NUFFIELD DEPARTMENT OF PRIMARY CARE HEALTH SCIENCES

Primary Care Clinical Trials Unit • Nuffield Department of Primary Care Health Sciences • University of Oxford • Gibson Building, 1st Floor • Radcliffe Observatory Quarter • Woodstock Road • Oxford OX2 6GG •

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

9 February 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 SA009:

1. New principle investigator for trust sites already participating in the study, table 1
2. New NHS regions for primary care sites, table 2. Individual sites not yet identified.

Many thanks

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

Table 1. New principle investigator for trust sites already participating in the study

Site	New PI
Salisbury NHS Foundation Trust	Dr Katrina Pettit
Stennack Surgery	Dr William Webb

Table 2. New NHS regions for primary care sites

Site_Name
PCT/CCG sites covered by North Thames
PCT/CCG sites covered by South Thames
PCT/CCG sites covered by North West London

Tricia Carver

From: Karen Melham
Sent: 12 February 2016 09:30
To: Tricia Carver
Cc: Ronja Bahadori; Research.Portfolio@ouh.nhs.uk
Subject: Sponsor authorisation for ARCHIE Amendment 9

Dear Tricia,

Thank you for sending for our review the amendment proposed to ARCHIE, to add sites and to change the PI at an existing site.
I can confirm that we as sponsor representative are content for this to be sent to the relevant REC for their review and approval.

Please remember to forward correspondence with the REC 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

The phased roll-out of the HRA approvals process continues, with further studies included since 30th November 2015.
For more information, see: http://www.hra.nhs.uk/about-the-hra/our-plans-and-projects/assessment-approval/
or contact CTRG to discuss how this may affect your work.

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)*

- [x] 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 review bodies are you applying to?

- [ ] HRA Approval
- [x] NHS/HSC Research and Development offices
- [ ] Social Care Research Ethics Committee
- [x] Research Ethics Committee
- [x] 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, the CI must create Site-Specific Information Forms for each site, in addition to the study-wide forms, and transfer them to the PIs or local collaborators.

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

◉ Yes ○ No

5a. Are all the research costs and infrastructure costs for this study provided by an NIHR Biomedical Research Centre, NIHR Biomedical Research Unit, NIHR Collaboration for Leadership in Health Research and Care (CLAHRC) or NIHR Research Centre for Patient Safety & Service Quality in all study sites?

◉ Yes ○ No

If yes and you have selected HRA Approval in question 4 above, your study will be processed through HRA Approval.

If yes, and you have not selected HRA Approval in question 4 above, NHS permission for your study will be processed through the NIHR Coordinated System for gaining NHS Permission (NIHR CSP).

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: 201300282221

B.3 Full title of the trial: The early use of Antibiotics for at Risk CHildren with InfluEnza in

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:	University 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:	
Fax:	01865572228
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	University of Oxford
Given name	Tricia
Family name	Carver
Address	Nuffield Department of Primary Care Health Sciences
Town/city	Radcliffe Observatory Quarter,Woodstock Road
Post code	OX2 6GG
Telephone	01865617842
Fax	01865617939
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_SA009
Version:
Date: 2016/02/09

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:

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	Kay
Middle name(if applicable)	
Family name	Wang
Qualification (MD...)	BA,BM BCh, MA, DRCOG, DCH, MRCGP, DPhil
Professional address	PCT/CCG sites covered by North Thames CRN

Given name	Kay
Middle name(if applicable)	
Family name	Wang
Qualification (MD...)	BA,BM BCh, MA, DRCOG, DCH, MRCGP, DPhil
Professional address	PCT/CCG sites covered by South Thames CRN

Given name	Kay
Middle name(if applicable)	
Family name	Wang
Qualification (MD...)	BA,BM BCh, MA, DRCOG, DCH, MRCGP, DPhil
Professional address	PCT/CCG sites covered by North West London CRN

G.1.2 Removal of an existing site

G.1.2.1 Principal investigator (provide details below)

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

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	Katrina
Middle name(if applicable)	
Family name	Pettit
Qualification (MD...)	MRCPCH; CCT General Paediatrics
Professional address	Salisbury NHS Foundation Trust

G.1.4.6 Indicate the name of the previous principal investigator:
Dr Scott-Jupp

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 12/02/2016 12:22.

Job Title/Post: Senior trial manager

Organisation: Univ of Oxford

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.

NHS
Health Research Authority

North West - Liverpool East Research Ethics Committee
Barlow House
3rd Floor
4 Minshull Street
Manchester
M1 3DZ

Tel: 0207 104 8002

12 February 2016

Tricia Carver
Senior Trial Manager
Nuffield Department of Primary Care Health Sciences
Clinical Trials Unit
Radcliffe Observatory Quarter
Woodstock Road
Oxford, OX2 6GG

Dear Ms Carver,

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:	**SA009**
Amendment date:	**09 February 2016**
IRAS project ID:	**121769**

Thank you for submitting the above amendment, which was received on 12 February 2016.

Research site	*Principal Investigator / Local Collaborator*
PCT/CCG sites covered by North Thames CRN	Kay Wang
PCT/CCG sites covered by South Thames CRN	Kay Wang
PCT/CCG sites covered by North West London CRN	Kay Wang
Salisbury NHS Foundation Trust	Katrina Pettit replaces Dr Scott Jupp

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

Ewa Grzegorska
REC Assistant

Email: nrescommittee.northwest-liverpooleast@nhs.net

Copy to: Dr Kay Wang,
University of Oxford

Ms Heather House,
R&D office, Joint Research Office

Tricia Carver

From: CLRN TV (OXFORD UNIVERSITY HOSPITALS NHS FOUNDATION TRUST) <tvclrn@nhs.net>
Sent: 04 April 2016 14:23
To: Kay Wang
Cc: Tricia Carver; CTRG Sponsorship Correspondence
Subject: FW: NIHR CSP - Ref. 121769 - Amendment can be implemented

Dear Dr Wang,

Re:121769 - The early use of Antibiotics in at Risk Children with InfluEnza-ARCHIE – Amendment: ARCHIE_SA009, 09-02-2016

This amendment has received the necessary regulatory approvals and been reviewed by all participating study sites. It can now be implemented at all sites unless a site has objected and withdrawn NHS Permission.

Please contact us using the contact details below if you require any further information.

Kind regards

Elaine

Elaine Cherry
Research Facilitator
NIHR Clinical Research Network: Thames Valley and South Midlands
Delivering research to make patients, and the NHS, better
tvclrn@nhs.net

****Please note this mailbox is monitored from 8am to 4pm Monday-Friday only****

www.crn.nihr.ac.uk/thamesvalley