



The University of
Nottingham

UNITED KINGDOM • CHINA • MALAYSIA

School of Clinical Sciences
Division of Stroke

Clinical Sciences Building
City Hospital Campus
Hucknall Road
Nottingham
NG5 1PB

t: +44 (0)115 823 1765

f: +44 (0)115 823 1767

Direct Dial: 0115 8230287
www.nottingham.ac.uk/scs/divisions/stroke

Head of Department:
Professor P M W Bath

2 August 2013

Dr L A Ruben
Chair of South East Research Ethics Committee
South East Coast Strategic Health Authority
Preston Hall
Aylesford
Kent
ME20 7NJ

Your reference:	08/H1102/112
Eudract Number:	2007-006749-42
Protocol No:	31350 & 08093 V1.4 Protocol 26/02/2013

Dear Dr Ruben and colleagues

Trial Title: Triple Antiplatelets for Reducing Dependency after Ischaemic Stroke

Please find enclosed a substantial amendment for the above trial to add new centres. We look forward to receiving your approval letter.

Yours sincerely

Sally Utton
TARDIS Trial Manager

Encs: SA03/13

cc: RGS, University of Nottingham

Substantial Amendment Notification Form (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*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: Ethics committee registration number of the trial :	Withdrawal of amendment application ☐ 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:	UK
A.2 Notification for authorisation to the competent authority:	☐ yes
A.3 Notification for an opinion to the ethics committee:	☐ yes

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	☐ no
B.1.1 If yes repeat this section as necessary.	

B.2 Eudract number: 2007-006749-42

B.3 Full title of the trial : Safety and efficacy of intensive versus guideline antiplatelet therapy in high risk patients with recent ischaemic stroke or transient ischaemic attack (TIA): a randomised controlled trial
Sponsor's protocol code number, version, and date: 31350 and 08093 TARDIS Protocol V1.4 26/02/13

C IDENTIFICATION OF THE SPONSOR RESPONSIBLE FOR THE REQUEST

C.1 Sponsor
C.1.1 Organisation: University of Nottingham
C.1.2 Name of person to contact: Mr Paul Cartledge
C.1.3 Address : Head of Research Grants and Contracts, University of Nottingham, Research Innovation Services, King's Meadow Campus, Lenton Lane, Nottingham NG7 2NR
C.1.4 Telephone number : 0115 951 5679
C.1.5 Fax number : 0115 951 3633
C.1.6 e-mail: paul.cartledge@nottingham.ac.uk

C.2 Legal representative³ of the sponsor in the European Union for the purpose of this trial (if different from the sponsor)
C.2.1 Organisation:
C.2.2 Name of person to contact:
C.2.3 Address :
C.2.4 Telephone number :
C.2.5 Fax number :

¹ OJ, C82, 30.3.2010, p. 1; hereinafter referred to as 'detailed guidance CT-1'.

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

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

C.2.6 e-mail:

D APPLICANT IDENTIFICATION (please tick the appropriate box)

D.1 Request for the competent authority	
D.1.1 Sponsor	YES
D.1.2 Legal representative of the sponsor	☐
D.1.3 Person or organisation authorised by the sponsor to make the application.	YES
D.1.4 Complete below:	
D.1.4.1 Organisation : University of Nottingham	
D.1.4.2 Name of person to contact : Sally Utton	
D.1.4.3 Address : Division of Stroke, Clinical Sciences Building, City Hospital Campus, Hucknall Road, Nottingham NG5 1PB	
D.1.4.4 Telephone number : 0115 823 0287	
D.1.4.5 Fax number : 0115 823 1771	
D.1.4.6 E-mail : Sally.utton@nottingham.ac.uk	

D.2 Request for the Ethics Committee	
D.2.1 Sponsor	YES
D.2.2 Legal representative of the sponsor	☐
D.2.3 Person or organisation authorised by the sponsor to make the application.	YES
D.2.4 Investigator in charge of the application if applicable ⁴ :	
• Co-ordinating investigator (for multicentre trial)	YES
• Principal investigator (for single centre trial):	☐
D.2.5 Complete below	
D.2.5.1 Organisation : University of Nottingham	
D.2.5.2 Name : Mrs Sally Utton	
D.2.5.3 Address : Clinical Sciences Building, Div of Stroke, c/o Nottingham City Hospital, Hucknall Rd, Nottingham NG5 1PB	
D.2.5.4 Telephone number : 0115 823 0287	
D.2.5.5 Fax number : 0115 823 1771	
D.2.6 E-mail : sally.utton@nottingham.ac.uk	

E SUBSTANTIAL AMENDMENT IDENTIFICATION

E.1 Sponsor's substantial amendment code number, version, date for the clinical trial concerned: (SA03/13)
--

E.2 Type of substantial amendment	
E.2.1 Amendment to information in the CT application form	no
E.2.2 Amendment to the protocol	no ☐
E.2.3 Amendment to other documents appended to the initial application form	no ☐
E.2.3.1 If yes specify:	
E.2.4 Amendment to other documents or information:	no ☐
E.2.4.1 If yes specify:	
E.2.5 This amendment concerns mainly urgent safety measures already implemented ⁵	no ☐
E.2.6 This amendment is to notify a temporary halt of the trial ⁶	no ☐
E.2.7 This amendment is to request the restart of the trial ⁷	no ☐

⁴ According to national legislation.

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

E.4 Information on temporary halt of trial⁸ N/A		
E.4.1	Date of temporary halt (YYYY/MM/DD)	
E.4.2	Recruitment has been stopped	no ☐
E.4.3	Treatment has been stopped	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 (free text): - Justification for a temporary halt of the trial - The proposed management of patients receiving treatment at time of the halt (<i>free text</i>). The consequences of the temporary halt for the evaluation of the results and for overall risk benefit assessment of the investigational medicinal product (<i>free text</i>).	

F DESCRIPTION OF EACH SUBSTANTIAL AMENDMENT⁹ (*free text*):

Previous and new wording in track change modus	New wording	Comments/explanation/reasons for substantial amendment
Update centres and Principal Investigators		

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

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

G.1	Type of change
G.1.1	Addition of a new site
G.1.1.1	Principal investigator (provide details below)
G.1.1.1.1	Given name Robert
G.1.1.1.2	Middle name (if applicable)
G.1.1.1.3	Family name Luda
G.1.1.1.4	Qualifications (MD.....) MD
Professional address: North Middlesex University Hospital NHS Trust, Sterling Way, London, London N18 1QX	
G.1.2	Addition of a new site
G.1.2.1	Principal investigator (provide details below)
G.1.2.1.1	Given name Olivia
G.1.2.1.2	Middle name (if applicable)
G.1.2.1.3	Family name Geraghty
G.1.2.1.4	Qualifications (MD.....) MD
Professional address. Imperial Healthcare NHS Trust, Charing Cross Hospital, Fulham Palace Road, London, W6 8RF	
G.1.2.2	Principal investigator (provide details below)
G.1.2.2.1	Given name John
G.1.2.2.2	Middle name (if applicable)
G.1.2.2.3	Family name Corrigan
G.1.2.2.4	Qualifications (MD.....) MD
Professional address. Western Health and Social Care Trust, Altnagelvin Area Hospital Site, Glenshane Road, Londonderry, BT47 6SB	
G.1.2.3	Principal investigator (provide details below)
G.1.2.3.1	Given name Toby
G.1.2.3.2	Middle name (if applicable)
G.1.2.3.3	Family name Black
G.1.2.3.4	Qualifications (MD.....) MD
Professional address. Salisbury NHS Foundation Trust, Salisbury District Hospital, Odstock Road, Salisbury, Wiltshire SP2 8BJ	
G.1.2.4	Principal investigator (provide details below)
G.1.2.4.1	Given name Imtiaz
G.1.2.4.2	Middle name (if applicable)
G.1.2.4.3	Family name Shah
G.1.2.4.4	Qualifications (MD.....) MD
Professional address. NHS Ayrshire & Arran, Covers University Hospital of Ayr and University Hospital of Crosshouse, NHS Ayrshire & Arran, University Hospital Crosshouse, Kilmarnock, KA2 0BE	
G.1.2.5	Principal investigator (provide details below)
G.1.2.5.1	Given name Anthony
G.1.2.5.2	Middle name (if applicable)
G.1.2.5.3	Family name Kenton
G.1.2.5.4	Qualifications (MD.....) MD
Professional address. University Hospitals Coventry & Warwickshire, Dept of Neurology, Clifford Bridge Road, Coventry, CV2 2DX	
G.1.2.6	Principal investigator (provide details below)
G.1.2.6.1	Given name Brigitte
G.1.2.6.2	Middle name (if applicable)
G.1.2.6.3	Family name Yip

G.1.2.6.4 Qualifications (MD.....) MD
Professional address. NHS Lanarkshire, Hairmyres Hospital, Eaglesham Road, East Kilbride, G75 8RG

G.1.2.7 **Principal investigator** (provide details below)

G.1.2.7.1 Given name Habib

G.1.2.7.2 Middle name (if applicable)

G.1.2.7.3 Family name Rehman

G.1.2.7.4 Qualifications (MD.....) MD

Professional address. Royal Albert Edward Infirmary, Wroughtington, Wigan & Leigh NHS Foundation Trust, Wigan Lane, Wigan, WN1 2NN

G.1.3 **Removal of an existing site**

G.1.3.1 **Principal investigator** (provide details below)

G.1.3.1.1 Given name

G.1.3.1.2 Middle name (if applicable)

G.1.3.1.3 Family name

G.1.3.1.4 Qualifications (MD.....) MD

G.1.3.1.5 Professional address

G.1.3.1.6

G.1.4 **Change of co-ordinating investigator** (provide details below of the new coordinating investigator)

G.1.4.1 Given name

G.1.4.2 Middle name

G.1.4.3 Family name

G.1.4.4 Qualification (MD.....)

Professional address

G.1.4.5 Indicate the name of the previous co-ordinating investigator

G.1.5 **Change of principal investigator at an existing site** (provide details below of the new principal investigator)

G.1.5.1 Given name

G.1.5.2 Middle name

G.1.5.3 Family name

G.1.5.4 Qualification (MD.....) MD

Professional address

G.1.5.5 Indicate the name of the previous co-ordinating 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 ☐ no

H.2.1 Do you want a .xml file copy of the CTA form data saved on EudraCT? ☐ 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).

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

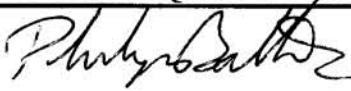
Please submit only relevant documents and/or when applicable make clear references to the ones already submitted. Make clear references to any changes of separate pages and submit old and new texts. Tick the appropriate box(es).

I.1 Cover letter	YES
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 document¹¹	☐
I.4 Supporting information	☐
I.5 Revised .xml file and copy of initial application form with amended data highlighted	no
I.6 Comments on any novel aspect of the amendment if any	

J SIGNATURE OF THE APPLICANT IN THE MEMBER STATE

J.1	I hereby confirm on behalf of the sponsor that • 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): NO
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): YES
J.3.1	Signature ¹³ : 
J.3.2	Print name: PHILIP BANN
J.3.3	Date : 6/8/13

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

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.