

Title: Amendments	
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Approver: University Research Ethics Committee	

### Document History

Version	Description of update	Date Effective
1.0	Slight change the HRA amendments email address; addition of 'non-notifiable' amendments, i.e. those that do not need regulatory approvals before implementing; changes to numbering given insertion of additional text; addition of related link with regard to section 3.10.	06/03/2020
2.0	Amendments made to sections 3.3, 3.7 and 3.13 following the implementation of a new online amendments tool on the IRAS system. Typographical changes and minor amendments made.	04/06/2020 (approved by University Research Ethics Committee 29/07/2020)

## 1. Scope

1.1 This Standard Operating Procedure (SOP) has been written in order to support students, Postgraduate Researchers and Academics who are undertaking a project with Bournemouth University (BU) as Sponsor, in identifying which approvals are required for their study amendments, and how to apply for them.

1.2 Staff will be required to obtain approval for substantial or non-substantial amendments in line with the HRA's guidance, in addition to applying for Research Ethics Committee (REC) approval, if required. Applicants will be required as standard to notify Research Development & Support (RDS) via the Research Ethics email so that the Head of RDS can sign-off the documentation.

## 2. Responsibilities

The *Chief Investigator (CI)/Researcher* or delegated individual is responsible for requesting authorisation of all amendments from the Sponsor prior to applying for the necessary approvals and notifying participating sites of the amendment. At BU the CI is (one of) the supervisory member of staff or Academic (*the Researcher*) undertaking the research.

The *Clinical Governance Advisor (CGA)*, on behalf of the Sponsor, is responsible for advising students, staff and Postgraduate Researchers on how to submit their amendments for approval and the necessary actions following this.

### 3. Procedure

#### Classification of Amendments by REC

3.1 Amendments are classified as substantial or non-substantial.

#### Substantial amendments – Definition and Procedure

3.2 A substantial amendment is defined as a change to the protocol or other essential documentation such as the participant information sheet or informed consent form, that is likely to affect to a significant degree:

- The safety, physical or mental integrity of the participants.
- The scientific value of the study.
- The conduct or management of the study
- The quality or safety of any investigational medicinal product (IMP) used

Examples of substantial amendments can be found on the HRA website

(<https://www.hra.nhs.uk/approvals-amendments/amending-approval/examples-of-substantial-and-non-substantial-amendments/>)

3.3 In order to make a substantial amendment to a study, the amendment should be signed off by the Sponsor after creating and submitting an amendment using the Amendment Tool on IRAS. Contact the study Chief Investigator to sign off the amendment. The Head of RDS should be contacted electronically and sent the Amendment Tool (excel file), to sign off the amendment on behalf of the Sponsor.

Once the form has been generated, click 'lock for submission' and then save the PDF copy generated. This file should then be submitted online. Further guidance is available on the [IRAS website](#).

3.4 The REC will validate the amendment and then categorise it. They will then send a validation letter which is when participating sites should be notified of the amendment and its category, and should be sent the amended documentation (if applicable) by the CI/Researcher. Remember to copy the CGA into correspondence.

According to the REC categorisation (IRAS, 2018):

**Category A** amendments have implications for, or affect, *all* participating NHS/HSC organisations hosting the research project (e.g. an addition of a blood test).

**Category B** amendments have implications for, or affect, *specific* participating NHS/HSC organisations hosting the research project (e.g. the change in PI at *one* site).

**Category C** amendments have *no implications* that require management or oversight by the participating NHS/HSC organisations hosting the research project. However the amendment should still be submitted for information (e.g. appointment of a new CI).

If the site takes less than 35 days, they can implement the amendment prior to the deadline. Additionally, sites may request longer to review the amendment and its implications.

3.5 The REC will review the amendment and issue one of the following outcomes –

**Unfavourable opinion** – the amendment will need to be re-visited and re-submitted.

**Favourable opinion no further review from HRA required** – this should be sent to participating sites (both research team and R&D). The site has 35 days to object to category A and B amendments. Category C amendments can be implemented immediately.

**Favourable opinion further assessment needed** – applicants will receive an email following further evaluation, after this then the notification to participating sites should take place.

The HRA coordinates REC approvals and will likewise issue their approval for the substantial amendment<sup>1</sup>.

#### Non-Substantial Amendments – Definition and Procedure

3.6 Non-substantial amendments are usually administrative changes to documents or minor changes such as changes in the CI's research team, or inclusion of new sites/changes in PIs at any participating sites (both for non-CTIMPs).

3.7 In order to submit a non-substantial amendment, use the [IRAS Amendment Tool](#), and send it the CGA and Head of RDS for Sponsor sign-off. The amendment will then be submitted online via the Amendment Tool. The team will not send a validation email but they will send a categorisation email –

- HRA Approval for the amendment confirmed
- HRA Approval for the amendment pending

In both cases, the CI/Researcher should communicate the above outcome to their participating sites' research teams and R&D, along with the amendment form and amended documentation (if applicable), copying in the CGA.

As above, sites have 35 days to object to category A and B amendments, category C amendments can be implemented straightaway. If the site takes less than 35 days, they can implement the amendment prior to the deadline. Additionally, sites may request longer to review the amendment and its implications as long as they do so before the 35 days has ended.

3.8 Where HRA review is required, they will review the amendment and issue approval. This should then be sent to participating sites with the final approved documents. Some Trust R&Ds will issue an agreement letter; which should then be filed in the Trial Master File

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<sup>1</sup> Please note, as of June 2018, HRA approval is now HRA and Health and Care Research Wales (HCRW) approval

(TMF). Under HRA procedure, R&D *does not* need to send agreement letters to the Sponsor, due to the 35 day deadline procedure, but some may choose to.

The Sponsor (CGA), alongside the CI/Researcher must ensure that no amendment is implemented at any participating site prior to final approvals, the confirmation from R&D or after the 35 day deadline.

#### Amendments that do not require notification

3.9 Where a study has not received HRA approval, rather NHS REC approval only, non-substantial amendments do not need to be notified to the REC. The Sponsor, at their discretion, may choose to forward the amendment for the REC's information. The amendment should still be reported to the Clinical Governance Advisor for auditing purposes.

3.10 Some activities undertaken during a project do not need to be submitted as amendments for review and categorisation. These include:

1. Addition of translated versions of participant facing documentation.
2. Where there has been a routine review or renewal process during the study with an outcome that does not change the research project. For example:
  - Where a Data Monitoring Committee meeting concludes a study should proceed without any changes.
  - Where insurance is renewed but there is no change to the level or breadth of cover.
  - Annual updates and reviews of study documentation that do not make any changes, such as an annually updated edition of the Investigator's Brochure where no changes are made except the last review date.
3. Changes to the research team at participating NHS/HSC organisations, except where it is the appointment of a new Principal Investigator (PI). Appointment of a new PI at a participating NHS/HSC organisation is notifiable as an amendment.
4. Updating of participant information wording to comply with GDPR requirements where only the unmodified standard wording provided by HRA, on behalf of the UK, has been used.
5. Addition of new Participant Identification Centres (PICs) in England. (HRA, 2019)

#### Requesting Authorisation of Amendments from the Sponsor

3.11 For research studies sponsored or co-sponsored by BU, the CI is responsible for notifying the Head of RDS (and Clinical Governance Advisor [CGA]) via email, of their intention to submit an amendment. The CGA will confirm whether the amendment is

substantial or non-substantial in line with the guidance above and advise as to which approval bodies should review.

3.12 As alluded to above, non-substantial amendments do not require REC approval (or MHRA in the case of CTIMP/medicinal/device studies), however it is best practice to notify each body, for information. Participating sites should be notified of all non-substantial amendments as they occur, copying in the CGA.

#### Reporting of Amendments to the MHRA (CTIMP/DEVICE STUDIES ONLY)

3.13 In order to notify the MHRA of a Substantial Amendment to a clinical trial authorisation, an amendment should be submitted via the Amendment Tool, alongside a completed European Commission “Annex 2” form (available via the Amendment Tool), a revised application form, and other documents, to the MHRA:

- Covering letter outlining the substantial and any non-substantial changes;
- Signed notification of amendment form from the European Commission website;
- Updated XML and PDF versions of the clinical trial application form if it’s changed since the last submission;
- Reasons for the proposed changes;
- Proposed changes to the protocol or other document (e.g. investigational medicinal product dossier), showing previous and new wording;
- Supporting data for the change, including:
  - Summaries of data
  - Updated overall risk-benefit assessment
  - Possible consequences for subjects already in the trial
  - Possible consequences for the evaluation of results

The submission should be made through the Common European Submission Platform (CESP) found at <https://cesportal.hma.eu/Account/Login?ReturnUrl=%2f>.

3.14 The application will be assessed within 35 days and if the application does not meet requirements, it will not be assessed. The MHRA will outline the reasons as to why the application is invalid, e.g. missing documents. The MHRA has the authority to make amendments to an authorisation, or to suspend or terminate a trial.

The outcome of the assessment will be delivered via post, with a fee of £225 for applications requiring assessment.

#### Implementing an Amendment

3.15 Amendments may only be implemented once all the necessary approvals have been received by the Sponsor (CGA).

3.16 The CI/Researcher must make any changes to submitted documentation as per the request of the REC and/or MHRA during their review, and should then resubmit the documents to the requesting body, copying in the CGA.

3.17 The CI/Researcher must ensure that the CGA is copied into all correspondence to site Principal Investigators (PI) and R&D teams once the amendment has been approved, and that they receive all approval documentation.

## Procedure after Necessary Approvals and R&D Agreement

3.18 It is advisable that the CI/Researcher or delegate keeps a log of study amendments and they must file in the TMF all approvals and correspondence with the REC/HRA/MHRA in the appropriate file sections (see BU RDS SOP 006 - File Management for Clinical Research).

The CI/Researcher should file all correspondence with the Sponsor and participating sites within the TMF also.

3.19 The CI/Researcher must provide the Sponsor (CGA) with an electronic copy of any documentation that was amended as a result of correspondence with the REC, R&D (and/or MHRA).

3.20 For multicentre projects, the CI/Researcher must ensure that all sites participating in the study are able to support and implement the amendment, and they should distribute the amendment and related documentation and approvals to the PI and Trust R&D.

3.21 The CI/Researcher should discuss with the CGA, any problems participating sites might have in supporting the amendment. It may be that the site is unable to continue supporting the study, and the Sponsor should address this.

3.22 The CI/Researcher/site PI must ensure that all staff involved in the study are aware of and comply with any amendments, confirming that the original NHS R&D agreement is unaffected by the amendment.

3.23 The CI/Researcher (via the CGA) is responsible for ensuring that BU's insurance will cover the study following the amendment. The CI or delegate should file the confirmation of cover in the TMF.

## **4. Abbreviations and definitions**

BU	Bournemouth University
CGA	Clinical Governance Advisor
CI	Chief Investigator
CTIMPs	Clinical Trial of an Investigational Medicinal Product
HRA	Health Research Authority
HSC	Health and Social Care (Northern Ireland)
IRAS	Integrated Research Application System
MHRA	Medicines and Healthcare Products Regulatory Agency
R&D	Research & Development (Trust Research Governance)
RDS	Research Development & Support
REC	Research Ethics Committee
TMF	Trial Master File

## **5. Related documentation and references**

BU RDS SOP 006 - File Management for Clinical Research

UK Policy Framework for Health and Social Care Research. (2017). Health Research Authority

myresearchproject.org.uk. (2018). IRAS Help - Maintaining your approvals - Amendments for projects conducted in NHS/HSC. [online] Available at:

<https://www.myresearchproject.org.uk/help/hlpamendmentsresearch.aspx> [Accessed 22 Jun. 2018] (*IRAS help pages*)

myresearchproject.org.uk. (2019). *IRAS Help - Maintaining your approvals - Amendments for projects conducted in NHS/HSC*. [online] Available at:

<https://www.myresearchproject.org.uk/help/hlpamendmentsresearch.aspx#Activities-not-notified-NHS-HSC> [Accessed 31 Jan. 2020].

myresearchproject.org.uk. 2020. *IRAS Help - Maintaining Your Approvals - Amendments*. [online] Available at:

<<https://www.myresearchproject.org.uk/help/hlpamendments.aspx#Amendment-Tool>> [Accessed 4 June 2020].