Health Research Authority

East of England - Cambridge South Research Ethics Committee

The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

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

10 May 2021

Dr David Inwald
Consultant in Paediatric Intensive Care
Cambridge University Hospitals NHS Trust
PICU
Addenbrooke's Hospital
Cambridge
CB2 0QQ

Dear Dr Inwald,

Study title:	**PRESSURE: PRotocolised Evaluation of permiSSive blood pressure targets versus Usual caRE. Evaluating the clinical and cost effectiveness of using a permissive blood pressure target to guide titration of vasoactive drugs in critically ill children with hypotension.**
REC reference:	**21/EE/0084**
Protocol number:	**A095842**
IRAS project ID:	**289545**

Thank you for your letter of 05 May 2021, responding to the Research Ethics Committee's (REC) request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair and another member of the REC.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Good practice principles and responsibilities

The UK Policy Framework for Health and Social Care Research sets out principles of good practice in the management and conduct of health and social care research. It also outlines the responsibilities of individuals and organisations, including those related to the four elements of research transparency:

1. registering research studies
2. reporting results
3. informing participants
4. sharing study data and tissue

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System.

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 research should be registered in a publicly accessible database and we expect all researchers, research sponsors and others to meet this fundamental best practice standard.

It is a condition of the REC favourable opinion that **all clinical trials are registered** on a publicly accessible database within six weeks of recruiting the first research participant. For this purpose, 'clinical trials' are defined as the first four project categories in IRAS project filter question 2. Failure to register a clinical trial is a breach of these approval conditions, unless a deferral has been agreed by or on behalf of the Research Ethics Committee (see here for more information on requesting a deferral: https://www.hra.nhs.uk/planning-and-improving-research/research-planning/research-registration-research-project-identifiers/

If you have not already included registration details in your IRAS application form, you should notify the REC of the registration details as soon as possible.

Further guidance on registration is available at: https://www.hra.nhs.uk/planning-and-improving-research/research-planning/transparency-responsibilities/

Publication of Your Research Summary

We will publish your research summary for the above study on the research summaries section of our website, together with your contact details, no earlier than three months from the date of this favourable opinion letter.

Should you wish to provide a substitute contact point, make a request to defer, or require further information, please visit: https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/

N.B. If your study is related to COVID-19 we will aim to publish your research summary within 3 days rather than three months.

During this public health emergency, it is vital that everyone can promptly identify all relevant research related to COVID-19 that is taking place globally. If you haven't already done so, please register your study on a public registry as soon as possible and provide the REC with the registration detail, which will be posted alongside other information relating to your project. We are also asking sponsors not to request deferral of publication of research summary for any projects relating to COVID-19. In addition, to facilitate finding and extracting studies related to COVID-19 from public databases, please enter the WHO official acronym for the coronavirus disease (COVID-19) in the full title of your study. Approved COVID-19 studies can be found at: https://www.hra.nhs.uk/covid-19-research/approved-covid-19-research/

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).

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, including early termination of the study
- Final report
- Reporting results

The latest guidance on these topics can be found at https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/.

Ethical review of research sites

NHS/HSC sites

The favourable opinion applies to all NHS/HSC sites taking part in the study, subject to confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or management permission (in Scotland) being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Copies of materials calling attention of potential participants to the research [PRESSURE Family Room Poster]	1.0	10 February 2021
Copies of materials calling attention of potential participants to the research [PRESSURE Participant Information Leaflet (Parents or Guardians)]	1.1	19 April 2021
Covering letter on headed paper [PRESSURE_IRAS 289545_Ethics re-submission cover letter_05 May 2021]		05 May 2021
IRAS Application Form [IRAS_Form_08032021]		08 March 2021
Letter from funder [NIHR128895 PRESSURE Grant Award Letter_03 December 2019]		03 December 2019
Letters of invitation to participant [Enrolment Covering Letter]	1.0	10 February 2021
Letters of invitation to participant [Enrolment Follow-Up Covering Letter (2)]	1.0	10 February 2021
Letters of invitation to participant [Bereaved-Enrolment Covering Letter (1)]	1.0	10 February 2021
Letters of invitation to participant [Bereaved-Enrolment Follow-Up Covering Letter (2)]	1.0	10 February 2021
Other [Follow-Up Email for questionnaire]	1.0	10 November 2020
Other [Follow-Up Letter for questionnaire]	1.0	10 November 2020
Other [Newsletter (Parents or Legal Guardians)]	1.0	10 February 2021
Participant consent form [PRESSURE Consent Form (Parent or Guardian)]	1.0	10 February 2021
Participant consent form [PRESSURE Bereaved Consent Form (Parent or Guardian)]	1.0	10 February 2021
Participant consent form [PRESSURE Assent form]	1.0	10 February 2021
Participant information sheet (PIS) [PRESSURE PIS less than 8 years]	1.0	09 February 2021
Participant information sheet (PIS) [PRESSURE PIS 8-10 years]	1.0	09 February 2021
Participant information sheet (PIS) [PRESSURE PIS 11+ years]	1.0	09 February 2021
Participant information sheet (PIS) [PRESSURE Bereaved-Participant Information Sheet (Parents or Guardians)]	1.1	28 April 2021
Participant information sheet (PIS) [Participant Information Sheet (Parents or Guardians) TC]	1.1	28 April 2021
Participant information sheet (PIS) [Participant Information Sheet (Parents or Guardians) Clean]	1.1	28 April 2021
Referee's report or other scientific critique report [PRESSURE letter response to board]		12 November 2019

Research protocol or project proposal [PRESSURE Protocol]	2.0	28 April 2021
Research protocol or project proposal [Tracked changes]	2.0	28 April 2021
Summary CV for Chief Investigator (CI) [David Inwald CV Oct 20]		01 October 2020
Summary, synopsis or diagram (flowchart) of protocol in non technical language [PRESSURE Trial Flow_V1.0_06-11-2020]	1.0	09 November 2020
Validated questionnaire [CHU-9D-Questionnaire]		
Validated questionnaire [PedsQL-Infant(1-12Months)_AU1.0_eng-GB1]		
Validated questionnaire [PedsQL-Infant(13-24Months)_AU1.0_eng-GB1]		
Validated questionnaire [PedsQL-4.0-Core-PT_AU4.0_eng-GB2 (age 2-4)]		
Validated questionnaire [PedsQL-4.0-Core-PYC_AU4.0_eng-GB2_(age 5-7)]		
Validated questionnaire [PedsQL-4.0-Core-PC_AU4.0_eng-GB2 (age 8-12)]		
Validated questionnaire [PedsQL-4.0-Core-PA_AU4.0_eng-GB2 (age 13-18)]		

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.

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 Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at: https://www.hra.nhs.uk/planning-and-improving-research/learning/

IRAS project ID: 289545 **Please quote this number on all correspondence**

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

Yours sincerely,

pp

Dr Leslie Gelling
Chair

Email: cambridgesouth.rec@hra.nhs.uk

Enclosures: “After ethical review – guidance for researchers”

Copy to: Ms Alanna Brown, ICNARC