St George's University Hospitals NHS
NHS Foundation Trust

Standard Operating Procedure (SOP)

Management of Amendments for studies hosted by St George's

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Author:	Subhir Bedi	**Title:**	Head of Research Governance and Delivery
Approved by:	Mark Cranmer, Director of the JREO	**Date:**	
Signature of Authorisor			

This is a controlled document.
The master document is posted on the JREO website and any print-off will be classed as uncontrolled.

Researchers and their teams are responsible for checking the JREO website for the most recent version. They may print off this document for training and reference purposes.

SOP Chronology		
SOP Version Number:	**Reason for Change:**	**Author:**
V1.0	Original Version	Subhir Bedi

1. Background

The European Clinical Trials Directive (EUCTD) 2001/20/EC was transposed into UK Regulations by The Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031) on the 1st May 2004. 'UK Regulations' will be the term used to cover the UK legislation and the EUCTD in this document. UK Regulations and subsequent amendments thereto set out the legal requirements for notification and approval of 'substantial amendments' arising from Clinical Trials of Investigational Medicinal Products (CTIMPs). To breach these requirements constitutes a breach in criminal law.

Studies that are not considered CTIMPS must still apply for formal approval of any substantial amendments under the terms of the Research Governance Framework.

Amendments are changes made to a clinical trial after a favourable ethical opinion and/or approval by a Competent Authority (*i.e.* HRA/MHRA in UK) has been given (1). Amendments can be made to any information relating to a trial. An amendment to a clinical trial can be either substantial or non-substantial in nature. Substantial Amendments require favourable opinion from the REC that granted a favourable opinion for the trial and from the Competent Authority before they can be implemented. Substantial amendments submitted to REC post 1st April 2016 will also need HRA approval. Once the amendment has been assessed against HRA standards relating to the legal and regulatory aspects of the study, the HRA will issue a 'Confirmation of Amendment Assessment'. After this has been issued and relevant REC/MHRA approvals received, the amendment can be implemented. Non -substantial amendments need to be submitted to the HRA only. The HRA will then assess and approve the amendment before implementation at sites.
For multi-site studies conducted in the UK, the amendments are further categorised and a presumed implementation following regulatory approval has been adopted. Unless an objection to the amendment within a reasonable time ~ (35 days) is raised the amendment will be implemented.

Amendments have been grouped into 3 different categories –

Category	Definition	Explanation
A	Amendment to research that ALL participating NHS organisations are expected to consider	Includes any amendment to a research study that has implications for, or affects, ALL participating NHS organisations hosting the research study. All participating NHS organisations will be informed of, and have access to the amendment, for example, additional trial related procedures to be performed onsite
B	Amendment to research that only affect certain/specific sites	Includes any amendment to a research study that has implications for, or affects, SPECIFIC participating NHS organisations hosting the research study. Only those participating NHS organisations affected by the amendment will be informed of the amendment. However, all participating NHS organisations will have access to the amendment through the relevant national coordinating function. Only those participating NHS organisations affected by the amendment are expected to consider the amendment to determine whether they are able to continue to confirm capacity and capability.
C	Amendment to research that participating sites are **not** expected to consider	Includes any amendment to a research study that has no implications that require management or oversight by the participating NHS organisations hosting the research study. All participating NHS organisations will have access to the amendment. Participating NHS organisations are NOT expected to consider the amendment or give continued confirmation for these amendments.

The Sponsor categorises the amendment as substantial or non-substantial, however for the purpose of this SOP, and for studies not sponsored by St George's, the primary consideration is the categorisation of the amendment by the HRA. The JREO, on behalf of St George's, should be sent all amendment notifications and documents for clinical research that takes place within St George's University Hospital's NHS Foundation Trust (SGHT) and/or St George's, University of London (SGUL).

2. Joint Research and Enterprise Office (JREO) Policy

All JREO SOPs will be produced and approved in accordance with the JREO SOP on SOPs and must be used in conjunction with local NHS Trust and St George's policies and procedures.

The JREO acts as the representative of both St George's University of London (SGUL) and St George's University Hospital's NHS Foundation Trust (SGHT). St George's will be the official name used on all SOPs to represent both institutions acting as clinical trials Sponsor.

3. Scope

This SOP covers the management of amendments and Urgent Safety Measures for hosted clinical research studies.

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4. Definitions

For general research management related acronyms or definitions used in this SOP refer to "General Research Definitions" working practice document JREOWPD0020

5. Responsibilities

JREO

This SOP is to be followed by members of the JREO

It is the responsibility of the Head of Research Governance and Delivery within the JREO to ensure that the SOP is updated when necessary. This responsibility can be delegated.

The assigned Research Governance and Facilitation team member (RGF) will be responsible for reviewing the amendment and updating the electronic JREO file.

Investigator

It is the Investigator's responsibility to ensure that amendments for hosted studies are submitted to the JREO for approval (**if not done by the sponsor**). It is their responsibility to ensure that the

changes are not implemented for Category A and or B (relevant to St Georges) prior to JREO confirmation.

Research Teams

Research teams should ensure that amendments are reviewed carefully. If there is any aspect of an amendment that the team are unsure about, they should liaise directly with the study Sponsor and the PI.

6. Procedure

Is the amendment substantial?

The CI/ Sponsor should determine whether the amendment is substantial or non-substantial and are responsible for submissions to the regulatory bodies and local sites.

Management amendments to studies hosted by St George's

Upon notification of an amendment the lead RGFO will register it on the amendments spreadsheet, and update the electronic JREO study file and EDGE.

The JREO will require the following documents (where relevant):

- REC Amendment Approval Letter – The lead RCFO will ensure that the documentation submitted has been approved by REC and that the correct versions have been submitted.
- HRA Amendment Confirmation-The RCFO will ensure that the documentation submitted has been approved by the HRA and that the correct versions have been submitted.
- MHRA Approval (if applicable) – The lead RCFO will ensure that all amendments for CTIMP studies hosted by St George's received MHRA approval of the amendment.
- Notice/Notification of Substantial Amendment (NOSA) - The lead RCFO will review the IRAS Form to ensure that the amendment to determine the changes proposed.

Where the HRA categorisation confirmation labels the amendment as a Category **"C" or "B" (not relevant to St Georges)** the RCFO only needs to acknowledge receipt of the amendment. No formal review or ongoing confirmation is required. The RCFO should update the electronic study JREO file and EDGE with the documents and correspondence provided and acknowledgement sent.

Where the HRA categorisation confirmation label the amendment as Category **"A" or "B" (relevant to St Georges)** formal review of the amendment implication is required. The RGF should review details of the amendment submission documentation to determine the effect it may have on the study locally. The RGF should identify any/all support departments approvals that will be required and work with local study team to ensure the changes can be accommodated on site. This could include Pharmacy, Pathology, Radiology, and Clinical Research Facility, Finance and Contracts as well as other departments.
If the amendment cannot be reviewed fully **within 35 days of notification** from the sponsor and or cannot be accommodated locally, the RCFO should notify the sponsor at the earliest opportunity.

If the amendment cannot be accommodated within St George's, the lead RCFO will inform the PI and Sponsor within a reasonable timeframe by e-mail. If no resolution can be reached, St Georges will be unable to confirm the amendment and host confirmation may be suspended or withdrawn. Physical letters will not be issued for amendments.

Investigator procedure for reporting Urgent Safety Measures
It is recommended that the CI/PI/sponsor contacts the JREO within 24 hours, should they plan to implement or have already implemented any urgent safety measures as defined in Section 4. Urgent Safety Measures can be implemented on site without prior JREO confirmation however a review of the ongoing implications maybe required. The HRA subsequent categorization

7. References

NIHR Clinical Trials Toolkit www.ct-toolkit.ac.uk

MHRA

HRA www.hra.nhs.uk

8. Appendices

8.1 **Confirmation of amendment notification email template**

8.2 Flowchart of HRA Amendment Process-

8.1 Confirmation of amendment notification email template:

From: St Georges JREO

To: Sponsor representative, Chief Investigator, Clinical Trial Unit/Study Manager/Study Coordinator (where applicable),

Cc: Principal Investigator or Local Collaborator, Lead Research Nurse/Coordinator, Support Departments, LCRN London South (NIHR CRN studies)

Subject: IRAS xxxxxx. Amendment Confirmation at **St Georges Healthcare NHS Foundation Trust/ St Georges, University of London**

Attachment: updated Signed agreement as appropriate

Dear Sponsor Representative,

RE: IRAS xxxxxx. Amendment (Number and or Date) Confirmation at **St Georges Healthcare NHS Foundation Trust / St Georges, University of London.**

Full Study Title:	
Site PI/LC	
Amendment Number and Date	
Current Protocol version:	
HRA Approval date:	

This email confirms that **St Georges Healthcare NHS Foundation Trust / St Georges, University of London** confirms the subjected amendment.

If you wish to discuss further, please do not hesitate to contact us and local team (cc-ed above).

Kind regards

INSERT PERSONAL SIGNATURE

8.2 Flowchart of HRA Amendment Process-