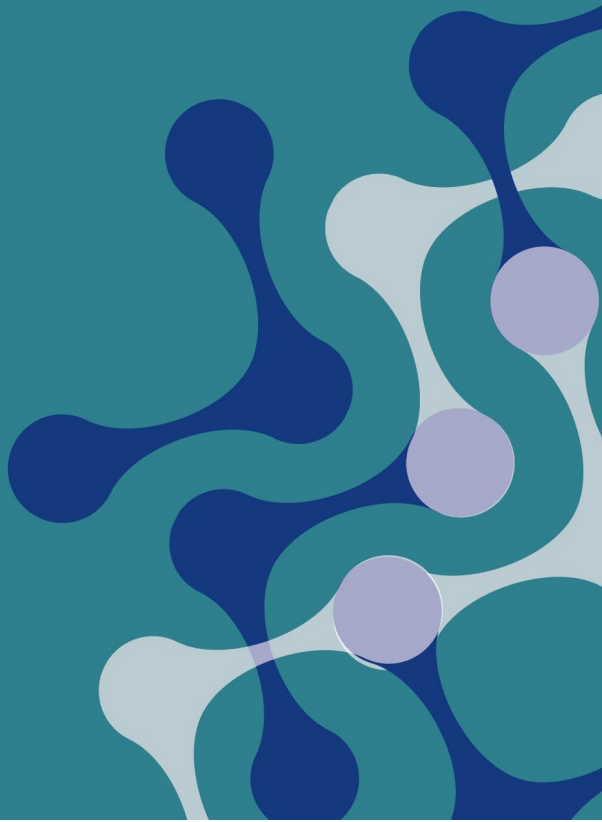
Office for Health and Medical Research

NSW Clinical Trials Quality Recognition Scheme

High Level Assessment Standards
2024



NSW GOVERNMENT

NSW Health

1 Reserve Road

St Leonards NSW 2065

(02) 9391 9228

www.health.nsw.gov.au

www.medicalresearch.nsw.gov.au

Further copies of this document can be downloaded from the NSW Health website: www.medicalresearch.nsw.gov.au

SHPN (OHMR) 241199

ISBN: 978-1-74231-007-7

Table of Contents

FRAMEWORK: The Quality Recognition Scheme (QRS) high level assessment standards were developed as part of the Early Phase Clinical Trial Framework (March 2017). Following broad support from the sector and endorsement by local health district and specialty health network Chief Executives, the Framework was approved by the Chief Health Officer.

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.

Quality Recognition Scheme Overview

- The QRS will be available for trial unit participation from February 2025 and administered by the Office for Health and Medical Research, Quality Recognition Scheme Central Office.
- The QRS standards will be locally adapted and be appropriately assessed to the setting, type of therapeutic intervention and population being studied.
- The criteria will be further developed, with technical input, during the operational phase to ensure that the QRS addresses the wide range of clinical trial types and site structures. Therefore, details in these guidelines are subject to change and will be adapted to operational issues that may arise.
- All trials carry risks, but early phase trials, particularly first-in-human and dose-escalation trials, have the highest clinical uncertainty. A risk matrix will be used to determine the order of selection for participation in the QRS.
- All clinical trial units are expected to have appropriate staff, procedures, and facilities to manage the risks relative to the trial services delivered.
- The QRS will recognise trial units that adequately prepare and account for this risk.
- Clinical Trial Unit/Site: The scope of the QRS will encompass both standalone units and named units within a hospital or academic setting (i.e. either a commercial organisations ward/s/specified area or a pre-defined non-commercial clinical research facility/unit/department, including their named or core personnel). The recognition will not cover the entire hospital and all the wards and personnel, or trials performed outside the named unit.
- The QRS will not address the conduct of individual trials, but rather trial unit operations, trial quality management and investigator skills and experience.
- This QRS aims to assist sites in gap analysis and preparation for current national schemes; the National Clinical Trials Governance Framework accreditation by the Australian Commission on Safety and Quality

in Healthcare, and the Good Clinical Practice (GCP) Inspection Program administered by the Therapeutic Goods Administration (TGA).

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 assessment of these standards DOES NOT reflect the full scope or does not replace to need for a standard regulatory GCP inspection or sponsor audit.

Quality Recognition Scheme High Level Assessment Standards

1. Clinical and medical governance oversight at site level	
Criteria	Assessment
1.1 Clinical/Medical governance accountability at sites including clear lines of responsibilities for investigators and other medical staff.	✓ Site specific policies or equivalent for medical (or clinical) governance statements, this may be dependent on the business structure of the site

1.2 Head of Site (HoS) maintains oversight and involvement in risk assessment and management of clinical trials.	✓ Evidence for sites covered under a hospital accreditation
2. Demonstrate efficient and effective system and processes to ensure quality	
Criteria	**Assessment**
2.1 Core Standard Operating Procedures (SOPs) at the site, to ensure compliance with relevant processes and GCP requirements including additional early phase trial requirements and procedures for trial documentation management. 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. 2.3 Efficient and effective system to monitor the quality of clinical trials including Quality Assurance (QA)/Quality Control (QC), internal audit, non-compliance management (e.g. Corrective Action/Preventive Action (CAPA)) and continuous improvement.	✓ Evidence of current and active SOPs for all relevant study activities, medical and clinical governance and training for the facility (refer to the QRS application guide for SOP list) ✓ Management of SOP life cycle ✓ Internal Monitoring and Review Plan ✓ Non-compliance and quality issue management procedures and evidence of continual monitoring
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 conducting a trial	
Criteria	**Assessment**
3.1 Established written procedure for risk assessment and evaluation, risk mitigation and monitoring or equivalent due diligence procedures should be in place to include the critical review of the relevant sources. 3.2 Risk Management Plan or equivalent is generated for each study, where all aspects of the trial and the associated risks are considered with appropriate actions put in place to mitigate and monitor those risks. 3.2.1 Full review of likely risks and mitigation strategies for any newly proposed trials **prior** to acceptance of the study 3.2.2 Topics to consider for the plan in the risk identification process should be tailored to the type of study, route of	✓ Risk Assessment and Management Plan template or equivalent checklist ✓ Evidence of previously completed risk assessments ✓ Dose escalation/de-escalation assessment and implementation ✓ Safety Management Plan and Reporting Plan template ✓ Other equivalent documented process e.g. integrated within SOP such as checklist/ templates ✓ Process of assigning resources against protocol requirements ✓ Process of assigning site responsibilities

administration and the nature of the IP and may include (but are not limited to): • Investigator Brochure (IB) including but not limited to physical and chemical characteristics, pre-clinical and clinical information related to pharmacology, toxicology, safety and tolerability profile, pharmacokinetics, pharmacodynamics and dose-response relationship (as applicable). • IB equivalent for medical device information including but not limited to procedure-related functions, performance-related functions, device safety (e.g. sterility), potential failure modes and clinical effects of failures on participants and the device (as applicable). • Study design and appropriateness of safety assessment, and assigning quality tolerance limits during protocol development, de risking primary endpoints for the trial i.e. safety/pharmacokinetics (GCP E6 (R2) 5.0.4). • Starting dose calculations, dosing regimen (including sentinel dosing), stopping criteria and dose escalation procedures. • Participants in life stages that may give rise to vulnerability. • Requirements and composition of a safety review or monitoring committee, including long-term follow-up. • Identification of potential medical emergencies and (serious) adverse reactions, the need to perform relevant specific mock scenarios and consider specific notification to Intensive Care Unit (ICU)/Emergency team, requirement of any specific antidotes or emergency treatments. • Staffing requirements for dosing days/IMP administration, overnight and subsequent observation period(s); additional training requirements. • Specific facility requirements and/or access to special wards and services (such as for dedicated phase 1 units	✓ Evidence of data reviewed and risk decision making logs

and/or Pharmacy facility requirements for sterile, or cytotoxic products and/or Genetically Modified Organisms (GMO)). • Internal monitoring and review plan should be in place for risk management procedures, to ensure there is continuous internal monitoring, especially for longer studies and providing rationale for the selection of the author(s), and the review and approval process. • Staff delegated to perform the risk assessment i.e. Principal Investigator (PI) or Medical Director of the site. 3.3 Evidence of continuous risk management and monitoring for protocols involving dose escalation (as applicable). 3.4 Evidence of continuous risk management and monitoring for medical device investigations (as applicable).	
4. Appropriate research team expertise for clinical trials	
Criteria	**Assessment**
4.1 Evidence of an appropriately composed, managed and led study team with the relevant collective knowledge to meet specific study requirements. 4.2 Principal Investigator: Relevant skills, demonstrated by experience and training in clinical trials, such as therapeutic area, patient populations, relevant to phase of trials including First Time in Human (FTIH)/First Time in Patients (FTIP) studies. 4.2.1 Relevant experience and training for specific IMP/IMD administration/insertion where applicable. 4.2.2 Experience/knowledge of clinical pharmacology in relevant therapeutic background (as required). 4.3 Other clinical trials personnel: 4.3.1 Evidence of an appropriate team composition with collective experience in clinical trials, accounting for the trial portfolio at site. 4.3.2 Existence of a mentoring/coaching system to support, train and develop	✓ Resource Management Plan or equivalent with documented evidence of expertise capacity (training, courses, studies, experience, etc.) and training plans ✓ Staff training records and/or training matrix documenting training completion including regular GCP and emergency training for the facility ✓ Evidence of training compliance review including regular competency assessments for routine procedures ✓ CVs, certifications and qualification evidence for all PIs and trial personnel ✓ Site roster review ✓ Site delegation logs (template and written process) ✓ Evidence of assessment process for visiting researchers ✓ Evidence of mentoring process

personnel e.g. those with no clinical trial experience, or no early phase experience. 4.3.3 Evidence of adequate supervision by senior personnel with relevant trial phase experience. 4.4 Appropriate resourcing and allocation /delegation of personnel. 4.4.1 Acceptable minimum personnel levels. 4.4.2 Process for allocation of PI and sub-investigators to facilities/research teams especially for FTIH. Mechanism for delegating responsibilities and tasks by PI to another appropriately qualified medical personnel especially when the PI is not on site during dose escalation days. 4.5 Approach to Visiting Researchers and temporary research personnel. 4.5.1 Process to assess visiting researchers and their suitability to act as PIs or sub-investigators. 4.5.2 Relevant experience. 4.5.3 Formal mentoring and supervision procedures.	
5. Adequate infrastructure and resources to conduct clinical trials and appropriately respond to medical emergencies	
Criteria	**Assessment**
5.1 Adequate infrastructure and resources to conduct clinical trials. Consent procedures which assure the rights and wellbeing of trial participants. Robust and formalised recruitment & eligibility review procedures to protect the participant from inappropriate recruitment to a clinical trial. Appropriate facilities and procedure for storage & dispensing of IP. IMP Administration: Site procedures assure correct dosing of trial participants i.e. procedure is available for administration where non-standard treatment or high -risk forms are necessary; and to assure the dose recipient is correctly identified and dosed according to protocol. 5.1.1 Risk management of facility factors contributing to the integrity and validity	✓ Hospital accreditation for sites within Public Health Organisations (PHOs) ✓ On-site audit of facilities and equipment ✓ Documentation for testing procedures ✓ Evidence of mock emergency scenarios performed and/or documented evidence of experienced emergency scenarios ✓ Evidence of relevant medical and clinical site personnel undergoing life support training with standard refresher frequency (as appropriate). ✓ Evidence of Service Level Agreement (SLA)/contract if applicable ✓ Evidence of procedures and/or templates ✓ Site visit assessment for pharmacy sterile, cytotoxic and GMO provisions (dependent on site)

of clinical trial bioanalytical and safety laboratory sample data. 5.1.2 Proper functioning of all clinical and laboratory equipment used for trials. 5.1.3 Safety reporting procedures in compliance with national regulations and GCP. 5.1.4 Site demonstrates adequate procedure in place for clinical trial contract management, insurances & indemnities 5.2 Adequate and appropriate site facilities to appropriately respond to medical emergencies. Based on the number of wards/beds and the layout of the site, there must be enough emergency trolleys (or acceptable alternative) to ensure easy and rapid access to clinical care. The emergency trolley contents should reflect the current PHO/Local Health District (LHD) guidelines or applicable emergency service guidelines to ensure staff easily locate required items on the trolley. Guidelines should include: 5.2.1 Emergency trolley management procedures including quality control measures which ensure equipment and medications for management of a clinical emergency is readily available and accessible. 5.2.2 Procedure in place to ensure ready availability of all necessary emergency medications whilst also maintaining appropriate storage and access control. 5.2.3 Site has appropriate facilities and equipment for medical supervision and emergency management of clinical trial participants. Appropriately trained trial site and other on the floor personnel for management of clinical emergencies. Site has procedure to ensure an immediate and appropriate clinical response to clinical trial participants in an acute emergency (i.e. a Clinical Emergency Response System (CERS) Plan) including cardiopulmonary arrest; hypotension, anaphylaxis & profound syncope. Site personnel are trained to identify a deteriorating patient and to initiate treatment during a clinical emergency; qualified/certified.	✓ Site visit assessment for biospecimen processing (dependent on site) ✓ IMP/IMD secure storage assessment ✓ Evidence of 24hr medical cover for participants ✓ Evidence of staff roster, procedures, participant contact card templates or equivalent ✓ Evidence of participant database (if kept)

5.2.4 Site personnel are trained to initiate treatment of a clinical emergency at various times of day and in various settings (scenario training). The meaning of "site personnel" equates to at a minimum, the nurses, PI and delegates and those personnel that would be responsible for participants clinical care and management whilst they are at the site. There should be provision of 24 hours medical cover as required by the study design both during and after dosing whilst in the clinic and after discharge from the clinic until the participants last follow-up visit. 5.2.5 Acceptable standards for the medical supervision of trial participants including out-of-hours medical cover. 5.2.6 Communication procedures for the exchange of urgent safety information with participants and primary/specialist care providers 5.3 Availability of ICU/Emergency in a reasonable proximity or equivalent 24-hour emergency provision. For standalone units, there should be a contract or service level agreement with an emergency and/or intensive care location within a reasonable distance or an equivalent 24-hour emergency provision. 5.4 Provision for emergency transfer and treatment: procedure in place and the ability to provide rapid and safe transfer of study participants to a facility with intensive care capability.	

Appendix 1: Regulatory Framework Resources

Description	Link
Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2), annotated with TGA comments	https://www.tga.gov.au/publication/note-guidance-good-clinical-practice
ISO 14155 Clinical Investigation of medical devices for human subjects-Good Clinical Practice	https://www.iso.org/standard/71690.html
Australia's National Statement on Ethical Conduct in Human Research (2023) issued by NHMRC	National Statement on Ethical Conduct in Human Research 2023 | NHMRC
Note for guidance on clinical safety data management: Definitions and standards for Expedited reporting (CPMP/ICH/377/95) Annotated with TGA comments	https://www.tga.gov.au/publication/note-guidance-clinical-safety-data-management-definitions-and-standards-expedited-reporting
Therapeutic Goods Legislation (the Therapeutic Goods Act 1989, the Therapeutic Goods Regulations 1990 and the Therapeutic Goods Medical Devices Regulations 2002)	https://www.tga.gov.au/legislation-legislative-instruments
Privacy: NSW Health Records and Information Privacy Act 2002 and Privacy Act 1988	https://www.legislation.nsw.gov.au/#/view/act/2002/71
Australian Clinical Trial Handbook: Guidance on conducting clinical trials in Australia using "unapproved" therapeutic goods, version 2.4, August 2021	https://www.tga.gov.au/sites/default/files/australian-clinical-trial-handbook.pdf
NHMRC, ARC & Universities Australia: Australian Code for the Responsible Conduct of Research 2018	https://www.nhmrc.gov.au/about-us/publications/australian-code-responsible-conduct-research-2018
The NHMRC Guidance: Safety monitoring and reporting in clinical trials involving therapeutic goods	https://www.nhmrc.gov.au/guidelines-publications/eh59
Australian Commission on Safety and Quality in Health Care (ACSQHC), National Clinical Trials Governance Framework	National Clinical Trials Governance Framework | Australian Commission on Safety and Quality in Health Care
Therapeutic Goods Administration (TGA) Good Clinical Practice inspections	Preparing for Good Clinical Practice (GCP) inspections | Therapeutic Goods Administration (TGA)

Appendix 2: Clinical Trial Definitions

In Scope: Investigational medicines, blood and blood products

Phase 0 or Early Phase I (Human Pharmacology – micro dosing)	An exploratory investigational new drug study also known as a "microdosing" study. Involves dosing a limited number of humans with a limited range of doses for a limited period.[1] Exploratory trials of this type establish whether the agent behaves in humans as expected based on preclinical animal studies. They gather preliminary data on pharmacodynamics or pharmacokinetics, select promising lead candidates, and/or explore bio-distribution characteristics. These studies do not offer any possibility of patient benefit.[2]
Phase I (Human pharmacology) **Escalation Phase for oncology studies**	Phase I studies usually test new drugs for the first time in a small group of people to evaluate a safe dosage range and identify side effects.[3] Medicines are usually given to small numbers of healthy volunteers, but sometimes to people affected by the disease the medicine is intended to treat. The purpose is to assess safety and tolerance. Trials may define or describe pharmacokinetics and pharmacodynamics, dosing, explore drug metabolism and drug interactions, identify preferred routes of administration. Phase 1a: single ascending dose. Phase 1b: multiple ascending doses.[2]
Phase I/II	A study that tests the safety, side effects, and best dose of a new treatment. Phase I/II clinical trials also test how well a certain type of cancer or other disease responds to a new treatment. In the Phase II part of the clinical trial, patients usually receive the highest dose of treatment that did not cause harmful side effects in the phase I part of the clinical trial. Combining phases I and II may allow research questions to be answered more quickly or with fewer patients.[4]
Phase II	Phase II studies test treatments that have been found to be safe in phase I but now need a larger group of human subjects to monitor for any adverse effects.[3]
Phase III	Phase III studies are conducted on larger populations and in different regions and countries and are often the step right before a new treatment is approved.[3]
Phase IV	Phase IV studies take place after country approval and there is a need for further testing in a wide population over a longer timeframe.[3]
Early Phase	Early phase trials can be broadly defined as non-therapeutic, exploratory trials in human participants who may be healthy volunteers or have a specific disease. They include FTIH/ FTIP trials (see below).
First time in human (FTIH)	Investigational medical product (IMP) administered to a human for the first time.

-

[1] Therapeutic Goods Administration (TGA). Australian clinical trial handbook V2.4 August 2021. Available at: www.tga.gov.au/sites/default/files/australian-clinical-trial-handbook.pdf
[2] US Department of Health and Human Services, National Institutes of Health. National Library of Medicine. Clinicaltrials.gov Learn about studies. October 2024. Available at: Learn About Studies | ClinicalTrials.gov
[3] World Health Organisation (WHO) Clinical trials overview. 2024 Available at: Clinical trials
[4] US Department of Health and Human Services, National Institutes of Health, National Cancer Institute. NCI Dictionaries. February 2024. Available at: www.cancer.gov/publications/dictionaries/cancer-terms/def/phase-i-ii-clinical-trial

First time in patient (FTIP)	This is a subset of FTIH, where it would be unethical to administer the IMP to a healthy volunteer. Therefore, the IMP is administered to a patient. It does not refer to a Phase II trial where the IMP was previously given to a healthy volunteer.[1]
First time in paediatric	The first time a medicine is used formally in a trial in a paediatric population, noting that the IMP may have previously been trialled in adult populations.
Healthy Volunteer	A well (generally healthy, not sick) person who agrees to participate in a clinical trial for reasons other than medical purposes and receives no direct health benefit from participating.
Patient Volunteer	A person who has a specific medical condition (e.g. asthma or diabetes etc.) relevant to the clinical trial who agrees to participate in a clinical trial for reasons other than medical purposes and is unlikely to receive a direct health benefit from participating.
Patient	A person being treated for a specific medical condition who has been invited or referred by their GP/consultant to participate in a clinical trial. Patients may receive a therapeutic benefit from the trial.[3]

Investigational Medical devices (IMD) ISO14155

Early feasibility study or pre-market pilot study	Exploratory investigations to determine preliminary safety and performance information to plan design modifications or provide support for a future pivotal study. A limited clinical investigation of a device early in development, typically before the device design has been finalised, for a specific indication (e.g. innovative device for a new or established intended use, marketed device for a novel clinical application). It usually involves a small number of participants (generally fewer than 10 initial participants).[1] Information obtained from an early feasibility study may guide device modifications. An early feasibility study does not necessarily involve the first clinical use of a device. This includes medical devices already on the market, that are being evaluated for new intended uses, new population, new materials or design changes.
First in human study (medical device)	A type of study in which a device for a specific indication is evaluated for the first time in human participants. Typically used for novel devices. Note: The first human use of a non-innovative device for a well understood clinical use could appropriately be evaluated under a traditional feasibility or pivotal (rather than FTIH or early feasibility).
Traditional feasibility study	A clinical investigation that is commonly used to capture preliminary safety and effectiveness information on a near-final or final device design to adequately plan an appropriate pivotal study. A traditional feasibility study does not necessarily need to be preceded by an early feasibility study.
Pivotal Study	Confirmatory investigations to evaluate performance and safety for a specified intended use to satisfy pre-market regulatory requirements.[1]
Post-market	Confirmatory investigations to establish performance and safety, for example, in broader populations OR Observational investigations or surveillance to gain better understanding of device safety, long term outcomes and health economics.[1]

Out of Scope: The following instances are out of scope.

i. Individual patient use (Special Access Scheme). The use of therapeutic goods in these circumstances is governed by clinical governance within the hospital and Local Health District (LHD). Most commonly this will be a Drugs and Therapeutic Committee within the hospital or LHD.

ii. The Authorised Prescriber Scheme allows multiple patients (class of patients with the same condition) to access therapeutic goods in Australia that have not been included in the Australian Register of Therapeutic Goods (ARTG).

iii. Trials where the interventions are not therapeutic goods as defined in the *Therapeutic Goods Act* 1989 (Cth) (e.g. surgery, allied health physical therapies).

The definition of 'early phase' in the context of the Framework is not intended to include:

Administration for the first time, of a medicine registered for a disease(s) to patients with a different disease provided, if applicable, the molecular target is the same and the dose is within the dose range of the registered indication(s). For example, a medicine which is registered in Australia (or by an internationally recognised regulatory authority e.g. US Food and Drug Administration, European Medicines Agency) for patients with a particular cancer, overexpressing a specific molecular target may be trialled in patients with another cancer type which also overexpresses the same target. That is, provided the dose requested is within the dose range for the registered indications. Such trials can be conducted under existing processes.

Appendix 3: Definitions and Abbreviations

Good Clinical Practice (GCP) is a standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial participants are protected.

Investigator's brochure (IB) is the document containing a summary or compilation of the clinical and non-clinical data on an investigational medicinal product/investigational medical device that are relevant to the study of the product in humans.

Investigational Product (IP): a pharmaceutical form of an active substance or placebo (medicinal) AND/OR a device intended to diagnose, prevent, monitor, treat or alleviate a disease or injury, being tested or used as a reference in a clinical trial, including products already with a marketing authorization but used or assembled (formulated or packaged) in a way different from the authorised form, or when used for an unauthorised indication, or when used to gain further information about the authorised form.

Schedule 8 (S8): **Controlled drug**. Schedule 8 (S8) drugs and poisons, otherwise known as Controlled Drugs, are substances and preparations for therapeutic use which have high potential for abuse and addiction. The possession of these medications without authority is an offence.

Sites/trial units: the scope of this Scheme will encompass both standalone trial units and named sites within a hospital or academic setting (i.e. either a commercial organisations ward/specified area or a pre-defined non-commercial clinical research facility/unit/department, including their named or core staff). The recognition will not cover the entire hospital and all the wards and staff, or trials performed outside the named unit