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

22 Mar2016

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 SA010:

1. Press release and sponsor acknowledgement
2. Notification of minor amendments:
    a. Wider media (pdf of request and sponsor acknowledgement)
    b. Parent preseason information cover letter (letter and sponsor acknowledgement)

Many thanks

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

Tricia Carver

From: Karen Melham
Sent: 23 March 2016 11:25
To: Tricia Carver
Cc: Research.Portfolio@ouh.nhs.uk
Subject: Sponsor Authorisation for Amendment 10 to ARCHIE Trial

Dear Tricia
Thank you for sending for our review the amendment proposed to the ARCHIE trial to use a press release as part of the promotional material to raise awareness of the study and encourage participation..
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

****Important Changes for Studies Involving the NHS in England ****

The route to seeking approval for studies involving the NHS in England has now changed. Applications are processed centrally through the Health Research Authority (HRA), concurrent with REC review. Please note that some study types are currently exempt. An overview of this new process can be found at:
http://www.highlights.rsc.mrc.ac.uk/HRAapproval/index.html
Please be aware that additional documents will need to be completed as part of the HRA Approval process. CTRG is happy to provide further guidance on these changes, and advise specifically on how they will 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)*

- ☑ 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
- ☑ 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, 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 primary

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_SA010
Version:
Date: 2016/03/22

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:
press release

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:
press release

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)*
NA

New wording:

Comments/ explanation/ reasons for substantial amendment:

The amendment concerns introduction of a press release in order to aid recruitment. This is in keeping with the recruitment/publicity strategy set out in the protocol.

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

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
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 23/03/2016 13:34.

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.

Researchers seek children for study aiming to reduce unnecessary antibiotic use

Researchers at the University of Oxford are looking for children with flu-like illness, who may be at greater risk of developing further complications from flu, to take part in a national study aiming to reduce unnecessary antibiotic use in the community.

For most children, flu is a mild and relatively short illness. However, for those with pre-existing medical conditions such as asthma, diabetes, and cerebral palsy, as well as some children who were born prematurely, flu may lead to more serious complications such as pneumonia and ear infections.

The ARCHIE study, funded by the National Institute for Health Research, is working with a selection of GP surgeries and hospitals across England to see whether early antibiotic treatment may prevent these children from developing further complications from flu.

Lead researcher, Dr Kay Wang, a practising GP and Academic Clinical Lecturer at Oxford University's Nuffield Department of Primary Care Health Sciences, said:

"The flu virus seems to particularly predispose children to bacterial infections, which may make children with flu-like illness even more unwell. We therefore want to find out whether targeting antibiotics specifically at children who we already know are more susceptible to bacterial infections can help prevent further complications and speed up recovery times."

Recent research conducted by Dr Wang and colleagues has shown that children who were born prematurely are around twice as likely to be admitted to hospital after developing flu or flu-like illness. The research also found that children with neurological conditions and diabetes were at greater risk of developing flu-related complications.

"If we find that early antibiotic treatment is effective in these children," continued Dr Wang, "this will help guide more accurate targeting of antibiotics in the community, and help minimise the development of antibiotic resistance due to unnecessary antibiotic prescribing."

"This year, fewer people have been consulting their doctor or nurse with flu-like illness. While this is great news for the NHS and the general public, it has made recruitment for our study rather challenging," added Dr Wang. "However, this year's flu season has also hit slightly later than usual, so we are still very much on the lookout for parents and children who might be interested in joining our study."

The researchers are calling on parents and children interested in taking part in their study to visit their nearest hospital or GP surgery (if they are participating) within the first five days of their child developing flu-like symptoms. Children will be tested to see whether they have the influenza virus and given a five-day course of study medication. Children may also have further optional tests to look at whether using antibiotics in this way may have implications for their effectiveness in treating future infections.

Further details about the study and a list of participating hospitals and GP surgeries can be found at www.archiestudy.com

Notes to editors

Participating GP surgeries and hospitals that are accepting their patients into the ARCHIE study:

South East:

Berkshire	Pangbourne	Boathouse Surgery
Berkshire	Wokingham	Wokingham Medical Centre
Berkshire	Ascot	Ascot Medical Centre
Berkshire	Bracknell	Evergreen Practice
Berkshire	Langley	Langley Health Centre
Berkshire	Crowthorne	New Wokingham Road Surgery
Hampshire	Southsea	Osborne Practice
Hampshire	Southsea	Portsdown Group Practice, Heyward Road Surgery
Hampshire	Winchester	Friarsgate Practice
Hampshire	Waterlooville	Forest End Surgery
Hampshire	Romsey	Abbeywell Surgery, Nightingale site
Hampshire	Cosham	Portsdown Group Practice
Hampshire	Portsmouth	Portsdown Group Practice, Somers Town
Hampshire	Cowplain	Cowplain Family Practice
Oxfordshire	Oxford	John Radcliffe Hospital
Oxfordshire	Wantage	Church Street Practice
Oxfordshire	Bicester	Bicester Health Centre
Oxfordshire	Oxford	South Oxford Health Centre
Oxfordshire	Faringdon	White Horse Medical Practice
Oxfordshire	Witney	Windrush Medical Practice
Oxfordshire	Carterton	Broadshires Health Centre
Oxfordshire	Whitney	Eynsham Medical Centre
Oxfordshire	Shrivenham	Elm Tree Surgery
Surrey	Yateley	Oaklands Practice
West Sussex	Chichester	St. Richard's Hospital
West Sussex	Worthing	Worthing Hospital

South West:

Bristol	Redfield	Wellspring Surgery
Bristol	Nailsea	Brockway Medical Centre
Bristol	Brentry	Bradgate Surgery
Bristol	Brislington	Nightingale Valley Practice, Brooklea Health Centre
Bristol	Westbury-on-Trym	Westbury-on-Trym Primary Care Centre
Bristol	Yatton	Mendip Vale Medical Practice
Cornwall	St. Ives	Stennack Surgery
Cornwall	Torpoint	Rame Medical Ltd
Cornwall	Truro	Royal Cornwall Hospital
Cornwall	Penzance	Alverton Practice
Devon	Plymouth	Stirling Road Surgery
Dorset	Poole	Poole Hospital NHS Foundation Trust
Dorset		Wareham Surgery
Gloucestershire	Cheltenham	Portland Practice, Hatherley branch
Gloucestershire	Cheltenham	Yorkleigh Surgery

North Somerset	Clevedon	Clevedon Medical Centre
Somerset	Yeovil	Yeovil District Hospital NHS Foundation Trust
Somerset	Taunton	Musgrove Park Hospital
Wiltshire	Salisbury	Salisbury NHS Foundation Trust
Wiltshire	Warminster	Avenue Surgery
Wiltshire	Calne	Patford House Surgery, Calne
Wiltshire	Swindon	Hawthorn Medical Centre

Midlands

Derbyshire	Derby	Derby Hospitals NHS Foundation Trust
Derbyshire	Calow	Chesterfield Royal Hospital NHS Foundation Trust
Leicestershire	Leicester	Leicester Royal Infirmary
Leicestershire	Leicester	Saffron Group Practice
Leicestershire	Hinckley	Castle Mead Medical Centre
Northamptonshire	Kingsthorpe	Kingsthorpe Surgery
Northamptonshire	Daventry	Danetre Surgery
Northamptonshire	Corby	Lakeside Healthcare
Nottinghamshire	Nottingham	Nottingham University Hospital NHS Trust
Warwickshire	Coventry	University Hospital of Coventry and Warwickshire

East of England:

Cambridgeshire	March	Cornerstone Practice
Cambridgeshire	Huntingdon	Acorn Surgery
Cambridgeshire	Peterborough	Wansford and Kings Cliffe Practice
Norfolk	Wymondham	Wymondham Medical Practice
Norfolk	Great Yarmouth	Nelson Medical Practice
Norfolk	Mundesley	Mundesley Medical Centre
Norfolk	Norwich	Roundwell Medical Centre
Norfolk	Norwich	Lawson Road Surgery
Norfolk	Norwich	Castle Partnership
Norfolk	Norwich	Norfolk & Norwich University Hospital NHS Foundation Trust
Suffolk	Beccles	Beccles Medical Centre
Suffolk	Ipswich	Ipswich Hospital NHS Trust

North West:

Cheshire	Crewe	Leighton Hospital Mid Cheshire NHS Foundation Trust
Lancashire	Blackburn	East Lancashire Hospitals NHS Trust
Lancaster	Lancashire	Queen Square Medical Practice
Merseyside	Wirral	Wirral University Teaching Hospital
Merseyside	Liverpool	Smithdown Children's Walk In Centre Liverpool

Merseyside	Liverpool	Brownlow Group Practice
Merseyside	Kirkby	Wingate Medical Centre
Merseyside	Liverpool	Alder Hey Children's NHS Foundation Trust Hospital
Merseyside	North Claughton	Claughton Medical Centre
Greater Manchester	Stockport	Stockport NHS Foundation trust
Greater Manchester	Bolton	Royal Bolton Hospital NHS Foundation Trust

North East and Yorkshire

County Durham	Durham	University Hospital of North Durham
Country Durham	Stockton	University Hospital of North Tees
Country Durham	Darlington	Darlington Memorial Hospital
West Yorkshire	Bradford	Bradford Royal Infirmary
South Yorkshire	Sheffield	Sheffield Children's NHS Foundation Trust

About the National Institute for Health Research:
This press release presents independent research funded by the National Institute for Health Research (NIHR) under the Programme Grants for Applied Research programme (RP-PG-1210-12012).
The National Institute for Health Research (NIHR) is funded by the Department of Health to improve the health and wealth of the nation through research. The NIHR is the research arm of the NHS. Since its establishment in April 2006, the NIHR has transformed research in the NHS. It has increased the volume of applied health research for the benefit of patients and the public, driven faster translation of basic science discoveries into tangible benefits for patients and the economy, and developed and supported the people who conduct and contribute to applied health research. The NIHR plays a key role in the Government's strategy for economic growth, attracting investment by the life-sciences industries through its world-class infrastructure for health research. Together, the NIHR people, programmes, centres of excellence and systems represent the most integrated health research system in the world. For further information, visit the NIHR website (www.nihr.ac.uk).

Oxford University's Medical Sciences Division is one of the largest biomedical research centres in Europe, with over 2,500 people involved in research and more than 2,800 students. The University is rated the best in the world for medicine and life sciences, and it is home to the UK's top-ranked medical school. It has one of the largest clinical trial portfolios in the UK and great expertise in taking discoveries from the lab into the clinic. Partnerships with the local NHS Trusts enable patients to benefit from close links between medical research and healthcare delivery.

Within the division, the Nuffield Department of Primary Care Health Sciences undertakes internationally acclaimed teaching and research that improves the primary care that GP practices deliver, and is ranked top in the UK. The department's research covers a broad range of primary care issues including cardiovascular and metabolic disease, health behaviours, infectious disease and child health, patient experience, research methods and evidence-based medicine. www.phc.ox.ac.uk

NUFFIELD DEPARTMENT OF PRIMARY CARE HEALTH SCIENCES

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ARCHIE

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

4 Mar 2016

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

ARCHIE needs to find ways to improve our recruitment and as the target population (children at risk to complication from flu) is a small fraction of patients seen by clinicians they are often missed. We have had some success by empowering parents so they can raise the idea of participating in study when they consult.

We have been considering a way to maximise this approach and would like to ask charities and groups who are in contact with our target population to publicise our study by pointing to our website. From our website they can find out about the study and where participating sites are located.

1. We would like to offer recruiting sites new text wording targeted at parents of children already identified by database search: The ARCHIE study www.archiestudy.com is looking for children with flu to take part this flu season. We want to find out whether using antibiotics within the first 5 days of a flu-like illness may help children recover more quickly and prevent flu-related complications e.g. pneumonia. Call (insert number) if you are interested in taking part.

2. We would like to tweet to organisations involved with the underlying conditions potentially associated with our target participants. We would start with: "@archiestudy is looking for children with flu-like illness "and refresh occasionally with similar short messages.

3. We would like to ask charities and groups who are in contact with our target population to publicise our study by pointing to our website using the appropriate option below:

   a. Advert without link

   The NIHR funded ARCHIE study (www.archiestudy.com)is looking for children with flu to take part this flu season. We want to find out whether using antibiotics within the first 5 days of a flu-like illness may help children recover more quickly and prevent flu-related complications e.g. pneumonia. Call (insert number) if you are interested in taking part.

   b. Web post

   The NIHR funded ARCHIE study (www.archiestudy.com) is looking for children within the first 5 days of a flu-like illness to take part. The study is aiming to find out whether treating certain children with antibiotics early during a flu-like illness might prevent them from becoming more unwell or developing further infections such as chest, throat, ear or sinus infections. Click here to find out more about what taking part would involve.

Many thanks,

Tricia Carver
Senior Trial Manager

Primary Health Care Archie

From: Karl Shepherd
Sent: 23 November 2015 10:18
To: Primary Health Care Archie
Cc: Sharon Tonner
Subject: RE: ARCHIE cover letter

Follow Up Flag: Follow up
Flag Status: Flagged

Dear Tricia,

Thank you for your email. I can confirm that the revised documents have been added to the study folder and also updated on our database here as a minor amendment.

No further action required.

Kind regards
Karl

Mr Karl Shepherd
Clinical Trials & Research Governance | Research Services
University of Oxford
Joint Research Office, Block 60, Churchill Hospital
Oxford ,Headington, OX3 7LE
T: +44 01865 (5)72221 **F:** +44 01865 (5)72228 **E:** Karl.Shepherd@admin.ox.ac.uk www.admin.ox.ac.uk/researchsupport

Linkedin: https://uk.linkedin.com/pub/karl-shepherd/103/961/98a

GCP face to face course dates/types available here: http://www.admin.ox.ac.uk/researchsupport/ctrg/training/gcpoxford/

Online GCP course details/registration available here: http://www.admin.ox.ac.uk/researchsupport/ctrg/training/gcponline/#d.en.121114

From: Primary Health Care Archie
Sent: 20 November 2015 17:24
To: Karl Shepherd
Cc: Sharon Tonner
Subject: ARCHIE cover letter

Dear Karl,
We had to stop using a GP cover letter we recently had approved (PDF attached). A couple parents were distressed as they did not realise their child was in a risk category. This may have been due to poor filtering of records by the GP, but in any event we wish to avoid this in the future. Therefore, we have completely reworded the letter using wording from the patient information leaflet and have removed the wording that alarmed parents (child has a long-term medical condition or disability …) .

We are hoping this new letter can be considered a minor amendment /notification. We wish to use this letter ASAP since the flu season is about to start.
I look forward to your response.

Kind regards,

Tricia

The early use of Antibiotics for at Risk CHildren with InfluEnza in primary care

The ARCHIE study is funded by the National Institute for Health Research's Programme Grants for Applied Research Programme

Nuffield Department of Primary Care Health Sciences
Clinical Trials Unit
Gibson Building, first floor
Radcliffe Observatory Quarter
Woodstock Road
Oxford, OX2 6GG

Direct line: 01865 617 842
FAX: 01865 617 939
Website: www.archiestudy.com
Twitter: @archiestudy

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

24 February 2016

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

ARCHIE needs to find ways to improve our recruitment and as the target population (children at risk to complication from flu) is a small fraction of patients seen by clinicians they are often missed. We have had some success by empowering parents so they can raise the idea of participating in study when they consult.

We have been considering a way to maximise this approach and would like to ask charities and groups who are in contact with our target population to publicise our study by pointing to our website. From our website they can find out about the study and where participating sites are located.

1. We would like to offer recruiting sites new text wording targeted at parents of children already identified by database search: The ARCHIE study www.archiestudy.com is looking for children with flu to take part this flu season. We want to find out whether using antibiotics within the first 5 days of a flu-like illness may help children recover more quickly and prevent flu-related complications e.g. pneumonia. Call (insert number) if you are interested in taking part.

2. We would like to tweet to organisations involved with the underlying conditions potentially associated with our target participants. We would start with: "@archiestudy is looking for children with flu-like illness "and refresh occasionally with similar short messages.

3. We would like to ask charities and groups who are in contact with our target population to publicise our study by pointing to our website using the appropriate option below:

   a. Advert without link

   The ARCHIE study www.archiestudy.com is looking for children with flu to take part this flu season. We want to find out whether using antibiotics within the first 5 days of a flu-like illness may help children recover more quickly and prevent flu-related complications e.g. pneumonia. Call (insert number) if you are interested in taking part.

   b. Web post

   The ARCHIE study (www.archiestudy.com) is looking for children within the first 5 days of a flu-like illness to take part. The study is aiming to find out whether treating certain children with antibiotics early during a flu-like illness might prevent them from becoming more unwell or developing further infections such as chest, throat, ear or sinus infections. Click here to find out more about what taking part would involve.

Many thanks,

Tricia Carver
Senior Trial Manager

North West - Liverpool East Research Ethics Committee

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

Tel: 0207 104 8009

23 March 2016

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

Dear Dr Wang

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:	**ARCHIE_SA010**
Amendment date:	**23 March 2016**
IRAS project ID:	**121769**

The amendment concerns introduction of a press release in order to aid recruitment. This is in keeping with the recruitment/publicity strategy set out in the protocol.

Thank you for submitting the above amendment, which was received on 23 March 2016. I can confirm that this is a valid notice of a substantial amendment and will be reviewed by the Sub-Committee of the REC at its next meeting.

Documents received

The documents to be reviewed are as follows:

Document	*Version*	*Date*
Covering letter on headed paper		22 March 2016
Notice of Substantial Amendment (CTIMP)	ARCHIE_SA 010	23 March 2016
Other [Email from sponsor]		23 March 2016
Other [Study press release]	1	22 March 2016
Other [Covering letter to parent/carer]	2	20 November 2015
Other [Wider Media]		04 March 2016
Other [Sponsor email]		08 March 2016
Other [Sponsor email]		23 November 2015

North West - Liverpool East Research Ethics Committee

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

Tel: 02071048127

26 April 2016

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

Dear Dr Wang

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:	**ARCHIE_SA010**
Amendment date:	**23 March 2016**
IRAS project ID:	**121769**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Covering letter on headed paper		22 March 2016
Notice of Substantial Amendment (CTIMP)	ARCHIE_SA 010	23 March 2016
Other [Email from sponsor]		23 March 2016

Other [Study press release]	1	22 March 2016
Other [Covering letter to parent/carer]	2	20 November 2015
Other [Wider Media]		04 March 2016
Other [Sponsor email]		08 March 2016
Other [Sponsor email]		23 November 2015

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

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.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

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

Yours sincerely

Signed on behalf of
Mrs Glenys Hunt
Chair

E-mail: nrescommittee.northwest-liverpooleast@nhs.net

Enclosures: *List of names and professions of members who took part in the review*

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

North West - Liverpool East Research Ethics Committee

Attendance at Sub-Committee of the REC meeting on 31 March 2016

Committee Members:

Name	*Profession*	*Present*	*Notes*
Professor Neil Pender	Professor of Orthodontics	Yes	
Dr Peter Walton	Lay Member	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Miss Amber Ecclestone	REC Assistant

Notification of the Committee's decision

The Committee will issue an ethical opinion on the amendment within a maximum of 35 days from the date of receipt.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval for the research.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

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

Yours sincerely

Amber Ecclestone
REC Assistant

Email: nrescommittee.northwest-liverpooleast@nhs.net

Copy to: *Dr Lorna Henderson, Oxford Health NHS Foundation Trust*

Ms Heather House, Oxford University NHS Trust

Tricia Carver

From: amendments hra (HEALTH RESEARCH AUTHORITY) <hra.amendments@nhs.net>
Sent: 06 April 2016 09:29
To: Tricia Carver; Kay Wang
Subject: RE: 13/NW/0621 ARCHIE N001 (IRAS 121769. Confirmation of Amendment Categorisation as Category C)

Dear Tricia Carver,

IRAS Project ID:	121769
REC Reference:	13/NW/0621
Short Study Title:	The early use of Antibiotics in at Risk Children with InfluEnza-ARCHIE
Date complete amendment submission received:	31/03/2016
Amendment No./ Sponsor Ref:	10
Amendment Date:	22/03/2016
Amendment Type:	**Substantial**

Thank you for submitting the above referenced amendment. In line with the UK Process for Handling UK Study Amendments I can confirm that this amendment has been categorised as:

Category C - An amendment that has no implications that require management or oversight by the participating NHS organisations

As such, the sponsor may implement this amendment **as soon as any relevant regulatory approvals are in place** (for participating organisations in England, this includes receiving a letter from the HRA Assessment to communicate that you are able to go ahead with the amendment).

As Chief Investigator/Sponsor, it remains your responsibility to ensure that the local research teams (if applicable) at each of your participating organisations are informed of this amendment.

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

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

Kind regards

Laura Greenfield

Laura Greenfield | Amendments Coordinator
Health Research Authority

Research Ethics Service (RES)
HRA, The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS
E: hra.amendments@nhs.net

T: 020 7104 8096
www.hra.nhs.uk

From: Tricia Carver [mailto:tricia.carver@phc.ox.ac.uk]
Sent: 31 March 2016 15:37
To: amendments-april hra (HEALTH RESEARCH AUTHORITY)
Subject: FW: 13/NW/0621 ARCHIE N001

Dear HRA reviewer.
I submitted a substantial amendment to the REC on the 23rd of March , but at that time I was unable to upload documents to the check list for the R&D submission due to formatting compatibility issues. I am now trying to submit to the R&D but as IRAS i/CSP is no longer used I must use the new HRA process, which the REC did not initiate as I submitted to them on the 23rd (last day of old system). Will you be able to provide me with an expedited review of 13/NW/0621 SA 010 as this is for a press release therefor very time sensitive.
Kind regards,
Tricia

From: Tricia Carver
Sent: 23 March 2016 11:46
To: 'LiverpoolEast NRESCommittee.NorthWest- (HEALTH RESEARCH AUTHORITY)' <nrescommittee.northwest-liverpooleast@nhs.net>
Cc: Karl Shepherd <karl.shepherd@admin.ox.ac.uk>; 'TVCLRN@nhs.net' <TVCLRN@nhs.net>; Primary Health Care Archie <archie@phc.ox.ac.uk>
Subject: 13/NW/0621 ARCHIE N001

Please find attached documents relating to a substantial amendment ARCHIE SA010 for the approval of a press release to add recruitment as influenza is in circulation at an unusual time and we need to act fast to raise awareness. I have also included recent minor amendment notifications.
The sponsor and lead R+D are copied in for their reference.

Kind regards,

Tricia Carver
Senior Trial Manager / Programme Manager

The early use of Antibiotics for at Risk CHildren with InfluEnza in primary care
The ARCHIE study is funded by the National Institute for Health Research's Programme Grants for Applied Research Programme
Nuffield Department of Primary Care Health Sciences
Clinical Trials Unit
Gibson Building
Radcliffe Observatory Quarter
Woodstock Road
Oxford, OX2 6GG

Direct line: 01865 617 842
FAX: 01865 617 939
Website: www.archiestudy.com
Twitter: @archiestudy

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Oxford University Hospitals NHS
NHS Trust

FP/SG/8801

Research & Development Department
Joint Research Office
Block 60
Churchill Hospital
Oxford
OX3 7LE

Stephanie.gilham@ouh.nhs.uk
Tel: 01865 223590
Fax: 01865 572242

27th April 2016

Dr Shelley Segal
Oxford Children's Hospital
Level 2 CHOX
John Radcliffe Hospital
Headley Way
Headington
Oxford
OX3 9DU

Dear **Dr Segal,**

Re: The early use of Antibiotics for at Risk CHildren with InfluEnza in primary care (ARCHIE): a doubleblind randomised placebo controlled trial

R&D Ref: 8801
REC Ref: 13/NW/0621
CSP No: 121769
EudraCT No: 2013-002822-21

Amendment Ref: Substantial Amendment 10

- Addition of press release to promotional material used for recruitment.

Thank you for submitting your protocol amendment to Oxford University Hospitals NHS Trust Research and Development office for approval.

I can confirm Trust Management Approval and Indemnity for the protocol amendment as described in your application. The documents approved are as listed in the Ethics Approval Letter date: **26th April 2016.**

This approval is subject to the formal approval by Ethics and, where appropriate, the MHRA remaining in place.

Trust Management Approval and Indemnity is dependent upon completion of satisfactory compliance with Trust policies and all regulatory requirements for the conduct of clinical research.

Please can I ask that you respond to this letter with current recruitment figures for this study for the OUH site. Regular updates on recruitment figures should be sent to our generic email address at ResearchRecruitment@ouh.nhs.uk

Yours sincerely

Fiona Parker
Research Support Services Manager