

WITS HUMAN RESEARCH ETHICS COMMITTEE: (MEDICAL)
(WITS INDEPENDENT ETHICS COMMITTEE)
STANDARD OPERATING PROCEDURE



SOP-IEC – 005 (VERSION 4)

IMPLEMENTATION DATE: JANUARY 2010

SUBJECT:	WITS IEC Secretariat Adverse Event Processing for Review														
DIVISION / SCOPE:	WITS HUMAN RESEARCH ETHICS COMMITTEE: (MEDICAL)														
AUTHOR: REVISION:	WITS CLINICAL RESEARCH IEC SECRETARIAT														
PURPOSE:	<p>This procedure describes the process to be followed by the WITS IEC Secretariat for the processing and reporting of AE's from human participants at WITS approved institutions to ensure compliance with the following guidelines:</p> <ul style="list-style-type: none"> • Guidelines for Good Practice in the Conduct of Clinical Trials in Human Participants in South Africa (2006) • International Conference on Harmonisation (ICH) Good Clinical Practices (GCP) Guideline (June 1996 Section 3), • FDA requirements for Institutional Review Boards (21 CFR Part 56). • MCC Reporting Adverse Drug Reactions in South Africa 														
PREVIOUS VERSIONS / (REASON FOR REVISION)	<p>SOP-IEC-005v1; 2 and 3 Administrative changes and additions in line with MCC SA adverse event reporting and / or updating of documents within the IEC</p>														
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APPROVALS:	<p align="center">Signature of Chairperson / Deputy Chairperson of IEC: Date: <i>Prof P Cleaton-Jones / Prof M Vorster</i></p>														



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1. DEFINITIONS AND ABBREVIATIONS

ADR	Adverse Drug Reaction
AE	Adverse Event
CFR	Code of Federal Regulations (USA)
FDA	Food and Drug Administration (USA)
GCP	Good Clinical Practice
ICH	International Conference on Harmonisation
IEC	Independent Ethics Committee (ICH GCP term)
SAE	Serious Adverse Event
SAGCP	Guidelines for Good Practice in the Conduct of Clinical Trials in Human Participants in South Africa (2000)
WCR	WITS Clinical Research

2. REFERENCES

- ◆ International Conference on Harmonisation (ICH) Good Clinical Practices (GCP) Guideline (June 1996 Section 3)
- ◆ Declaration of Helsinki 2008
- ◆ 21 Code of Federal Regulations Part 312.32 – IND Safety Reports
- ◆ Guidelines for Good Practice in the Conduct of Clinical Trials in Human Participants in South Africa (2000)
- ◆ MCC Reporting of Adverse Drug Reactions in South Africa

3. SAE'S ORIGINATING AT WITS APPROVED SITES

Capture of appropriate ADR data fields on the Wits Clinical Research Database to produce appropriate analysis reports for the WITS IEC

Responsible person	Action to be taken
IEC Secretariat	1 Receive ADR /AE reports from the Investigator and/or Sponsor
	2 Capture appropriate fields onto the database as identified in Attachment 2 (ADR data capture fields Version 1 dated 15 Jan 2003)
	4 Acknowledge receipt and processing of ADR report to Sponsor and Investigators

4. SOUTH AFRICAN AND FOREIGN SAE PROCESSING AND REPORTING

◆ SERIOUS, UNEXPECTED, ADVERSE DRUG REACTIONS OCCURRING AT OTHER SOUTH AFRICAN AND FOREIGN SITES

Report as part of the 6-monthly progress reports
Format of report: Line listing

Responsible person	Action to be taken
IEC Secretariat	1 Acknowledge receipt of reports to Sponsor and Investigators

5. Attachments

Attachment 1: SAE data capture fields
Attachment 2: Report produced for IEC SAE



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Extract from Policy Document below:

REF: POLICY DOCUMENT – POL-IEC – 001 (VERSION 5).

3.4. Reporting of Adverse Drug Reactions and other Safety Information to the Wits IEC

DEFINITIONS:

Adverse Event:

Any untoward medical occurrence that may present during treatment with a medicine/intervention but which does not necessarily have a causal relationship with this treatment

Adverse Drug Reaction or Adverse Reaction:

A response to a medicine/intervention which is noxious and unintended
The phrase response means that the causal relationship between the medicinal product/intervention and the adverse event is at least a reasonable possibility.

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 or Serious Adverse Drug Reaction:

Any untoward medical occurrence that:

- ◆ results in death,
- ◆ is life-threatening,
- ◆ requires patient hospitalisation or prolongation of existing hospitalisation,
- ◆ results in persistent or significant disability/incapacity, or
- ◆ is a congenital anomaly/birth defect.

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

REPORTING REQUIREMENTS FOR EVENTS OCCURRING AT WITS HREC APPROVED SITES:

- ◆ **All deaths**
- ◆ **Serious, unexpected, adverse drug reactions which are fatal or life threatening**
Report within 7 calendar days after first knowledge.
The initial notification should be followed by as complete a report as possible within an additional 8 calendar days
*Format of report: SAE form **
- ◆ **Serious, unexpected, adverse drug reactions which are not fatal or life threatening**
Report as soon as possible and not later than 15 calendar days after first knowledge
*Format of report: SAE form **
- ◆ **All Serious Adverse Events**
- ◆ **Non-serious unexpected adverse drug reactions**
Report as part of the 6-monthly progress reports
*Format of report: Line listing **



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OTHER REPORTING REQUIREMENTS:

- ♦ **Serious, unexpected, adverse drug reactions occurring at other South African and Foreign sites**
Report as part of the 6-monthly progress reports
*Format of report: Line listing **

 - ♦ **New information which may affect the safety of participants or the conduct of a trial**
Report within 3 calendar days of first knowledge and in the six-monthly progress report
Format of report: Detailed report

 - ♦ **Change in the nature, severity or frequency of expected Adverse Drug Reactions**
Report within 15 days after first knowledge and in the 6-monthly progress report
Format of report: Detailed report
- * www.mccza.com
- ♦ *Click on:*
 - ♦ Documents
 - ♦ Guidelines Human Medicine
 - ♦ Reporting Adverse Drug Reactions in South Africa
 - ♦ Forms – Human & Veterinary Medicine
 - ♦ Form ARF 1 Adverse Drug Reactions Reporting Form



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SOP-IEC – 005 - ATTACHMENT 1

SAE DATA CAPTURE FIELDS

1	Protocol title
2	SAE Identification (Case ID, Subject initials)
3	Report type (Initial/ Follow-up)
4	Country
5	Serious Adverse Event (Diagnosis) (Event title)
6	Reporting Criteria (Patient died, Involved or prolonged hospitalization, Involved persistence of significant disability or incapacity, Life-threatening, Congenital anomaly/birth defect)
7	Date of onset of SAE
8	Assessment of causality (Related/suspected, Not related/not suspected) (i.e. Relationship to study medication)
9	Outcome
10	Date IEC Secretariat notified



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SAE Grading System

	<i>SAE OUTCOME</i>	
1	Death	Trial drug related
2		Illness unrelated to trial drug
3		Accident unrelated to trial drug
4		Progressive disease
1	Hospitalization	Trial drug related
2		Illness unrelated to trial drug
3		Accident unrelated to trial drug
4		Progressive disease
1	Disability / Incapacity	Trial drug related
2		Illness unrelated to trial drug
3		Accident unrelated to trial drug
4		Progressive disease
1	Life Threatening	Trial drug related
2		Illness unrelated to trial drug
3		Accident unrelated to trial drug
4		Progressive disease
1	Other Significant Event	Trial drug exposure during pregnancy
2		Trial drug overdose



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Definitions and Abbreviations

AE	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.
ADR	Adverse Drug 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
SAE	Serious Adverse Event	Any untoward medical occurrence that at any dose: <ul style="list-style-type: none"> ◆ Results in death ◆ Is life-threatening ◆ Requires inpatient hospitalisation or prolongation of existing hospitalisation ◆ Results in persistent or significant disability/incapacity <p>Or</p> <ul style="list-style-type: none"> ◆ Is a congenital anomaly/birth defect
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 immediate risk of death from the event as it occurred. (This does not include an event, that had it occurred in a more severe form, might have been life threatening)
Other Significant Event		Includes important medical events which may jeopardise the patient or require intervention to prevent one of the listed SAE outcomes
Suspected		An SAE which is suspected to be related to the trial drug
Unexpected		An adverse event, the specificity or severity of which is not consistent with the Investigator's Brochure for an unapproved investigational product

