multiple documents, please merge them into one document and upload them together.

Application Form Module 5: Standard Operating Procedures

Framework Criteria:

Module 5 demonstrates to assessors that sites have current and active standard operating procedures (SOPs) for site activities. It addresses:

- Criteria 2.1 - Core Standard Operating Procedures (SOPs) at the site, to ensure compliance with relevant processes and GCP requirements including additional early phase trials requirements and procedures for trial documentation management.
- Criteria 2.2 - Oversight of SOP creation, implementation, internal monitoring and review of current processes in place to ensure SOPs are current and active at the site.

Clinical trial sites should have a core suite of SOPs to ensure clinical trial conduct complies with GCP requirements. Ideally, sites will have written SOPs to address every aspect of their activities. While the QRS uses the term "SOP", OHMR acknowledge that sites may address these requirements using other means that are better suited to the site's needs. Other documents may include local policies, manuals, work instructions, guidelines, or logs. Routine operational process documents should aim to provide detailed instructions that standardise trial related procedures at the clinical trial unit. Please upload the most relevant document available at your site to address the requested SOP.

Table 5: Module 5 contents – SOPs

Module Section	Context
SOP index	A list of the site's available SOPs demonstrates the routine operational process documents. It will also evidence additional SOPs that are available to the site team that may not need uploading into the system.
Document type	Please select the types of documents available at the site. You are not expected to have all these documents. Selecting the document types will create tables for you to be able to upload the relevant document. **Work instructions (WIs):** can be uploaded under 'Submission of Additional Documents'
Standard Operating Procedures	Please complete the fields for each SOP. This will support the assessor to work through the relevant documentation. Where the site does not have a SOP for a process, please specify this in the form. You can use the optional 'additional comments' section to type in your process or note that you have already provided this information in an earlier module. If the application form requests a SOP that has already been uploaded into a different section, **please do not upload it again**. Please complete the "SOP Name" field. Appendix A provides more information on SOP expectations.

Application Form Module 6: Declaration

The declaration page confirms that the Head of Site*:

- supports the QRS application
- verifies that the provided information is accurate
- has confirmed support for site QRS application from site **Chief Executive or Director of Research**
- agrees to the site being listed on the OHMR website as an NSW Health quality recognised clinical trial unit for up to three years.

*Under the QRS, the "Head of Site" is defined as the person with the "overall responsibility and accountability for clinical trials at the site". Whereby, they are expected to maintain active oversight and awareness of clinical trials. For example, a Clinical Trial Unit Manager or Clinical Trials Operations Manager. In the absence of an operational lead, the Principal Investigator, who is responsible for the medical oversight of clinical trials at the site, can sign the declaration.

Appendix A: QRS Standard Operating Procedures

SOPs define a site's procedures and provide insight into organisational management, staff responsibilities, and the controls/oversight of trials at site. The QRS will verify that the submitted SOPs are approved, current, and version controlled in accordance with the site defined standards for SOP management.

Table 6 provides a list of clinical trial procedures considered relevant to management of clinical trials including a summary of suggested content. Given the variance in site procedures and management of site procedural documents, the list is not intended to mandate the content of individual SOPs. More than one process may be incorporated into one SOP/document as appropriate for the site (e.g. operations manual, quality manual).

The SOP list below is not exhaustive, and sites should ensure all activities are formalised adequately. The QRS expects sites to have a suite of SOPs in place for general clinical trial management and GCP compliance.

Please note sites are only required to supply SOPs or routine operational process documents that are:

- referenced in the application form
- specifically relevant to the review of clinical trial conduct.

Any other standard GCP SOPs, not falling into the categories above, do not need to be provided, however, please list them in the SOP index.

Suggested inclusions for GCP Standard SOPs are listed for reference only.

Table 6: Site management procedures

Procedure Purpose	Suggested inclusions and/or outcomes
Site Management & Governance Ensure management leadership, organisation, communication, and oversight of clinical trials.	• Describes management structure & composition of the leadership team. • Describes **operation** of leadership team, including its composition, role/functions. • Describes how management maintains awareness and oversight of operational issues. • Describes leadership team meeting formats, frequency, attendees, agenda, required functional reports, and meeting output (minutes / reports). • Identifies person(s) responsible for management decisions. • Describes pathways for issue escalation to management including timelines. • Describes communication strategies to ensure staff are notified of changes in procedures, study, and safety issues. • Describes issue reporting pathway/timelines to Sponsor.
Quality & Compliance Management Ensure systems are in place to achieve the required quality standards including	• Identifies applicable quality standards/regulations. • Identifies person (ideally independent to operations) responsible for quality assurance. • Describes how compliance will be achieved.

quality monitoring systems that identify quality non-compliance; correct non-compliance and prevent repetition of quality issues.	• Describes how compliance will be monitored. • Defines internally reportable quality issues. • Describes how quality issues are reported to management. • Describes how quality issues are managed including incident review, root cause analysis, risk-based determination of corrective actions and actions to prevent recurrence of the quality issues i.e. Corrective and Preventative Action (CAPA) plan, and follow-up to ensure CAPA completed. • Identifies person(s) responsible for CAPA. • Maintains register of quality issues to track management and analyse trends. • Ensures compliance with non-compliance/deviation reporting requirements for all applicable agencies. • Ensures expedited reporting of significant GCP/Protocol non-compliance to sponsors.
Management of SOPs Ensures implementation of functionally appropriate, GCP/regulatory compliant, and management approved procedures.	• Clear process for creation and management of SOPs. • Procedures identify staff responsible for performing/overseeing an activity. • Development, review, and approval procedure ensures functional accuracy and regulatory/GCP compliance of the SOP. • SOPs are authorised for use by management. • Documents are uniquely identifiable (e. g. dated and/or versioned). • Date effective is noted. • SOPs are readily available to relevant staff. • Document control ensures only current effective SOP is in use. • Person responsible identified for management of SOPs (i.e. Document Controller). • Staff notified/trained in new/revised procedures as documents are released. • Training is documented. • Periodic review for currency: review outcomes documented. • A Master SOP index is maintained which records all SOPs in use at the site, including effective dates. • Change history is maintained. • Superseded or obsolete documents are retained. • Compliance with SOPs monitored. • Changes in procedures or regulations trigger SOP revision.
Staff Qualification & Training	• Defines site roles and responsibilities. • Site role and/or position description includes minimum qualifications and experience.

	• Defines minimum training requirements for staff, including minimum training to participate in specific trials such as early phase, medical device, paediatric. • Staff required to demonstrate competency PRIOR to performing any safety critical tasks unsupervised. • Defined minimum qualification, experience, and training for Investigators, including currency in emergency management experience, prior EPCT experience (if relevant), and appropriate pharmacological knowledge. • Site staff are trained in GCP with periodic refreshers within the expected timeframe. • Site specific training requirements includes life support as appropriate to role with annual refreshers. • Staff maintain currency in training: periodic refreshers and/or recertification within expected timeframes. • Defined, maintained, and retained training records which include CV, position descriptions, certificates, and training logs. • Ongoing verification of staff qualifications and tracking of training, refreshers, and re-certification to ensure continuity of competency. • Ensures temporary research personnel and/or visiting researchers are appropriately qualified, trained, and supervised with training records maintained. • Includes mentoring or a form of mentoring for new personnel.
Staff Resourcing	• Describes process for allocation of personnel to clinical trials. • Minimum staffing requirements identified for different trials conducted. • Minimum staffing adjusted according to study design, workload, intensity, overnight cover etc. • Acceptable site standards for medical supervision and emergency management of participants. • Ensures 24-hour medical cover according to study safety risks. • Describes management activities to ensure staffing adequacy throughout the study. • Ensures staffing contingencies identified. • Includes credentialling of potential Investigators based on trial requirements. • Trials allocated to site staff equal to their experience and qualifications OR with systems to ensure appropriate supervision including allocation to lower risk studies. • Ensures support of staff with little/no clinical trial experience including supervision of junior staff. • Ensures an escalation pathway is identified for urgent escalation of issues.

Delegation of Clinical Trial Responsibilities Ensure delegation to clinical trial qualified staff to perform significant study tasks.	• Ensures allocation of only appropriately qualified and trained staff to study-specific tasks. • Ensures only Investigators with relevant skills, demonstrated by appropriate experience is delegated clinical trial specific tasks. • Study delegation log records study-specific personnel requirements and staff responsibilities. • Staff delegated by Principal Investigator (PI) to study-specific responsibilities before performing tasks. • Ensures 24/7 medical cover. • Sufficiently trained and qualified back-up staff delegated and available to cover absences of core team members. • Describes handover procedures to ensure continuity of staff providing cover or changes in the study team. Records of handover are maintained.
Equipment Management Ensure proper functioning and accuracy of equipment	• Ensures availability of appropriate, functioning clinical equipment. • Maintains an asset register of equipment used for clinical trials. • Periodic service/calibration of equipment with maintenance and service records retained. • Only appropriately trained staff permitted to operate equipment, with training logs maintained. • Ensures instructions for equipment use are available, including a functional check of equipment prior to use. • Cleaning regimen. • Removal of non-functioning equipment from use. • Ensure contingency in place for critical equipment malfunction.
Record Keeping Ensure GCP compliant record keeping, document management & retention	• Requires GCP record keeping standards (i.e., Good Documentation Practice). • Ensures privacy of participant information. • Ensures confidentiality of participant and sponsor records. • Ensures site documents and participant records maintained in electronic systems are secure, accurate (audit trail), and durable (back-up/recovery). • Records (paper/electronic) securely retained for required archiving period.
Risk Management Ensure continuous risk identification, evaluation, mitigation & monitoring.	• Defines risk. • Describes method and/or template for performing and documenting risk identification, assessment, evaluation, mitigation and monitoring [e.g. Risk Management Plan (RMP) or equivalent]. • Describes procedure for RMP generation, approval, review, and revision (as applicable).

	• Describes who performs, provides input, reviews, and approves RMPs (as applicable). • Describes required information to be able to determine risk. For EPCT must include review of product pharmacology, safety, tolerability, and pharmacokinetics/pharmacodynamics. • Defines format and circulation of outputs to relevant staff. • Defines frequency of review and revision. • RMP ensures compatibility of site resources and experience PRIOR to acceptance of study. • RMP includes assessment of the quality/accuracy of sponsor provided data. • RMP identifies potential emergency scenarios and, if applicable, required consultation with the responsible clinical emergency/code blue team. • EPCT RMP addresses dose escalation and de-escalation strategy risk review (as applicable). • RMP ensures participant safety reviews prior to, during, and after study involvement including long-term safety follow-up.
Business Continuity Ensure protection of clinical trial participants, materials, and records.	• Risk based plans in place to ensure continuity of care of study participants and continuance of critical trial activities. • Ensure safe evacuation of participants in an emergency. • Ensures staff are trained and the evacuation procedure is regularly tested. • Ensures contingency of electrical power. • Has a succession plan for key clinical trial staff to ensure continuity of care and adequate trial handover.
Contract Management Ensure responsibilities of all parties involved in clinical trial is documented and agreed (contract management).	• Ensures a contract is in place with the Sponsor prior to receipt of any investigational product at site or prior to consenting the first participant (whichever is earlier). • Ensures periodic review of contract for currency. • Third party contracts are adequately reviewed.
Insurance & Indemnity Ensure adequate Insurances & Indemnities in place for the protection of participants.	• Ensures the adequacy of compensation, indemnity, and insurance for the protection of participants. • Indemnity Agreement in place to compensate participants for harm resulting from the trial. • Reviews adequacy of sponsor insurance(s). • Ensures currency of insurance(s). • Ensures appropriate professional indemnities and insurances in place for staff, in the event of negligence claims.

Management of 3rd Parties Ensure qualification and oversight, of third-party providers for safety critical services.	• Vendors/suppliers are verified as qualified for responsibilities/services prior to use. • Vendors responsibilities are agreed upon and documented. • Vendor contracts reference the applicable compliance requirements. • Mechanism for oversight of vendor performance described. • Records maintained evidencing vendor oversight. • Periodic review and re-qualification of vendors. • A list of approved vendors is maintained.
Management of Medical Emergencies (Including Emergency Medical Cover) Ensure an immediate and appropriate medical response to clinical trial participants in an acute clinical emergency	• Ensures a Clinical Emergency Response System (CERS) Plan/Protocol exists for management of a clinically deteriorating participant. • Ensures CERS Plan/Protocol developed or reviewed by staff with appropriate emergency management qualifications and experience. • CERS Plan/Protocol defines monitoring practices for early recognition of medical deterioration. • Thresholds/definitions for medical deterioration should be defined. • Ensures medically endorsed treatment protocols for diagnosis and response to medical deterioration. • Ensures easily activated system to summon assistance for medically deteriorating participant. • Defines actions required to ensure immediate and appropriate medical response to deterioration past defined thresholds to resuscitate/stabilise participants in acute emergency. • Describes who will respond and how they will be contacted. • Ensures appropriately trained staff (See separate SOP). • Identifies provider/location of emergency department (ED)/intensive care unit (ICU). • Ensures trial specific rescue medicine and/or antidotes are available PRIOR to dosing; staff know where and how to use them. • Ensures provision of 24-hour medical cover as required by the study design. • Ensures intensive medical supervision (“bedside”) for high-risk dosing/study activities. • Ensures defined escalation pathways for medical cover. • Ensures participants provided with instruction and contact numbers to rapidly access medical care. • Unblinding procedures are rapidly carried out in an emergency (as applicable).
Medical Emergency Training	• Staff training and refresher training for emergency resuscitation procedures. • Scenario testing of likely medical emergencies.

Ensure any staff member in the presence of a participant is appropriately qualified, trained and ready to respond to medical emergencies.	• Ensures testing of emergency responses in key treatment areas and other areas frequented by participants. • Maintenance of scenario training records and outcomes. • Consultation with the responsible clinical emergency/code blue teams. • System testing is documented (both real and scenario) with learning points circulated to staff. • Periodic review of emergency procedures for improvements. • Training includes emergency unblinding.
Facilities & Equipment for Emergency Management Ensure availability of appropriate facilities and equipment for participant supervision and emergency management	• Ensures areas routinely accessed by participants are reviewed for safety and emergency management. • Ensures readily accessible and properly functioning call bells. • Describes emergency trolley(s) management. • Ensures availability of appropriately functioning equipment for continuous monitoring of a participant. • Ensures "line of sight" supervision of participants. • Ensures participants are dosed in appropriate areas to allow for emergency treatment. • Ensures participant lockable areas (e.g., toilets) accessible by site staff in an emergency.
Rapid Emergency Transfer to ED/ICU Ensure rapid transfer of participant to specialist emergency/ICU care.	• Identifies ED/ICU facility. • Identifies transfer facility in reasonable proximity to site. • Ensures ED/ICU acceptance of trial participants. • Describes how transfer is initiated including necessary contact details. • Describes method of transfer including accompanying person(s). • Ensures provision of continuous medical support during transfer. • Identifies person(s) responsible for receipt of participant. • Timely provision of all relevant medical information regarding the investigational product, the clinical trial, and the participant(s) medical history to the receiving hospital. • Communication escalation pathways ensure relevant parties are notified as necessary. • Ensures records of transfer are maintained. • Ensures regular testing of the transfer plan. Include "worst case scenario" in establishing maximum estimated travelling time.
Informed Consent ***GCP Standard SOP***	• Consent SOP ensures participant consent is freely given and informed consent is documented, prior to performing any study specific procedure.

	• Where payments are made to clinical trial participants, the form and frequency of payments are documented in the consent form and approved by the ethics committee prior to use. • Where a site uses "generic consent and screening" as part of recruitment strategies, the screening Participant Information sheet/ Consent Form (PICF) is approved by the HREC prior to use.
Participant recruitment, enrolment, and eligibility ***GCP Standard SOP***	• Any recruitment advertising is approved by the ethics committee prior to use. • Site maintains a secure, validated, fit-for-purpose, searchable database of potential participants, which includes information of previous trial participation (as applicable). Database captures significant safety information which prevents them from being invited/recruited inappropriately to a future trial. • Volunteers consent to be included in the database. • Where a site enrols participants from outside the institution, recruitment procedures should describe how the participants medical history and associated eligibility criteria are verified. • Defines how long medical history is valid before it must be reviewed again. • Defines policy for acceptability of verbal medical history. • Medical history review includes assessment of previous trial history. • Procedure to guard against participant over-volunteering is defined. • Site has a policy for washout periods. • Medical history reviewed by Investigator to assure eligibility PRIOR to first dose. • Investigator documents that participant meets all eligibility criteria PRIOR to first dose. • Ensures identity of trial participants at each visit: this may require photographic ID to ensure the person screened is the person dosed. In-patients are identified via a secure wrist band.
Storage & Dispensing of Investigational Product (IP) ***GCP Standard SOP***	• Ensures IP is handled by qualified and trained personnel. • Ensures appropriately licensed, access restricted, and secure storage for IP. • Sufficient space for safe storage of IP including ability to segregate stock not to be used. • Ensures IP is stored under required environmental conditions with records of storage conditions maintained. • Ensures deviations from required environmental conditions are identified with an action plan to minimise the risk of use of affected materials. • Equipment used for the storage and/or management of IP is maintained and calibrated to ensure proper functioning.

	• Investigational Medicinal Product (IMP) is verified as being in good condition prior to administration to a study participant. • Sufficient secure storage to segregate stock/records from unauthorised persons i.e. maintain blinding. • Ensure maintenance of GCP compliant IP accountability records.
Administration/Use of IP ***GCP Standard SOP***	• Ensure only eligible participants dosed, with ongoing eligibility criteria for each participant throughout a trial. • Ensures participants are only dosed following written instruction for the protocol required treatment by a medically qualified, study-trained, and delegated investigator. • Ensures the quality of IMP before dosing. • Dosing or device implementation procedure for each route of administration and/or intervention described. • Ensures any equipment used for dosing is appropriately serviced, calibrated, and verified as properly functioning prior to use. • Ensure participants are correctly dosed with records maintained of treatments administered. • Procedures include 2nd person quality checks of safety critical dispensing and administration steps. • Procedures to ensure appropriate medical supervision of participants before, during, and after dosing.
Management of biological samples ***GCP Standard SOP***	• Ensure safe collection, handling, processing, storage, and shipping of infectious substances. • Ensure staff are appropriately qualified/trained for management of biospecimens. • Ensure appropriately maintained and calibrated equipment for the processing, storage, and temperature monitoring of biospecimens. • Establish systems to detect and respond to temperature deviations. • Ensures records of evidence for protocol compliant processing, management, and storage of biospecimens. • Records maintained for sample movement. • Contingency plans ensure continuity of storage conditions. • Third-party providers of laboratory are assessed and monitored to ensure appropriate qualification and management of samples.
Safety Reporting ***GCP Standard SOP***	• Ensure identification of safety events, evaluation, and reporting in compliance with national and protocol requirements. • Maintains contact details to enable urgent notification of safety information to participants. • Defines the reporting timelines, processes, and notified parties. • Ensures participant primary carers are informed of safety events.

Appendix B: Sample site visit agenda

Time	Agenda Item	Minimum attendees
9:00am	Opening meeting & introductions	Head of Site
9:15am	Clinical & medical governance – organisation & leadership	Head of Site & Site Medical Head
11:00am	Facility Tour Clinical areas: consent, assessments Dose administration areas Overnight accommodation Pharmacy / IMP/ IMD storage & dispensing Biospecimen processing & storage	Delegated site staff member
12:30pm	*Lunch*	
1:00pm	Study management	Principal Investigator(s)
1:30pm	Clinical & Quality Management Systems	Head of Site or person responsible for quality systems
2:00pm	Document review	Delegated site staff member (as required)
4:30pm	Closing meeting	Head of Site

Appendix C: Abbreviation Glossary

Abbreviation	Meaning
ACSQHC (NSQHS)	Australian Commission on Safety and Quality in Health Care (National Safety and Quality Health Service)
AED	Automated External Defibrillator
AHPRA	Australian Health Practitioner Regulation Agency
ALS	Advanced Life Support
ANZCOR	Australian and New Zealand Committee on Resuscitation
BCP	Business Continuity Plan
CAPA	Corrective and Preventative Action
CE	Chief Executive
CERS	Clinical Emergency Response System
CRO	Contract Research Organisation
CPR	Cardiopulmonary resuscitation
CRF	Case report form
CV	Curriculum Vitae
ED	Emergency Department
EPCT	Early Phase Clinical Trials
FIH	First In Human
GCP	Good Clinical Practice (This refers to the International Council for Harmonisation Guideline for Good Clinical Practice)
GMO	Genetically modified organisms
GMP	Good Manufacturing Practice
HREC	Human Research Ethics Committee
IB	Investigator's Brochure
ICU	Intensive Care Unit
IMD	Investigational Medical Device
IMP	Investigational Medical Product
MET	Medical Emergency Team
NATA	National Association of Testing Authorities
OHMR	Office for Health and Medical Research
NSW	New South Wales
PD	Position Description
PI	Principal Investigator

PICF	Participant Information sheet/Consent Form
QA	Quality Assurance
QMS	Quality Management System
QRS	Quality Recognition Scheme
RGO	Research Governance Office
RMP	Risk Management Plan
SAE	Serious adverse event
SOP	Standard Operating Procedure
TGA	Therapeutic Good Administration
UK MHRA	United Kingdom's Medicines and Healthcare Products Regulatory Agency
USA FDA	United States of America Food and Drug Administration
WI	Work Instruction

Appendix D: References

a) Australian and New Zealand Committee on Resuscitation. *Guidelines 10.1-10.6 Education & Implementation*, ANZCOR. https://www.anzcor.org/home/education-and-implementation/

b) Australian and New Zealand Committee on Resuscitation. *Guidelines 11.2- 11.9 Adult Advanced Life Support,* ANZCOR, https://www.anzcor.org/home/adult-advanced-life-support/

c) Australian and New Zealand Committee on Resuscitation, *ANZCOR Guidelines 14.1 – 14.3 Acute Coronary Syndrome,* ANZCOR. https://www.anzcor.org/home/acute-coronary-syndromes/

d) Australian and New Zealand Committee on Resuscitation. *Guidelines 2-8 Basic Life Support,* ANZCOR. https://www.anzcor.org/home/basic-life-support/

e) Australian and New Zealand Committee on Resuscitation. *Guidelines 9.2.1 – 9.2.13 First Aid Management of Medical Conditions,* ANZCOR. https://www.anzcor.org/home/new-guideline-page-2/

f) Australian and New Zealand Committee on Resuscitation, *ANZCOR Resuscitation Guidelines,* ANZCOR. https://www.anzcor.org/

g) Australian Commission on Safety and Quality in Healthcare. *NSQHS Standard: Essential elements for recognising and responding to acute physiological deterioration 2021.* ACSQHC. https://www.safetyandquality.gov.au/publications-and-resources/resource-library/national-consensus-statement-essential-elements-recognising-and-responding-acute-physiological-deterioration-third-edition

h) Australian Commission on Safety and Quality in Healthcare. *National Clinical Trials Governance Framework 2022.* ACSQHC. https://www.safetyandquality.gov.au/publications-and-resources/resource-library/national-clinical-trials-governance-framework-and-user-guide

i) Clinical Excellence Commission, NSW Health. *Policy Directive PD2020_018 Recognition and management of patients who are deteriorating 2020,* NSW Government. https://www1.health.nsw.gov.au/pds/ActivePDSDocuments/PD2020_018.pdf

j) Clinical Trials: Thinking Smarter *Project 3. Early Phase Trials Best Practice Checklist.* CT:IQ. https://ctiq.com.au/current-projects/project-3-2/

k) Department of Health and Aged Care Therapeutic Goods Administration. *ICH GCP E6 (R2) - Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice ICH E6(R2) - Annotated with TGA comments 2016.* Australian Government. https://www.tga.gov.au/resources/resource/international-scientific-guidelines/international-scientific-guideline-ich-guideline-good-clinical-practice.

l) European Medicines Agency *Guidelines on Strategies to Identify & Mitigate Risks for First-In-Human and Early clinical trials with Investigational Medicinal Products 2018*, EMA.https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-strategies-identify-mitigate-risks-first-human-early-clinical-trials-investigational_en.pdf

m) Medicines and Healthcare products Regulatory Agency. *Phase 1 Accreditation Scheme Requirements, version 4.1 2015,* MHRA.https://www.gov.uk/guidance/mhra-phase-i-accreditation-scheme

n) National Health and Medical Research Council. The *National Statement on Ethical Conduct in Human Research (2007)* (National Statement (2007) updated 2018. NHMRC. https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018#block-views-block-file-attachments-content-block-1/.

The Association of the British Pharmaceutical Industry. *Guidelines for phase I clinical trials 2018 edition.* ABPI. https://www.abpi.org.uk/publications/guidelines-for-phase-i-clinical-trials-2018-edition.