Standard Operating Procedures for Submission of Amendments to Sponsored Studies

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- When using this document ensure that the version you are using is the most up-to-date either by checking on the Research Governance webpages[1] for any new versions or by contacting the author to confirm the current version
- Staff and students may print off this document for training and reference purposes but are responsible for regularly checking for the current version. Any print-off of this document will be classed as uncontrolled
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Acknowledgement BSUHT

[1] http://www.sussex.ac.uk/staff/research/governance

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1.0 Purpose & Scope

The UK Policy Framework for Health and Social Care Research (2017) sets out the broad principles of good research governance in the research areas of health and social care. The Policy Framework applies to all research that relates to the responsibilities of the Secretary of State for Health.

This SOP sets out the process for seeking approval for protocol amendments to studies for which the University of Sussex had granted formal agreement to be the Sponsor.

The scope of the document is for all schools at the University of Sussex, all members of staff with substantive employment and students registered at the University (including Brighton and Sussex Medical School).

2.0 Standards for Research

The University of Sussex, through its *Code of Practice for Research*[2] is committed to promoting and upholding the highest quality academic, professional and ethical standards in all its activities and seeks to foster a culture of professional integrity.

2.1 Good Clinical Practice (GCP)

The University expects that researchers undertake *all clinical research involving human participants* in accordance with the principles of GCP.

Good Clinical Practice (GCP) is an international ethical and scientific quality standard for the design and conduct of clinical research involving humans[3]. GCP is a set of core principles, which applies to all clinical investigations that could affect the safety and wellbeing of human participants. GCP is internationally recognised as best practice and compliance (including up to date training) and is a legal obligation in the UK/Europe for all trials of investigational medicinal products. GCP was developed by the regulatory authorities represented in the Tripartite International Conference on Harmonisation and provides international assurance that:

(i) Data and reported results of clinical investigations are credible and accurate, and;
(ii) The rights, safety and confidentiality of participants in clinical research are respected and protected.

2.0 Responsibilities

The *Chief Investigator* (CI) is responsible for making a request to the University of Sussex to act as Sponsor and fulfilling the terms of the 'Conditions of Sponsorship Agreement' issued when the study has been formally accepted for Sponsorship. However, the University recognises that CIs may delegate this responsibility to another member of the research team with sufficient knowledge of the research activity.

The CI will, however, remain ultimately responsible for any submissions made to the MHRA, HRA and an NHS Research Ethics Committee or to the URGC Sponsorship Sub-Committee (SSC) (or any other body with research governance functions) on behalf of the study.

[2] https://www.sussex.ac.uk/webteam/gateway/file.php?name=code-of-practice-for-research-june-2018.pdf&site=377
[3] https://ichgcp.net/

The SSC is responsible for reviewing and approving applications for amendments to Sponsorship on behalf of the University. The Sub-Committee allows for the use of Chair's action on a case-by-case basis when the CI can make a robust case that waiting for the next Sub-Committee meeting date will be detrimental to the study. In all instances, the Sub-Committee receives details of any approved business between meeting dates to maintain its oversight.

3.0 Procedure

The Chief Investigator (CI) or delegated individual is required to submit an application for an amendment to Sponsorship. The nature of the amendment (Substantial or Non-Substantial) determines how the SSC will review the amendment request.

3.1 How to determine whether the amendment is Substantial or Non-Substantial (Non CTIMPs)

The HRA provides the following guidance on the distinction between different categories of amendment[4].

Examples of substantial amendments:

- changes to the design or methodology of the study, or to background information likely to have a significant impact on its scientific value;
- changes to the procedures undertaken by participants;
- changes likely to have a significant impact on the safety or physical or mental integrity of participants, or to the risk/benefit assessment for the study;
- significant changes to study documentation such as participant information sheets, consent forms, questionnaires, letters of invitation, letters to GPs or other clinicians, information sheets for relatives or carers;
- a change of sponsor(s) or sponsor's legal representative;
- appointment of a new chief investigator
- a change to the insurance or indemnity arrangements for the study;
- inclusion of a new trial site (not listed in the original application) in a CTIMP;
- appointment of a new principal investigator at a trial site in a CTIMP;
- temporary halt of a study to protect participants from harm, and the planned restart of a study following a temporary halt;
- a change to the definition of the end of the study;
- any other significant change to the protocol or the terms of the REC application.

Examples of non-substantial amendments:

- minor changes to the protocol or other study documentation, e.g. correcting errors, updating contact points, minor clarifications;
- updates of the investigator's brochure (unless there is a change to the risk/benefit assessment for the trial);
- changes to the chief investigator's research team

[4] https://www.hra.nhs.uk/approvals-amendments/amending-approval/examples-of-substantial-and-non-substantial-amendments/
IRAS also provides information on 'Amendments for projects conducted in NHS/HSC' https://www.myresearchproject.org.uk/help/hlpamendmentsresearch.aspx

- changes to the research team at particular trial sites (other than appointment of a new principal investigator in a CTIMP);
- changes in funding arrangements;
- changes in the documentation used by the research team for recording study data;
- changes in the logistical arrangements for storing or transporting samples;
- inclusion of new sites and investigators in studies other than CTIMPs;
- extension of the study beyond the period specified in the application form.

The Research Governance Officer can receive initial queries on processes– researchsponsorship@sussex.ac.uk.

3.3 *When* to request an amendment

Following NHS Research Ethics Committee approval, all research should comply with the protocol approved by the HRA and the approving NHS Research Ethics Committee.

Changes to the research activity from the approved protocol may only occur when approval has been

- granted by the HRA and the NHS REC (substantial amendments) or
- when the HRA confirms receipt of the Notification of Non-Substantial/Minor Amendments

3.4 Applying for an amendment – the Sponsorship Sub-Committee

Applicants should be aware of meeting dates and submission deadlines as indicated on http://www.sussex.ac.uk/staff/research/governance/sponsorship/applysponsorship .

3.4.1 Non-Substantial Amendments

Applicants should complete a Notification of Non-Substantial/Minor Amendments(s) for NHS Studies[5] form together with any relevant supporting documents to researchsponsorsip@sussex.ac.uk. The email should briefly explain the reason for the request. The CI (or the delegated member of the research team) should submit the modified study documents, showing both the previous and new wording, with the form.

The SSC cannot review and decide on applications that are incomplete or missing the required minimum documentation.

3.4.2 Substantial Amendments

Applicants should complete a Notice of Substantial Amendment form in IRAS[6] (IRAS login needed) and prepare new versions of all amended supporting documents (e.g. PIS, Consent Form, Statement of Activities, Protocol etc.). You should submit the modified documents, showing both the previous and new wording, with the form.

[5] https://www.hra.nhs.uk/documents/1327/notification-non-substantialminor-amendmentss-nhs-studies.docx
[6] https://www.myresearchproject.org.uk/

The CI (or the delegated member of the research team) should send a PDF of the draft of the completed IRAS form and supporting documents (showing updated version control details) to researchsponsorsip@sussex.ac.uk. The email should briefly explain the reason for the request.

4. Amendments to Clinical Trials of Investigational or Medicinal Products (CTIMPs)

The notification of amendment for a CTIMP to the SSC requires the following:

(a) a signed cover letter, including:

- in its subject line the EudraCT number and the sponsor reference with the title of the trial and the sponsor's amendment code number allowing unique identification of the substantial amendment.
- a highlighted indication of any special issues related to the amendment and indication where the relevant information or text is in the original application
- identification of any information not contained in the Amendment Notification Form that might impact on the risk to trial participants;

(b) the Amendment Notification Form,

(c) a description of the amendment:

- an extract from the amended documents showing previous and new wording in track changes, as well as the extract only showing the new wording;
- if the changes are so widespread or far-reaching that they justify an entire new version of the document, a new version of the entire document. In this case, an additional table should list the amendments to the documents. In this list researchers should group together identical changes. The new version should feature the date and an updated version number.

(d) supporting information including, where applicable:

- summaries of data,
- an updated overall risk/benefit assessment,
- possible consequences for subjects already included in the trial,
- possible consequences for the evaluation of the results;

Researchers should submit all documents to researchsponsorship@sussex.ac.uk .

Applicants should be aware of SSC meeting dates and submission deadlines as indicated on http://www.sussex.ac.uk/staff/research/governance/sponsorship/applysponsorship .

The CI or his research team may not implement amendments until the MHRA, NHS REC and the HRA grants approval.

3.5 Review by the URGC Sponsorship Sub-Committee

For all studies, it is the responsibility of the sponsor to determine whether an amendment is substantial or non-substantial.

The SSC shall review and decide whether to grant approval to both substantial and non-substantial amendment requests.

There are three main decision outcomes from the meeting:

- **Full approval of the application as submitted** - The Research Governance Officer will issue a letter confirming the approval.
- **Provisional approval** pending the addressing of issues identified.
- **Rejected** with comments.

The SSC can request further information and/or documentation of the CI as necessary. The CI (or nominated individual) may need to be available to answer any additional questions raised by the SSC.

Non-Substantial Amendments

Following approval, the Research Governance Officer will issue an approval letter that the CI will send with the Notification of Non-Substantial/Minor Amendments(s) for NHS Studies form to the HRA.

Substantial Amendments

Following approval, the Research Governance Officer will issue an approval letter that the CI will add to the supporting documents in IRAS for submission to the HRA and reviewing NHS REC.

3.6 Right to withdrawal of Sponsorship

In line with its responsibilities as a recognised Sponsor of research, the University may withdraw Sponsorship that it has granted if there has been a breach of the 'Conditions of Sponsorship Agreement' or if matters come to light through the study that have significant legal, regulatory, financial or reputational consequences to the University.

4.0 References

UK Policy Framework for Health and Social Care Research

https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/

Medicines for Human Use (Clinical Trials) Regulations 2004 and subsequent amendments

http://www.legislation.gov.uk/uksi/2004/1031/contents/made

Code of Practice for Research, University of Sussex
http://www.sussex.ac.uk/staff/research/documents/code.pdf

Good Clinical Practice, International Conference on Harmonisation of technical requirements for registration of pharmaceuticals for human use
http://ichgcp.net/

APPENDIX A: Conditions of Sponsorship Agreement

Conditions of Sponsorship Agreement

The University of Sussex will act as Sponsor, as defined by the Medicines for Human Use (Clinical Trial) Regulations 2004 and the UK Policy Framework for Health and Social Care Research (2017) for the above research project provided that the Chief Investigator adheres to the following conditions of sponsorship:

a) HRA approval has been received for the study.

b) Confirmation of Capacity & Capability is received from relevant NHS Trusts before any patients or participants are recruited.

c) The CI (Chief Investigator) and members of the research team will comply with all applicable regulations; including the principles from the UK Policy Framework for Health and Social Care Research (2017) the Medicines for Human Use (Clinical Trials) regulations 2004 and subsequent amendments (if a CTIMP), ICH GCP, the Data Protection Act 1998, the Human Tissue Act 2004 and any other relevant guidance and/or legislation.

d) The CI and members of the research team will comply with the University's *Code of Practice for Research*[1]

e) All research team members are appropriately GCP trained throughout the duration of the study.

f) Ensuring that the study is registered on an appropriate registry prior to recruitment of the first patient if applicable.

g) Ensuring that the clinical trial data is generated, documented and reported in accordance with the protocol, GCP and regulatory requirements.

h) A delegation log is completed and kept up to date throughout the duration of the trial.

i) A Trial Master File (TMF) must be set up containing essential documents in accordance with the Trial Master File Index provided and must be maintained throughout the research study.

j) If deemed appropriate by the Sponsor, a site initiation meeting is performed before the study commences and research staff training in the protocol is documented.

k) The research study is conducted in accordance with the protocol and any significant deviations are reported to the Sponsor (researchsponsorship@sussex.ac.uk).

l) Any proposed amendments to the research study are submitted to researchsponsorship@sussex.ac.uk for review and approval as per the Standard Operating Procedures for Sponsorship Approval.

m) Serious Adverse Events (SAEs) are reported to the Sponsor immediately and according to the study's protocol.

n) All SAEs are assessed in order to determine whether the SAE is a Suspected Unexpected Serious Adverse Reaction (SUSAR) as well as any new safety information that becomes available during the trial.

o) If the study is a CTIMP, Development Safety Update Reports are submitted annually to the Sponsor prior to review by the relevant authorities.

p) Annual Progress Reports are submitted to the Sponsor and the REC.

q) Urgent Safety Measures (USM) must be notified to the Sponsor, MHRA and the REC within 3 days of implementing the measure.

r) Any serious breaches of GCP or the protocol must be reported to the Sponsor, MHRA and the REC immediately.

s) Any other correspondence between the MHRA and the REC is copied to the Sponsor (researchsponsorship@sussex.ac.uk).

t) The Trial Master File (TMF) and other associated documentation must be made available for monitoring, auditing or inspection purposes.

u) At the end of the study, an End of Trial Notification/Declaration is sent to the Sponsor, the MHRA (if applicable) and the REC within 90 days of the end of the study, or within 15 days if the trial is terminated prematurely.

v) The end of trial study report must be submitted to the Sponsor, the MHRA (if applicable) and the REC within one year of the end of the trial.

w) The study documentation must be archived in accordance with the applicable University policies.

x) The Chief Investigator will ensure appropriate oversight of the study at all times and agrees to meet with the Sponsor for a Sponsor Review Meeting at intervals agreed at the time of sponsorship.

xi) The Standard Operating Procedures of the Brighton & Sussex Clinical Trial Unit (BSUH CTU) shall apply to all Clinical Trials (CTIMPs) that have is overseen by the Unit

By signing the declaration on IRAS form, I agree to adhere to the above conditions of sponsorship.

Please notify researchsponsorship@sussex.ac.uk when the first participant has been recruited