

Positively welcoming Actively respectful Clearly communicating Visibly reassuring

Document Title: Substantial Amendments for RF Sponsored Studies

Document Number: 016

Version:	2
Ratified by:	R&D Committee
Date ratified:	30/11/2017
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Department:	Research and Development
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Date issued:	04/12/2017
Review date:	04/12/2020
Target audience:	All research staff
Intranet:	04/12/2017
Key related documents:	SOP003 Reporting Amendments RFLRDWPD0007 Amendments
This document supports: <i>Standards and legislation</i>	Medicines for Human Use (Clinical Trials) Regulations 2004 and all associated amendments. UK Policy Framework for Health and Social Care (2017)
Date equality analysis completed.	30/11/2017
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Version Control

Version	Date	Author	Status	Comment
1	30 September 2014	Heidi Saunders	Final	New Document
1.1	03 OCT 2017	Lucy Parker	Final	SOP Review Date Time Extension
2	04 OCT 2017	Lucy Parker	Final	Removal of references to the MHRA and CTIMPs Name change of SOP from protocol amendments for RF Sponsored Studies to Amendments for RF Sponsored Studies Update from Research Governance Framework for Health and Social care (2005) to UK Policy Framework for Health and Social Care (2017)

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1. INTRODUCTION

This document sets out the procedures to be followed by all Royal Free London NHS Foundation Trust staff that are responsible for dealing with Protocol Amendments for research projects Sponsored by Royal Free London NHS Foundation Trust.

This SOP has been produced in accordance with ICH/GCP Guidelines, the Medicines for Human Use (Clinical Trials) Regulations 2004 and the Medicines for Human Use (Clinical Trials) Amendment Regulations 2006. This SOP outlines the procedure for dealing with Protocol Amendments for research projects Sponsored by Royal Free London NHS Foundation Trust.

If changes are made to the study protocol the Research and Development Office requires to be notified of the intended amendments, to enable reviews and confirmation of continued authorisation to be given.

2. OBJECTIVE

This document defines the Trust's procedure for changes to research protocol following Trust approval for studies Sponsored by Royal Free London NHS Foundation Trust.

The document clarifies the situation when an amendment is required and the approval and implementation process so as to meet the standards described in Good Clinical Practice (GCP).

For studies hosted at Royal Free London NHS Foundation Trust sites, SOP003 Reporting Amendments should also be followed.

3. DEFINITIONS

RF - Royal Free London Hospital NHS Foundation Trust

RM&G - Research Management & Governance

R&D - Research & Development

Sponsor - Individual, organisation or group taking on responsibility for securing the arrangements to initiate, manage and finance a study. A group of individuals and/or organisations may take on Sponsorship responsibilities and distribute them by agreement among the members of the group, provided that, collectively, they make arrangements to allocate all the responsibilities in this research governance framework that are relevant to the study.

CI - Chief Investigator (CI) is the authorised health care professional who takes primary responsibility for the conduct of the trial. There is only one Chief Investigator per Member State.

PI - Principal Investigator (PI) is the person who takes responsibility for the initiation and conduct of the study at site. There is one Principal Investigator at each site participating in a research study. For a single site study the Chief investigator may also take on the role of Principal investigator

GCP - Good Clinical Practice (GCP) is an international ethical and scientific quality standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and

reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

TMF - The Trial Master File (TMF) contains all essential documents held by the Sponsor /Chief Investigator which individually and collectively permits the evaluation of the conduct of a trial and the quality of the data produced.

4. SCOPE

This SOP outlines the procedure for making amendments to active studies Sponsored by Royal Free London NHS Foundation Trust.

5. EQUALITY STATEMENT

The Royal Free London NHS Foundation Trust is committed to creating a positive culture of respect for all individuals, including job applicants, employees, patients, their families and carers as well as community partners. The intention is, as required by the Equality Act 2010, to identify, remove or minimise discriminatory practice in the nine named protected characteristics of age, disability (including HIV status), gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, sex or sexual orientation. It is also intended to use the Human Rights Act 1998 to treat fairly and value equality of opportunity regardless of socio-economic status, domestic circumstances, employment status, political affiliation or trade union membership, and to promote positive practice and value the diversity of all individuals and communities.

This document forms part of the trust's commitment. You are responsible for ensuring that the trust's policies, procedures and obligation in respect of promoting equality and diversity are adhered to in relation to both staff and service delivery.

The equality analysis for this SOP is attached at Appendix 2.

6. DUTIES

The Trust is committed to the delivery of world class care and expertise to both staff and patients, and our values of positively welcoming, actively respectful, visibly reassuring and clearly communicating are fundamental to the delivery of this. This policy has been developed with our values in mind, and is intended to be implemented within the spirit of these values.

This SOP applies to all personnel that are conducting research at the Trust including: staff that are full or part-time employees of the Trust, those working at the Trust with employment contracts funded partially or wholly by third parties, those working at the trust under honorary contract or under the remit of a valid research passport, those seconded to and providing consultancy to the Trust, and to students undertaking training at the Trust.

It is the responsibility of the Chief Investigator to

- submit the relevant amendment form or letter and required supporting documents to the R&D Office, NHS Research Ethics Committee and the HRA correctly completed.

- ensure approval or acknowledgement is received from the relevant authorities before implementing an amendment.

It is the responsibility of the Study Sponsor to confirm whether an amendment is substantial or not.

The investigator should not implement any deviation from, or changes of the protocol without agreement by the Sponsor and prior review and documented approval/favourable opinion, except where necessary to eliminate an immediate hazard(s) to trial subjects (urgent safety measure)

7. DETAILS OF THE PROCEDURE

Person Responsible	Task
CI	<p>The Chief Investigator makes amendments to the research protocol or supporting documentation.</p> <p>Amendments may be non-substantial or substantial.</p> <p>A substantial amendment is defined as an amendment that is likely to affect to a significant degree any of the following:</p> <ul style="list-style-type: none"> • the safety or physical or mental integrity of the subjects of the trial, • the scientific value of the trial, • the conduct or management of the trial, or • The quality or safety of any investigational medicinal product used in the trial. <p>Non-substantial amendments are minor changes that are not considered substantial as described above. Non-substantial amendments do not require submission to REC and /or MHRA but must be submitted to the HRA.</p> <p>For non-substantial amendments, the CI should use the template form available at www.hra.nhs.uk/documents/2014/11/notification-non-substantialminor-amendmentss-nhs-studies.docx</p>
Research Portfolio Manager	<p>It is the responsibility of the Study Sponsor to confirm whether an amendment is substantial or not. For RF Sponsored studies, the CI should contact the R&D Office (rf.randd@nhs.net) to seek advice regarding the assessment of the amendment. This may involve initial discussion regarding the amendment, followed by a review of amended protocol and notice of amendment form. Any amended documents should be controlled by the allocation of a new version number and date.</p> <p>If the amendment is classed as a substantial amendment, the R&D Office will ask the CI to email Notice of Substantial Amendment Form along with any other associated paperwork to the R&D inbox rf.randd@nhs.net and a member of the R&D</p>

	<p>team will review the amendment. If amendment is acceptable, the R&D Manager or the assigned Research Portfolio Manager signs the notice of substantial amendment form as the Sponsor Representative. The CI will then forward documentation to the Ethics Committee (if required), and Health Research Authority (HRA) (if required).</p>
CI	<p>7.1 Generating Notice of Substantial Amendment Forms – REC review required – NON CTIMP</p> <p>Notice of substantial amendment forms are created in IRAS; the system automatically generates the type of notice of substantial amendment form that is appropriate to the project category.</p> <p>The CI should summarise the change(s) included in the amendment and briefly explain the reasons in each case on the notice of amendment.</p> <p>The CI should submit the documents that have been modified, showing both the previous and new wording so that the changes can be readily identified, along with the completed substantial amendment form to their assigned Research Portfolio Manager in the RF R&D Office.</p> <p>Where the amendment could significantly affect the scientific value of the research, further evidence of scientific and/or statistical review should also be provided.</p> <p>The NRES Notice of Substantial Amendment form generated in IRAS must be used. The form should be electronically authorised in IRAS by the Sponsor and the CI. Without any of the authorisations, the amendment will not be validated.</p> <p>Once signatures are in place, the amendment can be submitted to the Ethics Committee that originally approved the study. The REC will pass the amendment onto the HRA for approval.</p>
CI	<p>7.2 Generating Notice of non-Substantial Amendment – HRA Only review required</p> <p>For non-substantial amendments, the CI should use the template form available at www.hra.nhs.uk/documents/2014/11/notification-non-substantialminor-amendmentss-nhs-studies.docx</p> <p>The CI should submit the documents that have been modified, showing both the previous and new wording so that the changes can be readily identified along with the completed non-substantial amendment form to their assigned Research Portfolio Manager in the RF R&D Office.</p> <p>Once the RF R&D Office has authorised the non-substantial amendment, the CI needs to send the amended documents and amendment form to the HRA email – hra.amendments@nhs.net</p>

	<p>7.3 Implementing the Amendment</p> <p>Approval of amendments from all regulatory bodies including Research and Development must be in place before the implementation of any protocol amendment.</p> <p>The Investigator must gain R&D approval prior to implementing the protocol amendment, except in the case of urgent safety measures.</p> <p>The Chief Investigator should submit:</p> <ul style="list-style-type: none"> • a copy of the substantial amendment form, • a copy of amended documentation (tracked and untracked), • any correspondence with the Ethics Committee relating to the amendment including the favourable opinion letter (if applicable) • a copy of the HRA approval email <p>to the R&D Office rf.randd@nhs.net if the study is active at Royal Free and any other R&D office where the study is active.</p> <p>The R&D Office will approve the implementation of changes to the protocol subject to favourable ethics opinion(if applicable) and approval of the amendment from the HRA.</p> <p>Once the R&D Office is satisfied that the amendment can be implemented within the Trust, confirmation will be sent (via email) to the investigator noting approval on behalf of the Trust.</p> <p>The Chief Investigator should file the approved amendment in the Trial Master File with the amended documents and ensure the previous versions are marked as superceded.</p> <p>The Chief Investigator should file the approval letter from the Ethics Committee, HRA and R&D Office in the corresponding sections of the Trial Master File.</p> <p>The Chief Investigator makes all staff involved with the study, including PIs and other sites, aware of any amendments to the protocol.</p> <p>The Chief Investigator ensures all research staff abide by the changes. Individual investigators who are unable to work to the amendment may decide to withdraw from the study.</p>
<p>Research Portfolio Manager</p>	<p>Should follow RFLRDWPD007 Amendments when an amendment is received.</p>

8. POLICY

This SOP is mandatory and non-compliance with it may result in disciplinary procedures.

9. RISK MANAGEMENT/ LIABILITY/MONITORING & AUDIT

- The SOP Working Group will ensure that this SOP and any future changes to this document are adequately disseminated.
- The R&D Office will monitor adherence to this SOP via the routine audit and monitoring of individual clinical trials and the Trust's auditors will monitor this SOP as part of their audit of Research Governance. From time to time, the SOP may also be inspected by external regulatory agencies (e.g. Care Quality Commission, Medicines and Healthcare Regulatory Agency).
- In exceptional circumstances it might be necessary to deviate from this SOP for which written approval of the RM&G Manager/Deputy R&D Director should be gained before any action is taken.
- SOP deviations should be recorded including details of alternative procedures followed and filed in the Investigator and Sponsor Master File.
- The R&D Office is responsible for the ratification of this procedure.

10. FORMS/TEMPLATES TO BE USED

www.myresearchproject.org.uk for substantial amendment forms

www.hra.nhs.uk/documents/2014/11/notification-non-substantialminor-amendmentss-nhs-studies.docx for non- substantial amendment notification template form

11. FLOWCHART

None

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APPENDIX 2

Royal Free London NHS Foundation Trust Equality Analysis guide and Tool

An equality analysis is a review of a policy, practice, function, business case, project or service change which establishes whether there is a negative effect or impact on particular social groups. This In turn enables the organisation to demonstrate it does not discriminate and, where possible, it promotes equality to meet the needs of the diverse patients and communities we serve.

This check list is a way to help you think carefully about the likely impact on equality groups and take action to improve services. This is also an opportunity to evidence positive practices in our services and demonstrate strategic integrity to ensure that our services and employment practices are fair, accessible and appropriate for all patients, visitors and carers, as well as our talented and diverse workforce.

Name of the policy / function / service development being assessed	Protocol Amendments
Briefly describe its aims and objectives:	This document defines the Trust’s procedure for changes to research protocol following Trust approval for studies Sponsored by Royal Free London NHS Foundation Trust.
Directorate and Lead:	Rachel Fay, R&D Manager
Evidence sources: DH, legislation. JSNA, audits, patient and staff feedback	Medicines for Human Use (Clinical Trials) Regulations 2004 and all associated amendments. UK Policy Framework for Health and Social Care (2017)
Is the Trust Equality Statement present?	Yes X No if no do not proceed with Equality Analysis (EA)

If you are conducting an EA on a procedural document please identify evidence sources and references, who has been involved in the development of the document, process or strategy, and identify positive or negative impacts. It is the discussion regarding the equality impact of the document that is important.

Equality Analysis Checklist

Go through each protected characteristic below and consider whether the policy, practice, function, business case, project or service change could have any impact on groups from the identified protected characteristic, involve service users where possible and get their opinion, use demographic / census data (available from public health and other sources), surveys (past or maybe carry one out), talk to staff in PALS and Complaints and Patient Experience.

Please ensure any remedial actions are Specific, Measureable, Achievable, Realistic, and Timely (SMART).

Equality Group	Identify negative impacts	What evidence, engagement or audit has been used?	How will you address the issues identified?	Identifies who will lead the work for the changes required and when?	Please list positive impacts and existing support structures
Age	None identified	R&D administrative document	N/A	N/A	This SOP includes the Trust Equality Statement, as well as the results from the Equality Assessment for this SOP. These actions are designed to embed the equality agenda and promote equality compliance within the Trust
Disability	None identified	R&D administrative document	N/A	N/A	
Gender Reassignment	None identified	R&D administrative document	N/A	N/A	
Marriage and Civil Partnership	None identified	R&D administrative document	N/A	N/A	
Pregnancy and maternity	None identified	R&D administrative document	N/A	N/A	
Race	None identified	R&D administrative document	N/A	N/A	

SOP016: Protocol Amendments

V2 04 OCT 2017

Uncontrolled document when printed or downloaded. Current SOP versions available <https://www.royalfree.nhs.uk/research/for-investigators/standard-operating-procedures-sops/>

Equality Group	Identify negative impacts	What evidence, engagement or audit has been used?	How will you address the issues identified?	Identifies who will lead the work for the changes required and when?	Please list positive impacts and existing support structures
Religion or Belief	None identified	R&D administrative document	N/A	N/A	
Sex	None identified	R&D administrative document	N/A	N/A	
Sexual Orientation	None identified	R&D administrative document	N/A	N/A	
Carers	None identified	R&D administrative document	N/A	N/A	

It is important to record the names of everyone who has contributed to the policy, practice, function, business case, project or service change.

Equality Analysis completed by: (please include every person who has read or commented and approval committee(s). Add more lines if necessary)	Organisation	Date
SOP Working Group	Royal Free London NHS Foundation Trust	20/10/2017
R&D Committee	Royal Free London NHS Foundation Trust	30/11/2017