Health Research Authority

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Professor Paul Dark
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First Floor, Summerfield House, Salford Royal NHS
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Salford, Greater Manchester
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23 October 2017

Dear Professor Dark

Letter of HRA Approval

Study title:	**Biomarker-guided duration of antibiotic treatment in hospitalised patients with suspected sepsis. The ADAPT-Sepsis Trial.**
IRAS project ID:	**209815**
Protocol number:	**R121074**
REC reference:	**17/SC/0434**
Sponsor	**University of Manchester**

I am pleased to confirm that **HRA Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications noted in this letter.

Participation of NHS Organisations in England

The sponsor should now provide a copy of this letter to all participating NHS organisations in England.

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.

Appendices

The HRA Approval letter contains the following appendices:

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

After HRA Approval

The document *"After Ethical Review – guidance for sponsors and investigators",* issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

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

In addition to the guidance in the above, please note the following:

- HRA Approval applies for the duration of your REC favourable opinion, unless otherwise notified in writing by the HRA.
- Substantial amendments should be submitted directly to the Research Ethics Committee, as detailed in the *After Ethical Review* document. Non-substantial amendments should be submitted for review by the HRA using the form provided on the HRA website, and emailed to hra.amendments@nhs.net.
- The HRA will categorise amendments (substantial and non-substantial) and issue confirmation of continued HRA Approval. Further details can be found on the HRA website.

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.

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 research management staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

Your IRAS project ID is **209815**. Please quote this on all correspondence.

Yours sincerely

Miss Helen Penistone
Assessor

Email: hra.approval@nhs.net

Copy to: *Ms Nicola McGowan (WCTU)*
Ms Katie Doyle, Salford Royal NHS Foundation Trust & Pennine Acute Hospitals NHS Trust (lead NHS R&D)
University of Manchester (sponsor)

Appendix A - List of Documents

The final document set assessed and approved by HRA Approval is listed below.

Document	*Version*	*Date*
Contract/Study Agreement template [mNCA]		
Contract/Study Agreement template [Malpractice Insurance Certificate]		01 June 2017
Copies of advertisement materials for research participants [ADAPT-Sepsis HTA 15-99-02 Branding]	Logo	08 June 2017
Covering letter on headed paper [HRA Covering Letter]		31 July 2017
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Signed Insurance Assessment Form]		13 June 2017
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Indemnity Statement]		31 July 2017
GP/consultant information sheets or letters [GP Letter]	1.0	27 July 2017
HRA Schedule of Events	3	23 October 2017
HRA Statement of Activities	2	07 September 2017
IRAS Application Form [IRAS_Form_04082017]		04 August 2017
Letter from funder [funding letter]		
Letter from sponsor [Sponsor Letter]	V1.0	01 August 2017
Other [Sponsor Indemnity Statement]	V1.0	01 August 2017
Other [Sponsor CT, Medical Malpractice and PI Confirmation]	V1.0	01 June 2017
Other	Lay Summary	08 September 2017
Other [HRA Reply Letter]		08 September 2017
Other [HRA Clarification Letter]		04 August 2017
Other [MHRA confirmation of non-CTIMP]		24 September 2015
Participant information sheet (PIS) [ADAPT-Sepsis PIS Patient at Commencement]	1.2	08 September 2017
Participant information sheet (PIS) [ADAPT-Sepsis PIS Recovery]	1.2	08 September 2017
Participant information sheet (PIS) [ADAPT-Sepsis CIS Consultee]	1.2	08 September 2017
Research protocol or project proposal [ADAPT-Sepsis Trial Protocol V1.2 20OCT2017 tracked changes]	1.2	20 October 2017
Summary CV for Chief Investigator (CI) [Paul Dark short CV]	July 2017	03 July 2017

Appendix B - Summary of HRA Assessment

This appendix provides assurance to you, the sponsor and the NHS in England that the study, as reviewed for HRA Approval, is compliant with relevant standards. It also provides information and clarification, where appropriate, to participating NHS organisations in England to assist in assessing and arranging capacity and capability.

For information on how the sponsor should be working with participating NHS organisations in England, please refer to the, *participating NHS organisations*, *capacity and capability* and *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* sections in this appendix.

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

Name: Ms Nicola McGowan

Tel: 02476151386

Email: adaptsepsistrial@warwick.ac.uk

HRA assessment criteria

Section	HRA Assessment Criteria	Compliant with Standards	Comments
1.1	IRAS application completed correctly	Yes	No comments
2.1	Participant information/consent documents and consent process	Yes	No comments
3.1	Protocol assessment	Yes	No comments
4.1	Allocation of responsibilities and rights are agreed and documented	Yes	The sponsor intends to use an unmodified version of the model non-commercial agreement to form an agreement with participating NHS organisations. Salford Royal Foundation Trust will act as host organisation as this is a NIHR funded study. This is reflected in the agreement.

Section	HRA Assessment Criteria	Compliant with Standards	Comments
4.2	Insurance/indemnity arrangements assessed	Yes	The sponsor has made arrangements for the payment of compensation in the event of non-negligent harm. 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	Yes	Funding to support the study has been granted by the NIHR. As per the Statement of Activities, sites will be paid a £50.00 per participant fee and lab quality assurance (RIQAS) software licence support will be available.
5.1	Compliance with the Data Protection Act and data security issues assessed	Yes	Throughout the study participants will be identified by their participant ID and initials.
5.2	CTIMPS – Arrangements for compliance with the Clinical Trials Regulations assessed	Not Applicable	No comments
5.3	Compliance with any applicable laws or regulations	Yes	All blood samples will be tested locally and then destroyed.
6.1	NHS Research Ethics Committee favourable opinion received for applicable studies	Yes	No comments
6.2	CTIMPS – Clinical Trials Authorisation (CTA) letter received	Not Applicable	The MHRA have confirmed that this is a non-CTIMP.
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 will be one site type where all site activities will be undertaken as per the study protocol and supporting documents. Currently only 1 site has been named in part C of the IRAS form. A non-substantial amendment should be submitted to add new sites. The Chief Investigator or sponsor should share relevant study documents with participating NHS organisations 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**. • Following issue of this letter, participating NHS organisations in England may now confirm to the sponsor their capacity and capability to host this research, when ready to do so. How capacity and capacity will be confirmed is detailed in the *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* section 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 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).
There will be a Principal Investigator at site as is appropriate for this study type. The sponsor has

requested support to identify Principal Investigators at sites and has detailed the requirements in the Statement of Activities.

Local staff will be provided with protocol and set-up training by Warwick CTU on behalf of the Sponsor. The sponsor expects that members of the local research team will have undertaken or will undertake NIHR CRN training in Good Clinical Practice.

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

It is expected that local staff who are substantively employed by the participating NHS organisation will undertake all research activities as listed in A18 and A19 of the IRAS application and, therefore, unlikely that any HR arrangements will be required for this study.

Where arrangements are not already in place, researchers undertaking these activities would be expected to obtain an honorary research contract from one NHS organisation (if university employed), followed by Letters of Access for subsequent organisations. This would be on the basis of a Research Passport (if university employed) or an NHS to NHS confirmation of pre-engagement checks letter (if NHS employed). These should confirm enhanced DBS checks, including appropriate barred list checks, and occupational health clearance.

Other Information to Aid Study Set-up

This details any other information that may be helpful to sponsors and participating NHS organisations in England to aid study set-up.

The applicant has indicated that they intend to apply for inclusion on the NIHR CRN Portfolio.

The first approach to potential participants to discuss the study may be by a Research Nurse or the treating clinician. The first approach may only be made by a Research Nurse at sites where the Research Nurse is a member of the direct care team.