Health Research Authority
North East - Tyne & Wear South Research Ethics Committee
Room 001
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Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

17 March 2017

Dr T Pillay
Clinical Lead Neonatologist
Royal Wolverhampton NHS Trust
New Cross Hospital
Wolverhampton
WV10 0QP

Dear Dr Pillay

Study title:	**OPTIPREM: Optimising neonatal service provision for preterm babies born between 27 and 31 weeks of gestation in England using national data, qualitative research and economic analysis.**
REC reference:	**17/NE/0080**
Protocol number:	**2016NEO87**
IRAS project ID:	**212034**

The Proportionate Review Sub-committee of the North East - Tyne & Wear South Research Ethics Committee reviewed the above application on 15 March 2017.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact hra.studyregistration@nhs.net outlining the reasons for your request. Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

Ethical opinion

On behalf of the Committee, the sub-committee gave a **favourable** ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

Conditions of the favourable opinion

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA Approval (England)/ NHS permission for research is available in the Integrated Research Application System, www.hra.nhs.uk or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations.

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database. This should be before the first participant is recruited but no later than 6 weeks after recruitment of the first participant.

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from the HRA. Guidance on where to register is provided on the HRA website.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion").

Summary of discussion at the meeting

The PR Sub-Committee raised the following issues and the chief investigator responded accordingly as follows.

Social or scientific value; scientific design and conduct of the study

There are three named researchers (all neonatologists) noted as representing the host organisations in addition to yourself. Conformation was requested if the neonatologists represent both NICUs and LNUs and if so, clarification was requested how the potential risk of bias would be handled and confirmation that both treatment areas would be represented in some way.

You confirmed that, with regard to N*ICU vs LNU representation, you are a neonatal network consultant and provide clinical cover to both LNU and NICU in your network. In addition, one of the key collaborators provides an advisory service within your neonatal network to LNU teams.*

This is an observational study encompassing all neonatal NICU and LNU in England. As a result, both areas will be included. There is unlikely to be any screening or selection bias associated with this.

In the experience of the NDAU in previous studies with a similar format (i.e. opt-out option for individual units, with data anonymised) there has been no neonatal unit electing to opt-out, and all units data have been used. For these reasons noted above, you believed that it was unlikely to be a risk of bias associated with this study due to representation between LNU and NICU.

Favourable risk benefit ratio; anticipated benefit/risks for research participants (present and future)

Clarification was requested if a safety committee would be set up to undertake interim safety reviews. The reason for this is that it could be possible that before the study ends it would have been identified that NICU or LNU (or vice versa) has much better survival rates and this would need to be acted on.

You explained that with regards to the Safety Committee, you had not intended to establish a Study Safety Committee to undertake interim safety reviews as a) this is a non-interventional study and b) the data will only be available to the study team at two time points, as opposed to being collected at more regular intervals as in for example a clinical trial.

The first release of data (first time point and comprising 2014-2016 data) will not be of sufficient sample size to be able to provide clear statistical evidence, but serve as a useful interim point of data analysis and preparation for the team. This first release will not have been subjected to the 'feedback loop' which was added for the 2017 data to ensure added quality and completeness to the data. It is likely that any interim findings will need to be confirmed using the higher quality 'prospective' data.

The results from the interim analysis based on this first release of data will be made available to the Study Steering Committee. Advice will be sought from the Committee in the event of clear statistical evidence of a difference between the types of units emerging from the interim analysis; although the researchers believe this will need validation as noted above using the more robust 2017 data with the added feedback loop. The study steering committee comprises a panel with experience in sitting on data monitoring and trial safety committees.

Other general comments

Also the Committee stated that they would be happy to review phase 4 as a substantial amendment but the nature of the amendment may mean it would need to go to a full committee anyway.

This was acknowledged.

Approved documents

The documents reviewed and approved were:

Document	*Version*	*Date*
Covering letter on headed paper [Covering Letter]	1	03 January 2017
IRAS Application Form [IRAS_Form_01032017]		01 March 2017
Letter from funder		05 December 2016
Letter from sponsor [Sponsor Letter]	1	28 February 2017
Letters of invitation to participant [Letter to Participating units]	1	28 February 2017
Other [Leaflet to neonatal unit staff]	1	04 March 2017
Other [additional poster for neonatal unit]	1	04 March 2017
Other [Email response to issues raised]		14 March 2017
Participant information sheet (PIS) [Participant information sheet]	3	28 February 2017
Referee's report or other scientific critique report [NIHR Full project description including referees comments and responses]	2	03 January 2017
Research protocol or project proposal [Final Protocol OPTIPREM]	2	03 January 2017
Summary CV for Chief Investigator (CI) [CV chief applicant]	1	27 February 2017
Summary, synopsis or diagram (flowchart) of protocol in non technical language [Project Flow diagram]	2	03 January 2017

Membership of the Proportionate Review Sub-Committee

The members of the Sub-Committee who took part in the review are listed on the attached sheet.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:
http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

With the Committee's best wishes for the success of this project.

17/NE/0080	**Please quote this number on all correspondence**

Yours sincerely
pp

Sarah Pothero

Mr Paddy Stevenson
Chair

Email: nrescommittee.northeast-tyneandwearsouth@nhs.net

Enclosures: *List of names and professions of members who took part in the review*

"After ethical review – guidance for researchers"

Copy to: *Mrs Sarah Glover, The Royal Wolverhampton NHS Trust*

North East - Tyne & Wear South Research Ethics Committee

Attendance at PRS Sub-Committee of the REC meeting held by correspondence

Committee Members:

Name	*Profession*	*Present*
Mr Paddy Stevenson (Chair)	Research Operations Manager	Yes
Mr Chris Barron	Research Radiographer	Yes
Dr Dorothy Coe	Senior Research Assistant & Lecturer in Nursing Skills	Yes

Also in attendance:

Name	*Position (or reason for attending)*
Ms Gillian Mayer	REC Manager