

Standard Operating Procedures for reporting harm to participants, protocol deviations and urgent safety measures in studies involving a pharmaceutical or other compound with physiological effects

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Purpose

This Standard Operating Procedure (SOP) specifies the overall procedure for Principal Investigators and the Committee to follow for a University of Cambridge sponsored study involving a pharmaceutical or other compound with physiological effects (an “active compound”) in the event of harm to a participant as a result of the study protocol, or a protocol deviation. This SOP describes the procedure for the Principal Investigator to record the event and notify the Committee. The Principal Investigation may need to notify other agencies.

Definitions

All compounds licensed under the Medicines Act are included in this category. However, some products may be considered as investigational medicinal products (IMP) and studies involving them as clinical trials of investigational medicinal products (CTIMP), in which case NRES approval should be sought. If there is any ambiguity investigators should contact the Medicines and Healthcare Products Regulatory Agency (MHRA) for confirmation.

A **Protocol Violation** is an intended failure to adhere to the protocol. A minor protocol violation does not impact on subjects’ safety or compromise the integrity of study data and thus does not need to be reported to the Committee.

An **Urgent Safety Measure** is an intended change from the protocol to eliminate an immediate hazard to participants. This can be undertaken by the Principal Investigator without prior approval from the Committee.

A **Protocol Deviation** is an unintended departure from the expected conduct of the trial and if classified as non-serious or minor in nature does not need to be reported to the Committee.

A **Serious Protocol Deviation** (i.e. a “serious breach” of a protocol) is an unintended breach of protocol, or the conditions or principles of Good Clinical Practice which is likely to affect to a significant degree the safety or physical or mental integrity of the study participants, or the scientific value of the research. For example, failure to obtain informed consent, study procedures not approved by the Committee (unless for immediate safety reasons), dispensing or dosing errors.

Procedure

Before Approval

- Investigators undertaking a study involving an active compound should complete Appendix A of the application form and submit the form along with the complete protocol for the study and any other supporting information.

- Studies involving active compounds will be reviewed by two members of the Committee, selected by their experience and/or expertise, with the addition of a co-opted member with specific expertise in clinical pharmacology or other relevant discipline.
- Letters of Approval will only be issued by the Committee once all the members of the Committee are satisfied with the application and responses to any issues raised plus a certificate of appropriate insurance.

During the Study: Harm to participants

- If any harm (an “adverse event”) should occur to a participant, the investigators should halt the study immediately and contact the Secretary of the Committee.
- The Secretary will ask the Principal Investigator to complete and submit to the Committee a Adverse Event form (see below) within 5 days of the original incident. A copy of this SOP will accompany the correspondence.
- The Secretary will confirm receipt of the Adverse Event form to the Principal Investigator.
- The Principal Investigator should then inform their Head of Department who will coordinate a report setting out what occurred and, if necessary, what steps are being taken to ensure that there is no recurrence of the incident. This report will be returned to the Committee within 15 days of the incident.
- A further investigation involving someone independent of the original study may be initiated by the Principal Investigator and/or the Committee. This report should also be returned to the Committee within 15 days of the incident.
- Once the completed documentation (i.e. Adverse Event form, HoD report and Independent Report, if necessary) has been returned to the Committee it will be circulated, if possible, to those Committee members and co-opted members who reviewed the original application. If these members are not available, other members with equivalent experience will be selected.
- The Committee will reach one of the following outcomes: a. Agreement that the study may continue with the modifications suggested (if necessary); b. Further investigations as specified by the Committee and re-review are necessary before a decision can be reached; c. The study must cease and not restart. This decision will be made within 15 days of the Committee having all necessary documentation.

During the Study: Serious protocol deviation

- If a serious breach of protocol takes place, the Principal Investigator should write to the Secretary of the Committee as soon as possible, but within 5 days, including in their report when the breach occurred; the location; who was involved; the outcome and any information given to participants; and what action will be taken to mitigate subsequent occurrence.
- The Secretary will confirm receipt of the report to the Principal Investigator and include a copy of this SOP.
- The report will be circulated, if possible, to those Committee members and co-opted members who reviewed the original application. If these members are not available, other members with equivalent experience will be selected.
- The Committee will reach one of the following outcomes: a. Agreement that the study may continue with the current protocol, modified as required; b. Further investigations as specified by the Committee and re-review of the protocol are necessary before a decision can be reached; c. The study must cease and not restart. This decision will be made within 15 days of the Committee having all necessary documentation.

During the Study: Urgent Safety Measure

- The Principal Investigator should write to the Secretary of the Committee as soon as possible, but within 5 days of the incident, including when the measures were implemented; the location; who was involved; the reason for taking the measures; the outcome and any information given to participants; and what permanent action, if any, will be taken to mitigate the need for a similar urgent safety measure in the future.
- The Secretary will confirm receipt of the report to the Principal Investigator and include a copy of this SOP.
- The report will be circulated, if possible, to those Committee members and co-opted members who reviewed the original application. If these members are not available, other members with equivalent experience will be selected.
- The Committee will reach one of the following outcomes: a. Agreement that the study may continue with the current protocol, modified as required; b. Further investigations as specified by the Committee and re-review of the protocol are necessary before a decision can be reached; c. The study must cease and not restart. This decision will be made within 15 days of the Committee having all the documentation.

REPORT OF AN ADVERSE EVENT (AE)

The Principal Investigator (PI) should report any AE that is both related to the research procedures and is unexpected. Send the report to the Research Ethics Committee within 5 days of the PI becoming aware of the event.

1. Details of Principal Investigator

Name:	
Address:	
Telephone:	
Email:	
Fax:	

2. Details of study

Full title of study:	
REC reference number:	
Sponsor:	

3. Type of event

Please categorise this event, ticking all appropriate options:

Death <input type="checkbox"/>	Life threatening <input type="checkbox"/>	Hospitalisation or prolongation of existing hospitalization <input type="checkbox"/>
Persistent or significant disability or incapacity <input type="checkbox"/>	Congenital anomaly or birth defect <input type="checkbox"/>	Other <input type="checkbox"/>

4. Circumstances of event

Date of Adverse Event:	
Location:	
Describe the circumstances of the event: <i>(Attach copy of detailed report if necessary)</i>	
What is your assessment of the implications, if any, for the safety of study participants and how will these be addressed?	

5. Declaration

Signature of Principal Investigator:	
Print name:	
Date of submission:	

6. Acknowledgement of receipt by REC:

The Research Ethics Committee acknowledges receipt of the above.

Signed:	
Name:	
Position on REC:	
Date:	

*Signed original to be sent back to Principal Investigator (or other person submitting report)
Copy to be kept for information by REC.*