

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 : <input type="checkbox"/> Date :
Date of start of procedure:	Authorisation/ positive opinion : <input type="checkbox"/> Date :
Competent authority registration number of the trial: Ethics committee registration number of the trial :	Withdrawal of amendment application <input type="checkbox"/> 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:		<input type="checkbox"/> yes
A.3 Notification for an opinion to the ethics committee:		<input type="checkbox"/> 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	<input type="checkbox"/> 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	<input type="checkbox"/>
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	<input type="checkbox"/>
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):	<input type="checkbox"/>
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: (SA01/13)

E.2 Type of substantial amendment

E.2.1 Amendment to information in the CT application form	YES
E.2.2 Amendment to the protocol	YES <input type="checkbox"/>
E.2.3 Amendment to other documents appended to the initial application form	no <input type="checkbox"/>
E.2.3.1 If yes specify:	
E.2.4 Amendment to other documents or information:	no <input type="checkbox"/>
E.2.4.1 If yes specify:	
E.2.5 This amendment concerns mainly urgent safety measures already implemented ⁵	no <input type="checkbox"/>
E.2.6 This amendment is to notify a temporary halt of the trial ⁶	no <input type="checkbox"/>
E.2.7 This amendment is to request the restart of the trial ⁷	no <input type="checkbox"/>

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 <input type="checkbox"/>
E.3.2	Changes in interpretation of scientific documents/value of the trial	no <input type="checkbox"/>
E.3.3	Changes in quality of IMP(s)	no <input type="checkbox"/>
E.3.4	Changes in conduct or management of the trial	no <input type="checkbox"/>
E.3.5	Change or addition of principal investigator(s), co-ordinating investigator	YES <input type="checkbox"/>
E.3.6	Change/addition of site(s)	YES <input type="checkbox"/>
E.3.7	Other change	no <input type="checkbox"/>
E.3.7.1	If yes, specify:	
E.3.8	Other case	Yes
E.3.8.1	If yes, specify	
		Update to protocol

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 <input type="checkbox"/>
E.4.3	Treatment has been stopped	no <input type="checkbox"/>
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):	
	<ul style="list-style-type: none"> 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 to protocol, v1.4	See attached separate document	See attached separate document
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

<p>G.1 Type of change</p> <p>G.1.1 Addition of a new site</p> <p>G.1.1.1 Principal investigator (provide details below)</p> <p>G.1.1.1.1 Given name Partha</p> <p>G.1.1.1.2 Middle name (if applicable)</p> <p>G.1.1.1.3 Family name Das</p> <p>G.1.1.1.4 Qualifications (MD.....) MD</p> <p>Professional address: Burton Hospitals NHS Trust, Queens Hospital, Belvedere Road</p> <p>G.1.2 Addition of a new site</p> <p>G.1.2.1 Principal investigator (provide details below)</p> <p>G.1.2.1.1 Given name Matthew</p> <p>G.1.2.1.2 Middle name (if applicable)</p> <p>G.1.2.1.3 Family name Smith</p> <p>G.1.2.1.4 Qualifications (MD.....) MD</p> <p>Professional address. Airedale NHS Foundation Trust, Ward 5, Stroke Unit, Airedale General Hospital, Steeton, Keighley, W Yorks BD20 6TD</p> <p>G.1.2.2 Principal investigator (provide details below)</p> <p>G.1.2.2.1 Given name Anthony</p> <p>G.1.2.2.2 Middle name (if applicable)</p> <p>G.1.2.2.3 Family name Oke</p> <p>G.1.2.2.4 Qualifications (MD.....) MD</p> <p>Professional address. Mid Staffordshire NHS Foundation Trust, Cannock Chase Hospital/Stafford Hospital, WS11 5XY/ST16 3SA</p> <p>G.1.2.3 Principal investigator (provide details below)</p> <p>G.1.2.3.1 Given name Ken</p> <p>G.1.2.3.2 Middle name (if applicable)</p> <p>G.1.2.3.3 Family name Fotherby</p> <p>G.1.2.3.4 Qualifications (MD.....) MD</p> <p>Professional address. The Royal Wolverhampton Hospital NHS Trust, New Cross Hospital, Wednesfield Road, Wolverhampton WV10 0QP</p> <p>G.1.2.4 Principal investigator (provide details below)</p> <p>G.1.2.4.1 Given name Moe</p> <p>G.1.2.4.2 Middle name (if applicable)</p> <p>G.1.2.4.3 Family name Sein</p> <p>G.1.2.4.4 Qualifications (MD.....) MD</p> <p>Professional address. Macclesfield District General Hospital, Victoria Road, Macclesfield, Cheshire SK10 3BL</p> <p>G.1.2.5 Principal investigator (provide details below)</p> <p>G.1.2.5.1 Given name Sunil</p> <p>G.1.2.5.2 Middle name (if applicable)</p> <p>G.1.2.5.3 Family name Herath</p> <p>G.1.2.5.4 Qualifications (MD.....) MD</p> <p>Professional address. Royal Albert Edward Infirmary, Wrightington, Wigan & Leigh NHS Foundation Trust, Wigan Lane, Wigan WN1 2NN</p> <p>G.1.2.6 Principal investigator (provide details below)</p> <p>G.1.2.6.1 Given name Ed</p> <p>G.1.2.6.2 Middle name (if applicable)</p> <p>G.1.2.6.3 Family name Gamble</p> <p>G.1.2.6.4 Qualifications (MD.....) MD</p> <p>Professional address. F15, University of South Manchester NHS Foundation Trust, Wythenshaw Hospital,</p>

Southmoor Road, Wythenshawe, Manchester M23 9LT

G.1.2.7 Principal investigator (provide details below)

G.1.2.7.1 Given name Colin

G.1.2.7.2 Middle name (if applicable)

G.1.2.7.3 Family name Jenkins

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

Professional address. Wye Valley NHS Trust, The County Hospital, Union Walk, Hereford, HR1 2ER

G.1.2.8 Principal investigator (provide details below)

G.1.2.8.1 Given name Robert

G.1.2.8.2 Middle name (if applicable)

G.1.2.8.3 Family name Namushi

G.1.2.8.4 Qualifications (MD.....) MD

Professional address. Pennine Acute Hospital NHS Trust, Fairfield General Hospital, Rochdale Road, Bury, Greater Manchester BL9 7TD

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 Ravi

G.1.4.2 Middle name

G.1.4.3 Family name Rangasamy

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

Professional address Basildon University Hospital, Nether mayne, Basildon, Essex, SS16 5NL

G.1.4.5 Indicate the name of the previous co-ordinating investigator: Dr Udayaraj Umasankar

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)	<input type="checkbox"/>
I.3 Entire new version of the document¹¹	<input type="checkbox"/>
I.4 Supporting information	<input type="checkbox"/>
I.5 Revised .xml file and copy of initial application form with amended data highlighted	YES
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 <ul style="list-style-type: none">• 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.
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J.2 APPLICANT OF THE REQUEST FOR THE COMPETENT AUTHORITY (as stated in section D.1): YES
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:
J.3.3 Date :

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.