LEICESTER'S RESEARCH

NHS
University Hospitals of Leicester
NHS Trust

UNIVERSITY OF LEICESTER

&

UNIVERSITY HOSPITALS OF LEICESTER NHS TRUST

JOINT RESEARCH SUPPORT OFFICE

STANDARD OPERATING PROCEDURES

UHL Research Support Office
SOP S-1016 UHL v8 April 2020

Standard Operating Procedure for Procedure in the Event of Non-Compliance in Research sponsored by University Hospitals of Leicester NHS Trust (UHL)

PCG Reference No: C19/2014

OFFICE BASE

Research & Innovation
Leicester General Hospital
Gwendolen Road
Leicester
LE5 4PW

1. Introduction

This Standard Operating Procedure (SOP) describes the process for responding to any form of non-compliance identified in research sponsored by University Hospitals of Leicester NHS Trust (UHL), including audit findings, protocol & / or regulatory deviations / violations, contractual issues, and whistleblowing not requiring implementation of SOP S-1019 UHL Suspected Fraud and Misconduct in Research.

2. Scope

This SOP applies to all individuals conducting research sponsored by the UHL

3. Definitions

Forms of non-compliance are described as *critical, major or other* in line with audit and inspection processes of regulatory authorities.

- A critical non-compliance can include instances where:
    - The safety, well-being or confidentiality of participants has been jeopardised or has the potential to be jeopardised.
    - Reported data are unreliable or absent.
    - Inappropriate, insufficient or untimely corrective action has taken place regarding major non-compliance
    - Lack of adequate documentation available to reconstruct the study or failure to maintain an appropriate Trial Master File (TMF).

- A major non-compliance can include instances of :
    - Significant and unjustified non-compliance with relevant legislation or Good Clinical Practice (ICH GCP).
    - A number of breaches of legislation or GCP within one area, indicating systematic quality assurance failure.
    - A failure to comply with legislative requirements including annual reporting requirements.

- An other finding can be identified as :
    - Any other finding that is neither critical nor major.

4. Procedures

Non-compliance identified by whatever means, will be investigated using appropriate monitoring and audit processes by the Sponsor. The procedures described below are general, and each instance of non-compliance will be assessed and responded to on a case by case basis. Failure to respond to reported non-compliance will result in escalation from other to major to critical, and finally by referral to SOP S-1019 UHL Suspected Fraud and Misconduct in Research.

4.1 Critical Non-Compliance

On identification of a critical non-compliance as defined in Section 3 the Chief Investigator (CI) will be alerted by the Sponsor. Depending on the nature of the critical non-compliance it may be necessary to give a notification by email with an outline of immediate action required. The initial notification will be followed up within 7 calendar days with a detailed report.

Dependent on the nature of the non-compliance the study may be suspended with immediate effect.

The Sponsor may suspend all studies associated with the CI at their discretion in consultation with the Director of Research and Innovation. Identification of a critical non-compliance may prompt audit and close monitoring of associated studies.

Suspension of the study will be notified by the Sponsor to the Research Ethics Committee (REC), HRA, all active research sites, and the MHRA as appropriate.

The CI must respond within 30 calendar days from the date of receipt of a detailed notification. It is expected that the Corrective Action Preventative Action (CAPA)Template as detailed in SOP S-1012 UHL will be used in all cases. This will ensure that the CI explains clearly what action they will take. It is not necessary that all the action will have been taken within the 30 days but it is expected that a plan of completion is outlined. Non-response within this timeframe will lead to suspension of the study in all cases, and possible suspension of associated studies.

If deemed appropriate, submission of a substantial amendment to restart the study will be permitted by the Sponsor once the non-compliance is resolved or adequate plans are in place to prevent repeat incidents.

Studies sponsored by UHL that have been suspended will be closely monitored, prior to restarting, after the first new participant is entered and regularly thereafter until the Sponsor is satisfied the study remains fully compliant.

On identification of a critical non-compliance all research staff will be required to retrain in Good Clinical Practice and to be assessed / reassessed in taking consent.

4.2 Major Non-Compliance

On identification of major non-compliance as defined in Section 3 the CI will be alerted by the Sponsor.

It should be noted that evidence of several major non-compliance events has the potential to escalate findings to the level of critical non-compliance.

On identification of a major non-compliance the CI will have 30 calendar days in which to respond and complete the CAPA plan. This requires the CI to explain what action they will take, not necessarily take the action at this point.

Failure to respond to notification of major non-compliance within 30 calendar days will constitute a critical non-compliance as per section 3 and may result in suspension of the study.

4.3 Other Non-Compliance

On identification of other non-compliance, that is neither major nor critical as defined in section 3 the CI will be alerted by the Sponsor.

From the date of notification to the CI there will be 30 calendar days allowed in which to formulate an action plan in response to the non-compliance. This requires the CI to explain what action they will take, not necessarily take the action. A CAPA must be completed as for 4.1 & 4.2

Failure to respond to notification of non-compliance will constitute a major non-compliance as per Section 3

5. Multi-Centre Studies

Where non-compliance is identified at any site, the Sponsor, in collaboration with the Chief Investigator and the Principal investigator / R&D/ Manager at the site, will manage instances in line with Sponsor SOPs.

6. Responsibilities

	Responsibility	Undertaken by	Activity
1	Chief Investigator	Chief Investigator	The Chief Investigator is responsible for ensuring that the study complies with legislation, Good Clinical Practice,the protocol and Sponsor standard operating procedures
2	Chief Investigator	Chief Investigator	The Chief Investigator is responsible for responding to notifications of non-compliance in line with this SOP.
3	Chief Investigator	Chief Investigator	The Chief Investigator is responsible for ensuring the research team are appropriately trained, experienced and qualified to deliver Good Clinical Practice, take informed participant consent and deliver the protocol (see SOP S-1008 UHL Training for Staff Engaged in Research and SOP S-1006 UHL Informed Consent for Research)
4	Sponsor	Head of Research Operations or delegate	The Sponsor will undertake to monitor and utilise quality assurance audit for studies, according to risk assessment which will be influenced by findings of non-compliance
5	Sponsor	Head of Research Operations or delegate	The Sponsor will report non-compliance to the Chief Investigator and request response from them
6	Sponsor	Head of Research Operations and R&I Director	The Director of Research and Innovation will take the final decision whether to suspend a study and associated studies
7	Sponsor	Head of Research Operations or their delegate	The Head of Research Operations will decide when action is sufficient to reinstate a trial or trials.
8	Sponsor	Head of Research Operations or their delegate	The Head of Research Operations will advise in respect of non-compliance and provide access to GCP training and consent assessment as appropriate.
9	Sponsor	Head of Research Operations or their delegate	The Sponsor will escalate action if response is insufficient.
10	Sponsor	Head of Research Operations or delegate	The Sponsor will undertake close monitoring and audit of reinstated studies.

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:** 1/10/20

REVIEW RECORD			
Date	**Issue Number**	**Reviewed By**	**Description Of Changes (If Any)**
April 2015	2	Carolyn Maloney	Changes of Logo and corporate identity
September 2015	3	Carolyn Maloney	Minor wording changes
August 2016	4	CM, LW, JJ	Consistency Checks
February 2017	5	Carolyn Maloney	Update to Logo
March 2018	6	CM	Wording changes – remove trial, replace with Study. Remove R&I Office, replace with Sponsor.
September 2018	7	CCL	Updated R&I logo
April 2020	8	LW,JJ,AM	Review and consistency checks

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