Research Agreements in NSW Health Organisations

Summary This Policy Directive aims to ensure compliance and clarity in clinical trials conducted at NSW Health sites; it is essential to have written agreements. Approved research agreements have been developed for specific types of trial arrangement, including clinical trial research agreements for pharmaceutical trials and clinical investigation research agreements for medical device trials.

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Distributed to Ministry of Health, Public Health System, Divisions of General Practice, NSW Ambulance Service, Private Hospitals and Day Procedure Centres

Audience Research Office Staff;Researchers;Heads of Departments Hosting and Supporting Research;Research Directors;All Chief Executives

Secretary, NSW Health

NSW Health

POLICY DIRECTIVE

Research Agreements in NSW Health Organisations

POLICY STATEMENT

NSW Health aims to provide a streamlined approach to research agreements between NSW Health organisations and those undertaking clinical trial and non-clinical trial research.

SUMMARY OF POLICY REQUIREMENTS

To ensure compliance and clarity in clinical trials conducted at NSW Health sites, it is essential to have written agreements. Approved research agreements have been developed for specific types of trial arrangement, including clinical trial research agreements for pharmaceutical trials and clinical investigation research agreements for medical device trials.

These agreements should be used as a standard form, without substantial alterations or contradictory provisions. However, sponsor-specific clauses can be included through a special conditions schedule, provided they do not undermine the main provisions of the agreement.

Research governance officers should promptly review submitted agreements, accepting those without changes or with approved sponsor-specific clauses.

If sponsors deviate from the approved agreements or make significant alterations, NSW Health organisations are advised to seek independent legal advice. This approach ensures consistency and compliance with policies while allowing for necessary flexibility in clinical trial set up.

REVISION HISTORY

Version	Approved By	Amendment Notes
PD2023_017 July-2023	Deputy Secretary, Clinical Innovation and Research Division	Updated Research Agreements for use in NSW Health Organisations. Revised the Joint Review of Sponsor Specific Clauses section. Added non-clinical trial research agreement.
PD2011_028 May-2011	Deputy Director-General Population Health	Issue of policy which replaces Clinical Trial Research Agreement for Public Health Organisations (Commercial Entities) (PD2009_033) and Clinical Trial Research Agreement Public Health Orgs (Collaborative or Cooperative Research Groups) (PD2009_032).
PD2009_033 June-2009	Deputy Director-General Population Health	Policy replacing Clinical Research: Standard Clinical Trial Research Agreement for NSW Public Health Organisations PD2008_039.

PD2009_032 June-2009	Deputy Director-General Population Health	New policy clinical trial research agreement that is required for use in clinical trials that are conducted in NSW public health organisations and sponsored by a collaborative or cooperative research group.
PD2008_039 June-2007	Director-General	
PD2008_038 June-2007	Director-General	

CONTENTS

1. BACKGROUND

Each clinical trial to be conducted at sites under the control of a NSW Health organisation and sponsored by an entity external to that NSW Health organisation must be governed by a written agreement clarifying the obligations, responsibilities and rights of the parties involved in the trial, in accordance with NSW Health Policy Directive *Research - Authorisation to Commence Human Research in NSW Public Health Organisations* (PD2010_056).

NSW Health, together with key stakeholders, have developed a number of standard Clinical Trial Research Agreements and Clinical Investigation Research Agreements (Research Agreements), which are designed to be used for certain clinical trial arrangements. The Research Agreements anticipate that the clinical trial is being conducted according to the principles of Good Clinical Practice (GCP) and, using an unapproved therapeutic good being supplied by a sponsor (external to NSW Health) to an Institution under the Therapeutic Goods Administration's Clinical Trial Notification or Clinical Trial Approval Schemes. As such, they do not cover all types of clinical trial arrangements.

While parties may make amendments to Research Agreements through the use of the special conditions schedule, so they may be more applicable to an individual trial arrangement, if those amendments alter the core architecture of the Research Agreement, then it is recommended that a bespoke agreement is used.

1.1. About this document

This Policy Directive sets out the approved Research Agreements for use in NSW Health organisations and outlines the processes to be employed for the use, review, and amendment of these agreements.

1.2. Key definitions

Clinical Trial Approval (CTA) Scheme	An approval process where the Australian clinical trial sponsor seeks approval from the Therapeutic Goods Administration to supply an unapproved therapeutic good in a clinical trial.
Clinical Trial Notification (CTN) Scheme	A notification process where the Australian clinical trial sponsor is required to notify the Therapeutic Goods Administration of the intent to sponsor a clinical trial involving an 'unapproved' therapeutic good.
Collaborative research group (CRG)	An academic and/or not-for-profit legal entity responsible for sponsoring, initiating, managing, developing, and coordinating a non-commercial trial.
Contract research organisation (CRO)	A company contracted by an international sponsor without a presence in Australia to act as the local sponsor for the trial in Australia.

Institution	For the purpose of this Policy Directive, institution refers to a NSW Health organisation that is a party to a Research Agreement.
NSW Health organisations	Public Health Organisations established under the *Health Services Act 1997* (NSW) and NSW Ambulance.
Principal investigator	The individual who takes responsibility for the overall conduct, management, monitoring and reporting of research conducted at a site and submits the project for site authorisation. While agreements provide a place for the principal investigator to sign the agreement, they are not a party to the research agreement.
Research Agreement	A legally binding agreement that governs the relationship between the sponsor and the Institution in conducting a clinical trial. The Medical Technology Association of Australia (representing the device sector) uses the term 'clinical investigations' instead of 'clinical trials,' and a clinical trial research agreement is known as a 'clinical investigations research agreement' for device studies. In this Policy Directive, for simplicity, both forms of agreement are referred to as 'Research Agreements', unless otherwise specified.
Research governance officer	The individual appointed within the NSW Health organisation who is responsible for the management and provision of a recommendation of applications for site authorisation and oversight of authorised research projects, including clinical trials.
Site	The facility, location, or service where the clinical trial is being conducted.
Site authorisation	Authorisation granted by the chief executive or delegate of the NSW Health organisation for the commencement of a research project including clinical trials.
Site-specific assessment (SSA)	A component of research governance undertaken by NSW Health organisations, to assess the suitability of the sites to be involved in the research project, including clinical trials.
Sponsor	The company, Institution or organisation, body or individual that takes overall responsibility for the conduct of the trial and usually initiates, organises, and supports the clinical trial.

Therapeutic Goods Administration (TGA)	The responsible body for regulating therapeutic goods including prescription medicines, vaccines, sunscreens, vitamins and minerals, medical devices, blood, and blood products.

1.3. Related NSW Health policies and guidelines

This Policy Directive should be read in conjunction with the following NSW Health policy directives and guidelines.

Policy Number	NSW Health Policy Directive and Guidelines
GL2011_001	*Research Governance in NSW Health Public Health Organisations*
PD2010_056	*Research - Authorisation to Commence Human Research in NSW Public Health Organisations*
PD2011_006	*Clinical Trials- Insurance and Indemnity*

2. APPROVED RESEARCH AGREEMENTS

The Research Agreements approved for use in NSW Health organisations are:

Clinical trial research agreements	Clinical investigation research agreements	Non-clinical trial research agreements
Medicines Australia Standard Form	Medical Technology Association of Australia Standard Form	Multi-Jurisdictional Multi-Party non-Clinical Trial Collaborative Research Agreement
Contract Research Organisation acting as the Local Sponsor	Contract Research Organisations acting as the Local Sponsor	
Collaborative (Or Cooperative) Research Group Studies	Post Market (Devices)	
Phase 4 Clinical Trial (Medicines)	Post Market (Devices) Contract Research Organisations acting as the Local Sponsor	
Phase 4 Clinical Trial (Medicines) Contract Research Organisations acting as the Local Sponsor		

There are two pathways for clinical trials as prescribed by the Therapeutic Goods Administration:

- The Clinical Trial Notification (CTN) Scheme
- The Clinical Trial Approval (CTA) Scheme.

These provide a means by which unapproved therapeutic goods can be lawfully supplied solely for the purpose of research in humans.

For clinical trials conducted under the Clinical Trial Notification or Clinical Trial Approval Schemes, the organisation that executes the Clinical Trial Research Agreement acting as the

local sponsor must also be identified as sponsor in the Therapeutic Goods Administration's Clinical Trial Notification or Clinical Trial Approval process.

2.1. Research Agreements

The Research Agreements are designed for use by different types of sponsors of clinical trials as well as for different clinical trial phases including:

- Pharmaceutical companies
- Contract research organisations
- Medical device companies
- Collaborative or cooperative research groups
- Pre-approval (phase I-III) clinical trials
- Post-approval (phase IV) clinical trials.

The organisation that executes the Research Agreement as sponsor must provide indemnity and evidence that it is covered by requisite insurance arrangements as set out in the relevant Research Agreement and which meet the requirements of the NSW Health Policy Directive *Clinical Trials - Insurance and Indemnity* (PD2011_006).

2.2. Clinical Trial Research Agreements

Clinical Trial Research Agreements have been developed for sponsored studies of pharmaceuticals.

2.2.1. Medicines Australia – Standard Form

The *Medicines Australia Standard Form* (standard form) for commercially sponsored trials is to be used when a pharmaceutical company is sponsoring a clinical trial that is to be conducted at sites under the control of NSW Health organisations.

The sponsoring pharmaceutical company must be an Australian entity. This could be an Australian pharmaceutical company or an Australian subsidiary of an international pharmaceutical company.

The standard form is also to be used for commercially sponsored trials when a pharmaceutical company subcontracts another party, for example a contract research organisation, to undertake certain clinical trial related activities or responsibilities but where the pharmaceutical company remains the sponsor of that trial.

2.2.2. Contract Research Organisation acting as the Local Sponsor

The *Contract Research Organisation acting as the Local Sponsor* agreement is to be used when a contract research organisation is sponsoring a clinical trial on behalf of an international sponsor that is to be conducted at sites under the control of NSW Health organisations.

The sponsoring contract research organisation must be an Australian entity. This could be an Australian contract research organisation or an Australian subsidiary of an international contract research organisation.

2.2.3. Collaborative or Cooperative Research Group (CRG) Studies – Standard Form

The *Collaborative or Cooperative Research Group (CRG) Studies – Standard Form* agreement is to be used when a non-commercial entity, including a collaborative or cooperative research group (research group), is sponsoring a clinical trial that is to be conducted at sites under the control of NSW Health organisations, and which satisfies the following criteria:

- The research addresses relevant clinical questions and not the pharmaceutical/ device company, or any other commercial needs
- The research group declares the nature of any sponsorship from any entity, including a pharmaceutical/ device company, that may benefit commercially from the research outcomes; and
- The research group is the primary author and custodian of the clinical trial protocol.

Depending on the nature of commercial entity sponsorship to the collaborative or cooperative research group, NSW Health organisations may determine that another form of agreement is more appropriate for the trial.

The sponsoring research group is to be an Australian entity. This could be an Australian research group or an Australian division of an international research group.

2.2.4. Phase 4 Clinical Trial (Medicines)

The *Phase 4 Clinical Trial (Medicines)* agreement must be used when a pharmaceutical company is sponsoring a clinical trial for a phase 4 study that is to be conducted at sites under the control of NSW Health organisations.

The sponsoring pharmaceutical company is to be an Australian entity. This could be an Australian pharmaceutical company or an Australian subsidiary of an international pharmaceutical company.

The intervention must fit within the criteria for a phase 4 clinical trial including:

- Being approved for the treatment of the disease targeted in the trial
- The drug has already been marketed
- The side effects of the drug are being studied.

2.2.5. Phase 4 Clinical Trial (Medicines) – Contract Research Organisation acting as Local Sponsor

The *Phase 4 Clinical Trial (Medicines) Contract Research Organisation acting as Local Sponsor* agreement must be used when a contract research organisation is sponsoring a clinical trial for a phase 4 study on behalf of an international pharmaceutical company that is to be conducted at sites under the control of NSW Health organisations.

The sponsoring contract research organisation must be an Australian entity. This could be an Australian contract research organisation or an Australian subsidiary of an international contract research organisation.

The intervention must fit within the criteria for a phase 4 clinical trial including:

- Being approved for the treatment of the disease targeted in the trial
- The drug has already been marketed
- The side effects of the drug are being studied.

2.3. Clinical Investigation Research Agreements

2.3.1. Medical Technology Association of Australia – Standard Form

The *Standard Clinical Investigation Research Agreement* (standard agreement) must be used when a medical device company is sponsoring a clinical trial that is to be conducted at sites under the control of NSW Health organisations.

The sponsoring medical device company must be an Australian entity. This could be an Australian medical device company or an Australian subsidiary of an international medical device company.

The standard agreement must also be used when a medical device company subcontracts another party for example, a contract research organisation, to undertake certain clinical trial related activities or responsibilities but remains the sponsor of that trial.

2.3.2. Contract Research Organisation acting as the Local Sponsor

The *Contract Research Organisation acting as the Local Sponsor* agreement is to be used when a contract research organisation is sponsoring a clinical trial on behalf of an international sponsor that is to be conducted at sites under the control of NSW Health organisations.

2.3.3. Post Market Clinical Trial (Medical Devices)

The *Post Market Clinical Trial (Medical Devices)* agreement is to be used for the post market medical device studies, which are 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, health economics.

2.3.4. Post Market Clinical Trial (Medical Devices) – Contract Research Organisation acting as Local Sponsor

The *Post Market Clinical Trial (Medical Devices) – Contract Research Organisation acting as Local Sponsor* agreement is to be used where a contract research organisation acts as, and assumes all the responsibilities of, a local commercial sponsor.

2.4. Multi-Jurisdictional Multi-Party non-Clinical Trial Collaborative Research Agreement

Multi-Jurisdictional Multi-Party Non-Clinical Trial Collaborative Research Agreement is to be used where two or more parties collaborating on a research project that is not a clinical trial.

3. SPECIAL CONDITIONS CLAUSES

The Research Agreements are designed to allow for the inclusion of sponsor specific clauses through a nominated schedule titled 'special conditions' at the back of the agreement.

The schedule is to be used for the introduction of sponsor specific operational requirements that are required to be executed to allow for the conduct of the clinical trial.

The schedule is not to be used to substantially amend the agreement, or to introduce provisions that contradict or otherwise undermine the substantive provisions or intent of the agreement, including those that:

- are clearly contrary to, or attempt to modify, the core provisions of the agreement
- seek to delete or substantially modify the essential clauses of the agreement. These include the provisions surrounding core publication rights, confidentiality, intellectual property, governing law and termination
- merely restate (or 'wordsmith') the existing provisions of the agreement
- seek to override the applicability of the agreement
- are contrary to government insurance arrangements or seek to require the NSW Health organisation to have certain types of insurance.

3.1. Joint reviews of special conditions clauses

NSW Health and representatives from other Australian jurisdictions' health agencies regularly conduct a joint review of sponsor specific clauses for inclusion in the nominated schedule of the research agreements. This panel is known as the Southern and Eastern Border States Review Panel (the review panel).

The review panel meets monthly to consider amendment requests from sponsors. Closing dates for submissions and the review panel meeting dates are published on the Medicines Australia website.

The purpose of the joint review is to ensure sponsors have single point of negotiation for their clauses to be considered rather than having to negotiate with each site individually.

3.1.1. New clauses and amendments to existing clauses

Although review by the review panel is not required to amend the special conditions, the service is recommended to assist clinical trial sponsors with timely, standardised review, where only one negotiation is required, rather than several.

This process only applies to the review of new clauses, and to amendments to existing pre-approved sponsor specific clauses, in participating states, for use in approved standard research agreements.

From time-to-time review and update of the research agreement templates are undertaken. Following changes to the research agreement template versions, sponsors do not have to submit previously approved clauses for re-approval.

If any minor issues (such as clause numbering) are affected through these changes, they can be accepted directly by individual Institutions. The process covers review of clauses for on-going use by the sponsor for clinical trials conducted in participating states, and for one-off multi-site studies that involve at least one of the participating states.

The review panel does not usually accept review of sponsor specific clauses for one-off single site studies. In these instances, clauses should be negotiated directly with the relevant NSW Health organisation.

3.1.2. Submission to the review panel

The sponsor is to prepare a submission for review using the standard pro forma template on the Medicines Australia website.

Where appropriate, the proposed clause must reference the relevant standard agreement clause that it will replace or amend. A justification must be provided for the inclusion of each of the proposed clauses. Where possible, the sponsor is to highlight the change to the original clause.

There is to be no application fee for submission to the review panel. The sponsor must submit the completed pro forma to the review panel contact listed on the Medicines Australia website.

The participating states will jointly review the submitted clauses. The timeline for review will be dependent on the number and complexity of the clauses submitted. If the panel assesses that the proposed amendments require external legal review, the sponsor is to be provided with an estimate of timeline and cost before the external legal review starts.

During the review, if necessary, the states' legal representative is to communicate directly with the sponsor's legal representative.

The participating states are to notify the sponsor of approved clauses with a version number and date, and which of the standard Research Agreements they are approved for.

Where amendments to pre-approved clauses are approved, the sponsor will be notified that the previously approved clauses are superseded and replaced by the new approved clauses, but that existing Research Agreements using the superseded clauses are valid until the end of the term of that agreement.

The approved clauses with their approval letter are to be submitted by the sponsor to the research governance officer as part of the site-specific assessment process.

NSW Health organisations are to refer submissions and queries relating to the review of 'special conditions' clauses to:

NSW Ministry of Health

Research Ethics and Governance Unit

Email: MOH-SEBS@health.nsw.gov.au

Phone: 02 9391 9920

4. REVIEW OF RESEARCH AGREEMENTS

In accordance with the NSW Health Policy Directive *Research - Authorisation to Commence Human Research in NSW Public Health Organisations* (PD2010_056), the principal investigator must submit the Research Agreement to the research governance officer responsible for the proposed trial site as part of an application for site specific assessment.

Research governance officers are to initiate reviews of research agreements at the earliest possible opportunity, following submission by the principal investigator.

NSW Health organisations must accept a Research Agreement without further review where an appropriate Research Agreement is submitted without any alteration.

Where the Research Agreement is submitted with only the addition of sponsor specific clauses that have been reviewed and approved by the Southern and Eastern Border States Review Panel (the review panel), NSW Health organisations must also accept this agreement without further review.

NSW Health organisations can reject any sponsor specific clauses reviewed and approved by the review panel for operational purposes. NSW Health organisations can also negotiate specific additional operational terms and conditions for a Research Agreement for a particular trial.

NSW Health organisations should obtain independent legal advice where the sponsor:

- uses an agreement other than one of the approved research agreements; or
- uses an approved Research Agreement but makes non-trivial/ significant alterations or additions to it other than the addition of sponsor specific clauses that have been reviewed and approved by the review panel.

NSW Health organisations should first inform the sponsor, where they choose to obtain independent legal advice.

Where the sponsor is a commercial entity, the legal advice will be at the expense of that commercial entity. A written undertaking is to be obtained from the sponsor to pay the legal costs incurred for the review of the submitted agreement.

Where the sponsor is a research group, NSW Health organisations should negotiate the payment of the costs for the legal advice with the sponsor, acknowledging that not all research groups will be in a position to meet these costs.