2 February 2016

Dr Koert de Waal
Neonatal Intensive Care
John Hunter Children's Hospital

Dear Dr de Waal,

Re: The Ultimate PDA trial: Early pharmacological treatment with supportive care versus supportive care alone in preterm Infants with patent ductus arterious (15/12/16/3.03)

HNEHREC Reference No: 15/12/16/3.03
NSW HREC Reference No: HREC/15/HNE/498

Thank you for submitting the above protocol for single ethical review for a multi-centre study. This project was first considered by the Hunter New England Human Research Ethics Committee at its meeting held on **16 December 2015.** This Human Research Ethics Committee is constituted and operates in accordance with the National Health and Medical Research Council's *National Statement on Ethical Conduct in Human Research (2007)* (National Statement) and the *CPMP/ICH Note for Guidance on Good Clinical Practice*. Further, this Committee has been accredited by the NSW Department of Health as a lead HREC under the model for single ethical and scientific review. The Committee's Terms of Reference are available from the Hunter New England Local Health District website.

As part of the procedure for ethical approval of research involving humans in Hunter New England Health the above protocol has reviewed by the Clinical Trials Subcommittee, an advisory group of the Hunter New England Human Research Ethics Committee.

I am pleased to advise, the Hunter New England Human Research Ethics Committee has determined that the above protocol meets the requirements of the *National Statement on Ethical Conduct in Human Research* and following acceptance of the requested clarifications and revised Information Statement by Dr Nicole Gerrand Manager, Research Support & Development under delegated authority from the Committee, grants ethical approval of the above project.

The following documentation has been reviewed and approved by the Hunter New England Human Research Ethics Committee:

Document	Version	Date
NEAF	Submission Code: AU/1/4AC2215	
Clinical Trial Protocol	Version 3.3	25 November 2015
SECTION 5 PROJECT: Describe the theoretical, empirical and/or conceptual basis, and background evidence, for the research proposal, eg. previous studies, anecdotal evidence, review of		

Hunter New England Research Support & Development Office
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Telephone: (02) 49214950 Facsimile: (02) 49214818
Email: HNELHD-HREC@hnehealth.nsw.gov.au
http://www.hnehealth.nsw.gov.au/ethics/Pages/Research-Ethics-and-Governance-Unit.aspx

literature, prior observation, laboratory or animal studies		
uPDA TRIAL Drug Protocol IBUPROFEN Non-steroidal anti-inflammatory drug		November 2015
uPDA TRIAL Drug Protocol INDOMETHACIN Non-steroidal anti-inflammatory drug		22 February 2013
Parent Information Sheet and Consent Form	Version 2.2	27 December 2015

For the protocol: **The Ultimate PDA trial: Early pharmacological treatment with supportive care versus supportive care alone in preterm Infants with patent ductus arterious**

Approval has been granted for this study to take place at the following sites:

- **John Hunter Children's Hospital, New Lambton NSW**
- **Royal North Shore Hospital, St Leonards NSW**

Approval from the Hunter New England Human Research Ethics Committee for the above protocol is given for a maximum of **5** years from the date of this letter, after which a renewal application will be required if the protocol has not been completed.

The *National Statement on Ethical Conduct in Human Research (2007),* which the Committee is obliged to adhere to, include the requirement that the committee monitors the research protocols it has approved. In order for the Committee to fulfil this function, it requires:

- A report of the progress of the above protocol be submitted at 12 monthly intervals. Your review date is **February 2016.** A proforma for the annual report will be sent two weeks prior to the due date.

- A final report must be submitted at the completion of the above protocol, that is, after data analysis has been completed and a final report compiled. A proforma for the final report will be sent two weeks prior to the due date.

- All variations or amendments to this protocol, including amendments to the Information Sheet and Consent Form, must be forwarded to and approved by the Hunter New England Human Research Ethics Committee prior to their implementation.

- The Principal Investigator will immediately report anything which might warrant review of ethical approval of the project in the specified format, including:

    - any serious or unexpected adverse events

        - Adverse events, however minor, must be recorded as observed by the Investigator or as volunteered by a participant in this protocol. Full details will be documented, whether or not the Investigator or his deputies considers the event to be related to the trial substance or procedure. These do not need to be reported to the Hunter New England Human Research Ethics Committee

        - Serious adverse events that occur during the study or within six months of completion of the trial at your site should be reported to the Manager, Research Support & Development Office, of the Hunter New England

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Human Research Ethics Committee as soon as possible and at the latest within 72 hours.

- All other safety reporting should be in accordance with the NHMRC's Safety Monitoring Position Statement – May 2009 available at http://www.nhmrc.gov.au/health_ethics/hrecs/reference/_files/090609_nhmrc_position_statement.pdf

- Serious adverse events are defined as:

  - Causing death, life threatening or serious disability.
  - Cause or prolong hospitalisation.
  - Overdoses, cancers, congenital abnormalities whether judged to be caused by the investigational agent or new procedure or not.

- Unforeseen events that might affect continued ethical acceptability of the project.

- If for some reason the above protocol does not commence (for example it does not receive funding); is suspended or discontinued, please inform Dr Nicole Gerrand as soon as possible.

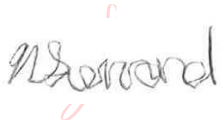
You are reminded that this letter constitutes ethical approval only. You must not commence this research project at a site until separate authorisation from the Chief Executive or delegate of your site has been obtained.

A copy of this letter must be forwarded to all site investigators for submission to the relevant Research Governance Officer.

Please quote **15/12/16/3.03** in all correspondence.

Should you have any concerns or questions about your research, please contact Dr Gerrand as per the details at the bottom of the page. The Hunter New England Human Research Ethics Committee wishes you every success in your research.

Yours faithfully



For: Ms M Hunter
Acting Chair
Hunter New England Human Research Ethics Committee

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