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Standard Operating Procedure for Reporting Research Incidents, Events and Complaints in UCL/UCLH sponsored non-CTIMPs

JRO SOP 9

SOP ID Number	Version Number	Effective Date	Review Date
JRO SOP 9	4	27/04/2020	27/04/2020
Author: **Name and Job Title**	Mona Hassan Research Quality and Safety Manager		
Authorised by: **Name and Job Title:**	Rajinder Sidhu Deputy Director, Research Support		
Target Audience	Joint Research Office, Research Management & Governance, Research staff conducting non-CTIMPs sponsored by UCL or UCLH (and managed by the JRO)		
Please check with the JRO Research Quality & Safety Manager that this is the latest version of the SOP.			

Revision Chronology			
Version	**Effective Date**	**Reasons for Change**	**Author**
JRO RMG RSS SOP-09 DRAFT version 1.0			Anna Jones & Patrik Pettersson
JRO RMG RSS SOP-09 DRAFT version 2.0		Inclusion of process for reporting UCL sponsored non-CTIMPs	Susan Kerrison
JRO RMG RSS SOP-09 version 1	19 Dec 2012	Inclusion of QA	Patricia Galligan
JRO RMG RSS SOP-09 version 2	31 January 2013	To clarify that SAE reporting is for non-CTIMPs only and SUSAR reporting is for hosted CTIMPs. Update of the flowchart in Appendix 1 as version 2.1 dated 31 January 2013.	Patricia Galligan
JRO RMG SOP 9 version 3	21 July 2014	The UCLH NHS permission template was updated on the 24 June 2014 to remove reporting of SUSARs to the JRO as host site (in addition to the Sponsor). The review timeframe was revised to every 3 years and the key criteria for inclusion in the audit checklist were outlined. Therefore the SOP has been revised to include the changes.	Patricia Galligan
JRO SOP 9 version 4	27/04/2020	With the introduction of UCLH SOPs it was deemed appropriate to separate reporting requirements for UCL sponsored non-CTIMPs and UCLH hosted studies. Research reporting requirements for UCLH hosted studies is now covered by UCLH SOP 6. SOP now includes reporting requirements for UCLH sponsored research; different methods of reporting research incidents to JRO, expansion of JRO research incident definitions and remit, inclusion of JRO Research Quality & Safety Unit, and updates to JRO reporting and escalation process. The process for suspending recruitment to UCL/UCLH sponsored research has been inserted. Information on what, where and how to report incidents for non-CTIMPs has been updated. The roles of the UCL and UCLH Data Protection Officers have been inserted into the SOP, to account for the	Mona Hassan

		responsibility of investigating data breaches in research, in line with the General Data Protection Regulation (Regulation (EU) 2016/679) and the UK Data Protection Act 2018. Research staff conducting non-CTIMPs have also been added as a target audience. The title of this SOP has been amended to reflect these changes.	

1. ACRONYMS

AE	Averse Event
CAPA	Corrective and Preventative Action
CI	Chief Investigator
CRIU	[BRC] Clinical and Research Informatics Unit
CTIMP	Clinical Trial of Investigational Medicinal Product
CTU	Clinical Trial Unit
GCP	Good Clinical Practice
HRA	Health Research Authority
ICH	International Conference on Harmonisation
JRO	Joint Research Office
MHRA	Medicines and Healthcare products Regulatory Agency
PI	Principal Investigator
QA	Quality Assurance
R&D	Research & Development
REC	Research Ethics Committee
RQSU	Research Quality and Safety Unit
RM&G	Research Management & Governance
SAE	Serious Adverse Event
SADE	Serious Adverse Device Event
SO	Sponsorship Officer
SOC	[UCL] Sponsorship Oversight Committee
SOP	Standard Operating Procedure
UCL	University College London
UCLH	University College London Hospitals NHS Foundation Trust
USADE	Unanticipated Serious Adverse Device Event

2. DEFINITIONS

CTIMP	An investigation in human participants, intended: a. To discover or verify the clinical, pharmacological and/or other pharmacodynamics effects of one or more medicinal product, b. To identify any adverse reactions and safety, or c. To study absorption, distribution, metabolism and excretion, with the object of ascertaining the safety and/or efficacy of those products. An IMP is a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products - used in a different form from the marketing authorisation - used for an indication not included in the summary of product characteristics (SmPC) - used to gain further information about the product as authorised in the clinical trial authorisation.
Non-CTIMP	The JRO define non-CTIMPs as observational and interventional research excluding CTIMPs, ATIMPs, and regulated device trials. **Observational research:** A study in which participants may undergo

	procedures or tests using various methods in order to investigate a research question, but there is no intervention or treatment altering clinical/standard care involved. Examples of observational research: **Interventional research:** A clinical study in which participants are assigned to receive one or more interventions (or no intervention) so that researchers can evaluate the effects of the interventions on biomedical or health-related outcomes. The assignments are determined by the study protocol. Participants may receive diagnostic, therapeutic, or other types of interventions. These types of studies change the clinical care that the participant is receiving. Examples of observational and interventional research: • a basic science study involving procedures with human participants • a study administering questionnaires/interviews for quantitative analysis, or using mixed qualitative/quantitative methodology • a study involving qualitative methods only • a study limited to working with human tissue samples (or other human biological samples) and data (specific project only) • a study limited to working with data (specific project only) • clinical investigation or other study of a **regulated CE marked** medical device falling under ISO 14155 • other clinical trial to study a novel intervention or randomised clinical trial (RCT) to compare interventions in clinical practice • **Mechanistic study**: A study or test designed to analyse the biologic or chemical events responsible for, or associated with, an effect observed, and to provide information concerning the molecular, cellular or physiological mechanisms by which substances exert their effects on living cells and organisms. These studies can explore the mechanisms of action of the intervention, the causes of differing responses, or promote an understanding of any potential adverse effects and how these could be reduced. They could also contribute to understanding of the disease process.
Concern	A perception that a set of circumstances or a potential error or hazard presents a risk which could lead to harm, loss or damage if not addressed.
Complaint	A written or spoken statement expressing dissatisfaction.
Data Breach	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, e.g. when it has been encrypted by ransomware, or accidentally lost or destroyed. Breaches of personal data collected as part of a research study must be reported to the JRO as sponsor, and relevant Data Protection Officer. The UCL or UCLH DPO will take the lead in investigating data breaches, with support from the JRO where required.

Host research site	The organisation at which the research procedures are taking place.
Research Incident	Any unintended or unexpected event that could have or did lead to harm, loss or damage to research participants, staff or members of the public receiving care or delivering services in a UCL/UCLH sponsored non-CTIMP study. Examples of the following should be reported to Sponsor: • Significantly affects the rights or wellbeing of a research participant • The scientific value of the study • It is an accident or other incident which results in injury or ill health • It is contrary to the specified or expected standard of patient care or service • It places patient(s) or staff member(s), or visitor(s), contractor(s) or members of the public at unnecessary risk • Non-compliance of the study/research staff with relevant legislation, ethical guidance, and Sponsor requirements, e.g. the UK Policy Framework for Health and Social Care Research, the EU General Data Protection Legislation (2016/679) and the UK Data Protection Act (2018), the Human Tissue Act (2004), the Mental Capacity Act (2005), etc. • It puts the Sponsor/research study in an adverse position with potential loss of reputation. • It puts the Sponsor/research study in an adverse position or at risk of loss or damage.
Near Miss	An event not causing harm but has the potential to cause injury or ill health. Reporting a 'near miss' event is as important as reporting incidents that occurred and caused harm, as the potential for recurrence may still exist and must be managed effectively.
Serious Breach of Protocol/GCP	A breach of protocol/GCP, which is likely to affect to a significant degree: (a) the safety or physical or mental integrity of the research participants; or (b) the scientific value of the study.
Protocol Deviation	A **minor** unintended departure from the expected conduct of the study protocol/SOPs, which **does not impact** the participants' safety or compromises the integrity of the study data. E.g. a study visit date being outside the window defined in the protocol, participants ticking rather than initialling their answers on their consent form.
Protocol Violations and Non-Compliances	Any significant deviation from the protocol, study, or sponsor procedures that **may impact** the participants' safety or affects the integrity of the study data; study conduct that is not approved by the sponsor/REC/HRA/R&D prior to its implementation. Examples: no evidence of informed consent having been taken, participants don't meet eligibility criteria, failure to report multiple research incidents, study started without appropriate regulatory/NHS approvals, study using unapproved documentation, etc.

	Additional examples of Non-Compliances: Non-compliances with the conditions of UCL or UCLH sponsorship authorisation, SOPs, policies or procedures, or non-compliances with the conditions of NHS Confirmations of Capacity and Capability (for participating research sites).
Adverse Event (AE)	Any untoward medical occurrence in a participant administered a licensed medicinal product or intervention, which **does not** necessarily have a causal relationship with this treatment. The PI should assess and confirm this was an AE, documented in patient medical notes, Case Report Forms, and the JRO non-CTIMP AE log.
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 d. results in persistent or significant disability or incapacity e. or is a congenital anomaly or birth defect f. any other safety issues considered medically important. Important medical events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardise the patient or may require intervention to prevent one of the other outcomes listed in the definition above should also be considered serious. Reportable SAEs are those that are **unexpected and related** to the research procedures/conduct/intervention.
Serious Adverse Device Effect (SADE)	An adverse event related to the use of an investigational medical device that has resulted in any of the consequences characteristic of a serious adverse event (see above). Note: planned hospitalisation for a pre-existing condition, or a procedure required by the protocol, without serious deterioration in health, is not considered a SADE, and doesn't require reporting to the JRO.
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.
Causality	The relationship between the research drug/device/procedure and the occurrence of research events and incidents will be assessed and categorised by the CI/PI, who will use clinical judgement to determine the relationship. Alternative causes, such as natural history of the underlying diseases, concomitant therapy, other risk factors etc. will be considered. • **Not related:** There is no relationship between the research intervention and the event, or another cause can by itself explain the occurrence of the event. • **Unlikely:** The event is likely to have another cause which can by itself explain the occurrence of the event.

	• **Possibly related:** Relationship between the research intervention and the event is reasonable but the event could have been due to another, equally likely cause. • **Probably related:** Relationship between the research intervention and the event is reasonable and the event is more likely explained by the research intervention than any other cause. • **Definitely related:** Relationship between the research intervention and the event is reasonable and there is no other cause to explain the event, and a reoccurrence is possible.
Expectedness of an AE/SAE	The expectedness of an AE/SAE must be determined according to the protocol and appropriate reference documents (e.g. SmPC, drug/device labelling or marketing information, etc.), as well as CI/PI assessment. **Expected:** AE/SAE previously identified and described in protocol or reference documents. **Unexpected:** AE/SAE not previously described in the protocol or reference documents.
Sponsor	The individual, organisation or group taking on responsibility for securing the arrangements to initiate, manage and finance a study.
Suspension to Recruitment	In certain instances, the JRO may need to temporarily suspend recruitment to a research study due to a research incident, in order for a JRO investigation to take place, and sponsor reporting and escalation processes followed. This is to ensure no participants/staff are unnecessarily put in harm's way, and the integrity of study conduct and data is maintained.
Urgent Safety Measure	An emergency measure taken by the sponsor/PI/CI to protect a research participant from an immediate hazard to their health and safety, without prior authorisation from a regulatory body.

3. JRO POLICY

Standard Operating Procedures (SOPs) are written working practice documents detailing routine procedures that must be followed to perform a given task.

All SOPs produced from the JRO must be used in conjunction with local NHS Trust and UCL policies and procedures.

The JRO represents UCL and UCLH as the Sponsor and UCLH as a participating site. The JRO is responsible for research management and governance processes as sponsor and host site representative. The JRO SOPs will provide the quality system to fulfil these requirements.

This SOP complies with the U.K Policy Framework for Health and Social Care Research 2017 (3rd edition, v3.3 07/11/2017) and its subsequent amendments, and Good Clinical Practice as outlined by the EU Clinical Trials Directive 2001/20/EC and EU Clinical Trial Regulation EU No. 536/2014 when it is implemented.

4. RELATED SOPs

JRO SOP 2	Granting UCL or UCLH Sponsorship for Observational Studies
JRO SOP 3	Granting UCL Sponsorship for Interventional Trials (excluding Clinical Trials of Investigational Medicinal Products, Advanced Therapy and Device Trials)
UCLH SOP 6	Reporting and Managing Incidents and Events in Studies
UCL Policy	Complaints From Research Subjects about UCL Sponsored Studies and Trials

5. BACKGROUND

Research teams are responsible for investigating, reporting and recording events and incidents that occur in relation to the conduct of a research study. This SOP describes the processes for when, how and where different kinds of research incidents relating to the safety of research participants and the integrity of the study should be reported. The JRO acts as UCL and UCLH sponsor representative, and must ensure there are oversight mechanisms in place to oversee and manage research incidents, events and complaints relating to the management and conduct of sponsored research.

It is the responsibility of the CI or PI (or delegated individual) to report these events to the Sponsor in the first instance, in accordance with the protocol, sponsor, and regulatory requirements. The Sponsorship Officer and Research Quality & Safety Manager will ensure that appropriate research incident reporting requirements are included in the relevant sections of the study protocol, during the sponsorship review process.

A flow diagram (see Diagram 1, page 15) summarises the reporting requirements for incidents involving research participants (either NHS patients or healthy volunteers), including further information on the review and escalation process of events reported.

The scope of this SOP includes all studies managed by the JRO's Research Management and Governance team, including:

- basic science studies involving procedures with human participants
- studies administering questionnaires/interviews for quantitative analysis, or using mixed qualitative/quantitative methodology
- studies involving qualitative methods only
- studies limited to working with human tissue samples (or other human biological samples) and data (specific project only)
- studies limited to working with data (specific project only)
- clinical investigations or other study of a CE marked medical device, being used for its intended purpose
- other clinical trials to study a novel intervention or randomised clinical trial (RCT) to compare interventions in clinical practice
- mechanistic studies (using licensed drugs).

The above observational and interventional study types will be hereafter referred to as "non-CTIMPs".

SOP Exclusions:

1. This SOP **does not** apply to UCL sponsored CTIMPs, ATIMPs, or regulated device trials managed by the JRO Clinical Trials team.
2. This SOP **does not** cover any studies run by a UCL Clinical Trials Unit (CTU). More specifically these include studies managed by:

    - MRC Clinical Trials Unit at UCL

- Comprehensive Clinical Trials Unit at UCL
- PRIMENT Clinical Trials Unit
- Cancer Research UK/UCL Cancer Trials Centre

Where a CTU is involved, the incident or complaint will be handled by the CTU, as delegated by the JRO.

3. This SOP **does not** cover host site reporting requirements for UCLH. Please refer to *UCLH SOP 9 Reporting and Managing Events and Incidents in Research,* or relevant NHS site reporting requirements for research incidents involving NHS participants.

6. PURPOSE AND SCOPE

This SOP outlines the JRO's reporting requirements for non-CTIMPs that are sponsored by UCL and UCLH, and managed by the JRO (Research Management and Governance team). This SOP describes when, how and where research events, incidents and complaints should be reported to the JRO as Sponsor, and how these are investigated by the JRO Research Quality and Safety team.

As part of sponsorship approval conditions, the CI and study teams must report to the JRO the following:

Reportable Research Incidents:

- Serious Adverse Events that are **unexpected and related** to the research procedures, conduct or management (based on CI/PI assessment, and comparison to list of expected events in the protocol)
- Protocol violations
- Serious breaches of Protocol or GCP
- Personal data breaches
- Complaints from research participants/staff
- Research concerns
- Near misses
- Non-compliances with sponsor requirements, research legislation, R&D approval conditions
- Serious Adverse Device Events (SADE) or Unexpected Serious Adverse Device Events (USADE) that are **unexpected and related** to the medical device used within the research study (based on CI/PI assessment, and comparison to list of expected events in the protocol).

Unexpected and related SAEs in non-CTIMPs should additionally be reported to the main REC that approved the study within 15 days of the CI becoming aware of the event, using the Non-CTIMP safety report to REC form[1]. The JRO will advise if these require additional reporting to the REC, or other regulatory bodies, and will support in the submissions.

[1] REC non-CTIMP SAE reporting: https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/safety-reporting/.

There are several ways to report to the JRO Research Quality and Safety Unit **(RQSU):**

Reporting Mechanism	How?	Type of Study	Additional Information
RQSU Email Address	research-incidents@ucl.ac.uk	UCL sponsored studies	Submit queries/reports/ emails
JRO Research Incident Report Form	REDCAP: https://redcap.slms.ucl.ac.uk/surveys/?s=NE5dypTdFo	UCL/UCLH sponsored studies	N/A
UCL RiskNet	https://ucl.oshens.com/AIR2/Incbook/incbook_tab_begin.aspx	UCL sponsored studies where incidents related to NHS patients occurred on UCL premises	Please select category '*NHS Patient Incident*'
DATIX	http://riskmanagement/datix/live/index.php?action=login	UCLH hosted studies	Please ensure you answer **yes** to the question: '*Was this incident related to a clinical trial or research study?*'

Non-reportable research incidents/events:
The following types of research events are not reportable to the JRO as Sponsor; the expectation is that research teams will have considered these during their protocol write up and noted these as expected or related/unrelated incidents (e.g. based on clinical evidence and/or clinical assessment). Research teams are therefore expected to keep a record of the incident in the relevant research incident logs (refer to Section 12 for applicable JRO non-CTIMP templates) within their site's Investigator Site File/CI Trial Master File, and make these available to the JRO upon request, for audit and monitoring purposes:

- Serious Adverse Events that are **expected and related or expected and unrelated** to the research procedures (and already documented within the protocol and confirmed as such by the CI/PI). Investigators may wish to record these in the JRO non-CTIMPs SAE log template.
- Adverse Events (records must be kept in the patient medical records/Case Report Forms/AE logs)
- Adverse reactions (records must be kept in the patient medical records/Case Report Forms/AE logs, and reported to manufacturers as required)
- Protocol deviations which **does not impact** the participants' safety or compromises the integrity of the study data (should be recorded in a protocol deviation log and retained at site in the Investigator Site File (ISF).

Please review the research protocol closely for information on what is reportable to the JRO as Sponsor. Protocols should include a list of expected and related or unrelated AEs and SAEs (where applicable) that don't require reporting to Sponsor and/or regulatory bodies (e.g. Research Ethics Committee). Otherwise, all **unexpected and related research events and incidents** should be reported to the JRO in the first instance.

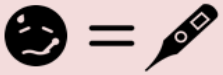
7. RESPONSIBLE PERSONNEL AND THEIR DUTIES

	Responsible Person	Summary of duties
1	CI (or delegated person)	Report events to the Sponsor in accordance with the protocol reporting process and timelines. The CI may delegate this responsibility to a member(s) of their team, but retains overall responsibility for the conduct of the study. Adhering to protocol and sponsor reporting procedures, including its conduct, the participants' safety and wellbeing, and ongoing suitability of protocol in light of research events, complaints and incidents. Ensuring that safety events (where applicable) are reviewed by an appropriate safety or data monitoring committees (where established).
2	PI (or delegated person)	Report events to the Chief Investigator and Sponsor in accordance with the protocol reporting process and timelines. Keep a record of all research events, incidents and complaints in the TMF/ISF, throughout duration of study, and seek advice from Sponsor where required. The PI is responsible for reviewing AE/SAEs and pertinent documentation (e.g. hospital notes, lab and diagnostic reports), and assessing intensity, causality, expectedness and seriousness. Where research events and incidents are related to the research intervention, **PIs must inform the participant and their clinical care team, and NHS site's R&D department, where applicable.**

3	JRO Research Quality and Safety Unit *Research Quality and Safety Manager* *Research Audit and Quality Officer* *Head of Clinical Research Governance* *Deputy Director of Research Support* *Director of Quality and Safety (Research)*	- Investigate and respond to research incidents reported to the JRO, on behalf of Sponsor - Provide guidance, advice and support to research teams - Escalate research incidents to Director of Quality & Safety (Research) - Escalate research incidents to relevant committee/group (as required, depending on nature, risk and complexity of study and research incident), e.g. JRO Quality & Safety Group, Sponsor Review Group, Sponsorship Oversight Committee, etc. - Report summaries of research incidents to UCL Clinical Research Governance Committee or UCLH Quality & Safety Committee - Where there is significant risk to research participants or integrity of study, authorised members of the JRO RQSU may suspend recruitment to the study until the incident has been satisfactorily resolved - Report research incidents to regulatory bodies and R&D departments, where required.

Definition of Incidents Table

INCIDENT	DEFINITION	REPORTABLE TO JRO?	REPORTING TIMELINE	REPORTING METHOD
Concern 	A perception that a set of circumstances or a potential error or hazard presents a risk which could lead to harm, loss or damage if not addressed.	YES	Within 3 working days of becoming aware	• Email concern to **research-incidents@ucl.ac.uk**
Complaint 	A written or spoken statement expressing dissatisfaction	YES	Within 3 working days of becoming aware	• Reportable to JRO as Sponsor by emailing **research-incidents@ucl.ac.uk** • If complaint is from NHS patients/staff involved in research, the **NHS Complaints Manager** should be notified too: Lesley Creasey, Interim Complaints Manager, lesley.creasey@nhs.net • The JRO and NHS Complaints Manager will seek to resolve complaints within 3 months (or longer, where agreed with the complainant)
Data Breach 	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, e.g. when it has been encrypted by ransomware, or accidentally lost or destroyed.	YES	Within 24 hours of becoming aware	• <u>UCL Sponsored Studies:</u> Report immediately to the following groups * UCL Information Security Group (ISG) & UCL Data Protection Officer: Please complete the form found on **https://www.ucl.ac.uk/legal-services/guidance/reporting-loss-personal-data** and forward any correspondence to the JRO to research-incidents@ucl.ac.uk * The JRO as the Sponsor: Please complete **JRO REDCAP Incident Reporting Form** at https://redcap.slms.ucl.ac.uk/surveys/?s=NE5dypTdFo • <u>UCLH Sponsored Studies:</u> Report immediately to the following groups * UCLH Head of Information Governance/Data Protection Officer: Please complete UCLH **Datix** Report on UCLH Intranet, answering 'yes' to "Was this patient taking part in a clinical trial or research project?" * The JRO as the Sponsor: Please complete **JRO REDCAP Incident Reporting Form** at https://redcap.slms.ucl.ac.uk/surveys/?s=NE5dypTdFo When reporting the data breach, please ensure the following information is included: • Full details of the nature of the breach • An indication of the volume of material involved • The sensitivity of the breach and any timeframes that apply • The actions taken to rectify the error

INCIDENT	DEFINITION	REPORTABLE TO JRO?	REPORTING TIMELINE	REPORTING METHOD
Adverse Event (AE) 	Any untoward medical occurrence in a participant administered a licensed medicinal product or intervention, which **does not** necessarily have a causal relationship with this treatment.	NO	N/A	• PI should assess and confirm that the incident was an AE (expected and/or related adverse events should be listed in the protocol) • PI should document the AE in the patient's medical notes, Case Report Forms and the JRO non-CTIMP AE Log which should be filed within the ISF/TMF
Serious Adverse Event (SAE) 	Any untoward medical occurrence that: • Results in death • Is life-threatening • Requires hospitalisation or prolongation of existing hospitalisation • Results in persistent or significant disability or incapacity • Is a congenital anomaly or birth defect • Any other safety issue considered medically important Important medical events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardise the patient or may require intervention to prevent one of the other outcomes listed in the definition above should also be considered serious.	YES (IF UNEXPECTED & RELATED TO THE STUDY)	Within 24 hours of becoming aware	• If SAE is **UNEXPECTED & RELATED** to the research procedures/conduct/intervention, please report to the JRO by completing the **JRO REDCAP Incident Reporting Form** at https://redcap.slms.ucl.ac.uk/surveys/?s=NE5dypTdFo • If SAE is expected & related to the research procedures/conduct/intervention, as per the protocol or SmPC, please do NOT report this to the JRO. These must be recorded in the patient's medical notes/eCRF and on the JRO non-CTIMP SAE Log and filed in the ISF/TMF
Serious Adverse Device Effect (SADE) 	An adverse event related to the use of an investigational medical device that has resulted in any of the consequences characteristic of a serious adverse event (see above).	YES (IF UNEXPECTED & RELATED TO THE STUDY'S CE MARKED MEDICAL DEVICE)	Within 24 hours of becoming aware	• If SADE is **UNEXPECTED & RELATED** to the study's CE marked medical device, please report to the JRO and manufacturers by completing the **JRO REDCAP Incident Reporting Form** at https://redcap.slms.ucl.ac.uk/surveys/?s=NE5dypTdFo • If SADE is expected & related to the study's CE marked medical device, as per the protocol please do NOT report this to the JRO. These must be recorded in the patient's medical notes/eCRF and on the JRO non-CTIMP SAE Log and filed in the ISF/TMF • Please note: planned hospitalisation for a pre-existing condition, or a procedure required by the protocol, without serious deterioration in health, is not considered a
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.	YES	Within 24 hours of becoming aware	• Please report to the JRO by completing the **JRO REDCAP Incident Reporting Form** at https://redcap.slms.ucl.ac.uk/surveys/?s=NE5dypTdFo • Please note: Anticipated Serious Device Effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk analysis report. Please do not report this to the JRO. These must be recorded in the patient's medical notes/eCRF and on the JRO

INCIDENT	DEFINITION	REPORTABLE TO JRO?	REPORTING TIMELINE	REPORTING METHOD
Protocol Deviation 	A **minor** unintended departure from the expected conduct of the study protocol/SOPs, which **does not impact** the participants' safety or compromises the integrity of the study data. E.g. a study visit date being outside the window defined in the protocol, participants ticking rather than initialling their answers on their consent form.	NO	N/A	• Record in a protocol deviation log and file in the ISF • The CI and study oversight groups/Clinical Trial Units should continually monitor protocol deviations to establish whether an amendment or training is needed or an escalation into a protocol violation or breach category is required. It is the responsibility of the CI to ensure research teams are trained to avoid repeat deviations from occurring.
Protocol Violations and Non-Compliances 	Any significant deviation from the protocol, study, or sponsor procedures that **may impact** the participants' safety or affects the integrity of the study data or study conduct that is not approved by the sponsor/REC/HRA/R&D prior to its implementation. Examples of Protocol Violations: no evidence of informed consent having been taken, participants don't meet eligibility criteria, failure to report multiple research incidents, study started without appropriate regulatory/NHS approvals, study using unapproved documentation Examples of Non-Compliances: Non-compliance with conditions of UCL or UCLH sponsorship authorisation, SOPs, policies or procedures, or non-compliances with the conditions of NHS Confirmation of Capacity and Capability (for participating research sites)	YES	Within 24 hours of becoming aware	• Please report to JRO as sponsor by completing the **JRO REDCAP Incident Reporting Form** at https://redcap.slms.ucl.ac.uk/surveys/?s=NE5dypTdFo
Serious Breach of Protocol/GCP 	A breach of protocol/GCP which is likely to affect to a significant degree: (a) the safety, physical or mental integrity of the research participant (b) the scientific value of the study	YES	Within 24 hours of becoming aware	• Please report to JRO as sponsor by completing the **JRO REDCAP Incident Reporting Form** at https://redcap.slms.ucl.ac.uk/surveys/?s=NE5dypTdFo • The JRO as sponsor is required to report serious breaches to REC/HRA (and MHRA, where applicable), within 7 days of becoming aware of the breach, therefore it is essential they are notified as soon as possible
Urgent Safety Measure 	An emergency measure taken by the sponsor/PI/CI to protect a research participant from an immediate hazard to their health and safety, without prior authorisation from a regulatory body.	YES	Report to Sponsor (JRO) Within 24 hours of becoming aware Report to Regulatory Bodies & Principal Investigators within 3 calendar days—Substantial Amendment	• The CI must report to JRO as sponsor by completing the **JRO REDCAP Incident Reporting Form** at https://redcap.slms.ucl.ac.uk/surveys/?s=NE5dypTdFo • The CI must report to regulatory bodies and Principal Investigators to protect participants in the study (in the form of a substantial amendment)

8. PROCEDURE

The below flow diagram summarises the reporting requirements for research incidents involving research participants in UCL/UCLH sponsored non-CTIMPs (either NHS patients or healthy volunteers), including the JRO review and escalation process of events reported:

Diagram 1: JRO Research Incidents Reporting Flowchart

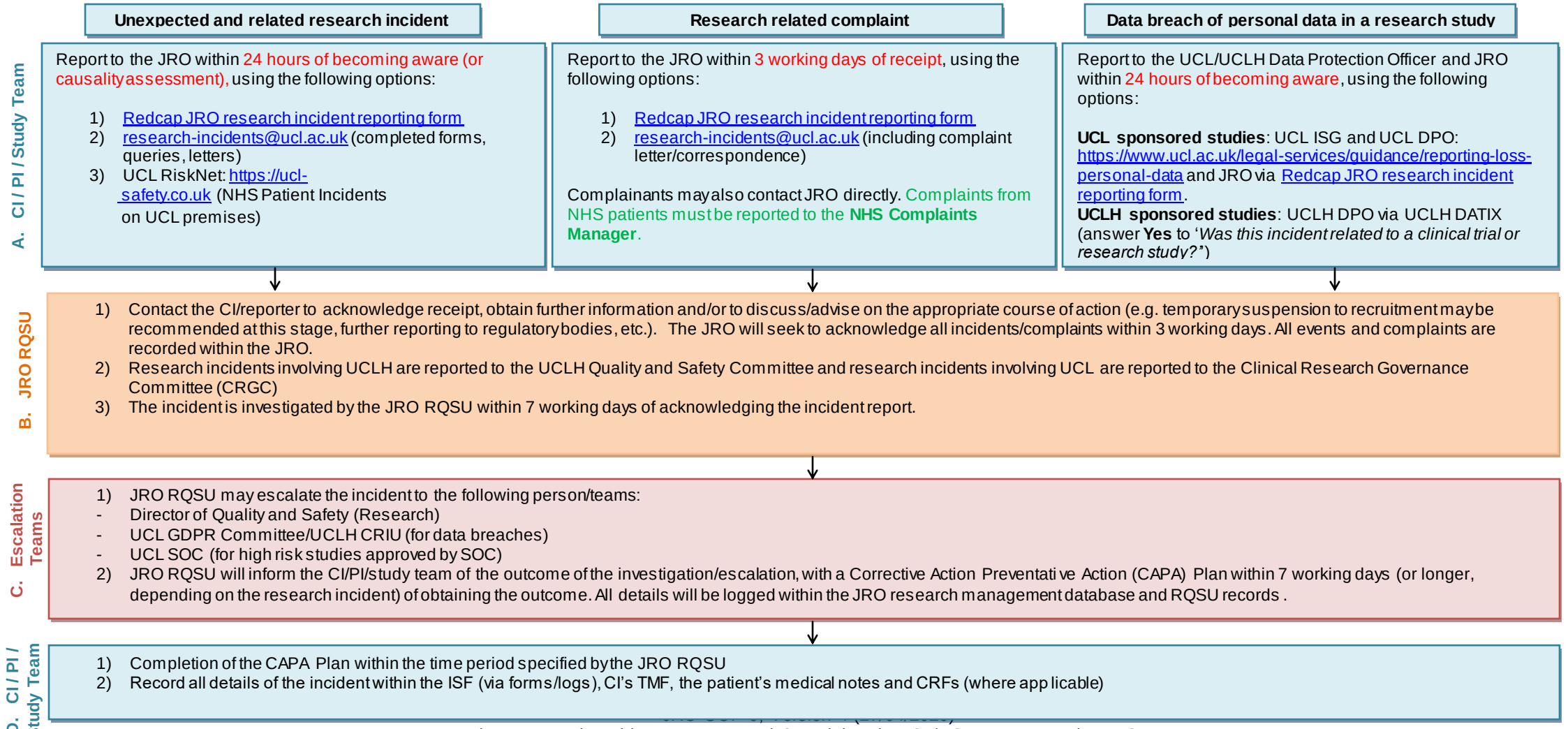
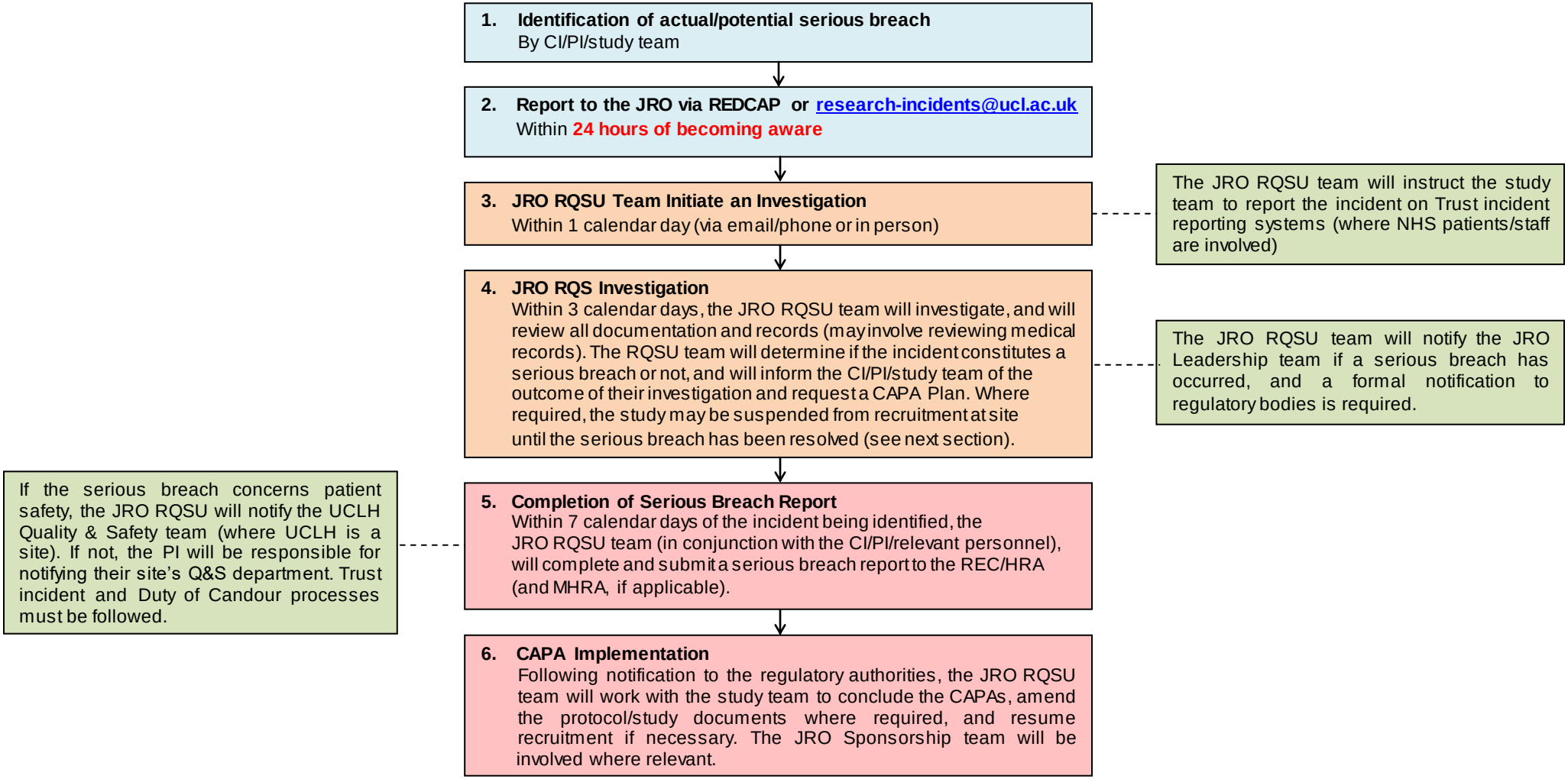


Diagram 2: Serious Breaches of Protocol/GCP

The below process must be followed in the event of an actual or potential serious breach:



JRO Suspensions to Recruitment

Authorised Managers[2] within the JRO may temporarily suspend recruitment or withdraw sponsorship for a study. This may occur when a study:

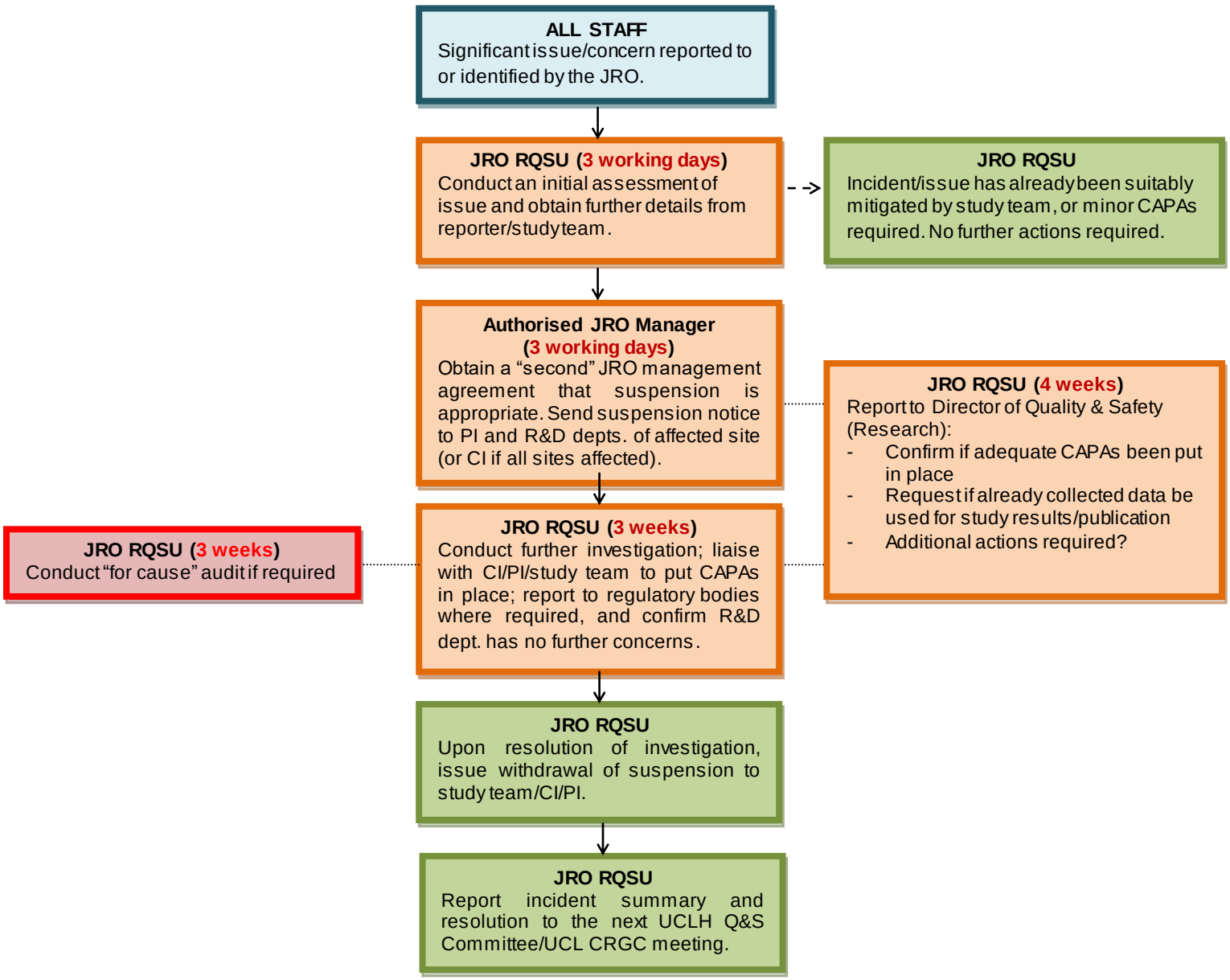
- Places research participants' rights and/or wellbeing at risk;
- Jeopardises the scientific integrity of the study and its data;
- Places UCL/UCLH at reputational or financial risk;
- Is currently being investigated by the JRO/funders/regulatory bodies/research team/etc.;
- Is non-compliant with research legislation, regulatory requirements or ethical guidance, e.g. the Human Tissue Act, General Data Protection Regulation, Good Clinical Practice, UCLH or R&D policies, procedures and Standard Operating Procedures;
- Has been initiated without the appropriate regulatory or NHS approvals;
- Has significant issues determined by the JRO.

The JRO may additionally facilitate the suspension of recruitment at specific participating research sites, where significant concerns have been identified.

The suspension will allow for the JRO to investigate and work with the study team to put measures in place to mitigate risk, and to ensure no further participants are affected. Diagram 3 illustrates the process followed by the JRO RQSU, which leads to suspension of non-CTIMP research. All JRO suspensions to recruitment will be decided following consultation and agreement from a second JRO manager.

[2] As defined in the *JRO Authorised Signatories* internal JRO document

Diagram 3: JRO Suspension Process



9. IMPLEMENTATION & TRAINING

Staff following this SOP shall confirm they have read and understood the procedures outlined above by completing their relevant signature log as a record of acknowledgement. RQSU staff shall be trained in this SOP.

10. PUBLICATION & COMMUNICATION

This SOP is authorised and published on the JRO website: http://www.ucl.ac.uk/joint-research-office. The electronic versions maintained here are the controlled copies; therefore, staff are encouraged to frequently review that they have the most up to date copies.

The original fully signed master copy is stored in a designated binder within the JRO and maintained by the Research Quality & Safety Manager and Research Audit & Quality Officer.

11. REVIEW & AUDIT

JRO SOPs will be reviewed every 3 years unless an earlier review is required. Any changes to the SOP will be recorded in the chronology table on page 2 of the SOP to ensure version control.

Procedural audits will be arranged by the RQSU to check the level of adherence to SOPs. Findings should feed into the review process of SOPs.

To check the level of adherence to this SOP, the following criteria will be included within the audit checklist:

1.	To ensure reporting requirements as outlined in the protocol have been adhered to.
2.	To ensure appropriate research incidents, events and complaints have been reported to JRO as sponsor, as per the requirements of this SOP.
3.	To confirm the number of events reported to the JRO followed the correct escalation process.
4.	To confirm research events, incidents and complaints have been appropriately documented by the JRO (e.g. within JRO research management database) and Chief Investigator/delegate (e.g. within TMF).
5.	To ensure that suspensions to recruitment in UCL/UCLH sponsored non-CTIMPs have followed the requirements of this SOP.

12. TEMPLATES/OTHER DOCUMENTS ASSOCIATED WITH THIS DOCUMENT

	Document	Stored
1.	JRO non-CTIMP SAE log	JRO shared drives
2.	JRO non-CTIMP AE log	JRO shared drives
3.	JRO non-CTIMP Protocol Deviation log	JRO shared drives
4.	JRO non-CTIMP Protocol Violation log	JRO shared drives
5.	Definition of Incidents Table	JRO shared drives

13. REFERENCES

JRO Website
https://www.ucl.ac.uk/joint-research-office/

UCL Complaints from Research Subjects About UCL Sponsored Studies and Trials policy
https://www.ucl.ac.uk/joint-research-office/

U.K Policy Framework for Health and Social Care Research (3rd Edition, 2017):
https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/

International Conference on Harmonisation Good Clinical Practice: E6 (R2)
http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2__Step_4.pdf

HRA Safety Reporting:
https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/safety-reporting/

REC Standard Operating Procedure (Section 10): https://www.hra.nhs.uk/about-us/committees-and-services/res-and-recs/research-ethics-committee-standard-operating-procedures/

14. SIGNATURE PAGE

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