APPENDIX 1

SYDNEY LOCAL HEALTH DISTRICT

CLINICAL TRIALS SUB-COMMITTEE

OF THE ETHICS REVIEW COMMITTEE (RPAH ZONE)

TERMS OF REFERENCE

1. Purpose

1.1 To advise such human research ethics committees within the SLHD and other organisations as approved by the SLHD Chief Executive (designated HRECs) on scientific aspects of clinical trials and innovative therapy.

2. Responsibilities

2.1 To review the scientific and safety aspects of clinical trial protocols in accordance with the *National Statement on Ethical Conduct in Human Research (2023)* and the following:

- the World Medical Association *Declaration of Helsinki*
- the CPMP/ICH *Note for Guidance on Good Clinical Practice* (CPMP.ICH-135/95), as adopted in Australia by the Therapeutic Goods Administration
- the ISO 14155:2020 *Clinical Investigation of Medical Devices for Human Subjects – Good Clinical Practice*
- the *Australian Device Requirement Version 4, DR4, May 1998*
- any requirements of relevant Commonwealth and NSW laws.

2.2 To advise designated HRECs on the following:

- scientific value, methodological validity and safety of clinical trials proposed to be undertaken within their organisation
- appropriateness of qualifications and expertise of investigators proposing to undertake clinical trials
- modifications to clinical trial protocols which would improve their safety and scientific value

- modifications to participant information sheets which would improve their accuracy and overall value as information documents

- appropriate mechanisms for and intervals of monitoring of approved clinical trials

- scientific appropriateness and safety of proposed amendments to clinical trial protocols

- significance of adverse event reports and other technical information pertaining to approved clinical trials

- scientific aspects of matters dealt with by designated HRECs, such as Access to Unapproved Therapeutic Goods – Authorised Prescribers, Access to Unapproved Therapeutic Goods via the Special Access Scheme and innovative therapy

- such other issues as are referred to it by the designated HRECs.

2.3 To undertake such monitoring of approved clinical trials as requested by the designated HRECs.

2.4 To promote scientific clinical research and education about research in the SLHD.

3. Status of the Sub-committee within the Organisation

3.1 The Clinical Trials Sub-committee is a Sub-committee of the SLHD Ethics Review Committee (RPAH Zone), reporting monthly to that Committee.

3.2 The Sub-committee shall have delegated authority to conduct assessments on behalf of the designated HRECs.

4. Composition of the Sub-committee

4.1 The composition of the Sub-committee shall reflect the mix of research activities across the SLHD, and shall include the following:

- chairperson

- deputy chairperson

- clinical pharmacologist

- pharmacist with appropriate experience

- a statistician experienced in the design of clinical trials

- persons with research experience and/or expertise relevant to the areas of research reviewed by the Sub-committee

- Executive Officer (non-voting member).

5. Appointment of Members and Terms of Appointment

5.1 The Chairperson and Deputy Chairperson shall be appointed by the SLHD Chief Executive following consultation with the Sub-committee and with other senior institutional officers, as deemed appropriate.

5.2 Members of the Sub-committee shall be appointed by the SLHD Chief Executive on the recommendation of the Chairperson.

5.3 The terms of appointment for the Chairperson and Deputy Chairperson shall normally be five years.

5.4 The term of appointment for Sub-committee members shall normally be three years.

5.5 Appointments may be renewed. Recommendations for renewal of appointment shall be made to the SLHD Chief Executive by the Chairperson.

5.6 Upon appointment, each member shall be required to sign a statement undertaking:

- that all matters of which he/she becomes aware during the course of his/her work on the Sub-committee will be kept confidential

- that any conflicts of interest which exist or may arise during his/her tenure on the Sub-committee will be declared.

6. Meetings

6.1 Meetings of the Sub-committee shall normally be held at approximately monthly intervals from January to November, or more frequently as necessary. Meetings shall be held in person or via video teleconference.

6.2 Meeting dates shall be determined in consultation with the designated HRECs.

6.3 Meeting dates and agenda closing dates shall be published appropriately.

6.4 It may be appropriate for members to provide written comments in lieu of attendance. A quorum shall exist for each research study under consideration when the views on it are available from at least four members.

7. Procedures

7.1 Clinical trial proposals shall be submitted to the Sub-committee on the approved application form, with supporting documents as specified in the *ICH Harmonised Tripartite Guideline - Guideline for Good Clinical Practice E6(R1) (Current Step 4 version, 9 November 2016)* (3.1.2), plus any other information required by the Sub-committee to enable it to fulfil its responsibilities.

7.2 The Sub-committee shall publish and regularly update the list of documents required for its consideration of clinical trial proposals.

7.3 In order to be considered at a scheduled meeting, clinical trial proposals and other correspondence shall be received at the RPAH Research Ethics and Governance Office at least seven (7) calendar days before the advertised meeting date.

7.4 The Sub-committee may seek advice from external sources. All expert reviewers are required to complete a Confidentiality Agreement and Conflicts of Interest Declaration Form prior to receiving any study documentation.

7.5 The Sub-committee has the power to delegate the following functions to the Chairman and/or other Sub-committee members, as appropriate:

- review of minor matters arising from the minutes of the previous meeting(s)
- review of quarterly reports on approved protocols which have not yet commenced
- review of adverse event reports
- any other administrative and/or minor matters requiring attention before the next scheduled Sub-committee meeting.

7.6 Clinical trial proposals and major amendments to approved clinical trials shall normally be considered at a scheduled Sub-committee meeting.

7.7 Minor amendments to approved clinical trials may be considered at a scheduled meeting of the Executive of the Ethics Review Committee (RPAH Zone).

7.8 A Sub-committee member involved in a clinical trial proposal under consideration shall absent him/herself from the meeting during the discussion and until a decision has been reached (see point 5.6 above).

7.9 The Sub-committee shall reach decisions by consensus after all members have been given the opportunity to express their views. In the event that a consensus cannot be reached, a decision may be taken by voting (show of hands). A two-thirds majority shall normally be required for a decision to be made. Dissenting views shall be recorded in the minutes.

7.10 Opinions on proposed studies shall be conveyed to the designated HRECs with written comments and justification. Proposed studies shall be assessed as either:

- approval recommended
- approval recommended, subject to the investigators providing satisfactory replies to questions raised by the Sub-committee
- deferred
- rejected.

7.11 Where approval has been recommended subject to provision by the investigator of satisfactory replies to the Sub-committee's concerns, such replies will be considered by the designated HRECs, but may be referred back to the Sub-committee for further advice.

7.12 Correspondence from investigators concerning proposed studies which have been deferred or rejected will be considered by the Sub-committee which may subsequently recommend approval or approval subject to further amendments/modifications.

7.13 The Sub-committee shall review quarterly reports of approved studies, sponsored by the SLHD under the Clinical Trial Notification (CTN) Scheme.

8. Responsibilities of the Executive Officer

8.1 The Executive Officer shall be responsible for the preparation of the meeting agendas, which will be circulated in electronic format no less than four (4) calendar days (including one weekend) before the meeting.

8.2 The Executive Officer shall be responsible for the preparation of the minutes of meetings (which shall clearly identify the trial and the documents reviewed), and of correspondence arising from the minutes. The Executive Officer has delegated authority from the Sub-committee to sign its correspondence.

8.3 In the case of a deferred or rejected proposal, the Executive Officer shall endeavour to notify the chief investigator of the Sub-committee's decision within five (5) working days, and no more than ten (10) working days, after each meeting.

8.4 The Executive Officer shall be responsible for the keeping of Sub-committee records, including the trial database, the protocol files and all other Sub-committee files.

8.5 The Sub-committee shall store minutes of its meetings, copies of all documentation which it considers, and correspondence for a period of at least fifteen (15) years after the completion of each clinical trial.

8.6 The Executive Officer shall undertake such other tasks as are requested by the Chairman and/or the Sub-committee.

9. Reporting to the designated HRECs

9.1 A written report (in the form of minutes) containing advice on each protocol referred to the Sub-committee by a designated HREC shall be provided on a monthly basis.

9.2 The Chairman (or nominee) of the Sub-committee shall attend each HREC meeting to provide a verbal report and any clarification required on the Sub-committee's deliberations.