

**STANDARD OPERATING PROCEDURE  
REPORTING OF ADVERSE EVENTS**  
(SA GCP Guidelines 3.12; 3.13; 3.14 pg 36)

Regulatory Framework :

Bill of Rights of the Constitution of South Africa  
National Health Act

Guidance Documents :

Health Professions Council of SA  
Ethics in Health Research: Principals, Structures and Processes  
European Association of Palliative Care  
MCC Guidelines : [www.mccza.com](http://www.mccza.com)  
South African Good Clinical Practice Guidelines – 2006  
Office of Human Research Protections : 21CFR50  
CIOMS  
ICH-GCP

While this document focuses on drug related adverse events its scope is wide enough to cover other adverse events including those of a socio/psychological nature.

The guidelines refer mainly to studies that involve drugs, but should any adverse event (not necessarily related to drugs) occur in the course of a research study these should also be reported to the HPCA Research Ethics Committee. The following is an extraction of that which appears in the MCC Guidelines.

**DEFINITIONS:**

(For clinical trials reporting time-lines of these events will be stipulated in the protocol. MCC guidelines must be strictly adhered to).

**Adverse Event:**

Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An adverse event (AE) can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

**Adverse Drug Reaction (ADR) or Adverse Reaction:**

All noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase 'responses to medicinal product' means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e. the relationship cannot be ruled out.

**Unexpected Adverse Reaction:**

One in which the nature, specificity, severity and outcome is not consistent with the applicable product information (i.e. with the approved package inserts for registered products, or the investigator's brochure or other product information for unregistered products).

**Serious Adverse Event :**

Any untoward medical occurrence that :

- ◆ Results in death
- ◆ Is life-threatening at the time of the event
- ◆ Requires inpatient hospitalisation or prolongation of existing hospitalisation
- ◆ Results in persistent or significant disability/incapacity
- ◆ Is a congenital anomaly/birth defect

**Unscheduled Hospitalisation :**

An event which causes the participant to be hospitalised or prolongs the duration of hospitalisation.

**Disability / Incapacity**

An event resulting in persistent or significant disability or incapacity is one which causes a substantial disruption of a participant's ability to conduct normal life functions.

**Life Threatening**

An adverse event that places the participant, in the view of the investigator, at risk of death from the event as it occurred.

**Other Significant Event**

Includes important events which may jeopardise the patient or require intervention to prevent one of the listed SAE outcomes.

**Unexpected**

An adverse event, the specificity or severity of which is not consistent with the Investigator's Brochure for an unapproved investigational product.

Medical and scientific judgement should be exercised when deciding if other situations are serious. Such instances could include medical events that may not be immediately life-threatening or result in death or hospitalisation, but which may jeopardise the patient or may require intervention to prevent one of the outcomes listed in the definition above. Examples include blood dyscrasias or convulsions not resulting in hospitalisation, or development of drug dependency or drug abuse.

**Medicines used under Section 21 of Act 101 (1965), not within a clinical trial**

The prescriber of a medicine approved for use under Section 21 of Act 101 (1965) for patients not enrolled in a clinical trial (for e.g., compassionate use, named-patient use, etc.), must report any serious suspected adverse drug reaction that occurred with the use of the medicine in the specified patient(s) within 15 calendar days of first knowledge by the prescriber.

**REPORT EVEN IF YOU ARE NOT CERTAIN THE PRODUCT CAUSED THE EVENT**

**Report Format and Details**

Applicants must complete an Adverse Event Report Form and submit it with **ALL** the **relevant** information available at the time of initial notification of an adverse drug reaction report, i.e. not only the minimum information required for a report. The attachment of discharge summaries, post-mortem reports, relevant laboratory data and other additional clinical data, is encouraged.

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The original words/description (verbatim) used by the initial reporter to describe the adverse reaction should be provided. The medicine (or trade) name must be provided as reported by the initial reporter.

Additional information, not available at the time of the initial report, should be provided in the form of follow-up reports.

**Submit the report** to the HPCA Research Ethics Committee who will review the incident and report back to you, in writing, their decision on the event.

This form is effective as soon as the Informed Consent document has been signed until 30 days after completion of participation by the participant.

**TABULATED SUMMARY OF REPORTING REQUIREMENTS  
Post-Registration ADR Reports (registered medicinal products)**

Type of ADR report	Time frame for reporting	Format
Local Reports (spontaneous/published/study): <ul style="list-style-type: none"> <li>• Serious (expected and unexpected)</li> <li>• Non serious (unexpected)</li> <li>• Non serious (expected)</li> </ul>	24-48 hours 24-48 hours 15 days	ADR form # ADR form # Not required
Foreign Reports (spontaneous/published/ study): <ul style="list-style-type: none"> <li>• Serious</li> </ul>	On request or relating to specific safety issue	As appropriate
Notification of Change in Nature, Severity or Frequency or Risk factors	15 days	Detailed report (including publications)
New information impacting on benefit-risk profile of product including international regulatory decisions	3 days	Detailed report (including publications)

# Applicant's in-house ADR report form or NADEMC ADR report form.

**Pre-Registration ADR/ADE reports (i.e. unregistered medicines being used under section 21 of Act 101, 1965 or Regulation 34 of Act 90, 1997)**

TYPE OF ADR REPORT	TIME FRAME FOR REPORTING	FORMAT
Local Reports: <ul style="list-style-type: none"> <li>• Fatal or life-threatening (unexpected)</li> <li>• Other serious (unexpected)</li> </ul>	24-48 hours 15 days	SAE form SAE form
All (local & foreign) reports: <ul style="list-style-type: none"> <li>• Serious (unexpected and expected) events</li> <li>• Non-serious unexpected reactions</li> </ul>	6-monthly <sup>##</sup> 6-monthly	Line listing Line listing
Notification of Change in Nature, Severity or Frequency of Risk factors	15 days and in 6 monthly report <sup>##</sup>	Detailed report
New information impacting on risk-benefit profile of product or conduct of trial	3 days and in 6-monthly report <sup>##</sup>	Detailed report

<sup>##</sup> 6-monthly progress report which should be submitted to Council during the entire duration of the clinical investigation.

### ADVERSE EVENT REPORTING FORM

Protocol Title : .....

Protocol Reference No. : .....

Date of approval : .....

SAE Identification (Case ID / Participant's initials) : .....

Report type : Initial / Follow-up :

Event Title : .....

Date of onset : .....

Reporting Criteria (Please circle one) : Death / Involved or prolonged hospitalisation /  
Persistent or significant disability or incapacity / Life threatening / congenital anomaly / birth  
defect

Assessment of causality in relationship to the study. (Please circle one) :

Related / Possibly related / Unlikely / Not related

Outcome : Recovered / Recovered with consequences / Ongoing / Other (explain)

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..... Date : .....

Principal Investigator

Please print name : .....