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:	
A.2 Notification for authorisation to the competent authority:	☐
A.3 Notification for an opinion to the ethics committee:	☐

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.1.1 If yes repeat this section as necessary.	

B.2 Eudract number:
B.3 Full title of the trial :
B.4 Sponsor's protocol code number, version, and date:

C IDENTIFICATION OF THE SPONSOR RESPONSIBLE FOR THE REQUEST

C.1 Sponsor	
C.1.1	Organisation:
C.1.2	Name of person to contact:
C.1.3	Address :
C.1.4	Telephone number :
C.1.5	Fax number :
C.1.6	e-mail:

C.2 Legal representative[3] **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 :
C.2.6	e-mail:

D APPLICANT IDENTIFICATION (please tick the appropriate box)

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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.

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.1.4.3	Address :	
D.1.4.4	Telephone number :	
D.1.4.5	Fax number :	
D.1.4.6	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[4]:	
	• Co-ordinating investigator (for multicentre trial)	☐
	• Principal investigator (for single centre trial):	☐
D.2.5	Complete below	
D.2.5.1	Organisation :	
D.2.5.2	Name :	
D.2.5.3	Address :	
D.2.5.4	Telephone number :	
D.2.5.5	Fax number :	
D.2.6	E-mail :	

E SUBSTANTIAL AMENDMENT IDENTIFICATION

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

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 ☐
E.2.3.1	If yes specify:	
E.2.4	**Amendment to other documents or information:**	yes ☐ no ☐
E.2.4.1	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 ☐

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**	**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** (YYYY/MM/DD)	
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 (free text)**:	

- Justification for a temporary halt of the trial
- 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)*.

F DESCRIPTION OF EACH SUBSTANTIAL AMENDMENT[9] *(free text)*:

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

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
G.1.1.1.2	Middle name (if applicable)
G.1.1.1.3	Family name
G.1.1.1.4	Qualifications (MD……..)
G.1.1.1.5	Professional address
G.1.2	**Removal of an existing site**
G.1.2.1	**Principal investigator** (provide details below)
G.1.2.1.1	Given name
G.1.2.1.2	Middle name (if applicable)
G.1.2.1.3	Family name
G.1.2.1.4	Qualifications (MD……..)
G.1.2.1.5	Professional address
G.1.3	**Change of co-ordinating investigator** (provide details below of the new coordinating investigator)
G.1.3.1	Given name
G.1.3.2	Middle name
G.1.3.3	Family name

[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.1.3.4 Qualification (MD…….)
G.1.3.5 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)
G.1.4.1 Given name
G.1.4.2 Middle name
G.1.4.3 Family name
G.1.4.4 Qualifications (MD……..)
G.1.4.5 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).	

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 :	

J SIGNATURE OF THE APPLICANT IN THE MEMBER STATE

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):☐

[10] This requires a EudraLink account. (See https://eudract.ema.europa.eu/ for details)
[11] Cf. Section 3.7.c. of the detailed guidance CT-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 :

[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.