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JOINT RESEARCH SUPPORT OFFICE

STANDARD OPERATING PROCEDURES

UHL Research Support Office
SOP S-1017 UHL V8 March 2020

Standard Operating Procedure for Green Light Process for Amendments to Research sponsored by University Hospitals of Leicester NHS Trust (UHL)

PGC Reference No: C35/2013

OFFICE BASE

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1. Introduction

This Standard Operating Procedure (SOP) describes the procedures used by the University Hospitals of Leicester NHS Trust (UHL) when completing the Sponsor Green Light Process for amendments to research that has previously received formal approval.

The outcome is that as Sponsor, the UHL is able to confirm that a revised Risk Assessment & Sponsor review has been appropriately conducted and that the Organisation is able to continue to act as research Sponsor.

2. Scope

This SOP applies to all research activity where the UHL acts as Sponsor.

3. Definition of Amendments

Amendments are viewed as changes to any research documentation that has been reviewed and approved by regulatory authorities and the Sponsor.

There are essentially two types of amendments.

- Substantial amendments
- Non-Substantial amendments

Both types of amendments require a different process as detailed below.

It is important to note that ANY change to ANY documentation, including administrative changes in a research study categorised as a Clinical Trial of an Investigational Medicinal product (CTIMP) must be sent to the Sponsor before the changes are implemented, or submitted to regulatory authorities, except in cases of Urgent Safety Measures which is discussed in detail in SOP S-1026 UHL.

3.1 Substantial Amendments

The definition of a substantial amendment can be found following this link: https://www.hra.nhs.uk/approvals-amendments/amending-approval/

It is the responsibility of the Sponsor to decide whether or not an amendment is substantial. In addition, the Sponsor must decide whether or not the amendment requires authorisation from the MHRA as well as a Favourable opinion from the Research Ethics Committee & HRA Approval.

A list of amendments that require authorisation from the MHRA can be found at Appendix 1. A list of amendments that require both authorisation from the MHRA and a REC Favourable Opinion can be found at Appendix 2. A list of amendments that require Favourable Opinion from the REC can be found at Appendix 3. A list of amendments that require no notification to REC or MHRA but do still require notification to the Sponsor can be found at Appendix 4.

In addition, the HRA process requires that each amendment is given a categorisation. Details of these categories can be found on the HRA Website. (www.hra.nhs.uk)

In addition to the MHRA, REC & HRA the Host Organisation R&I Office may also be required to review amendments prior to implementation at the NHS site. This should be noted during the Sponsor Amendment Green Light process and recorded in the appropriate workflows for amendments. Acknowledgement for amendment and sponsor green light will be issued and confirmed using the sponsor 22 workflow in EDGE

3.2 Non-Substantial Amendments

Research involving Clinical Trials of Investigational Medicinal Product

ANY change to ANY documentation, including administrative changes in a research study categorised as a Clinical Trial of an Investigational Medicinal product (CTIMP) must be sent to the Sponsor before the changes are implemented, or submitted to regulatory authorities, except in cases of Urgent Safety Measures which is discussed in detail in **SOP S-1026 UHL**.

Research not involving Investigational Medicinal Products

Where amendments are deemed to be Non-Substantial/Administrative/Minor as listed in Appendix 3, and not for research involving Clinical Trials of Investigational Medicinal Products, the amendment must be submitted to the sponsor prior to submission to the HRA / REC using UHLSponsor@uhl-tr.nhs.uk. A Non Substantial amendment form must be completed as part of the process which is available on the HRA Website. At the current time all NSAs are required to be submitted to the HRA for approval and categorisation, but it is recommended that the HRA website is checked prior to submission as there are plans to revise the process.

3.3 Process for ALL Amendments

All amendments must be sent to the UHLSponsor@uhl-tr.nhs.uk for review by the Head of Research Operations or a delegate. All documentation to be amended along with relevant amendment forms must be included for an amendment to be regarded as 'valid'. Once a valid submission has been received the Head of Research Operations or their delegate will review the documentation and confirm that the amendment is 'substantial'. This process may take up to 14 calendar days.

The Head of Research Operations or their delegate will review the amendment documentation, and will revise the initial Sponsor Risk Assessment and / or Sponsor review attributes / workflows (as detailed in SOP S-1003 UHL) as necessary. This may require further review by Research Management Meeting or the R&I Executive Committee if the amendment affects the risk outcome in accordance with SOP S-1003 UHL Sponsor Risk Assessment.

If an amendment includes the addition of new sites or Third Parties, the relevant SOP S-1014 UHL Sponsor Green Light Process and / or SOP S-1005 UHL Contracts will be implemented.

If necessary a face-to-face meeting with the Chief Investigator and / or study personnel will be requested to discuss the proposed amendment in detail prior to Sponsor Amendment Green Light confirmation.

The Head of Research Operations or their delegate will complete the relevant attributes / Workflows in the EDGE system, during the review of amendment documentation. When the documentation review and revised risk assessment has been completed, and relevant action has been taken or is in progress to mitigate any additional risk identified, the Head of Research Operations will confirm to the Chief Investigator or their delegate Sponsor permission to submit the amendment to relevant regulatory authorities.

Sponsor Amendment Green Light will be confirmed on receipt of documentary evidence that the relevant permissions, any additional contracts or agreements are in place, confirmation of indemnity and regulatory authority approvals have been received. Copies of all relevant documentation will be uploaded to EDGE. A Sponsor Amendment Green Light confirmation email will be sent allowing implementation of the amendment to take place

It is important to remember that the Sponsor must be sent a copy of any revised study documentation and details of changes in key personnel during the lifecycle of a research study.

3.4 Multi-Centre Studies

Once approved by all appropriate regulatory authorities it is the responsibility of the Chief Investigator to ensure that the amended documentation is submitted to each site for local authorisation. Confirmation of no objection / approval from each site will be recorded within the EDGE system.

4. Non- Compliance

Where it is identified that the processes detailed above have not been followed, the **SOP S-1016 UHL Non-Compliance** will be implemented at a minimum of a Major finding.

5. Responsibilities

	Responsibility	Undertaken by	Activity
1	Chief Investigator or their delegate	Chief Investigator or their delegate	Submit all documentation relating to the amendment to the UHLSponsor@uhl-tr.nhs.uk
2	Sponsor	Head of Research Operations or delegate	Commence review of Risk Assessment & Sponsor review as appropriate
3	Sponsor	Head of Research Operations or delegate	Completion of relevant Entities / Workflows in the EDGE system,
4	Sponsor	Head of Research Operations or delegate & Chief Investigator	Provide authorisation to submit to relevant regulatory authorities..
	Sponsor & Chief Investigator	Head of Research Operations or delegate & Chief Investigator	Ensure no implementation of amended documentation commences prior to receipt of Sponsor Amendment Green Light email.
	Sponsor	Head of Research Operations or delegate & Chief Investigator	Provide Sponsor Green Light for Amendment once all relevant approvals are in place
	Chief Investigator	Chief Investigator or delegate	Ensure all sites receive all documentation and provide local confirmation of capacity and capability prior to implementation of the amendment at site

6. Monitoring and Audit Criteria

Key Performance Indicator	Method of Assessment	Frequency	Lead
All research sponsored by UHL has appropriate Risk Assessment	Included in the monitoring / audit programme.	Random audits / monitoring conducted on a risk based assessment of research activity	Head of Research Operations or delegate

This table is used to track the development and approval of the document and any changes made on revised / reviewed versions

DEVELOPMENT AND APPROVAL RECORD FOR THIS DOCUMENT			
Author / Lead Officer:	Carolyn Maloney		**Job Title:** Head of Research Operations
Reviewed by:	R&I Management Meeting		
Approved by:	Professor Nigel Brunskill		**Date Approved:** 11/06/2020

REVIEW RECORD			
Date	**Issue Number**	**Reviewed By**	**Description Of Changes (If Any)**
March 2015	2	R&D Management Meeting	Change of Logo and name of R&I
July 2016	3	CM, LW, JJ	Consistency check. Adding process for HRA>
December 2016	4	CM	Adding of EDGE system
February 2017	5	CM	Update to Logo
March 2018	6	CM	Addition of management through EDGE
September 2018	7	CCL	Update to R&I logo
March 2020	8	LW/CM	Revision of wording and removal of Loughborough university

DISTRIBUTION RECORD:			
Date	**Name**	**Dept**	**Received**

Appendix 1 - List of amendments requiring MHRA authorisation only

New toxicological or pharmacological data or new interpretation of toxicological to pharmacological data of relevance for the investigator
Changes to the reference safety information for the development safety update report (DSUR)
Changes to the investigational medicinal product dossier
Reduction in the Sponsor's planned level of monitoring for the trial

Appendix 2 - List of amendments requiring MHRA & REC authorisation

Change to the main objective of the trial
Change of the primary or secondary end-points likely to have a significant impact on the safety or scientific value of the trial
Use of a new measurement for the primary end-point
New toxicological or pharmacological data or new interpretation of toxicological or pharmacological data which is likely to impact on the risk-benefit assessment
Addition of a trial arm or placebo group
Significant change of inclusion or exclusion criteria (for example, age range) likely to have a significant impact on the safety or scientific value of the trial
Change of a diagnostic or medical monitoring procedure likely to have significant impact on the safety or scientific value of a trial
Withdrawal of an independent data monitoring committee
Change of investigational medicinal product(s)
Change of dosing/mode of administration of investigational medicinal product(s)
Any other change of trial design likely to have a significant impact on primary or major secondary statistical analysis or on the risk-benefit assessment
Change of the sponsor to sponsor's legal representative
Temporary halt of the trial or temporary halt at a trial site, and re-start of the trial following a temporary halt
Change of the definition of the end of the trial

Appendix 3 - List of amendments requiring REC Favourable Opinion

Significant changes to information provided to subjects – for example, subject information sheets, consent forms, diaries, letters to GPs or other clinicians, letters to relatives/carers (whether generic to the whole trial or specific to particular trial site).
Significant changes to recruitment and consent procedures, including the inclusion of adults lacking capacity in the trial
Significant increase to the radiation exposures to subjects from the protocol
Change of insurance or indemnity arrangements for the trial
Change to the payments, benefits or incentives to be received by subjects or researchers in connection with taking part in the trial, or any other change giving rise to a possible conflict of interest on the part of any investigator/collaborator
Change of the Chief Investigator
Change of Principal Investigator at a trial site
Addition of new trial site not listed with the original request for authorisation and REC application
Change to the definition of a trial site
Any other significant change to the conduct or management of the trial at particular trial sites
Early closure or withdrawal of a site
Any other significant changes to the terms of the REC application

Appendix 4 – Amendments not normally requiring notification

Changes to the identification of the trial (for example, change of title)
Increase in duration of the trial, provided that the exposure to treatment is not extended, the definition of the end of trial is unchanged and there is no change to monitoring arrangements
Changes to the numbers of subjects planned in the UK as a whole or at individual trial sites, provided that there is no change to the total number of subjects in the trial or the increase/decrease is insignificant in relation to the overall sample size
Change in the documentation used by the research team to record trial data (for example, case report form or data collection form)
Additional safety monitoring which is not part of an urgent safety measure but is taken on a precautionary basis
Changes to the research team other than to the Chief or Principal Investigators
Changes to contact details
Changes to the internal organisation of the sponsor or persons to whom tasks have been delegated
Changes to the logistical arrangements for transporting or storing samples
Changes to technical equipment
Inclusion or withdrawal of another Member State or third country
Minor clarifications to the protocol
Minor clarifications or updates of subjects information documentation
Corrections of typographical errors