Annex 2: Notification of Amendment Form

REQUEST FOR AUTHORISATION OF A SUBSTANTIAL AMENDMENT TO A CLINICAL TRIAL ON A MEDICINAL PRODUCT FOR HUMAN USE TO THE COMPETENT AUTHORITIES AND FOR THE OPINION OF THE ETHICS COMMITTEES IN THE COMMUNITY

For official use:

Date of receiving the request:	Grounds for non acceptance / negative opinion: yes ❑ no ❑ If yes, date:
Date of start of the procedure in the CA:	Authorisation / positive opinion: yes ❑ no ❑ Date :
Competent authority/Ethics committee registration number of the trial :	

To be filled in by the applicant:
This form is common for request for authorisation from the Competent Authority and for the opinion from an Ethics Committee. Please indicate the relevant purpose in a box.

Member State in which the amendment is being submitted: UK

REQUEST FOR AUTHORISATION TO THE COMPETENT AUTHORITY: ☐

REQUEST FOR OPINION OF THE ETHICS COMMITTEE: ☒

NOTIFICATION FOR INFORMATION ONLY:

- to the competent authority ☒
- to the Ethics committee ☐

A 1. TRIAL IDENTIFICATION (When the amendment concerns more than one trial, repeat this form as necessary.)

EudraCT number: 2004-000991-15

Full title of the Trial:

ASCEND: A Study of Cardiovascular Events in Diabetes. A randomised 2x2 factorial study of aspirin versus placebo, and of omega-3 fatty acid supplementation versus placebo, for primary prevention of cardiovascular events in people with diabetes.

Sponsor's protocol code number :	Version	Date (yyyy-mm-dd):
CTSUASCEND1	7	2004-05-19

REQUEST FOR AUTHORISATION OF A SUBSTANTIAL AMENDMENT

A 2. AMENDMENT IDENTIFICATION :

Amendment to 'protocol'	☒	If checked specify sponsor's amendment code number, version and date
Sponsor's protocol amendment code number :	Version	Date (yyyy-mm-dd) :
CTSUASCEND1-1	**7**	**2004-05-19**

Amendment to 'initial request for authorisation'	☐	If checked specify sponsor's amendment code number, version and date
Sponsor's request amendment code number :	Version	Date (yyyy-mm-dd) :

REQUEST FOR AUTHORISATION OF A SUBSTANTIAL AMENDMENT

B. IDENTIFICATION OF THE SPONSOR RESPONSIBLE FOR THE REQUEST

B 1. Sponsor

Organisation:	University of Oxford	
Name of person to contact -	Given name :	Jane
Name of person to contact	Middle name :	Margaret
Name of person to contact -	Family name :	Armitage
Street address :	Clinical Trial Service Unit, Harkness Building Radcliffe Infirmary	
Town / city :	Oxford	
Post code : OX2 6HE	Country : UK	
Telephone number :		01865 404888
Fax number :		01865 404871
e-mail:		Jane.armitage@ctsu.ox.ac.uk

B 2. Legal representative [1] of the sponsor in the Community for the purpose of this trial (if different from the sponsor)

Organisation:		
Name of person to contact -	Given name :	
Name of person to contact -	Middle name :	
Name of person to contact -	Family name :	
Street address :		
Town / city :		
Post code :	Country :	
Telephone number :		
Fax number :		
e-mail:		

[1] as stated in article 19 of Directive 2001/20/EC

REQUEST FOR AUTHORISATION OF A SUBSTANTIAL AMENDMENT

C. APPLICANT IDENTIFICATION, (please tick the appropriate box)

C1. Request for the competent authority ☐
- Sponsor : ☐ - Legal representative of the sponsor ☐ - Person or organisation authorised by the sponsor to make the application**.** In that case, complete below: ☐

C2. Request for the Ethics Committee ☐
- Sponsor : ☒ - Legal representative of the sponsor ☐ - Person or organisation authorised by the sponsor to make the application**.** In that case, complete below: ☐
In the case of the investigator in charge of the application, complete on next page.

Organisation:	
Name of person to contact Given name :	
Name of person to contact Middle name :	
Name of person to contact Family name :	
Street address:	
Town / city :	
Post Code:	
Telephone number:	
Fax number:	
e-mail:	

Organisation:	University of Oxford
Name of person to contact Given name :	Jane
Name of person to contact Middle name :	Margaret
Name of person to contact Family name :	Armitage
Street address:	Clinical Trial Service Unit, Harkness Building Radcliffe Infirmary
Town / city :	Oxford
Post Code:	OX2 6HE
Telephone number:	01865 404888
Fax number:	01865 404871
e-mail:	jane.armitage@ctsu.ox.ac.uk

REQUEST FOR AUTHORISATION OF A SUBSTANTIAL AMENDMENT

- Investigator in charge of the application:
- Coordinating investigator (for multicentre trial) : ☐
- Principal investigator (for multicentre trial) : ☒

In the case of the Investigator, complete below

Name:	Dr Jane Armitage
Street address:	Clinical Trial Service Unit Harkness Building Radcliffe Infirmary
Town / city :	Oxford
Post Code:	OX2 6HE
Telephone number:	01865 404888
Fax number:	01865 404871
e-mail:	jane.armitage@ctsu.ox.ac.uk

D. TYPE OF AMENDMENT (please tick the appropriate box)

This amendment concerns mainly urgent safety measures already implemented: ☐ yes ☒ no

Reasons for the amendment:

Changes in safety or integrity of trial subjects: ☐ yes ☒ no
Changes in interpretation of scientific documents / value of the trial: ☐ yes ☒ no

Changes in quality of IMP(s): ☐ yes ☒ no

Changes in conduct or management of the trial:
Change or addition of site, principal investigator(s), co-ordinating investigator: ☐ yes ☒ no
Change of sponsor, legal representative, applicant ☐ yes ☒ no
Change in transfer of major trial related duties ☐ yes ☒ no

If yes, specify:

Other change: ☒ yes ☐ no

If yes, specify

Addition of a request for an optional urine sample during the 2 month pre-randomisation Run-in, and a urine sample collection at least once during follow-up in a random sample of participants.

Other case: ☐ yes ☒ no

If yes, specify:

Content of the amendment:
an amendment to information in the application form : ☐ yes ☒ no
an amendment to the protocol ☒ yes ☐ no
an amendment to other appended documents ☒ yes ☐ no

If yes, specify:

Changes required to Information leaflet and Consent Form for blood and urine sampling (see attached).

Other case : ☐ yes ☐ no

If yes, specify:

REQUEST FOR AUTHORISATION OF A SUBSTANTIAL AMENDMENT

E. REASON FOR AMENDMENT (one or two sentences) :

Measurement of urinary albumin to creatinine ratio will allow more precise stratification of participants by baseline cardiovascular risk, since urinary microalbuminuria is an important predictor of risk. Long-term storage of urine samples may allow future analyses of new or emerging biochemical risk factors for diabetes.

F. BRIEF DESCRIPTION OF THE CHANGES :

Addition of a request for an optional urine sample during the pre-randomisation Run-in period, and for urine to be assessed at least once during follow-up on a random sample of participants.

REQUEST FOR AUTHORISATION OF A SUBSTANTIAL AMENDMENT

G: LIST OF THE DOCUMENTS APPENDED TO THE NOTIFICATION FORM :

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).

- ☒ **Covering letter stating the type of amendment and the reason(s)**
- ☒ **Summary of the proposed amendment**
- ☒ **List of modified documents (identity, version, date)**
- ☒ **If applicable, pages with previous and new wording**
- ☐ **Supportive information**
- ☐ **When applicable, revised XML file and copy of initial application form with amended data highlighted**

I. SIGNATURE OF THE APPLICANT IN THE MEMBER STATE :

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
- it is reasonable for the proposed amendment to be undertaken.

APPLICANT of the request for the competent authority (as stated in section C1): Date: Signature: Print Name:	APPLICANT of the request for the Ethics Committee (as stated in section C2): Date: Signature: Print Name: