NSW HEALTH

# NSW HEALTH EARLY PHASE CLINICAL TRIALS HRECS SCHEME

## EXPRESSION OF INTEREST GUIDELINES

JULY 2018

CLOSING DATE:
28 SEPTEMBER 2018

NSW GOVERNMENT

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# 1 Introduction and purpose of this document

The NSW Ministry of Health, through the Office for Health and Medical Research is implementing two practical schemes to provide a high quality and efficient environment to conduct early phase trials, with the ultimate aim of improving health outcomes for NSW residents.

a) NSW Health early phase clinical trials HRECs Scheme and
b) Quality Recognition Scheme for early phase clinical trial sites in NSW.

These schemes will make NSW a centre of excellence in clinical trials.

This document provides information to HRECs responding to the call for expressions of interest to be NSW Health early phase clinical trials HRECs in NSW. It details the NSW Health early phase clinical trials HRECs Scheme, the application and selection processes, and monitoring requirements.

The two schemes are informed by a framework to support early phase clinical trials across NSW[1]. The framework received broad support from the sector and endorsement by local health district and specialty network Chief Executives, the Chief Health Officer and Deputy Secretary Population and Public Health.

| **Goal for the NSW Health early phase clinical trials HRECs Scheme** |
| --- |
| **Ensure timely and high quality processes for the approval to commence early phase trials** |

This scheme will be operational for the first time in 2019. Expressions of Interest will run every three years. It will be reviewed and adjusted as it becomes operational. Therefore, the details in this EOI are subject to change over time and will be adapted to operational issues that may arise.

[1] http://www.health.nsw.gov.au/ohmr/Pages/early-phase-clinical-trials.aspx

## 2 Rationale for the HREC Scheme

As part of developing the Early Phase Clinical Trials Framework for NSW,[2] extensive stakeholder consultation was undertaken. Consultation revealed that HREC committees often encounter difficulties reviewing early phase trials, particularly if trials were complex and required a depth of scientific expertise not common to most HRECs.

Through consultation it became clear that the status quo does not adequately support HRECs to review early phase trials in a timely fashion. Some broader issues identified were:

- State or national policy does not provide specific guidance on the conduct of risk assessment for early phase trials by HRECs;
- The changing definition and context of Phase 1 and early phase trials in terms of emerging trial designs and novel therapies;
- The concern from all stakeholders about adverse events in Phase 1 trials, in the light of recent international events in the UK and France; and
- State and national policies require HRECs to have the full suite of appropriate scientific skills to review early phase trials, however, access to scientific specialisations to review early phase trials are not readily available in a timely manner.

## 3 Overview of the scheme

To address these issues, NSW Health, through this Expression of Interest (EOI) process, will appoint up to five early phase clinical trials HRECs. They will be drawn from all private and public HRECs in Australia that are certified by NHMRC to review early phase clinical trials in NSW. The number of appointed HRECs will depend on both the workload and the availability of appropriate expertise. The Ministry of Health will mandate the use of these NSW Health early phase clinical trials HRECs for the review of early phase trials in NSW Public Health Organisations (PHOs) in the forthcoming review of PD2010_055 (due in 2018) . The Ministry encourages non-PHOs within NSW to use these HRECs where appropriate.

**This scheme has been designed to integrate with current schemes that streamline the approval process for clinical trials across Australia. The Therapeutic Goods Administration's Clinical Trial Notification (TGA's CTN) scheme and the National Mutual Acceptance (NMA) scheme will continue to operate as they currently do and will be complemented by this scheme.**

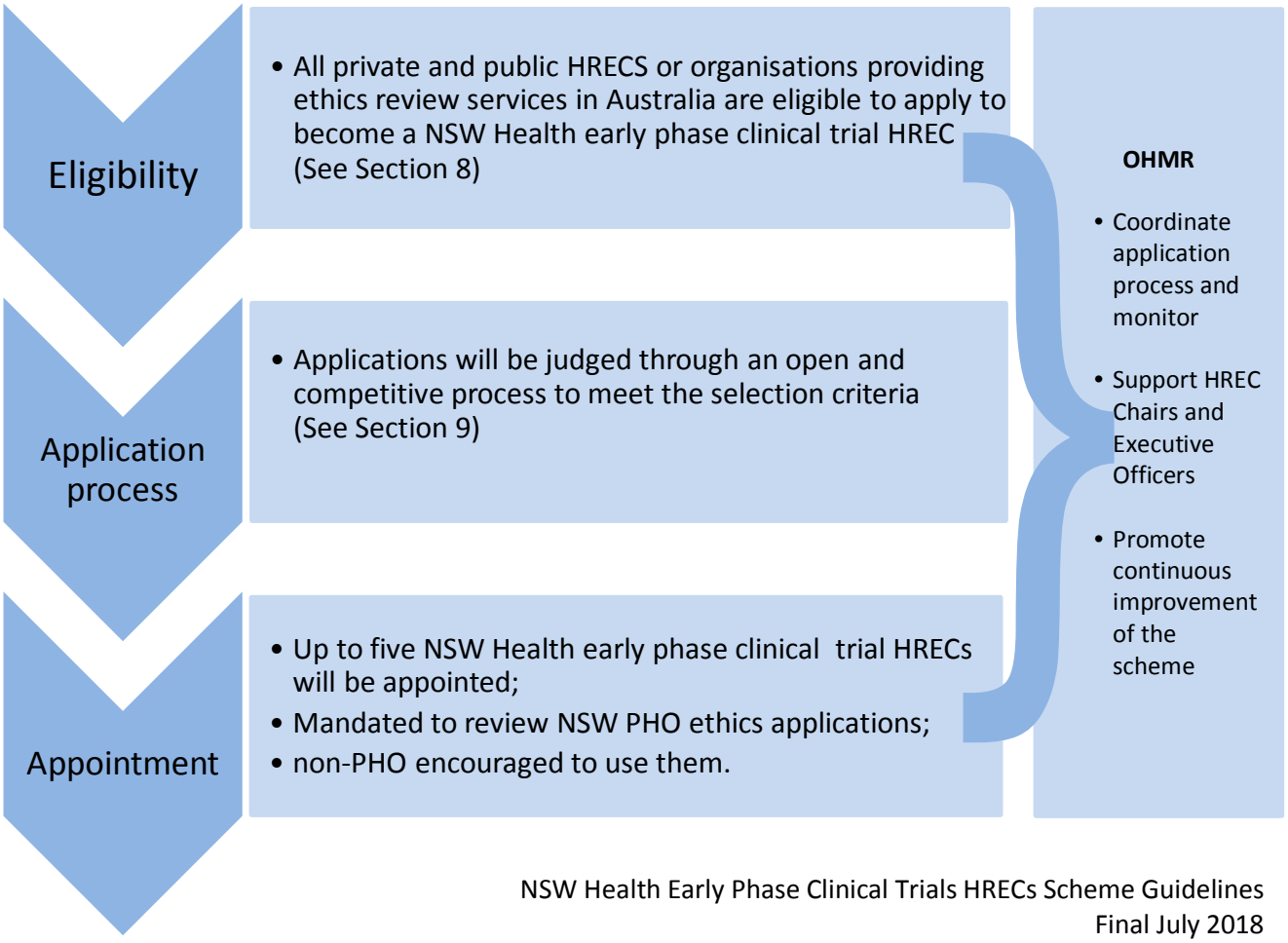
[2] http://www.health.nsw.gov.au/ohmr/Pages/early-phase-clinical-trials.aspx

This scheme allows for the continued acceptance of ethical approval from interstate HRECs under the NMA scheme. The NMA scheme allows multi-site early phase trials to commence in NSW having been reviewed by an NHMRC certified HREC from a participating jurisdiction. This means that a specialist early phase review would not be required for multicentre studies, where the lead site is outside of NSW. The interstate-HREC must be certified under the NHMRC National Certification Scheme and also be a Certified Reviewing HREC under the NMA scheme.

There may be instances where a NSW Health early phase clinical trials HREC is not recognised under the NMA scheme: for example, an appointed private ethics review provider. In this instance, the private ethics reviewer will only be able to accept applications for NSW-only early phase sites and their review will not be recognised by other states.

Any NSW Health early phase clinical trials HREC will continue with its usual business and also consider the ethics approval of early phase clinical trials in NSW. See Figure 1 for an overview of the scheme and Appendix 1 for a practical flowchart detailing the approval process from an applicant's perspective.

**Figure 1: Overview of the NSW Health early phase clinical trials HRECs scheme**



# 4 NSW Health List of Early Phase Clinical Trial Expert Technical Reviewers

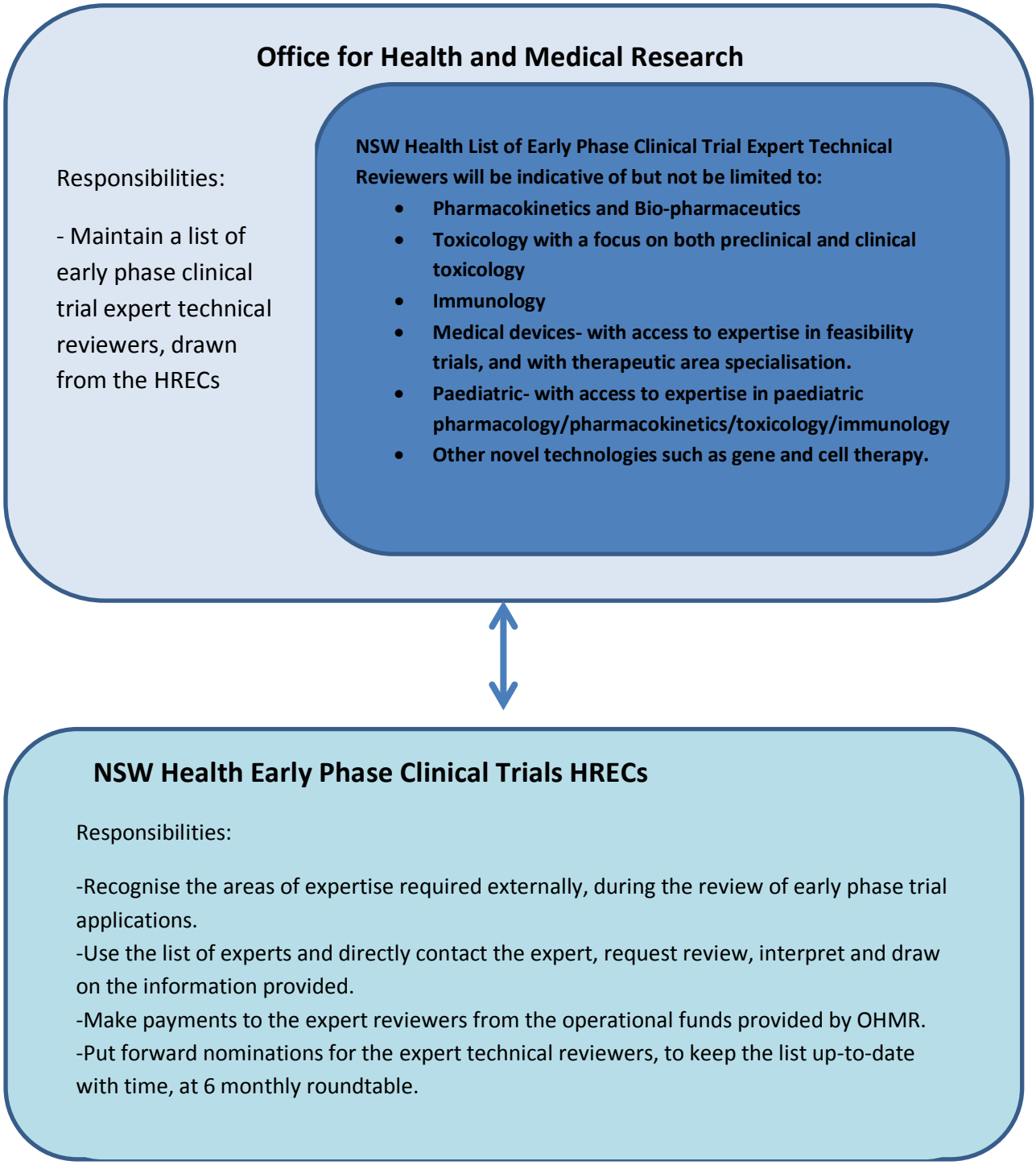
Office for Health and Medical Research will publish a list of early phase clinical trial experts who can assist with technical review of ethics applications. The list of experts will be created based on advice from the HREC Chairs. The areas of expertise will be indicative of but not be limited to:

- Pharmacokinetics and Bio-pharmaceutics
- Toxicology with a focus on both preclinical and clinical toxicology
- Early phase Clinical Trialist (design specialists)
- Immunologist
- Medical devices- with access to expertise in feasibility trials, and with therapeutic area specialisation.
- Paediatric- with access to expertise in paediatric pharmacology/pharmacokinetics/toxicology/immunology.
- Other novel technologies such as gene and cell therapy.

The list will be living and updated as required. NSW Health early phase clinical trials HRECs will assess early phase trials applications and identify the areas of expert review required externally.

Refer to Figure 2 below for further details.

## Figure 2: NSW Health List of Early Phase Clinical Trial Expert Technical Reviewers



# 5 Scope and Definitions of Early Phase Clinical Trials

In keeping with international trends, including the UK Medicines and Healthcare Products Regulatory Agency (MHRA)[3] and European Medicines Agency (EMA)[4], **the Framework encompasses a broad definition that includes all variants of early phase trials up to, and including Phase I/II but not including, Phase II**. This will ensure that definitions are in keeping with international norms and the changing context of early phase trials. (Appendix 2 – List of detailed definition)

The schemes will cover all early phase trials involving products which are defined as therapeutic goods[5] in the *Therapeutic Goods Act* 1989 (Cth) including:

- Medicines
- Medical devices
- Biological
- Other therapeutic good.

Emerging technologies, such as cell therapies are also included.

# 6 Governance of the scheme and Roles and Responsibilities

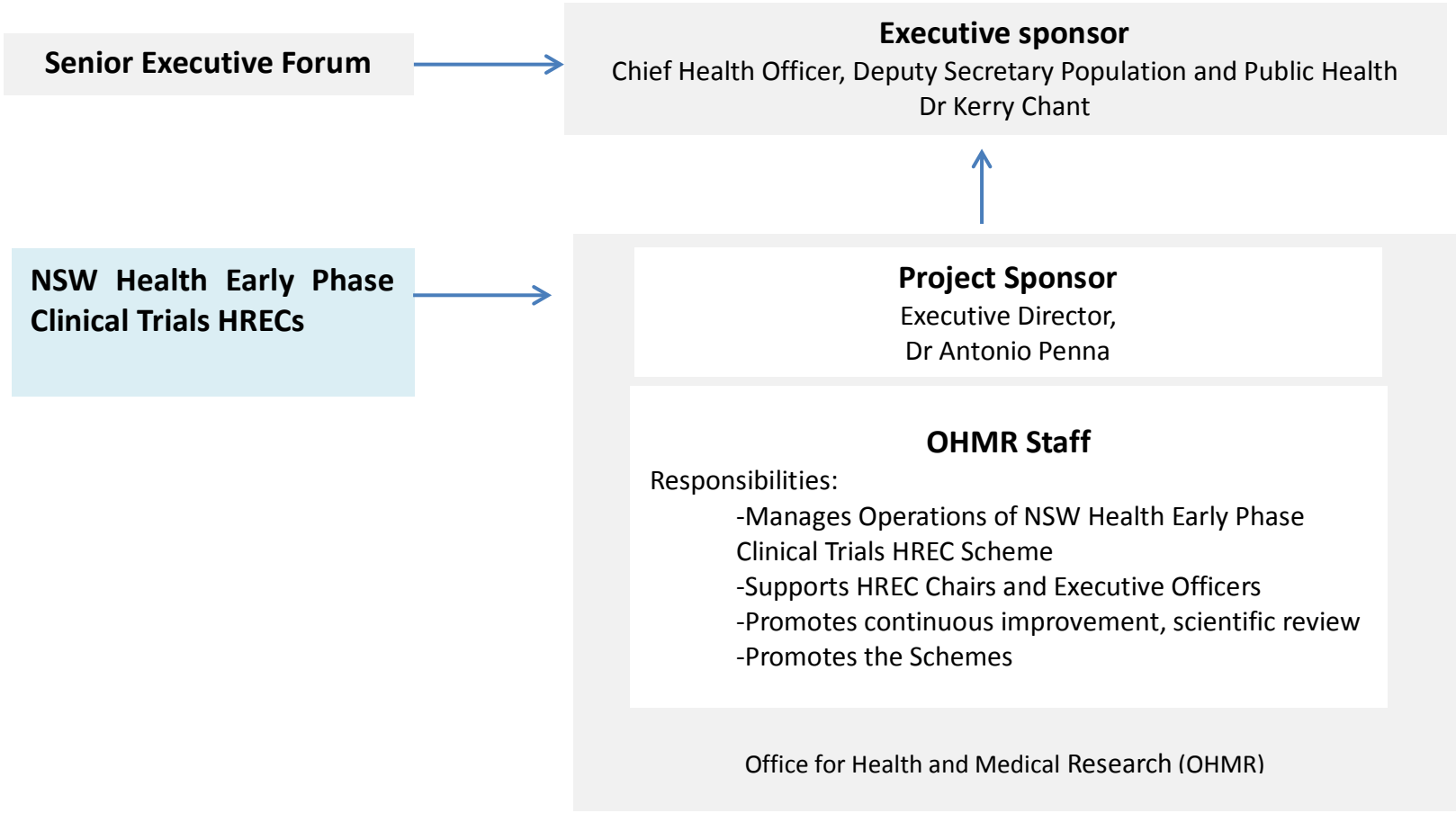
Figure 3 below provides the overview of the governance structure of the Scheme

[3] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/473579/Phase_I_Accreditation_Scheme.pdf Accessed 9 August 2016.

[4] http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/07/WC500210825.pdf Accessed 9 August 2016.

[5] https://www.tga.gov.au/sites/default/files/australian-clinical-trial-handbook-01.pdf

## 6.1 Figure 3: Governance Structure – Operational Phase 2019



## 6.2 Roles and responsibilities of OHMR

OHMR will be responsible for the overall management of the NSW Health early phase clinical trials HRECs scheme. Responsibilities include:

- Develop the appointment criteria for the early phase trials clinical trials HRECs with a HREC technical working group.
- Develop and manage the EOI process for appointing NSW Health early phase clinical trials HRECs.
- Enter into contracts with the appointed NSW Health early phase clinical trials HRECs that addresses issues such as insurance.
- Develop a risk assessment tool for the NSW Health early phase clinical trials HRECs, including clinical aspects, non-clinical aspects and quality aspects, and support for when to refer to the CTX scheme.
- Provide secretariat support to a 6 monthly meeting of the NSW Health early phase clinical trials HREC Chairs and Executive Officers.
- Monitor the performance of NSW Health early phase clinical trials HRECs to ensure compliance with the criteria including timeliness and use of operational funds provided by OHMR.
- Where appropriate, support quality assurance recommendations made by Chairs and Executive Officers (e.g. support training, development of proformas, etc.).
- Promote the usage of the NSW Health early phase clinical trials HRECs and negotiate their use with organisations other than NSW PHOs.
- Maintain a list of early phase clinical trial expert technical reviewers.

## 6.3 Roles and responsibilities of early phase clinical trials HREC Chairs and Executive Officers

As a support and quality assurance measure, the Chair (or representative Chair of an organisation with multiple committees) and Executive Officer of the appointed early phase clinical trials HRECs will meet together six-monthly to **discuss**:

- Harmonising the early phase clinical trial definitions and changes in the nature of trials and how they can be addressed in reviews,
- Consistency of review, monitoring process time, decision making (including auditing of committees' decision-making) and review of success metrics,
- Issues with reviewing early phase trials,
- Changes in processes or procedures for conducting ethics review of early phase clinical trial research projects (including standard operating procedures/templates etc.),
- Composition of the of expert technical reviewers list to ensure it is up to date and/or makes nominations where appropriate,
- Process and the timeliness of access to the list of early phase clinical trial expert technical reviewers,
- Feedback from on advice provided by the expert technical reviewers,
- Key performance indicators of the scheme, including timeliness and use of operational funds provided by OHMR and make recommendations as needed and
- Any other matters of common concern.

OHMR will provide the secretariat for these meetings.

## 6.4 Role and responsibilities of the NSW Health early phase clinical trials HRECs

- Continue to fulfil their standard role in reviewing research proposals involving human participants to ensure that they are ethically acceptable and in accordance with relevant standards and guidelines.
- Provide safe and high quality scientific and ethics review of all applications within 30 working days benchmark (with the aim to work towards achieving 20 working days benchmark) as defined by days 'on the clock'[6] from submission closing date to initial review decision and all amendments within 10 working days.
- Invite ethical and scientific input during the review process from a delegate of the Chief Executive(s) of all organisations hosting trial sites to be received by the date of the HREC meeting.
- Request review, interpret and draw on the information provided by the early phase clinical trial expert technical reviewers with appropriate expertise, for decision making.
- Work in harmonisation with other NSW Health early phase clinical trials HRECs to conduct the ethics review of the early phase clinical trial applications.
- Provide data to OHMR on performance as required.
- Enter into a contract with OHMR.
- Membership requirements in accordance with the National Statement and NHMRC certification.

## 6.5 Roles and responsibilities of NSW PHOs

- Accept the ethics review of any NSW Health early phase clinical trials HREC that is appointed by NSW Health under this scheme.
- To accept the review of any interstate NHMRC Certified HREC if the early phase trial is under the NMA scheme.
- The Chief Executives of NSW Local Health Districts and Speciality Networks will be given the opportunity to provide a local expert to review the trials that will take place in their facilities, if an application is submitted to a NSW Health early phase clinical trials HREC. This is to ensure that local matters that impact on ethics are taken into account within ethics committee deliberation. Therefore the Local Health Districts and Speciality Networks should

[6] Initial application clock start date: The submission closing date for the HREC meeting at which the ethics application is first considered. Where a sub-committee meets to consider applications before they proceed to a full HREC meeting, the closing date for submissions for the sub-committee meeting should be entered as the start date.
Final application clock stop date: Date of the final HREC decision letter that is provided to the investigator.

respond in a timely fashion to the specialist early phase clinical trials HREC by providing a review, by the date of the HREC meeting. Late submissions cannot be considered by the HREC.

### 6.6 Roles and responsibilities of institutions or other entities hosting the NSW Health early phase clinical trials HRECs

- Approve the application for the HREC to be appointed by NSW Health to review early phase trials under this scheme.
- Ensure the roles and responsibilities for the HREC are aligned to meet the early phase clinical trial scheme requirements as detailed in the contract.

## 7 Support for and Benefits of the Scheme for the NSW Health Early Phase HRECs

### 7.1 OHMR Support

NSW Health early phase clinical trials HRECs will receive additional support from OHMR if the committee is within a University or public health organisations within NSW. Applicants will need to present a business case supported by the host institution. The business case outlined in the application should indicate the in-kind and funding support provided by the host institution. Through this, there is an expectation that the host institution will demonstrate its support for early phase clinical trial ethical assessment.

Funds up to $50,000 as a one off payment in the first year will be available to support change management. Change management will include but not be limited to:

- appropriate change management activities to transition to the new operational arrangements to meet the timeline benchmarks,
- clear and transparent communication to stakeholders,
- appropriate changes to administrative processes and adherence to other relevant administrative protocols.

Funds up to $50,000 per annum will be available to support the HRECs plans to review early phase clinical trials:

- pay for additional scientific review as required by HRECs. HRECs are to draw on the networks of experts, such as the list of expert technical reviewers and HREC members with the appropriate expertise (for all public entities)

- support plans to achieve the rapid turnaround time of reviews (for public entities in NSW)

OHMR will provide additional support for capability development across the NSW Health Early Phase Clinical Trials HRECs, including:

- initial support to develop capacity to review early phase trials (for public entities in NSW), including orientation tool, education and training
- ongoing support for continuous professional development including education and training.

The Chairs of the NSW Health Early Phase Clinical Trials HRECs will advise OHMR on what capability development activities are required overtime.

## 7.2 Benefits for NSW Health early phase clinical trials HRECs will be:

- Committees will receive funds to support capacity development, additional scientific review and continuous professional development.
- Committees will be part of a continuous improvement processes to be responsive to national/international guidance.
- Committees will achieve continuous improvement and development of consistency of practice through 6 monthly meeting of the appointed HREC Chairs and Executive Officers.
- NSW Health early phase clinical trials HRECs appointed in NSW would be well positioned to apply for recognition within the NMA.

# 8 Eligibility criteria for HRECs to apply

1. All private and public HRECs or organisations providing ethics review services within Australia are eligible to apply to be appointed by NSW Health as HREC to assess early phase trials conducted within NSW.
2. HRECs applying must be certified under the NHMRC National Certification Scheme (for ethics review of Phase 1 clinical trial research).
3. Public Health Organisation HRECs within National Mutual Acceptance (NMA) participating jurisdictions must be a Certified Reviewing HREC under the NMA scheme.
4. All private and public HRECs, host institutions of a HREC or an organisation providing ethics review services is required to be/is responsible for ensuring that it is covered by adequate insurance[7] for the purposes of conducting a review of early phase clinical trials. This insurance must also cover HREC members, including those who are not employed by the host institution.

[7] Adequate insurance is defined as follows:

- Public liability insurance in the amount of not less than $20m in respect of each and every occurrence and in the aggregate for any one period of cover;
- Professional Indemnity insurance in the amount of not less than $10m in respect of any one occurrence and in the aggregate for any one period of cover including run-of cover for a period of 6 years; and
- Directors and Officers insurance in the amount of not less than $10m in respect of each and every occurrence.

# 9 Selection criteria for NSW Health Early Phase Clinical Trials HREC

## 9.1 Selection criteria:

1. The HREC must demonstrate that it can satisfy the minimum membership requirements of the *National Statement* and NHMRC certification.
2. The HREC must demonstrate that it has the following standing members:
   - At least one Clinical Pharmacologist or regular access to clinical pharmacologist who is not a standing member and
   - Two other members with expertise in early phase clinical trials.
3. The HREC must be willing to use the NSW Health list of early phase clinical trial expert technical reviewers to access experts for review of early phase clinical trial research projects. In addition they must demonstrate that they will have access to persons with expertise in the areas of:
   - clinical care and treatment appropriate to the research being reviewed at a given meeting, if not otherwise covered by those members who are appointed under the relevant category (under the *National Statement* requirements). For example in the following clinical areas as appropriate for a given application: oncology, haematology, cardiology, orthopaedics, neurology respiratory medicine and paediatrics
4. The HREC must demonstrate that it has a track record of reviewing early phase clinical trials.
5. The HREC must demonstrate that it can conduct the scientific review of pre-clinical data for ethics review of early phase clinical trial research projects.
6. The HREC must demonstrate that it can assess whether appropriate oversight processes are in place for dose escalation including the role and responsibilities of the investigator(s), sponsor and safety committees.
7. The HREC must agree to use the NSW Health risk assessment tool that will include guidance on when to refer to the CTX scheme. (Still in development)
8. The HREC must demonstrate that it has a plan in place to adhere to designated 30-working days benchmark and aim to work towards achieving 20-working days benchmark (including clock starts and stops) for review and approval times of early phase clinical trial research projects. It must also adhere to approval for all amendments within 10 working days.
9. The HREC must have appropriate processes in place for the monitoring of approved clinical trial research projects.[8]
10. The HREC must demonstrate a depth of understanding about NSW governance, policy and legislative requirements in relation to the approval and conduct of early phase clinical trial research projects.

[8] https://www.nhmrc.gov.au/guidelines-publications/eh59

11. Host institution must be supportive of the business case for the HREC, to conduct ethics review of early phase clinical trials and must be willing to enter into a contract with Office for Health and Medical Research. In doing so, it agrees to provide additional support to the HREC administration.

## 9.2 Further Sub-specialisation Areas

In addition to that listed above, HRECs may wish to apply for sub-specialisation in specific therapeutic areas. For example:

1. Medical devices- with access to expertise in feasibility trials, and with therapeutic area specialisation.
2. Oncology
3. Haematology
4. Cardiology
5. Orthopaedics
6. Neurology
7. Immunology
8. Paediatric- with access to expertise in paediatric pharmacology.
9. Respiratory Medicine
10. Other novel technologies such as gene and cell therapy.

Such applications will need to provide proven track record in sub-speciality areas.

## 10 Application and Selection Process

The NSW Health early phase clinical trials HRECs will be selected through a three-step application and appointment process:

1. HRECs complete and submit an application form and this will involve a self-assessment against the eligibility and selection criteria noted in sections 8 and 9, along with any associated documents to OHMR. The application needs to be approved by the Head of Organisation of the entity hosting the HREC.
2. A selection panel will assess the applications and may invite HREC Chairs and their institution's CE, or a delegate, for an interview. Selection panel will then provide advice to OHMR.
3. Chief Health Officer appoints the early phase clinical trials HRECs.

| Stage of Application | Activity | Indicative Dates * |
|---|---|---|
| Calls for HREC Expression of Interests | Advertise | 19 Jul 2018 |
| Registration for Information Session | Online registration open to register attendance | 24 July 2018 |
| Information Session | 1 hour Information session via Teleconference | 10 August 2018 |
| HREC EOIs closes | Expression of Interest will close | 28 September 2018 |
| HREC EOI assessment | Selection Panel meeting to assesses the applications | 04 October 2018 |
| HREC Interview Process | OHMR may invite HREC chairs and their institution's CE, or delegate for an interview | 10 October 2018 |
| Appointment of Specialist Early Phase HRECs | Reporting requirements, funding agreement and payment processes. | 26 October 2018 |

***These dates are indicative and subject to change. Please refer to the website for latest updates[1].**

## 11 Duration of NSW Health Early Phase Clinical Trials HRECs

Committees will be appointed for three years, and then they will need to reapply. Applications for EOIs will open every three years to coincide with the end of the three year appointment.

## 12 Ongoing Monitoring and Management

The specialist early phases clinical trials HRECs will be required to provide annual reporting to OHMR against the appointment criteria for the scheme, including review times. OHMR will reserve the right to withdraw the appointment of an early phase clinical trials HREC if it ceases to comply with the selection criteria.

OHMR may also conduct a user satisfaction survey of sponsors and investigators who have submitted their applications to an appointed early phase clinical trials HREC.

NSW Health early phase clinical trials HRECs will also be required to notify OHMR when there are changes to the committee membership or processes to conduct ethics or scientific review of early phase clinical trials.

## 13 Contract

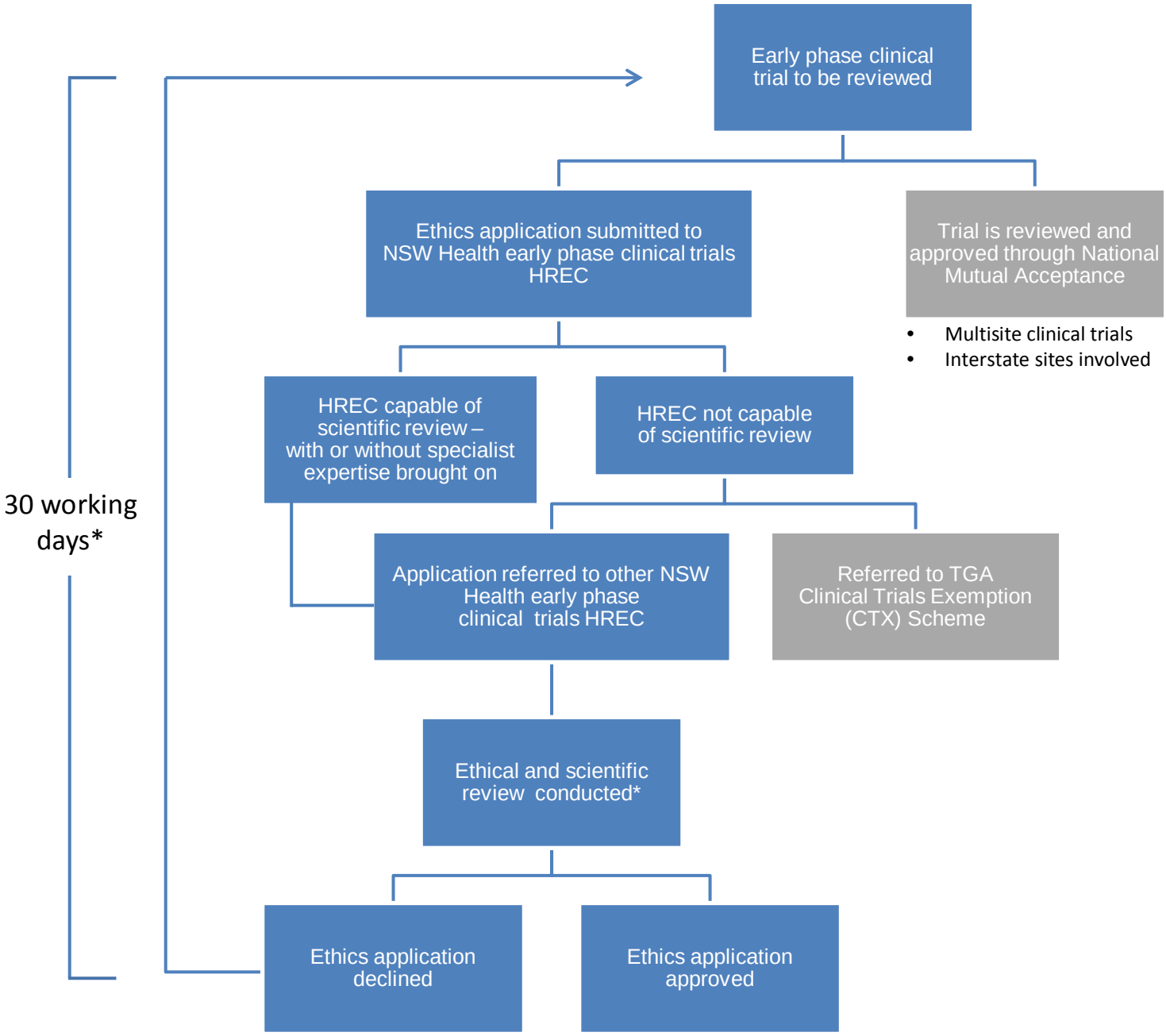
The host institution will sign a Contract with Office of Health and Medical Research, NSW Ministry of Health.

The latest draft of the "Agreement for Funding of Services" is available on our website:
http://www.health.nsw.gov.au/ohmr/Pages/early-phase-clinical-trials.aspx

**Further information regarding the Scheme may be directed to:**

Ashika Kumar, Senior Project Officer
Office for Health and Medical Research
NSW Ministry of Health
Tel. (02) 9461 7034
Email: earlyphasetrials@moh.health.nsw.gov.au

## Appendix 1: Ethics approval process for early phase clinical trials




* See 'Role and responsibilities of the NSW Health early phase clinical trials HRECs' Section 6.3 of the Early Phase Clinical Trials Framework for NSW[1].

*This will include Question and Answer (Q&A) between the NSW Health early phase clinical trials HRECs and the study team.

## Appendix 2: Definitions of Early Phase Trials

**Introduction:** These definitions are adapted from the definitions contained in the early phase clinical trials Framework for NSW. These definitions will provide the basis of determining whether an application needs to be reviewed by an NSW Health appointed specialist early phase clinical trials HRECs.

Definitions will be living and will be reviewed and adjusted as the scheme becomes operational. The arbitrator for the scope of definitions is Office for Health and Medical Research, NSW Ministry of Health.

## In Scope

### Investigational medicines, blood and blood products

| | |
|---|---|
| Phase 0 | An exploratory investigational new drug study also known as a "microdosing" study. Exploratory trials of this type establish whether the agent behaves in humans as expected based on preclinical animal studies, gather preliminary data on pharmacodynamics or pharmacokinetics, select promising lead candidates, and/or explore bio-distribution characteristics. Phase 0 studies do not replace formal Phase I drug trials and do not offer any possibility of patient benefit. They are intended to accelerate drug development as part of the US Food and Drug Administration (FDA) Critical Path Initiative by quickly weeding out ineffective drugs early in the development process. (No therapeutic or diagnostic intent.)[9] |
| Phase 1 | Phase I studies involve the first administration of the medicine to humans. 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 may be 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 dose.[10] |
| Early Phase | All types of Phase I trials (including phase 1b and any other variant) using either healthy volunteers, volunteer patients and/or patients, including First in human and First time in patient(see below). |
| First in human | Investigational medical product (IMP) administered to a human for the first time. |
| First time in patient | This is a subset of FIH, 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. |
| First time in paediatric | The first time a medicine is used formally in a trial in a paediatric population, noting that the medicine 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 the GP/consultant to participate in a clinical trial. Patients may receive a therapeutic benefit from the trial.[11] |
| 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. Combing phases I and II may allow research questions to be answered more quickly or with fewer patients. [12] |

[9] US Food and Drug Administration

[10] https://www.tga.gov.au/sites/default/files/australian-clinical-trial-handbook-01.pdf

[11] UK Medicines and Healthcare Products Regulatory Agency, 2015

[12] https://www.cancer.gov/publications/dictionaries/cancer-terms/def/phase-i-ii-clinical-trial

### Investigational Medical devices

| | |
|---|---|
| Early feasibility 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 may be used to evaluate the device design concept with respect to initial clinical safety and device functionality in a small number of subjects (generally fewer than 10 initial subjects) when this information cannot practically be provided through additional nonclinical assessments or appropriate nonclinical tests are unavailable. 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. |
| 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 subjects. |
| 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 | A clinical investigation designed to collect definitive evidence of the safety and effectiveness of a device for a specified intended use, typically in a statistically justified number of subjects. It may or may not be preceded by an early and/or a traditional feasibility study.[13] |

## Out of Scope

The following instances are out of scope.

- Individual patient use (Compassionate use of medicine). 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.
- 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:

- the 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).

[13] US Food and Drug Administration. 2013. Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies Guidance for Industry and Food and Drug Administration Staff.

For example a medicine which is registered in Australia (or by an internationally recognised regulatory authority e.g. 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.

If the dose requested is higher than that in the registered indication then this trial would fall within the processes of the Framework. As the Framework is implemented further examples of studies that would be out of scope will be made available.

Phase II Clinical Trial:

- are done to study an intervention in a larger group of people (several hundreds) to determine efficacy and to further evaluate its safety. [14]
- These are therapeutic exploratory trials[15].
- Phase IIa demonstrate clinical efficacy or biological activity through pilot studies and/or explore therapeutic dose range.
- Phase IIb determine optimum therapeutic dose and regimen (with efficacy as primary endpoint). These trials resolve uncertainties regarding the design and conduct of subsequent trials.

[14] https://www.australianclinicaltrials.gov.au/what-clinical-trial/phases-clinical-trials

[15] https://www.tga.gov.au/book-page/clinical-trial-phases-and-stages

## Appendix 3: Abbreviations

| | |
|---|---|
| CTN | Clinical Trial Notification |
| CTX | Clinical Trials Exemption |
| EMA | European Medicines Agency |
| EOI | Expression of interest |
| FDA | US Food and Drug Administration |
| FIH | First-in-human |
| FTIP | First time in patient |
| GCP | Good Clinical Practice (refers to the current version of GCP) |
| GMP | Good Manufacturing Practice |
| HREC | Human Research Ethics Committees |
| ICH | International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use |
| IMP | Investigational medical product |
| LHD | Local Health District |
| MHRA | UK Medicines and Healthcare Products Regulatory Agency |
| MRI | Medical Research Institute |
| NHMRC | National Health and Medical Research Council |
| NMA | National Mutual Acceptance |
| OHMR | Office for Health and Medical Research |
| PHO | Public Health Organisation |
| SOP | Standard operating procedure |
| TGA | Therapeutic Goods Administration |