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Email: hra.approval@nhs.net
Research-permissions@wales.nhs.uk

06 July 2018

Dear Dr Gale,

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**WithHolding Enteral feeds Around packed red cell Transfusion to prevent necrotising enterocolitis in preterm neonates: a multi-centre, electronic patient record (EPR), randomised controlled point-of-care pilot trial**
IRAS project ID:	**154432**
REC reference:	**18/LO/0900**
Sponsor:	**Imperial College London**

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

How should I continue to work with participating NHS organisations in England and Wales?
You should now provide a copy of this letter to all participating NHS organisations in England and Wales, as well as any documentation that has been updated as a result of the assessment.

Following the arranging of capacity and capability, participating NHS organisations should **formally confirm** their capacity and capability to undertake the study. How this will be confirmed is detailed in the "*summary of assessment*" section towards the end of this letter.

You should provide, if you have not already done so, detailed instructions to each organisation as to how you will notify them that research activities may commence at site following their confirmation of capacity and capability (e.g. provision by you of a 'green light' email, formal notification following a site

initiation visit, activities may commence immediately following confirmation by participating organisation, etc.).

It is important 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 of the research management function for each organisation can be accessed here.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within the devolved administrations of Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) has been sent to the coordinating centre of each participating nation. You should work with the relevant national coordinating functions to ensure any nation specific checks are complete, and with each site so that they are able to give management permission for the study to begin.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?
HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?
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.

I am a participating NHS organisation in England or Wales. What should I do once I receive this letter?
You should work with the applicant and sponsor to complete any outstanding arrangements so you are able to confirm capacity and capability in line with the information provided in this letter.

The sponsor contact for this application is as follows:

Name: Miss Becky Ward
Tel: 02075949495
Email: becky.ward@imperial.ac.uk

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **154432**. Please quote this on all correspondence.

Yours sincerely,

Emma Stoica
Senior Assessor

Email: hra.approval@nhs.net

Copy to: *Miss Becky Ward, Imperial College London*
Damon Foster , Chelsea And Westminster NHS Foundation Trust

List of Documents

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

Document	*Version*	*Date*
Copies of advertisement materials for research participants [WHEAT Parent Poster]	1.0	24 April 2018
Covering letter on headed paper [Covering letter]	N/A	30 April 2018
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [WHEAT sponsorship and insurance confirmation email 24.04.18]	N/A	24 April 2018
HRA Schedule of Events [SoE recruiting site]	1.0	24 April 2018
HRA Schedule of Events [SoE CCS]	1.0	24 April 2018
HRA Statement of Activities [SoA recruiting site]	1.0	24 April 2018
HRA Statement of Activities [SoA CCS]	1.0	24 April 2018
IRAS Application Form [IRAS_Form_30042018]		30 April 2018
Letter from funder [C Gale funding letter]	N/A	16 December 2015
Letter from sponsor [Sponsorship confirmation letter]	N/A	24 April 2018
Letter from statistician [Statistician covering letter v1.0 16.04.18]	1.0	16 April 2018
Other [List of NHS sites]		06 July 2018
Other [Research ethics committee decision-making efficent neonatal trial BMJ C Gale Sept 16]		14 September 2016
Other [WHEAT screenshots badgerNet]	V1.0	03 April 2018
Other [WHEAT Pilot trial privacy notice]	1.0	05 July 2018
Participant information sheet (PIS) [WHEAT PIL]	2.0	26 June 2018
Participant information sheet (PIS) [WHEAT PIL Tracked]	2.0	26 June 2018
Referee's report or other scientific critique report [Peer Review Certificate C Gale fellowship]	N/A	09 April 2018
Research protocol or project proposal [WHEAT Protocol]	1.0	24 April 2018
Summary CV for Chief Investigator (CI) [Chris Gale CV]		03 April 2018
Summary of any applicable exclusions to sponsor insurance (non-NHS sponsors only) [Imperial College London Insurance Certificate 2017]	N/A	01 August 2017
Summary, synopsis or diagram (flowchart) of protocol in non technical language [WHEAT Trial summary]	1.0	12 April 2018

Summary of assessment

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

Assessment criteria

Section	Assessment Criteria	Compliant with Standards	Comments
1.1	IRAS application completed correctly	Yes	The sponsor clarified that there are 13 NHS organisations in total (of which nine are listed in IRAS form part C. There are two or more locations / hospitals hosting the research in some of the NHS organisations. All NHS sites are listed in a separate document (Other [List of NHS sites]).
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	Statements of Activities for each site-type (Recruiting Sites and Shared Care Sites) have been provided and will act as agreement of the respective NHS organisations to participate. The sponsor is not requesting and does not expect any other site agreements.
4.2	Insurance/indemnity arrangements assessed	Yes	No comments
4.3	Financial arrangements assessed	Yes	The sponsor is not providing any funding to either type of NHS organisations for participating in the trial, as confirmed in the Statements of Activities.
5.1	Compliance with the Data Protection Act and data	Yes	No comments

Section	Assessment Criteria	Compliant with Standards	Comments
	security issues assessed		
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	No comments
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	No 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 and Wales

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 are two types of participating NHS organisations in the study:

1. Recruiting Sites. These sites will identify and recruit participants and undertake all research activities pertinent to the study.

2. Shared Care Sites. These sites will only take part in trial if/when a baby is transferred and are not known at present.

Statements of Activities and Schedules of Events have been provided to aid the set-up of the study at the participating NHS recruiting sites and Shared Care Sites respectively. The Schedules of Events detail all activities to be undertaken at each site-type.

The Chief Investigator or sponsor should share relevant study documents with participating NHS organisations in England and Wales 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. Where applicable, the local LCRN contact should also be copied into this correspondence.

If chief investigators, sponsors or principal investigators are asked to complete site level forms for participating NHS organisations in England and Wales which are not provided in IRAS, the HRA or HCRW websites, the chief investigator, sponsor or principal investigator should notify the HRA immediately at hra.approval@nhs.net or HCRW at Research-permissions@wales.nhs.uk. We will work with these organisations to achieve a consistent approach to information provision.

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 Wales, and the minimum expectations for education, training and experience that PIs should meet (where applicable).

Principal Investigators should be in place at the Recruiting Sites, and have been identified as listed in Part C of the IRAS form and the table above.

Principal Investigators should also be in place at the Shared Care Sites. These are not known presently however the sponsor indicated that they are not requesting support to identify Principal Investigators at these sites.

The minimum training expectations that the sponsor expects of PIs, including details of any training to be provided by the sponsor, are detailed in the Statements of Activities. GCP training is not a generic training expectation, in line with the HRA/HCRW/MHRA 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

As a point of care trial where all trial data will be obtained from clinical information entered into an existing neonatal EPR at the point of care, staff involved in the study should already have in place contractual relationship with the host organization, therefore no additional arrangements (honorary research contracts or letters of access) are expected for this study, at either site type.

Other Information to Aid Study Set-up

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

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