A Guide to the Ethics Approval and Research Governance Authorisation Processes for Clinical Trials* conducted in public health organisations in NSW

Last updated: October 2024

* Some of the information is also relevant to other types of health research involving human participants.

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Acronyms

AE	Adverse Event
ARTG	Australian Register of Therapeutic Goods
CIOMS	Council for International Organizations of Medical Sciences
CE	Chief Executive
CPI	Coordinating Principal Investigator
CTC	Clinical Trial Coordinator
CTA	Clinical Trial Approval (Scheme)
CTN	Clinical Trial Notification (Scheme)
CTRA	Clinical Trial Research Agreement
CV	Curriculum Vitae
GCP	Good Clinical Practice
HoD	Head of Department
HREA	Human Research Ethics Application
HREC	Human Research Ethics Committee
NCTGF	National Clinical Trials Governance Framework
NHMRC	National Health and Medical Research Council
NMA	National Mutual Acceptance (Scheme)
PHO	Public Health Organisation
PI	Principal Investigator
PICF	Patient Informed Consent Form
RA	Research Assistant
REGIS	Research Ethics & Governance Information System
RGO	Research Governance Office
SC	Study Coordinator
SSA	Site Specific Assessment (or STE in REGIS)
TGA	Therapeutic Goods Administration

Purpose

This guide is designed to provide new researchers and clinical trial staff an overview of the Ethics and Research Governance processes for clinical trials conducted in public health organisations in NSW. Some of the information is also relevant to other types of health research involving human participants. The guide has been developed with a focus on the health organisations that are members of Sydney Health Partners (Nepean Blue Mountains, Northern Sydney, Sydney, Western Sydney Local Health Districts, and the Sydney Children's Hospital Network) but may be relevant to other health organisations within NSW.

Links to key documents are provided within the guide, with other References and other background information at the end.

Requirements Prior to Trial Commencement

Clinical trials conducted in NSW need to complete the following processes before they can begin.



Ethics review and approval

Ethics approval is an integral part of the research process. Ethical review ensures the rights, safety and welfare of participants, and that participants are provided enough details to make informed, autonomous decisions about participating in a research study.

All research involving humans, including clinical trials, must have ethics approval from an NHMRC-accredited Human Research Ethics Committee (HREC). A list of accredited HRECs can be found here: https://www.nhmrc.gov.au/research-policy/ethics/human-research-ethics-committees.

For multi-centre clinical trials conducted in public health organisations (such as hospitals within NSW, ACT, QLD, SA, VIC and WA), in most cases one Human Research Ethics Application (HREA) is required under the National Mutual Acceptance (NMA) scheme. Certain research projects (e.g. those involving Aboriginal people) may need additional HREC approval. Refer to the Specialist HREC review section for details. More information on NMA scheme can be found here: https://www.medicalresearch.nsw.gov.au/national-mutual-acceptance/.

The following main principles have been described as fundamental to the conduct of ethical research. Click on the hyperlinks below to find out more:

- Social and clinical value
- Scientific validity
- Fair subject selection
- Favourable risk-benefit ratio
- Independent review
- Informed consent
- Respect for potential and enrolled subjects

Research Governance review and authorisation

Research governance authorisation is separate from ethics approval. While ethics approval focuses on the well-being of participants, governance authorisation is much broader and focuses on the responsibilities and risks to the institution leading or participating in a clinical trial. This includes the protection of research participants, the safety of study procedures and the quality of research, but also privacy and confidentiality, resource use and financial management, legal and regulatory matters, risk management, and monitoring arrangements.

In NSW, a Site Specific Assessment (SSA) application is required for all research conducted at that site including clinical trials. The application must be reviewed by a research governance officer and then authorised by the organisation's Chief Executive (CE) or their delegate before commencement. Separate research governance authorisation is generally required for each site involved in the research study or clinical trial.

Although research governance authorisation can only be finalised after ethics approval is received, some institutions encourage parallel submissions (i.e. submitting a research governance application whilst waiting to receive ethics approval) to help reduce time delays. See Completing the HREA and SSA concurrently in REGIS section for more details.

Differences between ethics and governance reviews

Research principles	**Ethics (anywhere)**	**Governance (site based)**
Beneficence	Does the benefit of the study outweigh the risk?	Is the organisation protected against any risks? Are the investigators insured? Is it our risk to protect? Should there be a contract detailing who bears the risk?
Respect	How will the privacy of participants be respected?	Has the data custodian provided support for access to medical records for research purposes?
Research Merit and Integrity	Will the study be able to answer the questions posed?	Is there money available to complete the study at this site? Are there resources available to complete the study at this site?

Research principles	Ethics (anywhere)	Governance (site based)
		Does the study have Human Research Ethics Committee (HREC) approval?
Justice	Is the process of recruiting participants fair?	Is the recruitment process in line with institutional policies? Does it facilitate equitable access for different participant groups?

Adapted from https://kr.schn.health.nsw.gov.au/research-support/ethics-and-governance

In practice, this means research will receive an ethical review to ensure the rights, safety and welfare of participants, and a governance review to ensure institutional acceptability.

A project will always receive both types of review, irrespective of whether the proposed research is single or multi-site.

Regulatory submission requirements for clinical trials

The Therapeutic Goods Administration (TGA) is Australia's regulatory authority for therapeutic goods. The TGA is responsible for regulating the use of therapeutic goods supplied in Clinical Trials in Australia under the Therapeutic Goods Legislation.

The legislation stipulates that a product may not be manufactured, imported, exported or supplied in Australia unless it is either entered onto the Australian Register of Therapeutic Goods (ARTG), or is "exempt" from the requirement for such entry. The Clinical Trial Notification (CTN) and Clinical Trial Approval (CTA) Schemes are two avenues that allow unapproved therapeutic goods to be supplied to members of the Australian public. Clinical trials that do not include unapproved therapeutic goods or are not using approved therapeutic goods outside of their approved indications, do not require regulatory submissions.

The Trial Sponsor is the entity that is responsible for submitting a CTN/CTA. Please refer to the TGA Clinical Trials Handbook for further information on the CTN and CTA schemes and how they may apply to your research.

BOTH ETHICS APPROVAL AND RESEARCH GOVERNANCE AUTHORISATION ARE REQUIRED PRIOR TO THE COMMENCEMENT OF A RESEARCH PROJECT OR CLINICAL TRIAL.

IF THE CLINICAL TRIAL INVOLVES AN UNAPPROVED THERAPEUTIC GOOD, OR IS USING AN APPROVED THERAPEUTIC GOOD OUTSIDE OF ITS APPROVED INDICATION, CTN/CTA SUBMISSION (BY THE SPONSOR) IS ALSO REQUIRED.

Applying for Ethics Review and Approval in NSW

All clinical research, including clinical trials, conducted in public health organisations in NSW requires submission of Ethics (and site governance) applications through the online Research Ethics and Governance Information System (REGIS) portal: https://regis.health.nsw.gov.au/. It is also used by TAS and ACT public health organisations.

Points to note:

- You will need to create an account to use REGIS
- The administrative contact (SC or RA) can create and prepare the application, but it is the responsibility of the Coordinating Principal Investigator (CPI) to submit the application (new or amendment)
- Researchers can track the progress of their applications through REGIS

Quick Reference Guides, videos and FAQ are available on the REGIS website:

https://regis.health.nsw.gov.au/how-to/

https://www.youtube.com/channel/UCYYI8wUSjJacGMF7pPAsIlA

https://regis.health.nsw.gov.au/help-desk-faqs/support/

What type of ethics application do I need?

Most health services have a Research Office and/or dedicated staff to help with ethics applications and inquiries. Reaching out early for advice is strongly encouraged.

Staff can also provide guidance on the most appropriate type of application, based on the risk profile of the research project as categorised in Figure 1.

Lower risk		**Higher risk** (Individual, group, community, societal or global)	
Minimal	**Low**	**Greater than low**	**High**
No risk of harm or discomfort; potential for minor burden or inconvenience*	No risk of harm; risk of discomfort (+/- foreseeable burden)	Risk of harm (+/- foreseeable burden)	Risk of significant harm (+/- foreseeable burden)

Figure 1. Risk profiles of research NHMRC National Statement on Ethical Conduct in Human Research 2023

For more information on risks refer to Chapter 2.1 of the National Statement.

What does a Human Research Ethics Committee (HREC) do?

HRECs protect the safety and welfare of human research participants.

They are responsible for providing an independent evaluation of proposed research studies, ensuring that the research does not proceed unless standards and regulations are met.

Some areas of review are:

- Research design and feasibility
- Recruitment and Consent
- Safety reporting
- Complaints
- Adverse Events
- Project suspensions

The HREC pays special attention to reviewing recruitment and consent processes, and to protecting the welfare of certain participants deemed to be vulnerable (e.g. children). For further information, see https://clinregs.niaid.nih.gov/country/australia#scope_of_review

Specialist HREC review

Certain research projects must undergo specialised HREC review before they can take place in a NSW Health organisation. This is in addition to review by a local or lead HREC, with the exception of early phase clinical trials which only require one review.

Justice Health HREC – for all research projects involving persons in custody in NSW and/or staff of NSW Justice Health. www.nsw.gov.au/health/justicehealth

Aboriginal Health & Medical Research Council (AH&MRC) HREC - for research projects that are explicitly aimed at Aboriginal people or communities in NSW, in total or as a part of a larger project. https://www.ahmrc.org.au/ethics-at-ahmrc/

NSW Population & Health Service Research Ethics Committee (PHSREC) – for all research projects requiring access (including linkage) to statewide data collections owned or managed by NSW Health or the Cancer Institute NSW. www.cancer.nsw.gov.au/research-and-data/nsw-population-health-services-research-ethics-com

Early Phase Clinical Trials - all Early Phase Clinical Trials (EPCT) should be submitted to one of two NSW Health EPCT HRECs for review and approval: Bellberry Ltd for adults, or Sydney Children's Hospital Network (SCHN) for children and young people. www.medicalresearch.nsw.gov.au/hrec-scheme/

Clinical Trials with Persons Unable to Provide Consent - under the Guardianship Act 1987 (NSW), a person who does not have capacity to consent may not participate in a clinical trial unless the trial has been approved by the Guardianship Tribunal. https://ncat.nsw.gov.au/case-types/guardianship/clinical-trials.html

What does Research Governance Review and Authorise?

The research governance review will consider the following:

- Ethics approval received by an accredited HREC
- Ethics approved study documents
- Investigators and study team have the appropriate training, experience and certification
- Site has facilities and resources to conduct the study assessments
- Study has adequate funding, budgets and financial management
- Clinical Trial Research Agreement (CTRA) or other Research Agreements
- Insurance and indemnity arrangements
- Regulatory submission (CTN/CTA) if applicable
- Trial sponsorship applications (for collaborative or investigator-initiated trials) if applicable

All research projects must undergo governance review before authorisation can be granted by the Chief Executive (or delegate) of the organisation.

Always check individual organisation's research governance guidelines and checklists. Organisations across SHP have developed and approved a common research governance checklist to help researchers prepare their applications.

In NSW, both ethics and governance applications are submitted through the online REGIS system. The site principal investigator (PI) can share the online SSA (STE) application with other team members (e.g. administrative contact, clinical trial coordinator, research assistant, etc.), and in REGIS can assign Edit or View rights.

Completing the HREA and SSA concurrently in REGIS

For institutions that allow parallel Ethics and Governance submissions, this can be completed in REGIS. REGIS creates and populates the SSA (STE) once the HREA (ETH) has been submitted. Once the SSA is complete it can be submitted by the PI, however the SSA cannot be authorised by the Chief Executive (or delegate) until the Ethics Committee has approved the HREA.

For instructions on how to complete the SSA in REGIS, please see the Quick Reference Guide: Completing a Site Specific Assessment.

Policies, Guidelines and Regulatory Frameworks

In Australia, clinical trials are regulated at a number of levels under Commonwealth, state and territory legislation and policy.

National level

- The National Statement on Ethical Conduct in Human Research (2023) describes the responsibilities of institutions and researchers for the ethical design, conduct and dissemination of results of human research, and of review bodies in the ethical review of research. https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2023

- The Australian Code for the Responsible Conduct of Research (2018) provides the foundations for high-quality research, and aims to ensure credibility and community trust in the research endeavour. It includes principles of integrity, accountability, independence/impartiality, respect and professional commitment. https://www.nhmrc.gov.au/about-us/publications/australian-code-responsible-conduct-research-2018

- The guide, Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods, outlines the responsibilities for monitoring and reporting adverse events and other safety issues. https://www.nhmrc.gov.au/about-us/publications/safety-monitoring-and-reporting-clinical-trials-involving-therapeutic-goods

- Therapeutic goods are regulated in Australia under the Therapeutic Goods Act 1989, the Therapeutic Goods Regulations 1990, and the Therapeutic Goods (Medical Devices) Regulations 2002. The TGA is responsible for administering the legislation. https://www.tga.gov.au/about-australian-therapeutic-goods-legislation
- The Australian Clinical Trial Handbook provides guidance on the legislative, regulatory and good clinical practice (GCP) requirements for the use of 'unapproved' therapeutic goods in clinical trials in Australia. https://www.tga.gov.au/resources/resource/guidance/australian-clinical-trial-handbook

- ❖ Good Clinical Practice (GCP) is the internationally accepted standard for designing, conducting, recording and reporting of clinical trials. All staff engaged in clinical trials require GCP certification. It is also required for accreditation under the National Clinical Trial Governance Framework (NCTGF). https://www.tga.gov.au/resources/publication/publications/ich-guideline-good-clinical-practice

- ❖ The National Standard Operating Procedures for Clinical Trials have been developed to assist organisations engaged in conducting clinical trials including teletrials to standardise their procedures for key operations. https://www.health.gov.au/resources/publications/national-standard-operating-procedures-for-clinical-trials?language=en

- ❖ All health service organisations conducting clinical trials in Australia are progressively being assessed against the National Clinical Trials Governance Framework (NCTGF). This ensures that clinical trials are delivered with high quality integration into clinical care, and have good clinical governance. Consumer involvement in clinical trials is also a key focus. https://www.safetyandquality.gov.au/standards/national-clinical-trials-governance-framework

State level (NSW) guides for ethics review

NSW Health has issued the following policies and guidelines:

- Human Research Ethics Committees - Standards for Scientific Review of Clinical Trials (PD2007_035)
- Research - Ethical & Scientific Review of Human Research in NSW Public Health Organisations (PD2010_055)
- Human Research Ethics Committees: Standard Operating Procedures for NSW Public Health Organisations (GL2013_009)
- Operations Manual: Human Research Ethics Committee Executive Officers (GL2010_014)
- Human Research Ethics Committees - Quality Improvement & Ethical Review: A Practice Guide for NSW (GL2007_20)
- HREC and Research Governance: Fee Policy for Review of Commercially Sponsored Research (PD2023_026)

State level (NSW) guides for research governance review

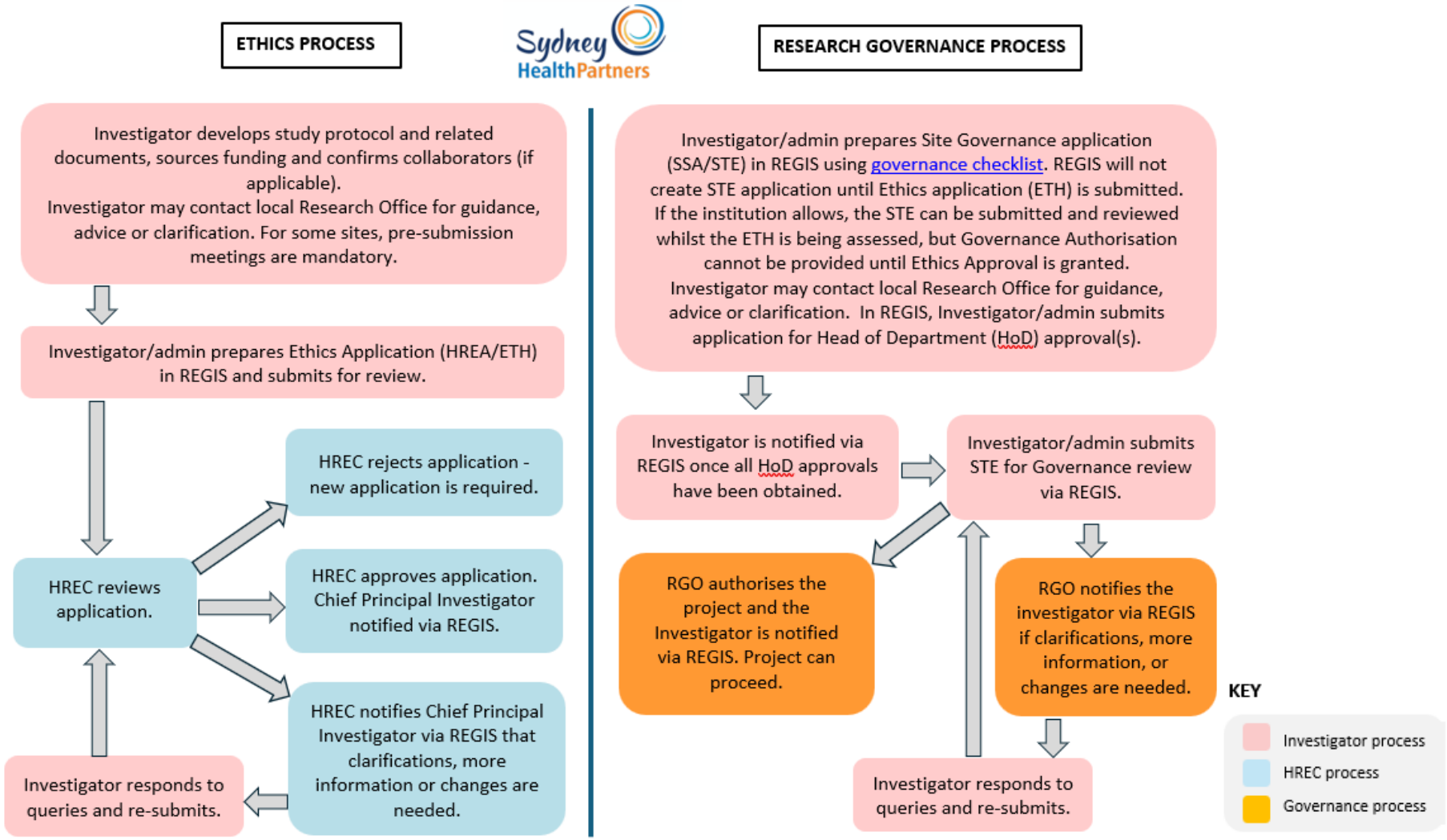
NSW Health has issued the following policies and guidelines:

- Clinical Trial Research Agreements for Use in NSW Public Health Organisations (PD2023_017)
- Clinical Trials - Insurance and Indemnity (PD2011_006)
- Research - Authorisation to Commence Human Research in NSW Public Health Organisations (PD2010_056)
- HREC and Research Governance: Fee Policy for Review of Commercially Sponsored Research (PD2023_015)

- Research Governance in NSW Public Health Organisations (GL2011_001)
- Operations Manual: Research Governance Officers (GL2010_015)

Please check for the most up-to-date policies and guidelines here:
https://www.medicalresearch.nsw.gov.au/policies-guidelines/

Overview of the Ethics and Research Governance Process in NSW Health Organisations



A detailed flow of Ethics and Governance through REGIS can be found here: https://regis.health.nsw.gov.au/media/1794/regis-inital-application-and-post-approval-flow-1.ppsx

Tips for Ethics and Research Governance Applications

Common ethics application mistakes leading to delays

- Not being familiar with the National Statement (especially Chapter 3.1)
- Poor study design - not appropriately designed to answer the research question, and study procedures are not adequately developed to meet ethical and regulatory requirements
- Not enough information and justification of burden, risks and benefits
- Lack of detail on study procedures or how participants will be recruited
- Not enough information on data collection and how data will be extracted
- Insufficient details on the identifiability of data (when and how it is de-identified and who has access to the identifiable data)
- Retention periods for data not specified or not as per local or international requirements
- Application is incomplete and missing mandatory documents (e.g. recruitment, data collection tool, PICF, CV)
- Logos added on master HREC documents
- Information in the HREA, protocol and PICF do not match
- HREC preferred Patient Information Consent Form (PICF) or other templates not used
- PICF or recruitment material contains typographical or grammatical errors
- Documents incorrectly named or have incorrect version number or date in footer
- Clean and tracked documents not included in re-submission
- PICF not suitable to the participant group (too technical or not clear)
- Insufficient details on risks/burdens to participants included in the PICF
- No plan for how incidental findings will be reported or shared with participants

Tips for success - ethics applications

- Check the HREC submission closing date
- Consult the Research Ethics Office to confirm the level of risk for your research project and the appropriate application form
- Read and follow the submission guidelines provided on the HREC website. Some projects may require peer or statistical review, or interstate Ethics forms (multi-site trials) so plan accordingly
- Utilise the current resources and templates available on the HREC website
- If your project involves biobanks, registries, opt out consent or a program of research, book a meeting with the Ethics Officer for further guidance
- Complete the Project Registration in REGIS – these details will be pre-populated into the Human Research Ethics Application (HREA)
- Check all study documents are accurate and consistent (proof-read)
- Ensure all the mandatory supporting documents are submitted (e.g. submission checklist, consents and fee payment)
- Check investigators listed in protocol are the same as in HREA
- Contact Ethics Officer for questions regarding the response letter (Note - it is rare for applications to be approved on the first round)

- Response to HREC queries – include cover letter, amended documents (version controlled)
- Ethics will send the approval to CPI and admin contacts via REGIS (ensure correct contact details are in REGIS)

Tips for success – research governance applications

- Read and follow the submission guidelines provided on the Research Governance Office (RGO) website
- Follow the steps in REGIS for how to create a site (STE) application
- Ensure PI and admin contacts are correctly listed in REGIS
- Organise a pre-submission meeting with the Governance Officer or attend a drop-in session (if required)
- Before completing the application:
    - Check if additional requirements apply for unapproved therapeutic good/device or Genetically Modified Organisms (GMOs)
    - Discuss contracts with the Governance Officer (before submitting your site application to minimise delays)
    - Arrange a Radiation Safety Assessment if the research project involves the use of X-rays, Dexa or CT scans
    - If your project involves access to, and use of health data, discuss your data requirements with the relevant data custodian
    - Discuss your research project with all relevant supporting Head of Department/s (HoDs) before you submit you application in REGIS (highly recommended) so they are aware and can approve quickly
    - Check that HoD contact details are current in REGIS
    - If required, arrange Contingent Worker Approval for any staff involved in the project who are not employed by the organisation (including students)
    - Make sure the site-specific PICFs etc have the local institution logo, correct local contact details, and the file name in the footer is version controlled
- Respond to queries as per the REGIS instructions, including any amended documents (version controlled). Contact them to discuss if needed.
- Final approval letter will be sent to PI and admin contacts via REGIS (ensure correct contact details are in REGIS)
- It is mandatory for all approved clinical trials conducted at NSW Health sites to be operated and managed in the Clinical Trial Management System (CTMS). Further information, including training and resources, are available at: https://www.medicalresearch.nsw.gov.au/clinical-trial-management-system/.

SHP Health Service Organisation Research Office Contacts

Nepean Blue Mountains LHD
Email Ethics: nbmlhd-hrec@health.nsw.gov.au
Email Governance: NBMLHD-RGO@health.nsw.gov.au
Website: https://www.nsw.gov.au/departments-and-agencies/nbmlhd/research-innovation/ethics

Northern Sydney LHD
Email: NSLHD-Research@health.nsw.gov.au
Website: https://www.nslhd.health.nsw.gov.au/Research/ResearchOffice/

Sydney Children's Hospital Network
Email Ethics: SCHN-ethics@health.nsw.gov.au
Email Governance: SCHN-Governance@health.nsw.gov.au
Website: https://kr.schn.health.nsw.gov.au/research-support/ethics-and-governance

Sydney LHD (Concord)
Email: SLHD-ConcordEthics@health.nsw.gov.au
Website: https://www.slhd.nsw.gov.au/concord/ethics/default.html

Sydney LHD (RPA)
Email: SLHD-RPAEthics@health.nsw.gov.au
Website: https://www.slhd.nsw.gov.au/rpa/research/

Western Sydney LHD
Email: wslhd-researchoffice@health.nsw.gov.au
Website: https://www.wslhd.health.nsw.gov.au/Education-Portal/Research/Research-Information/wslhd-research-office

Other NSW Health organisation contacts can be found here:
https://www.medicalresearch.nsw.gov.au/ethics-governance-contacts/

SHP further information and contacts

For more information on Sydney Health Partners Research Directory
https://sydneyhealthpartners.org.au/resources/research-directory/

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Research Director
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References and other background information

NSW Health Research Handbook
https://www.medicalresearch.nsw.gov.au/ethics-governance-overview/

NSW Health and Medical Research – Ethics and Governance Resources
https://www.medicalresearch.nsw.gov.au/ethics-governance/

What are the most common reasons for return of ethics submissions? An audit of an Australian health service ethics committee.
https://journals.sagepub.com/doi/10.1177/1747016121999935

The Belmont Report
https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html

2016 International ethical guidelines for health-related research involving humans
https://cioms.ch/publications/product/international-ethical-guidelines-for-health-related-research- involving-humans/

The Nuremburg Code (1947)
https://media.tghn.org/medialibrary/2011/04/BMJ_No_7070_Volume_313_The_Nuremberg_Code.pdf