Health Research Authority

Professor Rupert Pearse
Professor of Intensive Care Medicine
Queen Mary University of London
Adult Critical Care Unit
Royal London Hospital
London E1 1BB

Email: hra.approval@nhs.net

12 December 2016

Dear Professor Pearse,

Initial Assessment Letter

Study title:	**Optimisation of Peri-operative Cardiovascular Management to Improve Surgical Outcome II (OPTIMISE II) Trial: Open, multi-centre, randomised controlled trial of cardiac output-guided fluid therapy with low dose inotrope infusion compared to usual care in patients undergoing major elective gastrointestinal surgery.**
IRAS project ID:	**209688**
REC reference:	**16/LO/2067**
Sponsor:	**Queen Mary University of London**

Thank you for your application for HRA Approval for the above referenced study. You will have already received notification that your application is valid for REC and proceeding to a REC meeting.

I have been assigned to this application and have undertaken my initial assessment, the findings of which are detailed in *Appendix B*. Please note that **this is not a letter of HRA Approval**, and the research should not begin at any participating NHS organisations in England before HRA Approval is issued.

Purpose

The purpose of this letter is to provide initial information from the HRA assessment to you, the sponsor and participating NHS organisations in England to enable the process of arranging capacity and capability to begin.

You should now provide a copy of this letter and the local document package to participating NHS organisations in England and work with them to coordinate local arrangements in preparation for HRA Approval on the basis described in this letter, even where certain arrangements detailed in *Appendix B* are still to be finalised.

Appendix B provides important information for sponsors and participating NHS organisations in England for arranging and confirming capacity and capability. **Please read *Appendix B* carefully**, in particular the following sections:

- *Participating NHS organisations in England* – this clarifies the types of participating organisations in the study and whether or not all organisations will be undertaking the same activities
- *Confirmation of capacity and capability* - this confirms whether or not each type of participating NHS organisation in England is expected to give formal confirmation of capacity and capability. Where formal confirmation is not expected, the section also provides details on the time limit given to participating organisations to opt out of the study, or request additional time, before their participation is assumed.
- *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* - this provides detail on the form of agreement to be used in the study to confirm capacity and capability, where applicable.

Further information on funding, HR processes, and compliance with HRA criteria and standards is also provided.

It is critical that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details and further information about working with the research management function for each organisation can be accessed from www.hra.nhs.uk/hra-approval.

Notification of Outcomes

I will continue to work with you to resolve any outstanding questions whilst local arrangements are finalised prior to HRA Approval. I may contact you by phone or email to seek clarification as I complete my assessment.

You will receive written notification of HRA Approval once the assessment has been completed and subsequent to any regulatory approvals required for your study (e.g. REC Favourable Opinion, MHRA Clinical Trial Authorisation, etc.). HRA Approval will not be issued until any specific conditions on these approvals have been met.

There is no need for you to send me the REC opinion or any other regulatory approvals, as I will receive these directly, although I may contact you to confirm that any applicable conditions have been met.

Appendices

This Initial Assessment Letter contains the following appendices:

- A – List of documents to be reviewed during HRA assessment
- B – Summary of initial HRA assessment

Scope

HRA Approval provides an approval for research involving patients or staff in NHS organisations in England.

If your study involves NHS organisations in other countries in the UK, please contact the relevant national coordinating functions for support and advice. Further information can be found at http://www.hra.nhs.uk/resources/applying-for-reviews/nhs-hsc-rd-review/.

If there are participating non-NHS organisations, local agreement should be obtained in accordance with the procedures of the local participating non-NHS organisation.

HRA training

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

Your IRAS project ID is 209688**.** Please quote this on all correspondence.

Yours sincerely,

Emma Stoica
Senior Assessor

Email: hra.approval@nhs.net

Copy to:

Miss Ann Thomson; sponsor contact
Dr Sally Burtles, lead NHS R&D contact
NIHR CRN Portfolio Applications Team

Appendix A - Documents received

The documents to be assessed as part of HRA Approval are as follows.

Document	*Version*	*Date*
Covering letter on headed paper [Cover letter]		07 November 2016
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Insurance]		04 November 2016
GP/consultant information sheets or letters [GP letter]	1.0	03 November 2016
IRAS Application Form [IRAS_Form_07112016]		07 November 2016
Letter from funder [interview outcome letter]		24 June 2014
Letter from sponsor [Letter from sponsor]		04 November 2016
Other [Statement of activities]	1.0	03 November 2016
Other [Schedule of events]	1.0	03 November 2016
Participant consent form [Informed consent form]	1.0	03 November 2016
Participant information sheet (PIS) [Patient information sheet]	1.0	03 November 2016
Research protocol or project proposal [Study Protocol]	1.0	02 November 2016
Summary CV for Chief Investigator (CI) [Rupert Pearse CV]		10 January 2015

Appendix B – Information for Sponsors and Participating NHS Organisations

The appendix below provides all parties with information that will be beneficial when discussing the arranging of capacity and capability with participating NHS organisations in England. The information in this appendix is intended to be an accurate reflection of the study at the time of issue of this letter. As part of the HRA Approval process, details may change prior to a Letter of HRA Approval being issued. NHS organisations should be assured that the HRA will continue to work with the sponsor on any HRA assessment criteria which are 'pending', and this should not impact on the arranging or capacity and capability.

The following person is the sponsor contact for the purpose of addressing participating organisation questions relating to the study:

Miss Ann Thomson
E-mail ann.thomson@qmul.ac.uk
Telephone 02078822556

HRA assessment criteria

Section	HRA Assessment Criteria	Compliant with Standards?	Comments
1.1	IRAS application completed correctly	Pending	Justification will be sought from the applicant as to why the study is not considered a clinical trial of an investigational medicinal product. Clarification will be sought from the applicant regarding the number of NHS organisations invited to participate.
2.1	Participant information/consent documents and consent process	Pending	For the purpose of HRA assessment revisions will be necessary to the participant information sheet and consent form in order to make them compliant with the HRA standards.
3.1	Protocol assessment	Pending	Assessment pending clarification as per section 1.1 above.
4.1	Allocation of responsibilities and rights are agreed and documented	Pending	The sponsor indicated that a mNCA will be used with the participating NHS organisations, and a template will be requested from the applicant. A Statement if Activities has been

Section	HRA Assessment Criteria	Compliant with Standards?	Comments
			provided to aid set up of the study at the participating NHS organisations in England.
4.2	Insurance/indemnity arrangements assessed	Pending	Clarifications will be requested from the sponsor regarding the conditions of the loan and insurance arrangements covering the cardiac output monitoring equipment. Where applicable, independent contractors (e.g. General Practitioners) should ensure that the professional indemnity provided by their medical defence organisation covers the activities expected of them for this research study.
4.3	Financial arrangements assessed	Pending	Details of funding provided by the sponsor to the NHS organisations in England are specified in the Statement of Activities. Evidence of funding from Edwards Lifesciences Corporation will be requested from the applicant.
5.1	Compliance with the Data Protection Act and data security issues assessed	Pending	Clarifications will be sought as to why patient identifiable data would be transferred to other countries, and also regarding the period of storage of personal data after the end of the study.
5.2	CTIMPS – Arrangements for compliance with the Clinical Trials Regulations assessed	Pending	See section 1.1
5.3	Compliance with any applicable laws or regulations	Yes	No comments
6.1	NHS Research Ethics Committee favourable opinion received for applicable studies	Pending	No comments
6.2	CTIMPS – Clinical Trials Authorisation (CTA) letter received	Pending	See section 1.1

Section	HRA Assessment Criteria	Compliant with Standards?	Comments
6.3	Devices – MHRA notice of no objection received	Not Applicable	No comments
6.4	Other regulatory approvals and authorisations received	Not Applicable	No comments

Participating NHS Organisations in England

This provides detail on the types of participating NHS organisations in the study and a statement as to whether the activities at all organisations are the same or different.
There is one type of NHS organisations participating in the study, carrying out all research activities as described in the Statement of Activities and Schedule of Events. The Chief Investigator or sponsor should share relevant study documents with participating NHS in England in order to put arrangements in place to deliver the study. The documents should be sent to both the local study team, where applicable, and the office providing the research management function at the participating organisation. For NIHR CRN Portfolio studies, the Local LCRN contact should also be copied into this correspondence. For further guidance on working with participating NHS organisations please see the HRA website. If chief investigators, sponsors or principal investigators are asked to complete site level forms for participating NHS organisations in England which are not provided in IRAS or on the HRA website, the chief investigator, sponsor or principal investigator should notify the HRA immediately at hra.approval@nhs.net. The HRA will work with these organisations to achieve a consistent approach to information provision.

Confirmation of Capacity and Capability

This describes whether formal confirmation of capacity and capability is expected from participating NHS organisations in England.
Participating NHS organisations in England **will be expected to formally confirm their capacity and capability** to host this research. • The sponsor should ensure that participating NHS organisations are provided with a copy of this letter and all relevant study documentation, and work jointly with NHS organisations to arrange capacity and capability whilst the HRA assessment is ongoing. • Further detail on how capacity and capacity will be confirmed by participating NHS organisations, following issue of the Letter of HRA Approval, is provided in the *Participating NHS Organisations* and *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* sections of this appendix. • The Assessing, Arranging, and Confirming document on the HRA website provides further information for the sponsor and NHS organisations on assessing, arranging and confirming capacity and capability.

Principal Investigator Suitability

This confirms whether the sponsor's position on whether a PI, LC or neither should be in place is correct for each type of participating NHS organisation in England, and the minimum expectations for education, training and experience that PIs should meet (where applicable).
Principal Investigators should be in place at each participating NHS organization. PIs have been identified for the NHS organisations listed in Part C of the IRAS form. Study specific SOPs will be provided during the SIV. The sponsor expectation is that PIs and local research teams should all have up to date GCP training. GCP training is not a generic training expectation, in line with the HRA statement on training expectations.

HR Good Practice Resource Pack Expectations

This confirms the HR Good Practice Resource Pack expectations for the study and the pre-engagement checks that should and should not be undertaken..
The activities at the participating NHS organization will be undertaken by local staff who would have adequate contractual relationship with the host organizations, therefore no additional arrangements (honorary research contracts or letters of access) are expected for this study.

Other Information to Aid Study Set-up

This details any other information that may be helpful to sponsors and participating NHS organisations in England in study set-up.
• The applicant has indicated that they intend to apply for inclusion on the NIHR CRN Portfolio.