CLINICAL TRIALS - SCHN SPONSORSHIP

POLICY©

DOCUMENT SUMMARY/KEY POINTS

- This policy outlines the application and review process for SCHN staff who wish to have SCHN act as Clinical Trial Sponsor.
- This policy describes:
  - The decision-making process of Sydney Children's Hospitals Network (SCHN) when agreeing to act as Sponsor for a Clinical Trial
  - Both Investigator and Sponsor responsibilities under Good Clinical Practice (GCP) and the process to be followed to ensure compliance with applicable regulatory requirement(s), guidelines, institutional policies and procedures.
- This policy provides the following assurances for clinical trials conducted within SCHN are compliant with Good Clinical Practice (GCP):
  - The rights, safety and well-being of participants are protected
  - Clinical trial data generated within SCHN is reliable and robust
  - That the initiation, management and financing (or arranging the financing) of the trial is appropriate and follows the medico-legal responsibility associated with its conduct.

Approved by:	SCHN Policy, procedure and Guideline Committee	
Date Effective:	1st August 2023	**Review Period**: 3 years
Team Leader:	Quality Research Manager	**Area/Dept**: Research Ethics & Governance

CHANGE SUMMARY

- Not applicable – this is the first version of this policy
- **11/04/24:** Minor review. Additional wording has been included under Section 3.7 outlining the notification requirements for the SCHN Sponsorship Committee. This update aims to keep the Committee informed about the clinical trial's progress and ensure that any amendments undergo appropriate organisational risk review.

READ ACKNOWLEDGEMENT

- Read Acknowledge Only – all staff engaged in research at SCHN

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1 Purpose

This policy outlines the application and review process for requesting the Sydney Children's Hospitals Network (SCHN) Sponsorship of a Clinical Trial including where the Clinical Trial is to be conducted under the Therapeutics Goods Administration (TGA) Clinical Trial Notification (CTN) or Clinical Trial Approval (CTA) schemes (CTN/CTA trial).

It describes the responsibilities that the SCHN assumes when agreeing to act as the Sponsor of a Clinical Trial and sets out the framework for meeting these responsibilities under Good Clinical Practice (GCP).

2 Scope and Applicability

This policy applies where SCHN is approached to be the Sponsor of a Clinical Trial and must be followed by all SCHN employees wishing to conduct a clinical trial that does not have an Australian Sponsor in place.

This applies to all SCHN employees, affiliates and to all relevant external persons and parties engaged in research activity at SCHN.

3 Policy

3.1 Definition of a clinical trial at SCHN

The National Statement on Ethical Conduct in Human Research defines clinical trials as being a form of research designed to find out the effects on an intervention, including a treatment or diagnostic procedure.

A clinical trial is any research study in which human participants volunteer to test new treatments, interventions or tests as a means to prevent, detect, treat or manage various diseases or medical conditions (https://www.australianclinicaltrials.gov.au/what-clinical-trial).

Clinical trials include but are not limited to:

- Surgical and medical treatments and procedures
- Experimental drugs
- Biological products
- Medical devices
- Health-related service changes
- Health-related preventative strategies
- Health-related educational interventions.

3.2 Regulated clinical trials (CTN/CTA trials)

In accordance with legislative and regulatory requirements:

- All Clinical Trials involving unapproved therapeutic goods in Australia (i.e. CTN/CTA trials), or use of a therapeutic good outside of its TGA approved indication/conditions, must have a formal Sponsor that is an Australian entity (an overseas company cannot be the Sponsor of a trial in Australia). Clinical Trial sponsors can be commercial companies, collaborative research groups, government entities including health service organisations, individual investigators, or universities (refer to the Australian Clinical Trial Handbook: Guidance on conducting clinical trials in Australia using unapproved therapeutic goods for further information).
- The Sponsor is responsible for the conduct of a CTN/CTA trial in accordance with GCP.
- Sponsors can formally delegate one or more of the elements of sponsorship such as the Sponsor's trial-related duties and functions, including safety reporting, to a third party such as a Contract Research Organisation (CRO) or an individual such as a Coordinating Principal Investigator (CPI, where multi-site trial) or Principal Investigator (PI, where trial is single site).
- **However, the SPONSOR is ultimately responsible for the quality and integrity of the Clinical Trial data and all delegated functions (see SCHN Research Governance website for SCHN delegations).**
- In these instances, the Sponsor must implement procedures to ensure appropriate oversight of all delegated functions and ensure these are specified in writing. The contracts and agreements between trial sponsors and third parties must ensure all roles and responsibilities are clearly defined.

3.3 Clinical trials not regulated by the TGA

For Clinical Trials not involving unapproved therapeutic goods and where there is no legislative basis for compliance with GCP, SCHN requires the principles of GCP to be followed where applicable.

For non-regulated clinical trials, SCHN will apply a streamlined review process for SCHN Sponsorship requests (Section 3.6.)

3.4 SCHN Sponsorship and the Sponsor's Responsibilities

- SCHN may act as the Sponsor for some investigator-led/collaborative group studies where the CPI/PI is an employee of SCHN and the Clinical Trial is coordinated/conducted at SCHN and other sites. However, approval to act as Sponsor is not automatic (see Section 3.6).
- As the Sponsor, SCHN must:
    - Be satisfied it understands the risks associated with the study, has the resources to meet the responsibilities attributable to the study Sponsor in accordance with GCP, and the study design meets relevant standards,

- Ensure that arrangements are put and kept in place for management, monitoring and reporting, and
- Undertake that all requirements as a Sponsor can be met.

- For CTN/CTA trials, the SCHN has delegated the operational responsibility for executing the role of trial Sponsor to the SCHN Research Office including submitting the CTN/CTA and providing the Sponsor declaration acknowledging overall responsibility for the trial (for reference see page 49, CTN form user guide).
- The CPI/PI must discuss the intention for SCHN to be the Sponsor for a Clinical Trial with the SCHN Research Governance Office as early as possible (SCHN-Governance@health.nsw.gov.au). It is recommended that this takes place before the ethics submission .

The SCHN Clinical Trials Sponsorship Committee (CTSC) reviews Clinical Trial Sponsorship applications and the trial risk assessment and provides a recommendation to the Executive on whether SCHN is to act as Sponsor for a Clinical Trial.

3.5 Conditions for Sponsorship

For Sponsorship to be considered by SCHN the following conditions must be met:

- The CPI/PI must be an employee of SCHN and have active GCP certification..
- There must be a commitment to enter formal agreements with all third parties including external investigators, manufacturers, laboratories etc.
- The CPI/PI must have extensive experience in conducting Clinical Trials and have a current GCP certificate (not greater than 3 years old).
- There must be adequate finances sought or secured to ensure sufficient resourcing to complete the trial including some delegated sponsor responsibilities where necessary (refer to the SCHN Research Governance website for the delegation of responsibilities agreement template).

3.6 Process for Confirming Sponsorship

- The CPI/PI must submit a Sponsorship request through the SCHN Research Governance Office via email (SCHN-Governance@health.nsw.gov.au).
- For all early phase clinical trials, SCHN Sponsorship must be confirmed by CTSC, or delegate before HREC approval is granted. If HREC approval is granted before CTSC approval has been provided, there is no guarantee that SCHN Sponsorship will be approved and researchers may have to re-submit their Ethics application.
- The process outlined in the following sections (3.6.1 to 3.6.9) is to be followed where SCHN is requested to be the Sponsor for a Clinical Trial.

3.6.1 Informal Meeting with the CPI/PI and SCHN Sponsor Representative

- The CPI/PI must organise to meet the SCHN Sponsorship Representative to discuss their potential application and Risk Assessment to the CTSC (SCHN-Governance@health.nsw.gov.au). The Sponsorship application form (Early Phase Clinical Trials and Non-Early Phase Clinical Trials) and Risk Assessment form are available on the SCHN Research Governance website.
- At this meeting, the Research Governance Office will guide the CPI/PI through the application process and items to be identified in the Risk Assessment. A draft protocol (must include appropriate peer review and input from a statistician) and Investigator's Brochure (IB) or equivalent should be available.

3.6.2 Submission of Sponsorship Application and Draft Risk Assessment

- After the initial meeting, the CPI/PI must prepare and submit an Application for Sponsorship and Risk Assessment to the SCHN Research Governance Office.
- All templates and forms are available under the Sponsorship section of the SCHN Research Governance website.

Early-Phase Clinical Trials (EPCT)

3.6.3 SCHN Clinical Trial Sponsorship Committee Review of Application

- Within 7 days of receipt of the Sponsorship Application and Risk Assessment, all documentation submitted will undergo a preliminary review by the SCHN Research Quality Manager. Initial queries will be sent to the study team for responses prior to the next step
- All documents received will be circulated for electronic interim review and comment to the SCHN Clinical Trial Sponsorship Committee members
- Feedback will be provided to the CPI/PI to address any queries regarding:
  - Completeness of application
  - Other potential risks
  - Possible risk mitigation strategies
  - Any potential barriers to SCHN Sponsorship

If the interim reviewers are satisfied that the criteria outlined in 3.5 are met, and the application and risk assessment are complete, the application will be formally referred to the CTSC for consideration at a meeting.

3.6.4 SCHN Clinical Trial Sponsorship Committee Review and Decision

- The CTSC will convene to consider the Sponsorship application.
- The SCHN Clinical Trial Sponsorship Committee Membership as per Terms of Reference.
- The CTSC will meet to review the Sponsorship Application and Risk Assessment.
- In determining approval, the SCHN Sponsorship Committee will consider:
    - The available infrastructure to act as Trial Sponsor;
    - The possible benefits to SCHN and SCHN patients;
    - The risks identified in the risk assessment;
    - The appropriate management of the study;
    - The proposed contractual arrangements; and
    - The research strategy of SCHN

The CTSC may request the CPI/PI to present to the Committee or seek further information or request further detail in order to approve the application for Sponsorship.

During the meeting the CTSC will determine:

- The overall risk rating of the trial
- The degree of CTSC (or delegate) oversight required
- Any further actions required for mitigating and/or monitoring the risks identified
- If additional documents for further review (including date for submission) are required such as:
    - data sharing plan
    - data management plan
    - monitoring plan

3.6.5 Response to feedback

- If any revisions/concerns are recommended by the CTSC, the CPI/PI needs to address these and re-submit the revised documents to the SCHN Research Quality Manager for review and approval by the SCHN CTSC.
- The response must be in writing within the nominated time-frame by the CTSC (usually 14 days) and address the concerns from the Committee in writing and provide a plan/solution to a level that satisfies the SCHN CTSC.

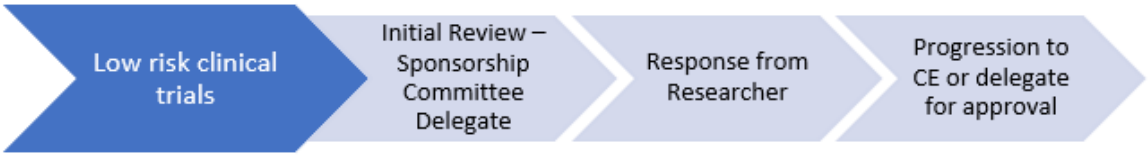
3.6.6 *In Principle Decision for SCHN to act as Sponsor*

- Once the CTSC considers that all concerns have been adequately addressed by the CPI/PI, they will endorse an in-principle decision for SCHN to act as Sponsor and progress the application to the SCHN Executive for final review and approval.
- ***Note***: This is not a final confirmation of SCHN Sponsorship approval. At this stage, the CPI/PI is able to submit the Expression of Interest application to SCHN HREC, however they are unable to submit the CTN/CTA application to the TGA or the HREA to SCHN HREC until final approval for Sponsorship is confirmed.

3.6.7 *SCHN Sponsorship Confirmation*

- The SCHN Executive will review the risk mitigation strategies provided by the CPI/PI and may have further concerns to raise.
- The CPI/PI must respond to these in writing to the Sponsor representative
- Once SCHN Sponsorship is approved by SCHN Executive, an email will be sent from the Sponsor Representative to the CPI/PI informing them of the decision SCHN agrees to act as trial Sponsor.
- An agreement will be sent to the CPI/PI outlining how the investigator and SCHN will fulfill responsibilities under the TGA legislation, including GCP
- The Agreement must be completed and returned by the CPI/PI.
- The Research Office will provide confirmation to the CPI/PI of clinical trials insurance coverage

Non-early Phase Clinical Trials



Clinical trials requesting SCHN Sponsorship that meet the criteria below should follow this pathway:

- Phase 2, 3 or 4 interventional drug/device trials with a non-commercial overseas Sponsor (eg: trials that are being run by an overseas consortium or collaborative group)
- Non-drug/Non-device clinical trials

3.6.8 SCHN Review of Application

- Within 7 days of receipt of the Sponsorship Application and Risk Assessment, all documentation submitted will be reviewed by the Sponsorship Committee Representative
- The application will be reviewed, and feedback provided to the CPI/PI to address any queries has regarding:
    - Completeness of application
    - Other potential risks
    - Possible risk mitigation strategies
    - Any potential barriers to SCHN Sponsorship

If the interim reviewers are satisfied and the criteria outlined in 3.5 are met, and the application and risk assessment are complete, a decision will be made for Sponsorship to be considered by the SCHN Chief Executive or Delegate.

3.6.9 SCHN Executive (or Delegate) Review and Decision

- Within 2 weeks of this interim decision, the application will be progressed to the SCHN Chief Executive or Delegate for review and approval.
- In determining approval, the SCHN Executive or Delegate will consider:
    - The available infrastructure to act as Trial Sponsor;
    - The possible benefits to SCHN and SCHN patients;
    - The risks identified in the risk assessment;
    - The appropriate management of the study;
    - The proposed contractual arrangements; and
    - The research strategy of SCHN

The approver will determine:

- The overall risk rating of the trial
- The degree of CTSC (or delegate) oversight required
- Any further actions required for mitigating and/or monitoring the risks identified
- If the CPI/PI to submit any additional documents for further review (including date for submission) such as:

- data sharing plan
- data management plan
- monitoring plan

3.6.10 SCHN Sponsorship Confirmation

- SCHN will review the risk mitigation strategies provided by the CPI/PI and may have further concerns to raise.
- The CPI/PI must respond to these in writing to the Sponsor representative
- Once SCHN Sponsorship is approved by SCHN CE or Delegate, an email will be sent from the Sponsor Representative to the CPI/PI informing them of the decision SCHN agrees to act as trial Sponsor.
- An agreement will be sent to the CPI/PI outlining how the investigator and SCHN will fulfill responsibilities under the TGA legislation, including GCP
- The Agreement must be completed and returned by the CPI/PI.
- The Research Office will provide confirmation to the CPI/PI of trials insurance coverage

3.6.11 HREC and Governance Application

Once the SCHN Sponsorship has been confirmed the CPI/PI may proceed with HREC, SSA applications and regulatory applications as agreed in the Sponsorship Arrangement Agreement.

Authorisation to conduct the Clinical Trial at SCHN must be provided in accordance with PD2010_056 – Research – Authorisation to Commence Human Research in NSW Public Health Organisations.

3.6.12 Submission CTN/CTA

SCHN Research Office oversees the institution's TGA account. The Research Governance Manager is the SCHN authorised representative responsible for submitting CTN/CTA on behalf of SCHN.

The CPI/PI must liaise with the Research Governance Office to ensure:

- A CTN is submitted prior to commencement of the trial, or
- the CTA is in place prior to submission to HREC.

The CPI is responsible for ensuring adequate trial resources are allocated to covering the cost of the CTN/CTA submission, along with any HREC and governance applications (where relevant (initial and any subsequent amendments).

3.7 Continued Sponsorship arrangements

The review of Sponsorship is a continuous process and continued Sponsorship is contingent on the Research Governance Office receiving relevant correspondence as the trial progresses including:

- All approval letters
- All amendments to the trial protocol that substantially impact the Sponsorship application risk assessment (the Risk Management Table should be updated and re-submitted).
- All safety reports as required by Australian legislation and relevant guidance provided by the NHMRC and TGA.
- All serious breaches of GCP/Protocol at the Sponsor and trial site level and accompanying Corrective and Preventive Action (CAPA) plan (see SCHN SOP Management of Serious Breaches of GCP and CAPA Process).
- Annual progress reports
- Any changes which may impact the Sponsorship risk assessment (i.e. loss of resources, (funding, skilled trial staff) which may impact the safety of participants or the quality/integrity of the trial data.

The above must be communicated to the Sponsorship Committee via email (SCHN-Governance@health.nsw.gov.au) before submission to the HREC and RGO.

3.8 Decision not to Sponsor a Trial

Should the CTSC determine that the institutional risks to the SCHN are not aligned with SCHN research strategy, the CTSC may not approve SCHN Sponsorship. The reason for rejecting an application will be provided to the CPI/PI in an email from the SCHN Director of Research.

3.9 Termination of Sponsorship

During the course of the study any trials that have had an increase in its risk rating since starting as per the Risk Management Table must be re-assessed by the CTSC. The CTSC may decide to withdraw Sponsorship, if necessary, and will notify the reviewing HREC of this decision. The trial will be suspended until further assessment can be made. The TGA must also be notified. The CPI/PI will be given clear notice, in writing, to cease all trial activities other than those deemed necessary essential for participant safety.

4 Definitions

Abbreviation or Term	Definition
Clinical Trial	A Clinical Trial is a form of research designed to find out the effects on an intervention, including a treatment or diagnostic procedure.
Coordinating Principal Investigator (CPI)	The person who takes overall responsibility for the design, conduct and reporting of a study. Where the research is conducted at a single site this is the PI.
CTN/CTA Trial	A Clinical Trial involving medicines, biologicals and/or medical devices conducted under the TGA Clinical Trial Notification or Clinical Trial Approval schemes.
CONSORT Statement	Consolidated Standards of Reporting Trials (CONSORT) - encompasses various initiatives developed by the CONSORT Group to alleviate the problems arising from inadequate reporting of randomized controlled trials.
Early Phase Clinical Trial (EPCT)	Early Phase Clinical Trial (EPCT) includes all clinical trial phases up to but not including Phase II, including studies with any Phase I component.
Good Clinical Practice (GCP)	A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial participants are protected. The term “GCP” within this document is with reference to two internationally accepted standards: (1) ICH GCP and (2) ISO 14155
Good Manufacturing Practice (GMP)	A system for ensuring that investigational products are consistently produced and controlled according to quality standards.
ICH GCP	The International Council for Harmonisation (ICH) of Technical Requirements for Pharmaceuticals for Human Use (ICH), Harmonised Guideline for Good Clinical Practice
Investigator’s Brochure	The Investigator's Brochure (IB) is a compilation of the clinical and non-clinical data on the investigational product(s) that are relevant to the study of the product(s) in human participants. Its purpose is to provide the investigators and others involved in the research project with the information to facilitate their understanding of the rationale for, and their compliance with,

	many key features of the protocol, such as the dose, dose frequency/interval, methods of administration and safety monitoring procedures.
Investigational Product (IP)	Any therapeutic good (including active comparators or placebos) being tested or used as a reference in a Clinical Trial.
ISO 14155	International Organisation for Standardisation - Clinical Investigation of Medical Devices for Human Subjects - Good Clinical Practice
Principal Investigator (PI)	Principal Investigator (PI) is the person responsible, individually or as a leader of the research team at a site, for the conduct of a clinical trial at that site. As such, the PI is responsible for adequately supervising his or her research team. Note: In a single centre investigator initiated study, the PI is also often the person who takes overall responsibility for the design, conduct and reporting of a study.
Protocol	A document that describes the rationale, objective(s), design and proposed analysis, methodology, monitoring, conduct and record-keeping of a clinical trial. The sponsor of a clinical trial is responsible for the protocol.
Risk Assessment	Risk assessment is the assessment, analysis and management of risks. It involves recognising which events may lead to harm in the future, and minimising their likelihood and consequence.
SCHN Clinical Trial Sponsorship Committee (CTSC)	The Committee established in Section 3.6 of this Policy
Site	A facility, location or institution (or group of institutions) that conducts a Clinical Trial/Study and comes under research authorisation sign off.
Sponsor	An individual, organisation or group taking on responsibility for securing the arrangements to initiate, manage and finance (or arranging the finance) for a study. The Sponsor carries the medico-legal responsibility associated with the conduct of a Clinical Trial. The sponsor takes overall responsibility for the conduct of a clinical trial, including responsibility for the protocol.
Therapeutic Goods Administration (TGA)	The Australian regulatory authority for therapeutic goods. The TGA is responsible for regulating the supply, import, export, manufacturing and advertising of therapeutic goods in Australia.

Treasury Managed Fund	"Treasury Managed Fund" or "TMF" refers to the NSW Treasury Managed Fund, which is the NSW Government's self-insurance and risk management scheme.
Coordinating Principal Investigator (CPI)	The person who takes overall responsibility for the design, conduct and reporting of a study. Where the research is conducted at a single site this is the PI.

5 Related Documents

5.1 SCHN References

1. SCHN Procedure (2023-064) Clinical Trials - Safety Reporting
2. SCHN Procedure (2019-024) Clinical Research - Statistical Design, analysis and reporting

5.2 External References

3. Australian Code for the Responsible Conduct of Research (2018)(the Code)
4. National Statement on Ethical Conduct in Human Research (2007) updated 2018 (National Statement)
5. ICH GCP – Good Clinical Practice Guidelines - Annotated by the TGA
6. ISO 14155 – International Organisation for Standardisation - Clinical Investigation of Medical Devices for Human Subjects - Good Clinical Practice
7. PIC/S Guide to Good Manufacturing Practice for Medicinal Products (Annex 13)
8. Australian Clinical Trial Handbook
9. NSW Health PD2010_056 - Research - Authorisation to Commence Human Research in NSW Public Health Organisations
10. NSW Health PD2011_006 Clinical Trials - Insurance and Indemnity
11. NSW Health PD2011_028 Clinical Trial Research Agreements for Use in NSW Public Health Organisations
12. NSW Health PD2023_007 Intellectual Property Arising from Health Research - NSW Department of Health
13. NSW Health PD2015_045 Conflicts of Interest and Gifts and Benefits
14. NSW Health PD2017_039 Safety Monitoring and Reporting for Clinical Trials Conducted in NSW Public Health Organisations
15. NSW Health PD2023_015 HREC and Research Governance: Fee Policy for Review of Commercially Sponsored Research