**FHS008hlp: Guidance on Preparing an Internal Adverse Event or Unanticipated Problem report - Pointers for researchers**

**How to report an internal adverse event or unanticipated problem**

* If the investigator judges that the event represents an unanticipated problem or adverse event that requires timely reporting, the PI must submit standard internal reporting form to notify the HREC and the sponsor and/or a central or independent monitoring committee (e.g. DSMB) as required under a monitoring plan described in the HREC-approved protocol.
* The standard internal reporting form must be completed even if other forms (e.g. sponsor, CIOMS, Medwatch, SAHPRA) have already been completed. Information such as a summary of the event, or drug company reports may be attached and submitted with the form.
* The investigator must independently determine and comment on whether the event was thought to be related, possibly related, unrelated or the relationship is unknown. The HREC therefore relies on the PI’s expertise to assess the causality of the problem or event, its seriousness and whether it was expected. Investigators must also recommend whether a change in the protocol is needed to minimise risks to participants, whether the consent form should be revised to reflect this risk and whether participants in the study should be re-consented in light of this risk.
* An amendment form reflecting changes to the protocol and consent/assent documentation may be appended to the adverse event report. Please follow the specific instructions posted on the HREC website for submitting amendments.

**Definitions**

**Unanticipated problems**

An ‘unanticipated’ problem is any incident, experience or outcome that meets **all** the following three criteria:

* Unexpected in terms of its nature, severity or frequency, or the research population being studied; or if anticipated it is not fully addressed or specified in information provided to the Human Research Ethics Committee (HREC) or to participants such as in initial protocol applications, any amendments, investigator brochures, scientific literature, product labelling, package inserts and HREC-approved informed consent documents or any existing documentation regarding the research conducted to date under the protocol;
* Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience or outcome may have been caused by the procedures involved in the research);
* Suggests that the research places participants or others at a greater risk of physical, psychological, economic or social harm than was previously known or recognised.

In summary, an unanticipated problem is:

|  |  |
| --- | --- |
| Unexpected | not in the consent form, investigator’s brochure, protocol package insert or label; or unexpected in its frequency, severity or specificity; |
| Related | to the research – caused by, or probably caused by, or associated with a device |
| Harmful | caused harm to participants or others, or placed them at increased risk of physical, psychological, economic or social harm |

Examples of unanticipated problems include:

* Loss of a laptop computer containing confidential information about participants or others
* A spouse physically abused by his or her partner for taking part in the study
* Publication in the literature or a Data and Safety Monitoring Report that indicates an unexpected change in the balance of risks and benefits in the study
* Finding that laboratory reports on blood or other samples were in error

**Adverse events**

An adverse event is defined as any untoward or unfavourable medical or psychological occurrence in a participant, including any abnormal laboratory finding, symptom or disease. An adverse event does not necessarily have a causal relationship with the research or any risk associated with the research.

**Unexpected adverse events**

Unexpected adverse events are those in which any of the following applies:

* The specificity or severity is not consistent with the current Investigator’s Brochure
* The event is inconsistent with the risk information in the current protocol application
* The event is occurring more frequently than anticipated

**Internal adverse event**

Internal adverse events are those experienced by participants enrolled at a site under the jurisdiction of UCT’s Faculty of Health Sciences.

**Serious adverse event (SAE)**

A serious adverse event is any adverse event in research that results in any of the following:

* Death
* A life-threatening incident (places the participant at immediate risk of death from the event as it occurred)
* Hospitalisation (initial or prolonged)
* Disability
* Congenital abnormality
* Requires medical or surgical intervention to prevent permanent impairment or damage (e.g. allergic bronchospasm requiring intensive treatment in the emergency room or at home)
* Inadvertent disclosure of confidential information if this presents an immediate risk to a participant such as from spousal or child abuse

**Timelines for Reporting**

**Reporting Unanticipated Internal Problems or Adverse Events**

**Unanticipated problems**

PIs must report to the Human Research Ethics Committee within seven calendar days after the investigator first learns of their occurrence all unanticipated problems that increase the risk of harm to participants or others.

**Fatal and life-threatening, unexpected adverse drug reactions**

PIs must report to the Human Research Ethics Committee as soon as possible but not later than seven calendar days after the investigator first learns of their occurrence all fatal and life-threatening adverse drug reactions in clinical trials.

**Serious and unexpected non-fatal adverse drug reactions**

PIs must report to the Human Research Ethics Committee as soon as possible but not later than fifteen calendar days after first learning of their occurrence all serious unexpected drug reactions that are not fatal or life-threatening.

**Expected adverse drug reactions**

PIs must notify the Human Research Ethics Committee within fifteen calendar days after the investigator first learns of their occurrence all adverse drug reactions that are expected but are judged to be occurring at a significantly higher frequency or severity than expected. The basis for these assessments must be included in the investigator’s report.

**Serious and unanticipated adverse device effects**

PIs must report to the Human Research Ethics Committee and to the sponsor (if applicable) as soon as possible but not later than seven calendar days after first learning about their occurrence all unanticipated adverse device effects [21 CFR 812.150(a)(1)]. The sponsor shall immediately conduct an evaluation of the unanticipated adverse device effect [21 CFR 812.46(b)(1)].

**New information that might impact the conduct of a clinical trial**

PIs must report to the Human Research Ethics Committee within three calendar days of first learning about their occurrence other unexpected adverse events, regardless of severity, that may alter the balance of risks and benefits in a study and as a result warrant consideration of substantive changes in the overall conduct of a clinical trial. The report could include individual case reports or a major safety finding from other sources.