

**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 COMMUNITY**

*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:	Withdrawal of amendment application <input type="checkbox"/> Date:
Ethics committee registration number of the trial:	

*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**

<b>A.1 Member State in which the substantial amendment is being submitted:</b>	<b>UK</b>
<b>A.2 Notification for authorisation to the competent authority:</b>	<input type="checkbox"/>
<b>A.3 Notification for an opinion to the ethics committee:</b>	<input checked="" type="checkbox"/>
<b>A.4 Notification for information only<sup>1</sup>:</b>	<input type="checkbox"/>
<b>A.4.1 To the competent authority</b>	<input checked="" type="checkbox"/>
<b>A.4.2 To the Ethics committee</b>	<input type="checkbox"/>

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

<b>B.1 Does the substantial amendment concern several trials involving the same IMP?</b>	yes <input type="checkbox"/> no <input checked="" type="checkbox"/>
B.1.1 If yes repeat this section as necessary.	

<b>B.2 EudraCT number:</b>	<b>2006-002827-18</b>
<b>B.3 Full title of the trial :</b> with cervical arterial dissection	Feasibility of a therapeutic trial in patients
<b>B.4 Sponsor's protocol code number, version, and date:</b>	<b>Ref No: 04/Q0803/215, 7, 2nd Oct 2007</b>

**C IDENTIFICATION OF THE SPONSOR RESPONSIBLE FOR THE REQUEST**

<b>C.1 Sponsor</b>	
C.1.1 Organisation:	St George's, University of London
C.1.2 Name of person to contact:	Dr Paul Craven
C.1.3 Address :	Cranmer Terrace, London, SW17 0RE
C.1.4 Telephone number :	020 8725 5013
C.1.5 Fax number :	020 8725 0794
C.1.6 e-mail:	pcraven@sgul.ac.uk

<sup>1</sup> For substantial amendments to information that only the CA has previously assessed (e.g. quality data in most of the MS), the sponsor should not only submit the amendment to the CA but also inform the ethics committee that they have made the notification indicating that it is "for information only". Similarly, the sponsor should inform the CA of any notification of a substantial amendment to information which was previously only assessed by the ethics committee (e.g. facilities for the trial).

**C.2 Legal representative<sup>2</sup> of the sponsor in the Community 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 :  
C.2.6 e-mail:

**D APPLICANT IDENTIFICATION, (please tick the appropriate box)**

**D.1 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:  
D.1.4.1 Organisation :  
D.1.4.2 Name of person to contact :  
D.1.5 Address :  
  
D.1.5.1 Telephone number :  
D.1.5.2 Fax number :  
D.1.5.3 E-mail

**D.2 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<sup>3</sup>:  
    • Co-ordinating investigator (for multicentre trial)   
    • Principal investigator (for single centre trial):   
D.2.5 Complete below  
D.2.5.1 Organisation : St George's, University of London  
D.2.5.2 Name : Professor John Norris  
D.2.5.3 Address : Clinical Neurosciences  
Jenner Wing  
Cranmer Terrace  
London SW17 0RE  
D.2.5.4 Telephone number : 020 8266 6468  
D.2.5.5 Fax number : 020 8725 2950  
D.2.6 E-mail : carotid@btopenworld.com

**E SUBSTANTIAL AMENDMENT IDENTIFICATION**

**E.1 Sponsor's substantial amendment code number, version, date for the clinical trial concerned: Ref**  
No: 04/Q0803/215, 7, 2nd Oct 2007

<sup>2</sup> As stated in Article 19 of Directive 2001/20/EC.

<sup>3</sup> According to national legislation.

<b>E.2 Type of substantial amendment</b>		
E.2.1	<b>Amendment to information in the CT application form</b>	yes <input type="checkbox"/> no <input checked="" type="checkbox"/>
E.2.2	<b>Amendment to the protocol</b>	yes <input type="checkbox"/> no <input checked="" type="checkbox"/>
E.2.3	<b>Amendment to other documents appended to the initial application form</b>	yes <input type="checkbox"/> no <input checked="" type="checkbox"/>
E.2.3.1	If yes specify:	
E.2.4	<b>Amendment to other documents or information:</b>	yes <input type="checkbox"/> no <input checked="" type="checkbox"/>
E.2.4.1	If yes specify:	
E.2.5	<b>This amendment concerns mainly urgent safety measures already implemented</b>	yes <input type="checkbox"/> no <input checked="" type="checkbox"/>
E.2.6	<b>This amendment is to notify a temporary halt of the trial</b>	yes <input type="checkbox"/> no <input checked="" type="checkbox"/>
E.2.7	<b>This amendment is to request the restart of the trial</b>	yes <input type="checkbox"/> no <input checked="" type="checkbox"/>

<b>E.3 Reasons for the substantial amendment:</b>		
E.3.1	<b>Changes in safety or integrity of trial subjects</b>	yes <input type="checkbox"/> no <input checked="" type="checkbox"/>
E.3.2	<b>Changes in interpretation of scientific documents/value of the trial</b>	yes <input type="checkbox"/> no <input checked="" type="checkbox"/>
E.3.3	<b>Changes in quality of IMP(s)</b>	yes <input type="checkbox"/> no <input checked="" type="checkbox"/>
E.3.4	<b>Changes in conduct or management of the trial</b>	yes <input type="checkbox"/> no <input checked="" type="checkbox"/>
E.3.5	<b>Change or addition of principal investigator(s), co-ordinating investigator</b>	yes <input checked="" type="checkbox"/> no <input type="checkbox"/>
E.3.6	<b>Change of sponsor, legal representative, applicant</b>	yes <input type="checkbox"/> no <input checked="" type="checkbox"/>
E.3.7	<b>Change/addition of site(s)</b>	yes <input type="checkbox"/> no <input checked="" type="checkbox"/>
E.3.8	<b>Change in transfer of major trial related duties</b>	yes <input type="checkbox"/> no <input checked="" type="checkbox"/>
E.3.8.1	If yes, specify:	
E.3.9	<b>Other change</b>	yes <input type="checkbox"/> no <input checked="" type="checkbox"/>
E.3.9.1	If yes, specify:	
E.3.10	<b>Other case</b>	yes <input type="checkbox"/> no <input checked="" type="checkbox"/>
E.3.10.1	If yes, specify	

<b>E.4 Information on temporary halt of trial</b>		
E.4.1	<b>Date of temporary halt</b> (YYYY/MM/DD)	
E.4.2	<b>Recruitment has been stopped</b>	yes <input type="checkbox"/> no <input checked="" type="checkbox"/>
E.4.3	<b>Treatment has been stopped</b>	yes <input type="checkbox"/> no <input checked="" 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	<b>What is (are) the reason(s) for the temporary halt?</b>	
E.4.5.1	Safety	yes <input type="checkbox"/> no <input checked="" type="checkbox"/>
E.4.5.2	Lack of efficacy	yes <input type="checkbox"/> no <input checked="" type="checkbox"/>
E.4.5.3	Other	yes <input type="checkbox"/> no <input checked="" type="checkbox"/>
E.4.5.3.1	If yes to other, specify :	
E.4.6	<b>Briefly describe (free text):</b>	
	<ul style="list-style-type: none"> <li>• Justification for a temporary halt of the trial</li> <li>• The proposed management of patients receiving treatment at time of the halt (<i>free text</i>):</li> <li>• 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>):</li> </ul>	

**F REASONS FOR SUBSTANTIAL AMENDMENT** (*one or two sentences*):

**A new chief investigator has been appointed for the CADISS study.**

**G BRIEF DESCRIPTION OF THE CHANGES** (*free text*):

**Professor Hugh Markus will be the new chief investigator for CADISS. Professor Hugh Markus will replace Professor John Norris.**

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

**H.1 Type of change**

**H.1.1 Addition of a new site**

**H.1.1.1 Principal investigator** (provide details below)

H.1.1.1.1 Given name

H.1.1.1.2 Middle name (if applicable)

H.1.1.1.3 Family name

H.1.1.1.4 Qualifications (MD.....)

H.1.1.1.5 Professional address

**H.1.2 Removal of an existing site**

**H.1.2.1 Principal investigator** (provide details below)

H.1.2.1.1 Given name

H.1.2.1.2 Middle name (if applicable)

H.1.2.1.3 Family name

H.1.2.1.4 Qualifications (MD.....)

H.1.2.1.5 Professional address

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

H.1.3.1 Given name

Hugh

H.1.3.2 Middle name

S

H.1.3.3 Family name

Markus

H.1.3.4 Qualification (MD.....)

MRCP, DM, FRCP

H.1.3.5 Professional address

Centre for Clinical Neurosciences

St George's, University of London

Cranmer Terrace

London SW17 0RE

H.1.3.6 Indicate the name of the previous co-ordinating investigator: Professor John Norris

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

H.1.4.1 Given name

H.1.4.2 Middle name

H.1.4.3 Family name

H.1.4.4 Qualifications (MD.....)

H.1.4.5 Professional address

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



**K SIGNATURE OF THE APPLICANT IN THE MEMBER STATE**

- K.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.

**K.2 APPLICANT OF THE REQUEST FOR THE COMPETENT AUTHORITY**(as stated in section C.1):

- K.2.1 Signature <sup>5</sup>:  
K.2.2 Print name :  
K.2.3 Date :

**K.3 APPLICANT OF THE REQUEST FOR THE ETHICS COMMITTEE** (as stated in section C.2):

- K.3.1 Signature <sup>6</sup>:  
K.3.2 Print name:  
K.3.3 Date :

<sup>5</sup> On an application to the Competent Authority only, the applicant to the Competent Authority needs to sign.

<sup>6</sup> On an application to the Ethics Committee only, the applicant to the Ethics Committee needs to sign.

**K SIGNATURE OF THE APPLICANT IN THE MEMBER STATE**

**K.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.

**K.2 APPLICANT OF THE REQUEST FOR THE COMPETENT AUTHORITY**(as stated in section C.1):

K.2.1 Signature <sup>5</sup>:

K.2.2 Print name :

K.2.3 Date :

**K.3 APPLICANT OF THE REQUEST FOR THE ETHICS COMMITTEE** (as stated in section C.2):

K.3.1 Signature <sup>6</sup>: *[Handwritten Signature]*

K.3.2 Print name: *PAUL CRAVEN*

K.3.3 Date: *19/12/08*

<sup>5</sup> On an application to the Competent Authority only, the applicant to the Competent Authority needs to sign.  
<sup>6</sup> On an application to the Ethics Committee only, the applicant to the Ethics Committee needs to sign.