South Central - Oxford C Research Ethics Committee
Health Research Authority (Bristol)
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Telephone: 0207 104 8241

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

08 December 2020

Professor Daniel Martin
Professor of Perioperative and Intensive Care Medicine
University of Plymouth
John Bull Building
Derriford
Plymouth
PL6 8BU

Dear Professor Martin

Study title:	**Evaluating the clinical and cost-effectiveness of a conservative approach to oxygen therapy for invasively ventilated adults in intensive care.**
REC reference:	**20/SC/0423**
Protocol number:	**01/10/20**
IRAS project ID:	**288506**

The Research Ethics Committee reviewed the above application at the meeting held on 27 November 2020. Thank you for attending, along with Mr Alvin Richards-Belle, to discuss the application.

Ethical Opinion

The members of the Committee present 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.

Mental Capacity Act 2005 (England and Wales)

I confirm that the Committee has approved this research project for the purposes of the Mental Capacity Act 2005 (England and Wales). The Committee is satisfied that the requirements of section 31 of the Act will be met in relation to research carried out as part of this project on, or in relation to, a person who lacks capacity to consent to taking part in the project.

Relevance of the Research to the Impairing Condition

The Committee agreed the research was connected with an impairing condition affecting persons lacking capacity or with the treatment of the condition. The members noted that patients allocated to the trial will all be undergoing intensive ventilation and hence will lack mental capacity to consent. Therefore, the research is highly relevant to the impairing condition.

Justification for Including Adults Lacking Capacity to Meet the Research Objectives

The Committee agreed the research could not be carried out as effectively if it was confined to participants able to give consent.

Arrangements for Appointing Consultees

The Committee considered the arrangements set out in the application for appointing consultees under Section 32 of the Mental Capacity Act 2005 (England and Wales) and the equivalent Section 135 of the Mental Capacity Act (Northern Ireland) 2016) to advise on whether participants lacking capacity should take part and on what their wishes and feelings would have likely to have been if they had capacity. After discussion the Committee agreed that reasonable arrangements were in place for appointing consultees.

The Arrangements for Recruitment in an Emergency Setting

The Committee noted that the research would take place in circumstances involving the provision of urgent treatment to participants lacking capacity.

The Committee agreed that, in the circumstances, it was justified to recruit participants prior to obtaining advice from a consultee under the provisions in Section 32(8) and (9) of the Mental Capacity Act 2005 (England and Wales) and the equivalent Section 136 of the Mental Capacity Act (Northern Ireland) 2016). The members noted the rationale for the emergency waiver is that not only will the patients be unable to consent in this emergency situation but that in addition any relatives are likely to not have the capacity to make decisions at such a time of great stress when their nearest and dearest are very unwell in intensive care needing emergency invasive ventilation. In addition, there is unlikely to be enough time, as participants must be enrolled within twelve hours of fulfilling the inclusion criteria in order to discuss the trial in a meaningful way.

Balance Between Benefit and Risk, Burden and Intrusion

The Committee noted that while the research would not benefit participants lacking capacity it is intended to provide knowledge of the causes, treatment or care of their impairing condition or a condition similar to their impairing condition. The Committee agreed that the risk to participants was likely to be negligible and the research would not significantly interfere with their freedom of action or privacy and would not be unduly invasive or restrictive.

Additional Safeguards

The Committee was satisfied that reasonable arrangements would be in place to comply with the additional safeguards set out in Section 33 of the Mental Capacity Act 2005 (England and Wales) and the equivalent Section 137 of the Mental Capacity Act (Northern Ireland) 2016).

Information for Consultees

The Committee was satisfied that the information to be provided to consultees about the proposed research was adequate to enable consultees to give informed advice about the participation of persons lacking capacity.

Mental Capacity Act (Northern Ireland) 2016

The Committee approved this research project for the purposes of the Mental Capacity Act (Northern Ireland) 2016. The Committee is satisfied that the requirements of Part 8 of the Act will be met in relation to research carried out as part of this project on, or in relation to, a person who lacks capacity to consent to taking part in the project.

Conditions of the Favourable Opinion

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

Number	Condition	Response from the Applicant
1	The Committee emphasised that if a participant with capacity consequently loses capacity throughout the study then the individual should either be withdrawn (but use the data already collected) or the advice from a personal/nominated consultee should be sought as the current protocol of participants continuing in the study contradicts the Mental Capacity Act.	
2	The Committee noted that only verbal consent will be taken from participants but in order to give consent, participants could communicate this via other methods e.g. through blinking and hand movement.	
3	The Committee requested that the opt-out form for personal consultees is removed from the study as, if a personal consultee cannot be sought, then, according to the Mental Capacity Act, a nominated consultee should be pursued.	
4	The Committee requested it is made explicit in the patient follow-up letter after the section "If you **do not wish** to fill in the questionnaire, then please tick the box on the front of the questionnaire and return it to us using the stamped, addressed envelope provided" that if the individual does not respond to the letter then they will continue to be included in the study.	
5	The Committee requested the Participant Information Sheet format is amended so the information is provided in one column rather than two.	

You should notify the REC once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. Revised documents should be submitted to the REC electronically from IRAS. The REC will acknowledge receipt and provide a final list of

the approved documentation for the study, which you can make available to host organisations to facilitate their permission for the study. Failure to provide the final versions to the REC may cause delay in obtaining permissions.

Confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or NHS management permission (in Scotland) 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 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

It is a condition of the REC favourable opinion that **all clinical trials are registered** on a publicly accessible database. For this purpose, 'clinical trials' are defined as the first four project categories in IRAS project filter question 2. Registration is a legal requirement for clinical trials of investigational medicinal products (CTIMPs), except for phase I trials in healthy volunteers (these must still register as a condition of the REC favourable opinion).

Registration should take place as early as possible and within six weeks of recruiting the first research participant at the latest. Failure to register 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/

As set out in the UK Policy Framework, research sponsors are responsible for making information about research publicly available before it starts e.g. by registering the research project on a publicly accessible register. Further guidance on registration is available at: https://www.hra.nhs.uk/planning-and-improving-research/research-planning/transparency-responsibilities/

You should notify the REC of the registration details. We routinely audit applications for compliance with these conditions.

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 HRA 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

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 taking part in the study, subject to confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or NHS 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).

Non-NHS/HSC sites

I am pleased to confirm that the favourable opinion applies to any non NHS/HSC sites listed in the application, subject to site management permission being obtained prior to the start of the study at the site.

Approved Documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Copies of advertisement materials for research participants [Relatives room poster]	1.0	20 October 2020
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Insurance certificate]		14 August 2020
IRAS Application Form [IRAS_Form_29102020]		29 October 2020

Letter from funder [Funder letter]		07 July 2020
Letter from sponsor [Sponsor letter]		20 August 2020
Letters of invitation to participant [Enrolment Covering Letter]	1.0	20 October 2020
Non-validated questionnaire [Health Services Questionnaire]	1.0	20 October 2020
Other [Personal Consultee Information Sheet]	1.0	20 October 2020
Other [Nominated Consultee Information Sheet]	1.0	20 October 2020
Other [Information Leaflet]	1.0	20 October 2020
Other [Postal Consent Form]	1.0	20 October 2020
Other [Telephone Consent Form]	1.0	20 October 2020
Other [Personal Consultee Opinion Form]	1.0	20 October 2020
Other [Postal Personal Consultee Opinion Form]	1.0	20 October 2020
Other [Telephone Personal Consultee Opinion Form]	1.0	20 October 2020
Other [Nominated Consultee Opinion Form]	1.0	20 October 2020
Other [Personal Consultee Enrolment Covering Letter]	1.0	20 October 2020
Other [Patient Follow-up Letter]	1.0	20 October 2020
Other [Patient Newsletter]	1.0	20 October 2020
Participant consent form [Consent Form]	1.0	20 October 2020
Participant information sheet (PIS) [Patient Information Sheet]	1.0	20 October 2020
Referee's report or other scientific critique report [Response to board comments]		22 May 2020
Research protocol or project proposal [UK-ROX Trial Protocol]	1.0	26 October 2020
Summary CV for Chief Investigator (CI) [Professor Daniel Martin CV]		15 September 2020
Validated questionnaire [EQ-5D-5L Questionnaire]	1.0	20 October 2020

Membership of the Committee

The members of the Ethics Committee who were present at the meeting are listed on the attached sheet.

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: 288506 **Please quote this number on all correspondence**

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

Yours sincerely

PP
Dr Lee Potiphar
Chair

E-mail: oxfordc.rec@hra.nhs.uk

Enclosures: List of names and professions of members who were present at the meeting and those who submitted written comments

Copy to: Mr Alvin Richards-Belle, Intensive Care National Audit & Research Centre (ICNARC)

South Central - Oxford C Research Ethics Committee

Attendance at Committee meeting on 27 November 2020

Committee Members:

Name	*Profession*	*Present*	*Notes*
Dr Leonard Brookes	Consultant to the Pharmaceutical Industry	Yes	
Dr Linda Cartwright (Alternate Vice Chair)	Retired Consultant Epidemiologist	Yes	
Dr Ben Caswell	Accountant	Yes	
Dr Nicholas Coupe	PhD Student	No	
Mrs Vivienne Laurie (Vice Chair)	Barrister	Yes	
Mrs Susan Lousada	Company Director (Property) & Non-legal member of first-tier tax tribunal	No	
Dr Nadia Muspratt-Tucker	ST3 Registrar in Obstetrics and Gynaecology	Yes	
Dr Lee Potiphar (Chair and Meeting Chair)	Senior Lecturer in Adult Nursing and Senior Tutor	Yes	
Ms Anna Rathmell	Medical Manager - GI	Yes	
Dr Pamela Susan Ross	GP Principal	Yes	
Mr Barjinder Sahota	Solicitor Advocate	Yes	
Dr David Scott	Lecturer	Yes	
Dr Sabeena Sharma	Consultant Anaesthetist	Yes	
Mr Ioan Wigley	Regulatory Affairs Manager	Yes	

Also in Attendance:

Name	*Position (or reason for attending)*
Mr James CHAL	Observer
Miss Charlotte Ferris	Approvals Officer
Mx Maeve Ip Groot Bluemink	Approvals Specialist
Mr Robert Moore	Observer
Ms Sharon Northey	Approvals Manager (QC Observer)
Ms Joanna Strickland	Approvals Specialist (QC Observer)