NUFFIELD DEPARTMENT OF PRIMARY CARE HEALTH SCIENCES

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ARCHIE

+44 (0)1865 617 842• archie@phc.ox.ac.uk

Mrs Glenys Hunt
Chair, NRES Committee North West – Liverpool East
HRA NRES Centre Manchester
Barlow House, 3rd Floor
4 Minshull Street
Manchester
M1 3DZ

28 June 2016

Dear Mrs Hunt,

Study title: The early use of Antibiotics for at Risk CHildren with InfluEnza in primary care (ARCHIE): a double-blind randomised placebo-controlled trial
REC reference: 13/NW/0621
Protocol number: ARCHIE001
EudraCT number: 2013-002822-21
IRAS project ID: 121769

With reference to the above study we would like to submit a substantial amendment SA011:

- Addition of new NHS Sites. (Table attached)

This is our first substantial amendment since the change to the new HRA approvals system so we have included the following:

- ARCHIE hra-schedule-events-excel-template 3Jun16 final
- ARCHIE statement-activities-final
- Participating Site Agreement template

Other previously reviewed and approved documents can be supplied as required.

Many thanks,

Tricia

Tricia Carver
Senior Trial Manager
on behalf of Chief Investigator, Dr Kay Wang

Attached:
ARCHIE SA11 Amendment form
ARCHIE SA11 IRAS_Export
Sponsor confirmation
ARCHIE hra-schedule-events-excel-template 3Jun16 final
ARCHIE statement-activities-final
Participating Site Agreement template

Site	PI	CRN
Chelsea and Westminster Hospital NHS Foundation Trust	Dr Dipali Shah	North West London
Barking, Havering & Redbridge University Hospital NHS Trust	Dr Kausick Banerjee	North Thames
Milton Keynes University Hospital NHS Foundation Trust	Dr Lazarus Anguvaa	Thames Valley & South Midlands
North Middlesex University Hospital NHS Trust	Dr Neeraj Jain	North Thames
Countess of Chester Hospital NHS Foundation Trust	Dr John Gibbs	North West Coast
South Tees NHS Trust James Cook University Hospital	Dr Arshid Murad	North East and North Cumbria
East Cheshire NHS Trust Macclesfield District Hospital	Dr Surendran Chandrasekaran	North West Coast
St Helens & Knowsley Teaching Hospital NHS Trust	Dr Rosaline Garr	North West Coast
Warrington & Halton Hospital NHS Foundation Trust	Dr Delyth Webb	North West Coast
Northumbria Healthcare NHS Trust North Tyneside General Hospital	Dr Belinda Bateman	North East and North Cumbria
Burton Hospitals NHS Foundation Trust Queen's Hospital	Dr Mansoor Ahmed	West Midlands
Tameside Hospital NHS Foundation Trust	Dr Anjali Petkar	Greater Manchester

Tricia Carver

From: Karen Melham
Sent: 28 June 2016 13:10
To: Tricia Carver
Cc: Ronja Bahadori; Research.Portfolio@ouh.nhs.uk
Subject: Sponsor Authorisation for Amendment 11 to ARCHIE trial

Follow Up Flag: Follow up
Flag Status: Flagged

Dear Tricia
Thank you for sending for our review the amendment proposed to ARCHIE to add 12 new NHS sites, and thereby to bring this study under HRA approval .
I can confirm that we as sponsor representative are content for this to be sent to the relevant REC for review and approval.

Please remember to forward correspondence and any final, REC-approved documents to karl.shepherd@admin.ox.ac.uk to ensure ongoing sponsorship and indemnity.

With best wishes,

Karen

Dr Karen Melham
Senior Clinical Research Support Manager | Clinical Trials & Research Governance (CTRG)
University of Oxford
Joint Research Office, Block 60, Churchill Hospital, Headington, Oxford, OX3 7LE
E: karen.melham@admin.ox.ac.uk **T:** 01865 227093
www.admin.ox.ac.uk/researchsupport

PID:8801-AMD

Welcome to the Integrated Research Application System

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please complete the questions in order. If you change the response to a question, please select 'Save' and review all the questions as your change may have affected subsequent questions.

Please enter a short title for this project (maximum 70 characters)
The early use of Antibiotics in at Risk Children with InfluEnza-ARCHIE

1. Is your project research?

(●) Yes ( ) No

2. Select one category from the list below:

(●) Clinical trial of an investigational medicinal product
( ) Clinical investigation or other study of a medical device
( ) Combined trial of an investigational medicinal product and an investigational medical device
( ) Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice
( ) Basic science study involving procedures with human participants
( ) Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
( ) Study involving qualitative methods only
( ) Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)
( ) Study limited to working with data (specific project only)
( ) Research tissue bank
( ) Research database

If your work does not fit any of these categories, select the option below:

( ) Other study

2a. Is this a commercially sponsored Phase 1 or Phase 1/2a trial involving healthy volunteers?

( ) Yes (●) No

2b. Will the study involve the use of any medical device without a CE Mark, or a CE marked device which has been modified or will be used outside its intended purposes?

( ) Yes (●) No

2c. Please answer the following question:

Is this trial subject to advice from the Expert Advisory Group on Clinical Trials and the Commission on Human Medicine prior to authorisation from MHRA? ○ Yes ◉ No

2d. Please answer the following question:

Is this a trial of a gene therapy medicinal product? ○ Yes ◉ No

2e. Please answer the following question(s):

a) Does the study involve the use of any ionising radiation? ○ Yes ◉ No

b) Will you be taking new human tissue samples (or other human biological samples)? ◉ Yes ○ No

c) Will you be using existing human tissue samples (or other human biological samples)? ○ Yes ◉ No

3. In which countries of the UK will the research sites be located?*(Tick all that apply)*

- ☑ England
- ☐ Scotland
- ☐ Wales
- ☐ Northern Ireland

3a. In which country of the UK will the lead NHS R&D office be located:

- ◉ England
- ○ Scotland
- ○ Wales
- ○ Northern Ireland
- ○ This study does not involve the NHS

4. Which applications do you require?

IMPORTANT: If your project is taking place in the NHS and is led from England select 'IRAS Form'. If your project is led from Northern Ireland, Scotland or Wales select 'NHS/HSC Research and Development Offices' and/or relevant Research Ethics Committee applications, as appropriate.

- ☐ IRAS Form
- ☑ NHS/HSC Research and Development offices
- ☐ Social Care Research Ethics Committee
- ☑ Research Ethics Committee
- ☑ Medicines and Healthcare products Regulatory Agency (MHRA) – Medicines
- ☐ Gene Therapy Advisory Committee (GTAC)
- ☐ Confidentiality Advisory Group (CAG)
- ☐ National Offender Management Service (NOMS) (Prisons & Probation)

For NHS/HSC R&D Offices in Northern Ireland, Scotland and Wales the CI must create NHS/HSC Site Specific Information forms, for each site, in addition to the study wide forms, and transfer them to the PIs or local collaborators.

For participating NHS organisations in England different arrangements apply for the provision of site specific information. Refer to IRAS Help for more information.

5. Will any research sites in this study be NHS organisations?

(●) Yes ( ) No

5a. Are all the research costs and infrastructure costs (funding for the support and facilities needed to carry out research e.g. NHS Support costs) for this study provided by a NIHR Biomedical Research Centre, NIHR Biomedical Research Unit, NIHR Collaboration for Leadership in Health Research and Care (CLAHRC), NIHR Patient Safety Translational Research Centre or a Diagnostic Evidence Co-operative in all study sites?

Please see information button for further details.

(●) Yes ( ) No

Please see information button for further details.

6. Do you plan to include any participants who are children?

(●) Yes ( ) No

7. Do you plan at any stage of the project to undertake intrusive research involving adults lacking capacity to consent for themselves?

( ) Yes (●) No

Answer Yes if you plan to recruit living participants aged 16 or over who lack capacity, or to retain them in the study following loss of capacity. Intrusive research means any research with the living requiring consent in law. This includes use of identifiable tissue samples or personal information, except where application is being made to the Confidentiality Advisory Group to set aside the common law duty of confidentiality in England and Wales. Please consult the guidance notes for further information on the legal frameworks for research involving adults lacking capacity in the UK.

8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or who are offenders supervised by the probation service in England or Wales?

( ) Yes (●) No

9. Is the study or any part of it being undertaken as an educational project?

( ) Yes (●) No

10. Will this research be financially supported by the United States Department of Health and Human Services or any of its divisions, agencies or programs?

( ) Yes (●) No

11. Will identifiable patient data be accessed outside the care team without prior consent at any stage of the project (including identification of potential participants)?

( ) Yes (●) No

SUBSTANTIAL AMENDMENT FORM [1]

NOTIFICATION OF A SUBSTANTIAL AMENDMENT TO A CLINICAL TRIAL ON A MEDICINAL PRODUCT FOR HUMAN USE TO THE COMPETENT AUTHORITIES AND FOR OPINION OF THE ETHICS COMMITTEES IN THE EUROPEAN UNION

For official use:

Date of receiving the request:	Grounds for non acceptance/negative opinion:
	Date:
Date of start of procedure:	Authorisation/ positive opinion:
	Date:
Competent authority registration number of the trial:	Withdrawal of amendment application:
Ethics committee registration number of the trial:	Date:

To be filled in by the applicant:

*This form is to be used both for a request to the Competent Authority for authorisation of a **substantial** amendment and to an Ethics Committee for its opinion on a **substantial** amendment. Please indicate the relevant purpose in Section A.*

A TYPE OF NOTIFICATION

A.1 Member State in which the substantial amendment is being submitted:

A.2 Notification for authorisation to the competent authority: ☐

A.3 Notification for an opinion to the ethics committee: ☑

(1) Cf. Section 3.7.b of the Detailed guidance on the request to the competent authorities for authorisation of a clinical trial on a medicinal product for human use, the notification of substantial amendments and the declaration of the end of the trial (OJ, C82, 30.3.2010, p.1) hereinafter referred to as 'detailed guidance CT-1'.

B TRIAL IDENTIFICATION *(When the amendment concerns more than one trial, repeat this form as necessary.)*

B.1 Does the substantial amendment concern several trials involving the same IMP? [2] ○ Yes ◉ No

B.2 EudraCT number:	2013-002822-21
B.3 Full title of the trial:	The early use of Antibiotics for at Risk CHildren with InfluEnza in primary care (ARCHIE): a double-blind randomised placebo-controlled trial
B.4 Sponsor's protocol code number:	ARCHIE001
B.4 Sponsor's protocol version number:	v2
B.4 Sponsor's protocol date:	12/02/2014

(2) Cf. Section 3.7. of the detailed guidance CT-1

C IDENTIFICATION OF THE SPONSOR RESPONSIBLE FOR THE REQUEST

C.1 Sponsor

Organisation:	Univeristy of Oxford
Contact Given name:	Heather
Contact Family name:	House
Address:	Joint Research Office, Block 60, Churchill Hospital
Town/city:	Headington, Oxford
Post code:	OX3 7LE
Telephone:	01865572228
Fax:	
E-mail:	ctrg@admin.ox.ac.uk

C.2 Legal representative [3] of the sponsor in the European Union for the purpose of this trial (if different from the sponsor)

Name of organisation:
Contact Given name:
Contact Family name:
Address:
Town/city:
Post code:
Telephone:
Fax:
E-mail:

(3) As stated in Article 19 of Directive 2001/20/EC.

D APPLICANT IDENTIFICATION, (please tick the appropriate box)

D1. Request for the competent authority

D.1.1 Sponsor ☐
D.1.2 Legal representative of the sponsor ☐
D.1.3 Person or organisation authorised by the sponsor to make the application. ☐
D.1.4 Complete below:

Name of organisation
Contact Given name
Contact Family name
Address
Town/city
Post code

Telephone
Fax
E-mail

D2. Request for the Ethics Committee

D.2.1 Sponsor ☐
D.2.2 Legal representative of the sponsor ☐
D.2.3 Person or organisation authorised by the sponsor to make the application. ☑
D.2.4 Investigator in charge of the application if applicable[4]:
- Co-ordinating investigator (for multicentre trial): ☐
- Principal investigator (for single centre trial): ☐

D.2.5 Complete below:

Name of organisation	Univeristy of Oxford
Given name	Tricia
Family name	Carver
Address	Nuffield Department of Primary Care Health Sciences, Radcliffe Observatory Quarter
Town/city	Woodstock Road, Oxford
Post code	OX2 6GG
Telephone	01865617842
Fax	
E-mail	Tricia.Carver@phc.ox.ac.uk

(4) According to national legislation.

E SUBSTANTIAL AMENDMENT IDENTIFICATION

E.1 Sponsor's substantial amendment information for the clinical trial concerned:

Code Number: ARCHIE_SA011
Version:
Date: 2016/06/22

E.2 Type of substantial amendment

E.2.1 Amendment to information in the CT application form ○ Yes ◉ No
E.2.2 Amendment to the protocol ○ Yes ◉ No
E.2.3 Amendment to other documents appended to the initial application form ○ Yes ◉ No
If yes specify:
E.2.4 Amendment to other documents or information: ◉ Yes ○ No
If yes specify:
New NHS sites
E.2.5 This amendment concerns mainly urgent safety measures already implemented[5]: ○ Yes ◉ No
E.2.6 This amendment is to notify a temporary halt of the trial[6]: ○ Yes ◉ No

E.2.7 This amendment is to request the restart of the trial[7]: ○ Yes ◉ No

(5) Cf. Section 3.9. of the detailed guidance CT-1.
(6) Cf. Section 3.10. of the detailed guidance CT-1
(7) Cf. Section 3.10. of the detailed guidance CT-1

E.3 Reasons for the substantial amendment:

E.3.1 Changes in safety or integrity of trial subjects	○ Yes	◉ No
E.3.2 Changes in interpretation of scientific documents/value of the trial	○ Yes	◉ No
E.3.3 Changes in quality of IMP(s)	○ Yes	◉ No
E.3.4 Changes in conduct or management of the trial	○ Yes	◉ No
E.3.5 Change or addition of principal investigator(s), co-ordinating investigator	○ Yes	◉ No
E.3.6 Change/addition of site(s)	◉ Yes	○ No
E.3.7 Other change	○ Yes	◉ No
E.3.7.1 If yes specify:		
E.3.8 Other case	○ Yes	◉ No
E.3.8.1 If yes specify:		

E.4 Information on temporary halt of trial:[8]

E.4.1 Date of temporary halt		
E.4.2 Recruitment has been stopped	○ Yes	◉ No
E.4.3 Treatment has been stopped	○ Yes	◉ No
E.4.4 Number of patients still receiving treatment at time of the temporary halt in the MS concerned by the amendment		
E.4.5 Briefly describe:		

Justification for a temporary halt of the trial *(free text)*:

The proposed management of patients receiving treatment at time of the halt *(free text)*:

The consequences of the temporary halt for the evaluation of the results and for overall risk benefit assessment of the investigational medicinal product *(free text)*:

(8) Cf. Section 3.10. of the detailed guidance CT-1

F DESCRIPTION OF EACH SUBSTANTIAL AMENDMENT[9]

Please use this section to detail each substantial amendment which is being notified. If you are notifying more than one substantial amendment, please use the "Add Amendment" button as required

Substantial amendment 1

Previous and new wording:*(tracked)*

New wording:

Comments/ explanation/ reasons for substantial amendment:

(9)Cf. Section 3.7.c. of the detailed guidance CT-1. The sponsor may submit this documentation on a separate sheet.

G CHANGE OF CLINICAL TRIAL SITE(S)/INVESTIGATOR(S) IN THE MEMBER STATE CONCERNED BY THIS AMENDMENT

Type of change:

G.1.1 Addition of a new site

G.1.1.1 Principal investigator (provide details below)

Given name	Dipali
Middle name(if applicable)	
Family name	Shah
Qualification (MD...)	MD
Professional address	Chelsea&Westminster Hospital NHS Foundation Trust, West Middlesex Uni Hospital Isleworth TW76AF
Given name	Kausick
Middle name(if applicable)	
Family name	Banerjee
Qualification (MD...)	MD
Professional address	Barking, Havering & Redbridge University Hospital NHS Trust, Queens Hospital, Romford, RM7 0AG
Given name	Lazarus
Middle name(if applicable)	Anguvaa
Family name	
Qualification (MD...)	MD
Professional address	Milton Keynes University Hospital NHS Foundation Trust, Milton Keynes, MK6 5LD
Given name	Neeraj
Middle name(if applicable)	
Family name	Jain

Qualification (MD...)	MD
Professional address	North Middlesex University Hospital NHS Trust, London N18 1QX
Given name	John
Middle name(if applicable)	Gibbs
Family name	
Qualification (MD...)	MD
Professional address	Countess of Chester Hospital NHS Foundation Trust, Chester, CH2 1UL

G.1.2 Removal of an existing site

G.1.2.1 Principal investigator (provide details below)

Given name	Arshid
Middle name(if applicable)	
Family name	Murad
Qualification (MD...)	MD
Professional address	South Tees NHS Foundation Trust James Cook University Hospital. Middlesborough, TS4 3BW
Given name	Surendran
Middle name(if applicable)	Chandrasekaran
Family name	
Qualification (MD...)	MD
Professional address	East Cheshire NHS Foundation Trust Macclesfield Genral Hospital, Macclesfield, SK10 3BL
Given name	Rosaline
Middle name(if applicable)	Garr
Family name	
Qualification (MD...)	MD
Professional address	St Helens & Knowsley Teaching Hospital NHS Trust, Prescot, L35 5DR
Given name	Delyth
Middle name(if applicable)	
Family name	Webb
Qualification (MD...)	MD

Professional address	Warrington & Halton Hospital NHS Foundation Trust, Warrington, WA5 1QG.
Given name	Belinda
Middle name(if applicable)	
Family name	Bateman
Qualification (MD...)	MD
Professional address	Northumbria Healthcare NHS Foundation Trust North Tyneside General Hospital, North Sheilds, NE29 8NH
Given name	Mansoor
Middle name(if applicable)	
Family name	Ahmed
Qualification (MD...)	MD
Professional address	Burton Hospitals NHS Foundation Trust Queen's Hospital, Burton Upon Trent, DE13 0RB
Given name	Anjali
Middle name(if applicable)	
Family name	Petkar
Qualification (MD...)	MD
Professional address	Tameside Hospital NHS Foundation Trust, Ashton-under-Lyne, OL6 9RW

G.1.3 Change of co-ordinating investigator (provide details below of the new coordinating investigator)

Given name	
Middle name(if applicable)	
Family name	
Qualification (MD...)	
Professional address	

G.1.3.6 Indicate the name of the previous co-ordinating investigator:

G.1.4 Change of principal investigator at an existing site (provide details below of the new principal investigator)

Given name	
Middle name(if applicable)	
Family name	
Qualification (MD...)	

Professional address

G.1.4.6 Indicate the name of the previous principal investigator:

H CHANGE OF INSTRUCTIONS TO CA FOR FEEDBACK TO SPONSOR

H.1 Change of e-mail contact for feedback on application*

H.2 Change to request to receive an .xml copy of CTA data ○ Yes ◉ No

H.2.1 Do you want a .xml file copy of the CTA form data saved on EudraCT? ○ Yes ◉ No

H.2.1.1 If yes provide the e-mail address(es) to which it should be sent (up to 5 addresses):

H.2.2 Do you want to receive this via password protected link(s)[10]? ○ Yes ◉ No

If you answer no to question H.2.2 the .xml file will be transmitted by less secure e-mail link(s)

H.2.3 Do you want to stop messages to an email for which they were previously requested? ○ Yes ◉ No

H.2.3.1 If yes provide the e-mail address(es) to which feedback should no longer be sent:

(*This will only come into effect from the time at which the request is processed in EudraCT).

(10) This requires a EudraLink account. (See eudract.emea.europa.eu for details)

I LIST OF THE DOCUMENTS APPENDED TO THE NOTIFICATION FORM (cf. Section 3.7 of detailed guidance CT-1)

Please submit only relevant documents and/or when applicable make clear references to the ones already submitted. Make clear references to any changes of separate pages and submit old and new texts. Tick the appropriate box(es).

I.1 Cover letter ☑

I.2 Extract from the amended document in accordance with Section 3.7.c. of detailed guidance CT-1 (if not contained in Part F of this form) ☐

I.3 Entire new version of the document[11] ☐

I.4 Supporting information ☐

I.5 Revised .xml file and copy of initial application form with amended data highlighted ☐

I.6 Comments on any novel aspect of the amendment if any :

(11) Cf. Section 3.7.c. of the detailed guidance CT-1

J SIGNATURE OF THE APPLICANT IN THE MEMBER STATE

Please submit only relevant documents and/or when applicable make clear references to the ones already submitted. Make clear references to any changes of separate pages and submit old and new texts. Tick the appropriate box(es).

J.1 I hereby confirm that/ confirm on behalf of the sponsor that (delete which is not applicable)

- The above information given on this request is correct;
- The trial will be conducted according to the protocol, national regulation and the principles of good clinical practice; and
- It is reasonable for the proposed amendment to be undertaken.

J.2 APPLICANT OF THE REQUEST FOR THE COMPETENT AUTHORITY*(as stated in section D.1):* ☐

J.2.1 Signature [12]: .....

J.2.2 Print name:

J.2.3 Date:

J.3 APPLICANT OF THE REQUEST FOR THE ETHICS COMMITTEE *(as stated in section D.2)***:** ☐

J.3.1 Signature [13]: .....

J.3.2 Print name:

J.3.3 Date:

This section was signed electronically by Mrs Tricia Carver on 29/06/2016 10:32.

Job Title/Post:

Organisation:

Email: tricia.carver@phc.ox.ac.uk

(12) On an application to the Competent Authority only, the applicant to the Competent Authority needs to sign.
(13) On an application to the Ethics Committee only, the applicant to the Ethics Committee needs to sign.

Primary Health Care Archie

From: Rogerson Matt (HEALTH RESEARCH AUTHORITY) <matt.rogerson@nhs.net>
Sent: 12 July 2016 10:19
To: Kay Wang; tma ouh (OXFORD UNIVERSITY HOSPITALS NHS FOUNDATION TRUST); Primary Health Care Archie
Cc: lorna.henderson@oxfordhealth.nhs.uk; amendments hra (HEALTH RESEARCH AUTHORITY)
Subject: FW: IRAS 121769. Confirmation of REC Validation and Categorisation of Amendment
Attachments: 13NW0621_121769_Confirmation_of_opinion.pdf

Dear Dr Wang,

IRAS Project ID:	121769
REC Reference:	13NW0621
Short Study Title:	The early use of Antibiotics in at Risk Children with InfluEnza-ARCHIE
Date complete amendment submission received:	29/06/2016
Amendment No./ Sponsor Ref:	SA11
Amendment Date:	29/06/2016
Amendment Type:	**Substantial**

Thank you for submitting the above referenced amendment. I am pleased to confirm that this amendment has been submitted to the REC for ethical review. Please find attached a copy of the validation letter.

In line with the UK Process for Handling UK Study Amendments I can confirm that this amendment has been categorised as:

- **Category B** - An amendment that has implications for, or affects, SPECIFIC participating NHS organisations

You should now provide this email, together with the amended documentation, to the research management support offices **and** local research teams at your participating NHS organisations in England that are affected by this amendment.

If you have participating NHS organisations in Northern Ireland, Scotland and/or Wales that are affected by this amendment, you should communicate directly with the relevant research teams to prepare them for implementing the amendment, as per the instructions below. You do not need to provide this email or your amended documentation to their research management support offices, as we will pass these to the relevant national coordinating functions who will do this on your behalf.

Subject to the four conditions below, you will be able to implement the amendment at affected participating NHS organisations in England **35 days after you notify them of the amendment**. A template email to notify participating NHS organisations in England is provided here.

Subject to the same four conditions, you will be able to implement your amendment at participating organisations in Northern Ireland, Scotland or Wales on 35 days from the date of receipt of the complete (UK wide) amendment submission.

- You may not implement this amendment until and unless you receive all required regulatory approvals, including REC favourable opinion (for participating organisations in England, this includes receiving confirmation of HRA Approval for the amendment). You should provide regulatory approvals to the research management support offices and local research teams at your participating NHS organisations in England that are affected by this amendment, plus to local research teams at any affected participating NHS organisations in Northern Ireland, Scotland or Wales*.
- You may not implement this amendment at any participating NHS organisations which inform you within the 35 day period that they require additional time to consider the amendment, until they notify you that the considerations have been satisfactorily completed.
- You may not implement this amendment at any participating NHS organisation that informs you that it is no longer able to undertake this study.
- For amendments adding new sites, you may not commence research activities at site until the nation specific processes to allow this are concluded, e.g. NHS Permission in Northern Ireland, Scotland or Wales and Confirmation of capacity and capability in England (if this amendment adds new sites in England, the HRA will shortly provide further information on expectations relating to their formal confirmation of capacity and capability).

Note: you may only implement changes described in the amendment notice or letter.

If you receive required regulatory approvals (for participating organisations in England, this includes receiving confirmation of HRA Approval for the amendment) after the 35 days have passed you may then immediately implement this amendment at all existing participating NHS organisations that have not requested additional review time, or are no longer able to undertake this study. As above, the 35 days does not apply to opening new sites and nation specific processes should be followed.

For existing participating organisations, there is no need for you to receive a letter of confirmation from the participating organisation that the amendment can be implemented, as the intended date of implementation is communicated through the above process. However, you may be able to implement this amendment ahead of the 35 day deadline, if all necessary regulatory approvals are in place and the participating organisation has confirmed that the amendment may be implemented ahead of the 35 day date.

Further to the details above, I can confirm that this amendment will be assessed by the HRA to confirm that it meets the expected criteria and standards. An Assessor from the HRA will contact you and you will receive separate notification that the HRA Assessment is complete. You should not implement this amendment at participating NHS organisations in England until the outcome of the HRA assessment is confirmed and the conditions detailed in the categorisation section above have been met.

Please do not hesitate to contact me if you require further information.

Kind regards

Matt Rogerson | REC Manager

Hampstead REC / Liverpool East REC
Health Research Authority

HRA Centre Manchester
3rd Floor, Barlow House

Minshull Street

Manchester M1 3DZ
E: nrescommittee.london-hampstead@nhs.net

nrescommittee.northwest-liverpooleast@nhs.net

matt.rogerson@nhs.net

T: 02071048127 | www.hra.nhs.uk

IMPORTANT – **Click here** for the latest details of the roll-out of HRA Approval in England

The HRA is keen to know your views on the service you received – our short feedback form is available **here**

Health Research Authority

North West - Liverpool East Research Ethics Committee

Barlow House
3rd Floor
4 Minshull Street
Manchester
M1 3DZ

Telephone: 02071048127

12 July 2016

Ms Heather House
Oxford University NHS Trust
R&D Lead, Research and Development Department, Joint Research Office, Block 60,
Churchill Hospital,
Oxford
Old Road
Headington
OX3 7LE

Dear Ms House

Study title:	**The early use of Antibiotics for at Risk CHildren with InfluEnza in primary care(ARCHIE): a double-blind randomised placebo-controlled trial**
REC reference:	**13/NW/0621**
Protocol number:	**ARCHIE001**
EudraCT number:	**2013-002822-21**
Amendment number:	
Amendment date:	**29 June 2016**
IRAS project ID:	**121769**

Thank you for submitting the above amendment, which was received on 29 June 2016.

Research site	*Principal Investigator / Local Collaborator*
Chelsea and Westminster Hospital NHS Foundation Trust	Dipali Shah
Barking, Havering & Redbridge University Hospital NHS Trust	Kausick Banerjee
Milton Keynes University Hospital NHS Foundation Trust	Lazarus Anguvaa
North Middlesex University Hospital NHS Trust	Neeraj Jain
Countess of Chester Hospital NHS Foundation Trust	John Gibbs
South Tees NHS Trust James Cook University Hospital	Arshid Murad
East Cheshire NHS Trust Macclesfield District Hospital	Surendran Chandrasekaran
St Helens & Knowsley Teaching Hospital NHS Trust	Rosaline Garr
Warrington & Halton Hospital NHS Foundation Trust	Delyth Webb
Northumbria Healthcare NHS Trust North Tyneside General Hospital	Belinda Bateman
Burton Hospitals NHS Foundation Trust Queen's Hospital	Mansoor Ahmed

Tameside Hospital NHS Foundation Trust	Anjali Petkar

The amendment relates solely to the addition of new site(s) and/or investigator(s) within the National Health Service (NHS) or Health and Social Care (HSC) in Northern Ireland. The site-specific assessment for the site(s) will therefore form part of the research governance review. The Site-Specific Information (SSI) Form for the site should be included with the application for R&D approval.

On behalf of the Committee, I am pleased to confirm the extension of the favourable opinion to the new site(s) and/or investigator(s), subject to management permission being given by the relevant NHS/HSC R&D office(s) prior to the study starting at the site.

Statement of compliance

This Committee is recognised by the United Kingdom Ethics Committee Authority under the Medicines for Human Use (Clinical Trials) Regulations 2004, and is authorised to carry out the ethical review of clinical trials of investigational medicinal products.

The Committee is fully compliant with the Regulations as they relate to ethics committees and the conditions and principles of good clinical practice.

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.

13/NW/0621	**Please quote this number on all correspondence**

Yours sincerely

Matt Rogerson
REC Manager

Email: nrescommittee.northwest-liverpooleast@nhs.net

Copy to: *Dr Kay Wang, University of Oxford*

NHS
Health Research Authority

Dr Kay Wang
University of Oxford
Radcliffe Observatory Quarter
Woodstock Road
Oxford
OX2 6GG

Email: hra.approval@nhs.net

01 August 2016

Dear Dr Wang

Letter of HRA Approval for a study processed through pre-HRA Approval systems

Study title:	**The early use of Antibiotics for at Risk CHildren with InfluEnza in primary care(ARCHIE): a double-blind randomised placebo-controlled trial**
IRAS project ID:	**121769**
Sponsor	**Oxford University**

Thank you for your request for HRA Approval to be issued for the above referenced study.

I am pleased to confirm that the study has been given **HRA Approval.** This has been issued on the basis of an existing assessment of regulatory compliance, which has confirmed that the study is compliant with the UK wide standards for research in the NHS.

The extension of HRA Approval to this study on this basis allows the sponsor and participating NHS organisations in England to set-up the study in accordance with HRA Approval processes, with decisions on study set-up being taken on the basis of capacity and capability alone.

If you have submitted an amendment to the HRA between 23 March 2016 and the date of this letter, this letter incorporates the HRA Approval for that amendment, which may be implemented in accordance with the amendment categorisation email (e.g. not prior to REC Favourable Opinion, MHRA Clinical Trial Authorisation etc., as applicable). If the submitted amendment included the addition of a new NHS organisation in England, the addition of the new NHS organisation is also approved and should be set up in accordance with HRA Approval processes (e.g. the organisation should be invited to assess and arrange its capacity and capability to deliver the study and confirm once it is ready to do so).

Participation of NHS Organisations in England

Please note that full information to enable set up of participating NHS organisations in England is not provided in this letter, on the basis that activities to set up these NHS organisations is likely to be underway already.

The sponsor should provide a copy of this letter, together with the local document package and a list of the documents provided, to participating NHS organisations in England that are being set up in accordance with HRA Approval Processes. It is for the sponsor to ensure that any documents provided to participating organisations are the current, approved documents.

For non-commercial studies the local document package should include an appropriate Statement of Activities and HRA Schedule of Events. The sponsor should also provide the template agreement to be used in the study, where the sponsor is using an agreement in addition to the Statement of Activities. Participating NHS organisations in England should be aware that the Statement of Activities and HRA Schedule of Events for this study have not been assessed and validated by the HRA. Any changes that are appropriate to the content of the Statement of Activities and HRA Schedule of Events should be agreed in a pragmatic fashion as part of the process of assessing, arranging and confirming capacity and capability to deliver the study. If subsequent NHS organisations in England are added, an amendment should be submitted to the HRA..

For commercial studies the local document package should include a validated industry costing template and the template agreement to be used with participating NHS organisations in England.

It is critical that you involve both the research management function (e.g. R&D office and, if the study is on the NIHR portfolio, the LCRN) 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.

After HRA Approval

In addition to the document, *"After Ethical Review – guidance for sponsors and investigators"*, issued with your REC Favourable Opinion, 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 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 email the HRA at hra.approval@nhs.net. Additionally, one of our staff would be happy to call and discuss your experience of HRA Approval.

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/.

If you have any queries about the issue of this letter please, in the first instance, see the further information provided in the question and answer document on the HRA website.

Your IRAS project ID is 121769. Please quote this on all correspondence.

Yours sincerely

Kate Radford

Applications Administrator

Email: hra.approval@nhs.net

Copy to: *Ms Heather House, Oxford University NHS Trust*
Dr Lorna Henderson, Oxford Health NHS Foundation Trust