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ICREC – SETREC
Safety Reporting

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Version	Date	Reason for Change
Version 1.0	14 March 2019	1st Edition
Version 2.0	17 April 2020	2nd Edition
Version 3.0	19 Oct 2020	Scheduled Review Administrative changes to SOP. JRCO name change to RGIT
Version 4.0	25 April 2022	Additional associated templates added to the SOP.
Version 5.0	14 Jun 2024	Scheduled review
Version 6.0	04 Mar 2025	Updates to reporting processes

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1. PURPOSE

This SOP describes the process for managing and reporting Adverse Events for Imperial College Research Ethics Committee (ICREC) and Science, Engineering and Technology Research Ethics Committee (SETREC).

2. INTRODUCTION

It is essential that all Serious Adverse Events which occur during the study participants' involvement in a research project are appropriately recorded and reported where appropriate in order to ensure their continuing safety.

It is important that this SOP is followed as failure to report incidents, or deal with incidents adequately, can result in ethics approval being withdrawn from an individual project, or, in extreme cases, from all research carried out by the Principal Investigator (PI). It is accepted that Adverse Events will vary depending on the type of research being conducted.

For CTIMP Trials, definitions should follow RGIT_SOP_001 *(cited on 10 Dec 2023)*.
For international non-EU Trials SAEs and SUSARs should be reported to the Competent Authority and Ethics Committee of the countries involved as per local reporting requirements. All SAEs should be reported to the RGIT study monitor rgit.ctimp.team@imperial.ac.uk within 24 hours after becoming aware of the event.

The Research Governance and Integrity Team acts on behalf of Imperial College Research Ethics Committee (ICREC) and Science, Engineering and Technology Research Ethics Committee (SETREC) for the purposes of adverse event reporting. The Head of Department (HoD) may be notified for escalation and oversight purposes.

2.1. Definitions

A Serious Adverse Event is any untoward, unfavourable occurrence to a study participant, whilst involved in a research project or any occurrence that may impact on the integrity of the research outcomes. It is accepted that these will change depending on the type of research being conducted. For medical research the following definitions should be used. For other research AEs will depend on the type of study.

2.1.1. Adverse Event (AE)

Any untoward medical occurrence in a study participant which does not necessarily have a causal relationship with the study treatment or procedure (e.g. abnormal laboratory findings, unfavourable symptoms or diseases).

2.1.2. Serious Adverse Event/Reaction (SAE)

Any adverse event or adverse reaction that:

- results in death

- is life-threatening
- requires hospitalisation, or prolongation of existing inpatients' hospitalisation.
- results in persistent or significant disability or incapacity
- is a congenital anomaly or birth defect
- is otherwise considered medically significant

3. PROTOCOL DEVIATION AND VIOLATION

A protocol that has received ethics approval (and regulatory approval as applicable) is a formal document defining what can and cannot be done as part of a research project and must be adhered to so that participant safety and research integrity can be maintained.

Deviations from protocol can occur for several reasons and depending on the occurrence can be classes as protocol deviation or protocol violation. A protocol deviation occurs when a process or criteria has not been actioned in line with the approved protocol. For example, a study visit outside defined visit schedule, or a variation in the management of a participant due to minor safety concerns. Deviations are occurrences which can be classed as minor and do not affect participant safety or the integrity of the research.

A protocol violation occurs when there is a consistent variation in practice from the defined protocol. For example, changes to the protocol that have not been approved by an ethics committee or regulator that are classed as substantial amendments. A violation is a significant occurrence or event which may affect participant safety or the integrity of the research.

A protocol deviation may become a violation if it occurs on multiple occasions and/or affects multiple participants. Where a protocol deviation is not judged to impact on safety or research integrity, a file note should be added to the Trial Master File and/or case report form (CRF) and source documents explaining the action taken and its justification.

Non-compliance with the inclusion and exclusion criteria is always classed as a significant protocol violation regardless of how minor the deviation appears to be, as these criteria define the participant group in relation to the scientific requirements of the protocol.

When a protocol violation is identified it is essential to inform the appropriate parties of the occurrence and any corrective actions that have been implemented. The CI/PI must notify the sponsor of the violation immediately upon identifying the issue. The sponsor will advise on what action is required and may initiate a triggered audit of research activity to assess the extent of the violation and its relation to any other protocol compliance issues.
Once a violation has been identified it may be necessary to inform the ethics committee and/or regulator of the incident and any corrective actions. The sponsor will inform the CI/PI of reporting requirements and direct them to submit a report explaining the event. Key areas to include in a report are:

- An overview of the incident and its cause

- Description of corrective action
- An assessment of likelihood of reoccurrence
- Outline of any changes to the protocol that may be required
- Timeline for corrective action and amendment approval (if applicable) If the protocol violation is deemed to be of a serious nature the sponsor may suspend the research project until all necessary corrective actions have been taken.

In some circumstances it may be necessary to deviate from protocol to protect the safety of a research participant, which is classed as an urgent safety measure.
An urgent safety measure occurs when a research participant has been identified as being at risk of harm in relation to their involvement in a research project and urgent action, which deviates from the protocol, is required to manage the event and protect the participant. Urgent safety measures should be notified immediately, and in any event within three days of the event occurring, to RGIT outlining that such measures have been taken and the justification of these.

4. PROCEDURE

The procedure for notification of Serious Adverse Events is as follows:

i. Identifying an Adverse Event
ii. Assessment and reporting of an Adverse Event
iii. Notification to the Head of Division/ Department
iv. Escalation of a Serious Adverse Event to ICREC/SETREC
v. Publication

4.1. Identifying an Adverse Event

It is the responsibility of the Principal Investigator(s) to continually monitor the progress throughout the study; this may be delegated to a suitably qualified or experienced member of the research team. If delegated, this should be formally documented, and the Research Governance and Integrity Team (RGIT) notified.

In addition, Imperial College London may audit the project as part of their Quality Assurance procedures.

Any serious adverse events identified either through monitoring, audit or by other means outside the normal study process must be reported to the Ethics and Research Governance Coordinator within 24 hours of the Serious Adverse Event being identified and confirmed.

4.2. Assessment and reporting of an Adverse Event

Each AE must be evaluated for seriousness, causality, and expectedness. The responsibility for this evaluation can be shared between the overall PI and PIs at local sites. It may be most appropriate for the PI at each local site to evaluate each event, before reporting it to the overall PI. It must be stated in the study protocol and the local SOP who will take responsibility for the assessment and reporting of such events.

AEs should be assessed for causality to any of the research procedures using the definitions below:

Unrelated	There is no evidence of any relationship to any of the research procedures
Unlikely	There is little evidence to suggest there is a relationship and there is another reasonable explanation for the event
Possible	There is some evidence to suggest a relationship, however the influence of other factors may have contributed to the event
Probable	There is evidence to suggest a relationship and the influence of other factors is unlikely
Definitely	There is clear evidence to suggest a relationship and other possible contributing factors can be ruled out
Not assessable	There is insufficient or incomplete evidence to make a clinical judgement of the relationship

All AEs should be recorded and the reporting requirements for SAEs should be detailed in the protocol. For non-CTIMP studies, if the AE is deemed serious and where in the opinion of the PI the event was:

- ‘related’: that is, it resulted from administration of any of the research procedures; and
- ‘unexpected’: that is, the type of event is not listed in the protocol as an expected occurrence.

the SAE should be reported to RGIT within 24 hours of the PI being aware of the event using the Report of Serious Adverse Event Form.

SAEs should also be reported as per any local requirements.

Agreements at the beginning of the study should be made for such SAEs that can be defined as disease-related and therefore not subject to expedited reporting.

4.3. Escalation of Serious Adverse Event to ICREC/SETREC

If the AE is deemed serious and where in the opinion of the PIthe event was:

‘related’: that is, it resulted from administration of any of the research procedures; and

‘unexpected’: that is, the type of event is not listed in the protocol as an expected occurrence.

if the study previously had been granted favourable opinion by ICREC/SETREC then the SAE will be notified to ICREC/SETREC.
After notification to RGIT the Ethics and Research Governance Coordinator will send the Report of Serious Adverse Events Form (and any other relevant documents) to all committee members by email. The Ethics and Research Governance Coordinator will

be the contact person for all correspondence with Imperial College Research Ethics Committee.

5. APPENDICES

Appendix 1: Notification Examples

Issue:	**Would ICREC/SETREC have expected this case to be notified?**
Participant Information Sheet and Informed Consent updated without amendment approval	Yes, if there was a significant impact on the safety of the participants or integrity of the research.
Visit date deviation	No. Minor protocol deviation, which does not meet the criteria for notification.
Investigator failed to report a single SAE as defined in the protocol	Yes, if there was a significant impact on the safety of participants or integrity of the research.
Investigator does not comply with the conditions of ethics approval (if any)	Yes. This would trigger immediate suspension of the research and escalation to ICREC/SETREC and the HoD.
Additional data not included in the protocol is routinely captured as part of the research activity	Yes. This would be classed as a violation of the approved research protocol.
A participant is injured or experiences significant emotional distress during the research procedure	Yes.
Breach of confidentiality and data security	Yes.

Appendix 2: ICREC Participant Information Sheet – RGIT_TEMP_075
Appendix 3: SETREC Participant Information Sheet - RGIT_TEMP_076
Appendix 4: ICREC Consent Form - RGIT_TEMP_077 Appendix 5: SETREC Consent Form - RGIT_TEMP_078