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### Amendments to Healthcare Research

**SOP Reference:** JRCO/SOP/006  
**Version Number:** 6.0  
**Effective Date:** 18/02/15  
**Review by:** 18/02/17  
**Author:** Becky Ward, Research Governance Manager  
**Approved by:** Gary Roper  
**Date:** 18/02/15

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<td>03/07/2006</td>
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1. **PURPOSE**

This SOP describes the procedure for making amendments, both substantial and minor, to the National Research Ethics Service (NRES) and the Medicines and Healthcare products Regulatory Agency (MHRA).

2. **INTRODUCTION**

Please note that this amendment SOP gives generic amendment advice. For further specific advice on amendments for studies that are adopted to the NIHR Portfolio and processed via the CSP system, please also refer to JRCO SOP 033.

For further specific advice on amendments for CTIMP (drug studies) please also refer to JRCO SOP 008.

Amendments are changes made to a research study after a favourable ethical opinion or approval by a regulatory body has been given. They can be made to a protocol, other essential documentation or other aspects of a study's arrangements. All research protocols should have a clear version number and date in order to maintain accurate records and audit trails. Any amendment to a research protocol should have a concordant amendment to the date and version number.

An amendment to a research project can be either **substantial** or **minor (non-substantial)** in nature.

2.1 **Substantial Amendment**

A Substantial Amendment can be defined as an amendment to the protocol or any other supporting documentation that is likely to affect to a significant degree:

1. The safety or physical or mental integrity of the subjects of the trial;
2. The scientific value of the trial;
3. The conduct or management of the trial; or
4. The quality or safety of any investigational medicinal product used in the trial.

All substantial amendments should be notified to the Research Ethics Committee that gave a favourable opinion (the REC) using a notice of substantial amendment (see section 3.1).

Examples of substantial amendments include:

1. Amendments related to the protocol:
   - Purpose of trial
   - Design of trial
   - Recruitment procedure
   - Measures of efficacy
   - Schedule of samples
   - Addition or deletion of tests or measures
   - Number of participants
   - Age range of participants
   - Inclusion criteria
   - Exclusion criteria
   - Safety monitoring
   - Duration of exposure to the investigational medicinal product(s)
Change of dose of the investigational medicinal product(s)
Change of comparator

2. Amendments to Other Study Documentation:
   - Participant information sheet
   - Consent form
   - Questionnaires
   - Letters of invitation
   - GP Letters or other clinicians
   - Information sheets for relatives or carers
   - IMP Dossier

3. Amendments related to the trial arrangements:
   - Change of the principal investigator at a trial site in a CTIMP
   - Change of the coordinating investigator
   - Inclusion of a new trial site (not listed in the original application) in a CTIMP *
   - Change of sponsor or legal representative
   - Change of the definition of the end of the trial
   - Change in IMP supplier
   *Addition of a new site should be sent to the MHRA as a substantial amendment but for NOTIFICATION ONLY.

2.2 Minor (‘Non-Substantial’) Amendments.

A minor amendment can be defined as a change to the details of a study which will have no significant implications for participants or for the conduct, management or scientific value of the study.

Examples of minor amendments include:
- Correction of typographical errors in the study documentation
- Minor clarifications to the protocol;
- Changes to the research team (apart from changes to Chief Investigator or Principal Investigator);
- Changes in funding arrangements;
- Changes in the documentation used by the research team for recording study data (i.e. Case Report Forms);
- Changes in the logistical arrangements for storing or transporting samples;
- Inclusion of new sites and investigators in non-CTIMP studies

3. PROCEDURES

If an amendment is required for a study, the Chief Investigator must first determine whether the amendment is substantial or non-substantial. Once a decision has been made on the nature of the amendment, the following procedures should be followed, depending on whether it is substantial or minor. Please note, the procedure will also differ according to whether the study is a Clinical Trial of an Investigational Medicinal Product (CTIMP) (including gene therapy) or other healthcare research. If your study is sponsored by Imperial College AHSC, you should send your amendment to the Joint Research Compliance Office, prior to submission to ethics, for sponsor approval.

If you are unsure how an amendment should be classified, you can seek advice from the Joint Research Compliance Office (JRCO).

3.1 Reporting of Substantial Amendments
Substantial amendments require a favourable opinion from the REC and/or the MHRA before they can be implemented. The only exception to this is where urgent safety measures need to be taken. Further information is detailed in section 3.6.

### 3.1.1 CTIMPS (Clinical Trials of Investigational Medicinal Products)

A substantial amendment to a CTIMP must be reported both to the Medicines and Healthcare products Regulatory Agency (MHRA) and the NHS REC which approved the study before the amendment is actioned.

The EU Notification of Substantial Amendment Form must be used to notify both the MHRA and the relevant NHS REC. This form is available in IRAS or may be obtained via EudraCT (see Appendix 1 or access https://eudract.ema.europa.eu/docs/forms/Substantial_Amendments.doc) The form structure is protected and only permits responses in the appropriate boxes.

The Substantial Amendment Form should be submitted by the chief investigator, or another person or organisation authorised by the Sponsor. The Chief Investigator should send a copy to the JRCO for projects in which Imperial College Academic Health Science Centre (AHSC) is the sponsor.

The Substantial Amendments Form should summarise the change(s) and briefly explain the reasons in each case. It is important that the form is completed using language comprehensible to a lay person.

Other documents required in the submission are:
- Description of the amendment
- Reasons for the proposed amendment
- Copy of the proposed changes to the protocol or any other documents demonstrating both the previous and new wording.
- Supporting data for the amendment, including any change to the risk benefit analysis

Please submit the changes to the documentation both in tracked change and clear version format. Where the modified documents (for example, the study protocol) are lengthy and the changes are not so widespread or significant as to justify a new version, it is acceptable for extracts to be provided or for the changes to be listed in a separate document.

The chief investigator may also include other supporting information, such as a summary of trial data, an updated safety analysis or a report from a trial monitoring committee. Where the amendment could significantly affect the scientific value of the research, further evidence of scientific and/or statistical review should be provided.

Further information can be found in the Submitting a CTA application to the MHRA.

### 3.1.2 MHRA Device Studies

MHRA Devices must be notified of all proposed changes to the investigation (not just those classed as substantial amendments for the purposes of ethical review) and the researcher Chief Investigator must wait for a letter of no objection from MHRA Devices before any changes are implemented. This includes any changes requested by the
REC. Failure to provide this notification could result in the manufacturer being liable to prosecution.

When notifying the MHRA of any changes, the following information should be provided in writing:

- MHRA reference number for the trial
- Details of the proposed change(s) to the clinical investigation plan or the design of the device
- Reason for the change
- A signed statement from or on behalf of the manufacturer that the proposed changes will not present any foreseeable risks to the patient, user or third party

Notifications should be sent directly to MHRA devices. For further details, please see: http://www.mhra.gov.uk/Howweregulate/Devices/Clinicaltrials/index.htm

3.1.3 All Other Research (Non-CTIMPS)

For all other research (which is not a CTIMP), the Chief Investigator for the study should complete a substantial amendment form for ethics, which can be generated from the IRAS application (see Appendix 2).

For studies submitted using the old NRES application form, you must now create a basic dataset in IRAS based on the information in your original application in the old NRES application form. You can use this basic dataset to generate a Notice of Substantial Amendment from IRAS.

The substantial amendment form should be submitted to the NHS Research Ethics Committee which gave a favourable opinion to the research (the REC), along with any updated documents, such as consent forms or protocols. Amendments cannot currently be electronically submitted to the REC through IRAS and must be emailed directly to the REC. A copy must also be sent to the JRCO if Imperial College AHSC is the research Sponsor.

3.1.5 Notifying amendments to ARSAC

ARSAC should be notified for information of any changes to the administration of radioactive materials during a study, such as:

- Dose changes
- New modalities
- New classes of study participant

These changes will normally meet the criteria for notifying substantial amendments to the. Please provide ARSAC with a copy of the Notice of Substantial Amendment when this is submitted to the REC, together with any supporting documentation (e.g. protocol, patient information sheets).

With a multi-site study, it is not necessary for the ARSAC certificate holder to notify ARSAC; the ARSAC certificate holder at the lead site or the trial co-ordinator can provide a single notification. ARSAC will contact certificate holders if further information is require and/or the changes could affect existing certification.
3.2 Reporting of Minor Amendments

Minor study amendments do not need to be reported to or approved by the REC and/or the MHRA. However, it is best practice to update the REC and the MHRA (for CTIMPs) with the minor amendments to your study by e-mail, and copy in the JRCO.

A CI can make a non-substantial amendment at any time but must keep records of these amendments.

3.3 REC procedures for reviewing substantial amendments

The co-ordinator of the REC will write confirming whether or not the notice of amendment is valid for review, normally within five working days of receipt.

Amendments may be reviewed either at a meeting of the REC subcommittee, or at a meeting of the full committee.

The REC will issue an ethical opinion on the amendment within a maximum of 35 days from the date of receipt of a valid notice of amendment. A copy will be sent to the sponsor and the MHRA.

Where an unfavourable opinion is given, the applicant may submit a modified amendment. The REC will give an opinion on a modified amendment within 14 days of receipt.

3.4 MHRA procedures for reviewing substantial amendments

Upon receipt of the Notification of Amendment form, the MHRA will review the amendment and should issue an opinion on the amendment within a maximum of 35 days from the receipt of a valid form. However, if the MHRA is over-burdened, the opinion may be delayed to beyond the 35 day deadline as set out in the Medicine for Human Use (Clinical Trials) Regulations 2004. The MHRA state in their acknowledgement letter that “It is the Authority’s intention within 35 days of the date of receipt of the request, to notify you, where appropriate, by either setting out the grounds for not accepting the proposed amendment of accepting the application for amendment with or without conditions. If you are not sent either notice then the amendment can be made.” However, although the MHRA state this on their standard letter, it would be prudent to wait for their approval.

3.5 Urgent Safety Measures

There must be arrangements for taking appropriate urgent safety measures to protect participants against any immediate hazard where new events relating to the conduct of the trial or the development of the IMP are likely to affect the safety of the subjects. In many studies, the individual best able to take these measures will be the Chief Investigator or another identified person or organisation – rather than the Sponsor directly. The protocol should identify the specific individual(s) who accept(s) this responsibility. Otherwise, the Sponsor remains directly responsible.

These safety measures, such as temporarily halting the trial, may be taken without prior authorisation from the MHRA but must be reported to the MHRA, Ethics Committee and sponsor. For all other substantial amendments, MHRA authorisation must be sought before the amendment is implemented.
4. **JRCO APPROVAL OF AMENDMENTS**

Please note that if your study is sponsored by Imperial College Academic Health Science Centre, then you must send a copy of the REC approval letter of the amendment, with any supporting documentation approved by the REC, to the Joint Research Compliance Office. JRCO will need to assess the amendment for any implications (e.g. regarding funding, contracts or imaging).

If your study is taking place on Imperial College Healthcare NHS Trust premises, or involves Imperial College Healthcare NHS Trust participants, then you must also obtain Trust R&D approval for your study, **prior** to the amendment being implemented (please see JRCO/SOP/032 ‘Trust Approval of Amendments to Healthcare Research’).

5. **REFERENCES**

http://www.hra.nhs.uk/

Submitting a CTA application to the MHRA SOP, ref: JRCO/SOP/008
## 6. APPENDICES

### 6.1 Substantial amendment form for CTIMP

**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 trial1)***

### 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

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<th>Authorisation/ positive opinion:</th>
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<td>Date:</td>
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<table>
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<tr>
<th>Competent authority registration number of the trial:</th>
<th>Withdrawal of amendment application</th>
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<tbody>
<tr>
<td>Ethics committee registration number of the trial:</td>
<td>Date:</td>
</tr>
</tbody>
</table>

*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?**
  - 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:**

---

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.
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)

<table>
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<tr>
<th>C.2.1</th>
<th>Organisation:</th>
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<tr>
<td>C.2.2</td>
<td>Name of person to contact:</td>
</tr>
<tr>
<td>C.2.3</td>
<td>Address:</td>
</tr>
<tr>
<td>C.2.4</td>
<td>Telephone number:</td>
</tr>
<tr>
<td>C.2.5</td>
<td>Fax number:</td>
</tr>
<tr>
<td>C.2.6</td>
<td>e-mail:</td>
</tr>
</tbody>
</table>

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.1.4.3 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

---
\(^3\) As stated in Article 19 of Directive 2001/20/EC.
\(^4\) According to national legislation.

SOP Ref: JRCO/SOP/006
Final v7.0 18/02/15
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<td>Amendment to the protocol</td>
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<td>Amendment to other documents appended to the initial application form</td>
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</tr>
<tr>
<td>E.2.3.1</td>
<td>If yes specify:</td>
<td></td>
</tr>
<tr>
<td>E.2.4</td>
<td>Amendment to other documents or information:</td>
<td>yes ☐ no ☐</td>
</tr>
<tr>
<td>E.2.4.1</td>
<td>If yes specify:</td>
<td></td>
</tr>
<tr>
<td>E.2.5</td>
<td>This amendment concerns mainly urgent safety measures already implemented(^5)</td>
<td>yes ☐ no ☐</td>
</tr>
<tr>
<td>E.2.6</td>
<td>This amendment is to notify a temporary halt of the trial(^6)</td>
<td>yes ☐ no</td>
</tr>
<tr>
<td>E.2.7</td>
<td>This amendment is to request the restart of the trial(^7)</td>
<td>yes ☐ no</td>
</tr>
</tbody>
</table>

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\(^5\) 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.3.8.1 If yes, specify: | yes □ no □ |

### E.4 Information on temporary halt of trial

| 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

<table>
<thead>
<tr>
<th>Previous and new wording in track change modus</th>
<th>New wording</th>
<th>Comments/explanation/reasons for substantial amendment</th>
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</thead>
</table>

### 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

**Principal investigator** (provide details below)

- **G.1.1.1** Given name
- **G.1.1.2** Middle name (if applicable)
- **G.1.1.3** Family name
- **G.1.1.4** Qualifications (MD……..)
- **G.1.1.5** Professional address

## G.1.2 Removal of an existing site

**Principal investigator** (provide details below)

- **G.1.2.1** Given name
- **G.1.2.2** Middle name (if applicable)
- **G.1.2.3** Family name
- **G.1.2.4** Qualifications (MD……..)
- **G.1.2.5** 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
- **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***

<table>
<thead>
<tr>
<th>H.2 Change to request to receive an .xml copy of CTA data</th>
<th>□ yes □ no</th>
</tr>
</thead>
<tbody>
<tr>
<td>H.2.1 Do you want a .xml file copy of the CTA form data saved on EudraCT?</td>
<td>□ yes □ no</td>
</tr>
</tbody>
</table>

- **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 APPENED 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).*

---

$^{10}$ This requires a EudraLink account. (See [https://eudract.ema.europa.eu/](https://eudract.ema.europa.eu/) for details)
## 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

- [ ]

## 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):

#### J.2.1 Signature  

#### 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  

#### 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.

SOP Ref: JRCO/SOP/006

Final v7.0 18/02/15

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6.2 Appendix 2 – IRAS Substantial Amendment Form for non CTIMP

**NOTICE OF SUBSTANTIAL AMENDMENT**

Please use this form to notify the main REC of substantial amendments to an existing ethics/risk clinical trial of investigational medicinal products (CTIMPs). For CTIMPs, please use the European Commission notice of substantial amendment form at [link to European Commission notice of substantial amendment form](#).

The form should be completed by the Principal Investigator and any associate investigator in a legible manner. Supportive information should be sought from the study sponsor before the amendment is submitted.

<table>
<thead>
<tr>
<th>Details of Chief Investigator:</th>
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<tbody>
<tr>
<td><strong>Title</strong></td>
</tr>
<tr>
<td>Work Address</td>
</tr>
<tr>
<td>PostCode</td>
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<table>
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<tr>
<th>Full title of study:</th>
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<table>
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<th>Lead sponsor:</th>
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<th>Name of REC:</th>
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<th>REC reference number:</th>
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<tr>
<th>Name of lead M&amp;O office:</th>
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<table>
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<tr>
<th>Date study commenced:</th>
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<table>
<thead>
<tr>
<th>Protocol reference (if applicable): current version and date:</th>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Amendment number and date:</th>
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</thead>
</table>

**Type of amendment:**

(a) Amendment to information previously given in IRAS

- [ ] Yes
- [ ] No

If yes, please refer to relevant sections of IRAS in the “summary of changes” below.

(b) Amendment to the protocol

- [ ] Yes
- [ ] No
Online Form

If any, please submit either the revised protocol with a new version number and date, highlighting changes in bold, or a document listing the changes and giving both the previous and revised text.

(a) Amend any information sheet(s) and consent form(s) for participants, or to any other supporting documentation for the study.

☐ Yes  ☐ No

If yes, please submit all revised documents with new version numbers and dates, highlighting revised text in bold.

Is this a modified version of an amendment previously notified and not approved?

☐ Yes  ☐ No

If yes, please explain the modifications made under "Summary of changes" below.

Summary of changes

Briefly summarise the main changes proposed in this amendment. Explain the purpose of the changes and their significance for the study.

If the amendment significantly alters the research design or methodology, or could otherwise affect the scientific value of the study, supporting scientific information should be given, or enclosed separately. Indicate whether or not additional scientific review has been obtained.

Any other relevant information

Applicants may indicate any specific issues related to the amendment, on which the opinion of a reviewing body is sought.

List of enclosed documents

<table>
<thead>
<tr>
<th>Document</th>
<th>Version</th>
<th>Date</th>
</tr>
</thead>
</table>

Declaration by Chief Investigator

☐ I confirm that the information in this form is accurate to the best of my knowledge and I take full responsibility for it.

☐ I confirm that the study sponsor has been notified of the proposed amendment.

☐ I consider that it would be reasonable for the proposed amendment to be implemented.

Date of submission: ____________________________