NHS
Health Research Authority

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Email: hra.approval@nhs.net

29 June 2017

Dear Dr Embleton

Letter of HRA Approval

Study title:	**Interactions between the diet and gut microbes and metabolism in preterm infants (INDIGO study).**
IRAS project ID:	**215037**
REC reference:	**17/NE/0169**
Sponsor	**Newcastle Hospitals NHS Foundation Trust**

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.

The attached document *"After HRA Approval – guidance for sponsors and investigators"* gives detailed guidance on reporting expectations for studies with HRA Approval, including:

- Working with organisations hosting the research
- 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.

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 **215037**. Please quote this on all correspondence.

Yours sincerely

Catherine Adams
Senior Assessor
Email: hra.approval@nhs.net

Copy to: *AAron Jackson, Newcastle Hospitals NHS Foundation Trust*

Appendix A - List of Documents

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

Document	*Version*	*Date*
Covering letter on headed paper	v1	27 April 2017
IRAS Application Form [IRAS_Form_04052017]		04 May 2017
Participant consent form [Revised Consent Newcastle]	v1.3	06 June 2017
Participant consent form [Revised Consent Chelsea]	v1.3	06 June 2017
Participant information sheet (PIS) [Revised PIL Chelsea]	v1.3	06 June 2017
Participant information sheet (PIS) [Revised PIL Newcastle]	v1.3	06 June 2017
Participant information sheet (PIS) [PIS additional MRI Chelsea]	v1	12 April 2017
Research protocol or project proposal [INDIGO Protocol]	v1.3	06 June 2017
Summary CV for Chief Investigator (CI) [Embleton CV]		01 January 2017
Statement of Activities (NUTH)	1.2	29 June 2017
Statement of Activities (C&W)	1.2	29 June 2017
Schedule of Events (NUTH)	1.1	9 June 2017
Schedule of Events (C&W)	1.1	9 June 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:

Mr Aaron Jackson

E-mail aaron.jackson@nuth.nhs.uk
Telephone 01912824823

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	A statement of activities is the agreement in use for this study. The sponsor has decided that a tripartite site agreement will no longer be used. A Material Transfer Agreement will be used however this has not been supplied.

Section	HRA Assessment Criteria	Compliant with Standards?	Comments
4.2	Insurance/indemnity arrangements assessed	Yes	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	The donor human milk diet products are provided free of charge and the study site will not have to provide either infant formula or breast milk fortifiers. Consumables required for collection of stool and urine samples will be provided by the research grant, and this will also cover the costs of sample analyses and MRI scans (at the Chelsea and Westminster site). This is confirmed in the Statement of Activities
5.1	Compliance with the Data Protection Act and data security issues assessed	Yes	No comments
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	Not Applicable	No comments

Section	HRA Assessment Criteria	Compliant with Standards?	Comments
	and authorisations received		

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.
All organisations will be undertaking the same activity as detailed in the protocol except that at Chelsea and Westminster an MRI will be undertaken. See section 4.3 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. • 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 capability 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).
A Principal Investigator is expected at participating organisations. The Newcastle team will also organise a site initiation training session by teleconference for the research team at Chelsea & Westminster 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.
Where arrangements are not already in place, research staff not employed by the NHS host organisation undertaking any of the research activities listed in the research application 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 in study set-up.
The applicant has indicated that they intend to apply for inclusion on the NIHR CRN Portfolio. During the study the stool and urine samples will be initially stored on the 2 neonatal units in a freezer. Selected anonymised samples will all be transferred to Northumbria using HTA approved couriers where they will be stored prior to batch analyses. Samples not selected for analysis will be destroyed. After this analyses, a smaller subset of samples will be transferred in one batch to Liverpool university for analysis of stool chemicals. No samples will be left over in Liverpool (the analytic process destroys the sample). Northumbria and Liverpool will adhere to SOPs relevant to the HTA and governance will be the responsibility of the respective universities Stool and urine samples left-over in Northumbria will either be destroyed, or a subset transferred to the Newcastle university biobank. Blood samples (Newcastle only) will be sent from the neonatal unit to NHS laboratories for analyses. Selected residual blood samples will also be transferred to the HTA approved Newcastle University biobank and subject to their governance and custodial arrangements.