Title: Reporting and Managing Events and Incidents in Research

SOP Number and Version: **UCLH SOP 6, Version 2**	**Effective Date:** 3rd February 2020 **Review Date**: 3rd February 2023

For Trust-wide SOPs, please check this is the **latest version of the SOP** on the Joint Research Office website: www.ucl.ac.uk/joint-research-office.

For Departmental SOPs, please check this is the **latest version of the SOP** with the Research Unit QA Manager.

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Revision Chronology:

Version Number:	Effective date:	Reason for change:	Author:
1	20/04/2015	First UCLH SOP on event reporting requirements for active studies.	Suzanne Binks
1.1	14/09/2015	Clarification on reporting requirements for SAEs for hosted studies.	Suzanne Binks
2	10/12/2018	SOP has been updated to latest UCLH SOP template; minor Title change ('Studies' changed to 'Research'). 1. Background section has been revised to include applicable research policy, guidance and legislation. 3. Procedure section has been revised to include additional details regarding Datix reporting of research incidents, new R&D JRO email address, and suspensions to research recruitment. A reference to UCLH recording of adverse events in patient medical records has now been included (as per Trust reporting requirements). Reporting of personal data breaches (in line with EU GDPR 2016/679 reporting requirements) inserted into SOP. Appendix 1 has been updated to include additional research incidents and their reporting requirements. Minor clarifications have been made throughout the document. References have been updated.	Mona Hassan **Additional SOP Reviewers:** *Shivali Trivedi, CCTU QA Manager* *Kirsty Adams, NIHR CRF QA Manager*
3	03/02/2020	SOP has been updated to reflect the changes made to the research incident reporting section of the UCLH Datix form. The question "was this patient taking part in a clinical trial or research project" has been changed to "was this incident related to a clinical trial or research study?" A section regarding UCLH Serious Incident investigations involving research has been added, and further information has been provided on JRO reporting and investigation requirements for each incident type listed in Section 3. Minor edits and updates to references and web links have been made throughout the document.	Mona Hassan Additional SOP reviewers: Arti Kara, JRO Research Audit & Quality Officer Kirsty Adams, CRF Quality Assurance Manager Celia St Clair, CCTU Quality Assurance Manager

ACRONYMS

AE	Adverse Event
AR	Adverse Reaction
CTIMP	Clinical Trial of an Investigational Medicinal Product
CCTU	Cancer Clinical Trials Unit
CI	Chief Investigator
CRF	Case Report Form
GCP	Good Clinical Practice
HRA	Health Research Authority
IB	Investigator Brochure
ISF	Investigator Site File
JRO	Joint Research Office
MHRA	Medicines and Healthcare Products Regulatory Agency
NIHR CRF	NIHR Clinical Research Facility
PI	Principal Investigator
R&D	Research and Development
REC	Research Ethics Committee
RN	Research Nurse
RU	Research Unit
SAE	Serious Adverse Event
SADE	Serious Adverse Device Effect
SmPC	Summary of Product Characteristics
SOP	Standard Operating Procedure
SUSAR	Suspected Unexpected Serious Adverse Reaction
SSAR	Suspected Serious Adverse Reaction
TMF	Trial Master File
UCLH	University College London Hospitals NHS Foundation Trust
USADE	Unexpected Serious Adverse Device Effect

1. BACKGROUND

A number of research related incidents and events can occur throughout a study. Some may be reportable to the Sponsor (and to regulatory bodies) and some may not be. In accordance with Good Clinical Practice (ICH GCP E6 and subsequent amendments; Directive 2001/20/EC), the Clinical Trials Directive (2001/20/EC), to be repealed by the Clinical Trials Regulation EU No. 536/2014), and the U.K. Policy Framework for Health and Social Care Research 2017 (and subsequent amendments), research sites are responsible for investigating, reporting and recording events and incidents that occur in relation to the conduct of a research study. **Appendix 1** provides definitions of events that may occur, whether these are reportable, and any further action to be taken should they arise. The process of reporting and recording events and incidents aims to safeguard research participants, and ensures the integrity of research data.

2. PURPOSE

The UCLH/UCL Joint Research Office (JRO) is responsible for research management and governance processes for studies taking place at UCLH. This SOP defines events that can occur within a study (see **Appendix 1**) and describes the process for the notification of such events to the JRO as representative of **UCLH as a host site.** This SOP covers host reporting requirements for all types of studies.

3. PROCEDURE

Appendix 1 shows which study events need to be reported and when. For further information about how to report such events to **UCLH as a host site**, please see the table below. For details on how to report events and incidents to the Sponsor and regulatory bodies, please confirm this with the Sponsor for the study.

	Actions (When? How?)	Responsible persons (Who?)
Research related incidents and near misses		
	Where an event meets the definition of a reportable incident or near miss, the JRO (and Research Unit, where applicable) must be informed by reporting the incident through **Datix** (the Trust incident reporting system), and ensuring that 'yes' has been answered to the question '*Was this incident related to a clinical trial or research study?'*. Reporters will subsequently be expected to provide additional study-specific details under the Datix form section: '**Research related incidents'**. The process for investigating and completing Datix incident reports is outlined in the Trust *Incident Reporting Policy* (available on myUCLH). The JRO will liaise with the reporter/PI to obtain further details, and advise on further actions and reporting requirements, where applicable.	All
Serious Adverse Events/Reactions		
	These should be reported to the Sponsor as soon as the event is identified and **within 24 hours.** An SAE form should be completed for all SAEs, and can be obtained from the Sponsor. All AEs and SAEs must additionally be recorded in UCLH patient medical records, according to UCLH reporting systems. Where an SAE is unexpected and related to the research, a copy of the SAE form should be emailed to the JRO (uclh.randd@nhs.net), and the event recorded on Datix.	PI or delegate
Urgent Safety Measures		
	The study PI should be alerted as soon as the requirement for an urgent safety measure has been identified by the Sponsor, or is suspected to have occurred at UCLH The PI must immediately inform Sponsors of suspected/actual Urgent Safety Measures within 24 hours of becoming aware. Urgent Safety Measures can be implemented immediately, prior to receiving HRA, REC, MHRA and R&D authorisation. The main REC must be notified immediately and within 3 days, in the form of a substantial amendment, that such measures have been taken and the reasons why. The substantial amendment documentation must be submitted to the JRO in parallel, by emailing uclh.randd@nhs.net,	PI or delegate

	including regulatory body approvals. Where the research is taking place in a delegated Research Unit, they must also be informed. Correspondence and notifications from the Sponsor/regulatory bodies/JRO must be documented within the ISF and patient notes. The UCLH study team must ensure patients are informed of urgent safety measures, as per guidance and timelines provided by the Sponsor.	
Protocol Violations and Serious Breaches (of Protocol or GCP)		
	The study PI should be alerted as soon as a serious breach or reportable violation has been identified or is suspected (where the safety of the participant and/or integrity of the trial have been compromised). The PI should immediately inform the Sponsor **within 24 hours** of becoming aware (following the Sponsor's procedures) and the JRO (and the relevant Research Unit where applicable). The incident should be reported to the JRO through Datix (answer 'yes' to the question *'is this a serious breach of protocol/Good Clinical Practice/regulatory requirements?'*). The breach/violation should be recorded in the ISF/TMF, and patient medical notes. Serious breaches of protocol or GCP will additionally need to be reported to regulatory bodies within 7 days of becoming aware; the Sponsor, in conjunction with the study team and JRO, will be responsible for determining this necessity (however, as per due diligence, anyone can report a suspected serious breach to the regulatory bodies, e.g. the PI, third party organisation, etc.[1]). The JRO will provide support with the investigation, and where possible, the completion of the serious breach report to regulatory bodies.	PI PI or delegate
UCLH Serious Incidents involving Research		
	A Serious Incident in the NHS can include acts and/or omissions occurring as part of NHS-funded healthcare that result in: - Unexpected or avoidable death of one or more people - Unexpected or avoidable injury to one or more people that has resulted in serious harm - Unexpected or avoidable injury to one or more people that requires further treatment by a healthcare professional in order to prevent the death of the service user or serious harm - Actual or alleged abuse, sexual abuse, physical or psychological ill treatment, or acts of omission which constitute neglect, exploitation, financial or material abuse, discrimination and organisational abuse, self-neglect, domestic abuse, human trafficking and modern day slavery where abuse occurred during the provision of NHS-funded care - A Never Event - An incident (or series of incidents) that prevents, or threatens to prevent, an organisation's ability to continue to deliver an acceptable quality of healthcare services - Major loss of confidence in the service, including prolonged adverse media coverage or public concern about the quality of healthcare or any organisation[2]. Where a research incident has occurred and is considered to be serious by the UCLH Quality and Safety Director (Research), Director of Research, or delegated member of the JRO, a UCLH Serious Incident investigation may be triggered (refer	UCLH research staff JRO

[1] GCP Serious Breaches, 2018 Edition: https://mhrainspectorate.blog.gov.uk/2019/05/24/gcp-serious-breaches-the-2018-edition/
[2] Serious Incident framework, March 2015: https://improvement.nhs.uk/documents/920/serious-incidnt-framwrk.pdf

	to the UCLH *Incident Reporting* Policy on myUCLH for further information). For incidents involving a UCLH research participant or research study, the UCLH Quality & Safety team will notify the JRO, whom will oversee the serious incident investigation, and nominate a lead investigator (usually external to the division for the purposes of objectivity). Any UCLH staff member involved in research may report a suspected or actual serious incident to the JRO, via the normal Datix incident reporting processes, or directly via uclh.randd@nhs.net. The JRO will review and determine whether it constitutes a serious incident (alongside the UCLH Quality & Safety team), and will conduct a 72 hour review to help establish the facts, determine the severity of the incident, support available to staff, and the responsibilities under the duty of candour, including support to patients and families. The JRO will follow the UCLH Serious Incident investigation processes.	
Personal Data Breaches (of data collected as part of a research study)		
	The General Data Protection Regulation (2016/679) broadly defines personal data breaches as a security incident that has affected the **confidentiality**, **integrity** or **availability** of personal data. There will be a personal data breach whenever any personal data is lost, destroyed, corrupted or disclosed; if someone accesses the data or passes it on without proper authorisation; or if the data is made unavailable, for example, when it has been encrypted by ransomware, or accidentally lost or destroyed. Personal data breaches in UCLH research must be immediately reported to the Sponsor, the Data Protection Officer, and the JRO. Any breaches must be documented in the TMF/ISFs, and must follow Sponsor/Data Controller[3] reporting processes. Data breaches in UCLH research trials/studies should be reported to the UCLH Data Protection Officer and the JRO via Datix. Under '**Incident Type'** please select 'yes' to the question '*was this incident related to a clinical trial or research study'*, and under the '*Main category'*, select '*IT related'*, and '*Sub category'*, select '*Software – Breach of the Data Protection Act'*. The UCLH Data Protection Officer is responsible for investigating data breaches in conjunction with the JRO, and will liaise with the reporter accordingly.	PI or delegate
Complaints		
	All complaints from NHS patients from UCLH should be reported in the first instance to the UCLH NHS Complaints Manager (contact details available on myUCLH). The JRO will work with the study team, division and complaints department to resolve the matter.	PI or delegate
Suspensions to Research Recruitment		
	Where concerns have been raised regarding the conduct or management of a study that relates to patient safety or research integrity, the JRO may suspend study recruitment until an investigation can be completed. Refer to *UCLH Policy: Suspension to Recruitment to a Research Study Hosted at UCLH* on myUCLH for further details.	JRO (Authorised Managers for Suspensions)

[3] *Generally, the Sponsor will be the Data Controller; however this may not always be the case. Please check with the study's Sponsor.*

4. IMPLEMENTATION & TRAINING

Staff following this SOP shall confirm they have read and understood the procedures outlined above by completing their relevant training log as a record of acknowledgement.

5. PUBLICATION & COMMUNICATION

This SOP is authorised and published on the JRO website: http://www.ucl.ac.uk/joint-research-office. The latest version of the SOP will be made available on the JRO website and the Research page on myUCLH.

The original fully signed master copy is stored in a designated binder within the JRO and maintained by the JRO Research Quality & Safety Manager (or Research Unit QA Manager if a Departmental SOP).

6. REFERENCES

Clinical Trails Toolkit: serious breach and safety reporting:
http://www.ct-toolkit.ac.uk/routemap/gcp-and-serious-breach-reporting/

Clinical Trials Regulation (EU No 536/2014):
https://ec.europa.eu/health//sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf

Health Research Authority:
https://www.hra.nhs.uk/

ICH GCP:
http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2__Step_4.pdf

ISO 14155: 2011: Clinical investigation of medical device for human subjects – Good Clinical Practice:
https://www.iso.org/standard/45557.html

JRO website:
http://www.ucl.ac.uk/joint-research-office

MHRA GCP Serious Breaches, 2018 Edition:
https://mhrainspectorate.blog.gov.uk/2019/05/24/gcp-serious-breaches-the-2018-edition/

Medicines & Healthcare products Regulatory Agency:
https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency

NHS Improvement: Serious Incident Framework (March 2015 revised version):
https://improvement.nhs.uk/resources/serious-incident-framework/

UCLH Datix incident reporting: http://riskmanagement/datix/live/index.php

UCLH Complaints reporting:
https://my.uclh.nhs.uk/Interact/Pages/Section/Default.aspx?Section=4763

U.K. 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/.

7. APPENDICES

Appendix 1 - Definitions of research events and reporting/recording requirements

REPORTING REQUIREMENTS FOR INCIDENTS AND EVENTS				
Event	**Definition**	**Reportable incident to the Sponsor**	**Reportable incident to JRO (Host)**	**Further action to be taken**
Incident or Near Miss	Any unintended or unexpected event that could have or did lead to harm, loss or damage that contains one or more of the following components: a. It is an accident or other incident which results in injury or ill health. b. It is contrary to specified or expected standard of patient care or service. c. It places patients, staff members, visitors, contractors or members of the public at unnecessary risk. d. It puts the Trust in an adverse position with potential loss of reputation. e. It puts Trust property or assets in an adverse position or at risk of loss or damage.	Check with Sponsor	**Yes**	See Sponsor's reporting requirements.
Adverse Event (AE)	Any untoward medical occurrence in a patient or clinical trial participant administered a medicinal product/intervention, which **does not** necessarily have a causal relationship with this treatment.	Check with Sponsor	No	This should be documented in the patient notes/CRF, followed up, and recorded in the in the ISF.
Adverse Reaction (AR)	Any untoward and unintended response to an investigational medicinal product/procedure **related** (a reasonable causal relationship) to any dose administered/intervention.	Check with Sponsor	No	This should be documented in the patient notes/CRF, followed up, and recorded in the ISF.
Serious Adverse Event (SAE)	Any untoward medical occurrence or affect that: a. results in death b. is life threatening c. requires hospitalisation or prolongation of existing hospitalisation	**Yes,** within 24 hours **Exception:** where this is an **expected SAE** listed in the protocol, IB or SmPC, this may	**Yes,** where this is unexpected and related to the research.	An SAE form should be completed and submitted where appropriate. This should also be documented in the patient notes/CRF,

	d. results in persistent or e. significant disability or incapacity f. is a congenital anomaly or birth defect g. any other safety issues considered medically important.	not need to be reported. Check with the Sponsor/protocol.		followed up, and recorded in the ISF. PIs should **actively seek** follow-up information on reported SAE/Rs.
Serious Adverse Reaction (SAR)	An adverse reaction that is classed in nature as serious and which **is consistent** with the information about the medicinal product listed in the relevant reference documentation: a. Summary of Product Characteristics (SPC) in the case of a licensed product being used within its licensed dosage and indication. b. An Investigator's Brochure (IB) or a simplified IMPD in the case of any other IMP or a licensed product being used outside its licensed dosage and indication.	Yes	No	This should be documented in the patient notes/CRF, followed up, and recorded in the ISF. PIs should **actively seek** follow-up information on reported SAE/Rs.
Suspected Unexpected Serious Adverse Reaction (SUSAR)	An adverse reaction that is classified in nature as both serious and unexpected. That is, it **is not consistent** with information laid out; a. in the protocol b. in the summary of product characteristics (SmPC) c. in the IB relating to the trial in question.	**Yes,** within 24 hours	**No**	An SAE form should be completed and submitted where appropriate. Sponsor to report fatal or life threatening SUSARs to MHRA and REC within 7 days. All other SUSARs within 15 days. This should also be documented in the patient notes/CRF, followed up, and recorded in the ISF.
Serious Adverse Event/Serious Adverse Device Effect (SADE)	Adverse event that: a) led to death, b) led to serious deterioration in the health of the subject, that either resulted in a life-threatening illness or injury, or a permanent impairment of a body structure or a body function, or in-patient or prolonged hospitalization, or	**Yes**, within 24 hours	**Yes**, where this is unexpected and related to the research medical device	An SAE/SADE form should be completed and submitted where appropriate. This should also be documented in the patient notes/CRF, followed up, and recorded in the ISF.

	medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function, c) led to foetal distress, foetal death or a congenital abnormality or birth defect Note: Planned hospitalisation for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event (*ISO 14155)*.			
Unanticipated Serious Adverse Device Effect (USADE)	Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report Note: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk analysis report (*ISO 14155)*.	**Yes**, within 24 hours	**Yes**, where this is unexpected and related to the research medical device	An SAE/USADE form should be completed and submitted where appropriate. This should also be documented in the patient notes/CRF, followed up, and recorded in the ISF.
Urgent Safety Measure	An emergency measure taken to protect a research participant from an immediate hazard to their health and safety.	**Yes,** immediately	**Yes**	See Sponsor's reporting requirements.
Protocol Deviation	An unintended departure from the expected conduct of the study protocol/SOPs.	Check with Sponsor	No	Protocol deviations should be logged in the ISF.
Protocol Violation	Can occur when there is a consistent variation in practice from trial protocol or SOPs. A violation can be classified as serious if there is a significant occurrence which affects participant safety or integrity of the research.	If patient safety or data integrity has been compromised, **yes.**	If patient safety or data integrity has been compromised, **yes.**	See Sponsor's reporting requirements.
Serious Breach of Protocol and/or Good Clinical Practice	Regulation 29A of the Medicines for Human Use (Clinical Trials) Regulations 2004 [Statutory Instrument 2004/1031], as amended by Statutory Instrument 2006/1928, contains a requirement for the notification of "serious breaches" of GCP or the trial protocol: A breach which is likely to effect to a significant degree – a. The safety or physical or mental integrity of the subjects of the trial; or	**Yes,** immediately	**Yes**	See Sponsor's reporting requirements.

	b. The scientific value of the trial.			
Personal Data Breaches	Breaches of patient personal data collected as part of a research study must be reported. The General Data Protection Regulation (2016/679) broadly defines personal data breaches as a security incident that has affected the **confidentiality**, **integrity** or **availability** of personal data.	**Yes,** immediately (and to the Data Controller's Data Protection Officer) **Generally, the Sponsor will be the Data Controller, however you must confirm with Sponsors and report accordingly.*	**Yes**	See Sponsor's reporting requirements.
Serious Incident	A Serious Incident in the NHS can include acts and/or omissions occurring as part of NHS-funded healthcare that result in: - Unexpected or avoidable death of one or more people - Unexpected or avoidable injury to one or more people that has resulted in serious harm - Unexpected or avoidable injury to one or more people that requires further treatment by a healthcare professional in order to prevent the death of the service user or serious harm - Actual or alleged abuse, sexual abuse, physical or psychological ill treatment, or acts of omission which constitute neglect, exploitation, financial or material abuse, discrimination and organisational abuse, self-neglect, domestic abuse, human trafficking and modern day slavery where abuse occurred during the provision of NHS-funded care - A Never Event - An incident (or series of incidents) that prevents, or threatens to prevent, an organisation's ability to continue to deliver an	**Yes,** for information. Sponsors are not traditionally involved in SI investigations, however may be contacted for further information, or made aware.	**Yes,** immediately	See this SOP's reporting requirements for research, and the *UCLH Incident Reporting* Policy.

	acceptable quality of healthcare services - Major loss of confidence in the service, including prolonged adverse media coverage or public concern about the quality of healthcare or any organisation[4].			

[4] Serious Incident framework, March 2015: https://improvement.nhs.uk/documents/920/serious-incidnt-framwrk.pdf