PHARMA DEVILS

PHARMACOVIGILANCE DEPARTMENT

STANDARD OPERATING PROCEDURE	
Department: Pharmacovigilance	**SOP No.:**
Title: Handling of Adverse Events & Safety Information	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

1.0 OBJECTIVE:

This Standard Operating Procedure (SOP) describes the management of reports on suspected Adverse Drug Reactions (ADR's) at the Pharmacovigilance (PV) Department of …….

The SOP rules the handling, the documentation and the reporting of suspected ADR from any source relating to medicinal products marketed or registered by …….. or on behalf of ……., or relating to Investigational Medicinal Products (IMP's) in clinical development or Adverse event (AE) arising from Bioavailability/Bioequivalence studies conducted at …….., Search and Review of Literature and Digital Media.

2.0 SCOPE:

This SOP applies to all …… employees/vendors involved in drug safety process at or on behalf of ……. in accordance with applicable reporting regulations.

3.0 RESPONSIBILITY:

3.1. **Pharmacovigilance Department:**

Responsible to collect process and report AE's and products safety information. Preparation, distribution, retrieval and destruction of this SOP.

3.2. **Pharmacovigilance Officer In-charge (PvOI):**

Review and Approval of reporting of AE's and products safety information. Review, training and effective implementation of this SOP.

3.3. **Third Party**

A third party e.g. client/vendor may be assigned to take over responsibilities for specific processes described in the related documents.

4.0 ACCOUNTABILITY:

Pharmacovigilance Officer Incharge

5.0 PROCEDURE:

The PV Department at ……. is responsible for establishing and maintaining the pharmacovigilance system for the …….. group by providing training, supervision and support functions including electronic case submission. However, the Licensing Partners (LP's)/subsidiaries are fully responsible for fulfilling all regulatory obligations concerning pharmacovigilance including their specific reporting obligations to the authorities in accordance with the national laws and international regulations.

Any employee of …….. who receives information regarding AE's or ADR's concerning products marketed by …….., independent from the source of the information, i.e. immediately but not later than within 24 hours of receipt, forwards this information to the PV Department.
On a global level, case management is a shared responsibility between LPs/subsidiaries and PV department. The LPs/subsidiaries without access to the safety database forward all case data together with an English translation including source data to PV for Data Entry (DE) via email or fax.
All case information should be entered in English language. DE convention should ensure standardized DE, high level of data consistency and reliable quality.

5.1 Sources of Individual Case Safety Reports (ICSR)

ICSRs may derive from different sources:

5.1.1 Spontaneous reports:
5.1.1.1 Reports received from health professionals or consumers
5.1.1.2 Reports from RAs (including those requiring active collection from authority webpages)
5.1.1.3 Reports from published (local and global) literature
5.1.1.4 Reports associated with a product (quality) complaint
5.1.1.5 Reports originating from medical information requests
5.1.1.6 Reports from digital media (e.g. web sites, web pages, social media, health portals) through active collections
5.1.1.7 Special situation reports
5.1.1.8 Reports of medication errors, drug interaction, off-label use, overdose, misuse, abuse, occupational Exposure, lack of effect or lack of efficacy
5.1.1.9 Reports of pregnancy
5.1.2 Clinical trial (CT) reports
5.1.3 Reports from non-interventional post authorization studies, compassionate use, patient support and disease programmes
5.1.4 Cases to be captured in the safety database
5.1.4.1 Valid unsolicited (spontaneous) reports including reports deriving from special situations:
5.1.4.2 Valid solicited reports:
5.1.4.3 Cases received from consumers
5.1.4.4 Case reports identified in the literature and digital media
5.1.4.5 ADR related to product quality complaints or falsified medicinal products
5.1.4.6 Cases received from license partners
5.1.4.7 Case reports from interventional studies sponsored by ……
5.1.4.8 Case reports from non- interventional post-authorization studies sponsored by
5.1.4.9 Pregnancy reports
5.1.4.10 Non-valid reports of suspected adverse reactions, for which the minimum information is Incomplete, are also recorded in the safety database for use in on-going safety evaluation activities. Initial receipt date for non-valid reports is considered the day any personnel of …… or an organization having a contractual arrangement with ……. gains awareness of the non-valid ICSR.

5.1.5 Cases not be captured in the safety database:

Cases that do not qualify to any of the criteria mentioned above will be logged in the Case Log (Annexure II). This includes cases which originate from non-…… territory and which include listed reactions and cases received from LP's not under the scope of the Pharmacovigilance Agreement (e.g. no-……..Territory or no ……..).

5.1.6 Case reporting requirements:

Cases will be reported to the RA as per the applicable timelines with respective to the regulatory requirements. Each …….. employee has an obligation to ensure they transmit ICSR's to …….. PV department as defined in SOP's in a timely manner. …….. LP's have SDEAs in place. The SDEA documents the pharmacovigilance contacts for the LP, the reporting obligations and responsibilities for both …… and the LP with respect to the products outlined in the distribution agreement and reporting to the CA's. In cases where a preliminary report shall be submitted to the local RA prior to getting additional information, a follow-up report shall be sent within regulatory timelines.

5.1.7 Handling of initial case information

Case processing follows a workflow ("case processing model") comprising the following steps:

- Case Receipt and Registration
- Triage
- DE
- QC
- Medical Review
- Distribution and Reporting
- Archiving

PV runs a validated safety database which includes an electronic workflow. The electronic workflow supports case processing from initialization of the case up to its distribution as well as to its closing.

5.1.8 Periodic reporting of adverse drug reactions

If local legislations do not require expedited reporting of specific ICSR's, e.g. non-serious reports, such ICSR's are reported in the course of periodic safety update reports (e.g. PSUR's or annual line- listing) or other aggregate reports as stipulated by local legislation.
Furthermore, cases are distributed in form of listings to LP companies according to contracts for reconciliation purposes.

5.1.9 Requesting follow-up

If deemed necessary during medical assessment or if minimal criteria are not present in the initial information, adverse reaction reports will be followed up. Identification of follow –up needs an requesting follow-up information is a parallel activity starting with the workflow step "Triage". …….. and LP's, which are involved in the workflow step, enter the need for follow-up in the cases. The information on needed follow-up requests can

alternatively be entered during DE or Medical Assessment, instead of during Triage. Completion of follow-up activities is a prerequisite for "Case Closure and Archiving". Depending on the report source, case seriousness and expectedness, follow- up information (e.g. additional demographic and medical information) is requested. Table 1 details the number of follow-up attempts to be made for cases initially received by ……...

Table 1: Number of follow-up attempts depending on report source, seriousness and expectedness of initial report.

Source	Serious		Non-serious	
	Unexpected	Expected	Unexpected	Expected
Healthcare professional	Three	Two	One	None
Consumer	Attempt to obtain HCP confirmation only if information is incomplete for proper assessment			

For every case for which minimum criteria are not available (non -valid cases), follow –up requests are mandatory to obtain minimum criteria, if feasible.

Follow-up activities are initiated immediately after case receipt. Further attempts are undertaken if requested information has not been received within four weeks.

The timing of follow-up of pregnancy cases with unknown outcome at the time of the initial report should be aligned with the anticipated delivery date. The items that should be considered for follow- up are listed in the Case Follow-up Request and Tracking Form. All follow-up attempts are documented by the DE person (Case Follow-up Request and Tracking Form).

5.1.10 Case closure and archiving

This workflow step includes:

- Case closure: Minimum criteria for case closure are: regulatory reporting completed and/or follow-up activities are completed.
- Archiving of source data: Once the case is closed, case documentation received on paper (i.e. source documents and relevant correspondence) is archived by the PV department and local responsible person with the associated CIOMS I form. Electronic data are archived centrally in the safety database attached to the respective case. Archiving is documented in the safety database as last step of the electronic workflow.

5.1.11 Nullification of cases

The nullification of individual cases would indicate that a previously transmitted report is completely void (nullified), for example when the whole case was found to be erroneous or in case of duplicate reports.

A nullified case is one that should no longer be considered for scientific evaluation. The process of the nullification of a case is by means of a notification by the sender to the receiver that this is no longer a valid case. However, the case should be retained in the safety database for auditing purposes.

6.0 DISTRIBUTION:

Not Applicable

7.0 REFERENCES:

Not Applicable

8.0 ABBREVIATIONS:

ADR	Adverse Drug Reaction
AE	Adverse Event
CA	Competent Authority
CIOMS	Council for International Organizations of Medical Sciences
CT	Clinical Trial
DE	Data Entry
GVP	Good Pharmacovigilance Practices
HOD	Head of Department
ICSR	Individual Case Safety Report
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
IMP	Investigational Medicinal Product
LP	Licensing Partner
MAH	Marketing Authorization Holders
NA	Not Applicable
PSUR	Periodic Safety Update Report
PV	Pharmacovigilance
PvOI	Pharmacovigilance Officer In-charge
QA	Quality Assurance
QC	Quality Control
RA	Regulatory Authority
SAE	Serious Adverse Event
SDEA	Safety Data Exchange Agreement
SOP	Standard Operating Procedure

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9.0 ANNEXURE:

S.No.	Title	Annexure No.	Format No.
1.	Adverse Event (AE) Report Form	I	
2.	Case Log	II	

10.0 REVISION HISTORY:

Revision No.	Effective Date	Reason for change	CC No.
1		New SOP	NA

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ANNEXURE I

ADVERSE EVENT (AE) REPORT FORM

Report Type: Initial Follow-up Follow-up No:			
Date of AE Report:			
Please fill and return this form to …….within 24 hours of knowledge of adverse event within 24 hours of knowledge of adverse event			
1. Patient Information			
Initials/identifier:	Date of Birth (e.g. 01 Jan 1940)	Ethnic Origin: White Asian Black/African American Other, Please Specify	
Sex: Male Female	Height(cm):	Weight(kg):	
Pregnant: [ ]Yes[ ] No	Country of occurrence:	Tel. No:	
2. Adverse Event Information			
AE term(s):			
Course of event:			
Onset of AE or date and time when AE occurred:		Date:	Time:
Onset of AE or date and time when event became serious ,if applicable:		Date:	Time:
Present Status: Ongoing→ AE currently treated □Yes □No Resolved Please Specify Date:_____Time:_____			
Casedescription:Detaileddescriptionoftheevent(Includerelatedsigns/symptoms,course,outcome)			
Reason for seriousness:			
Resulted in death life-threatening required in patient hospitalization or prolongation of Existing hospitalization resulted in persistent or significant disability/incapability(as per reporter's opinion)/congenital anomaly/birth defect other medically important event(reporter's discretion)			
Intensity: Mild Moderate Severe			
Reporter's Causality: [ ] certainly[ ] probably[ ] possibly[ ] unlikely[ ] conditional[ ] un assessable [ ] not related			
Outcome of AE: Completely recovered/resolved Ongoing Fatal Lost to follow-up Unknown Recovered with sequel AE→ Specify:_____			
If outcome Is fatal: Cause of death:_____Date:_____Time:_____ Report of Autopsy available? □No □Yes (Please attach copy to this report) Further information:_____			
Lab test Details(with dates, results and normal range):_____			
3. Drug Details			
Name of the drug:_____Strength:_____Indication:_____			
Route of Admin:_____Dosage form:_____Dose:_____			
Frequency:_____Expiry date: DD/MM/YYYY			
Start date:(dd.mm.yyyy) Stop date:(dd.mm.yyyy) Ongoing:			

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	Action taken with suspect drug: None Dosage changed temporarily: Date:_____Dosage reduced Dosage increased Drugs top temporarily: Date:_____ Drug restarted: Date:_____ Drug withdrawn permanently Dosage not changed Unknown Not applicable		
	Additional suspect drug(if any) details as above:		
	Event abated after drug Stopped or dose reduced:	Event reappeared after Reintroduction of suspect drug:	If yes, did reaction recur?
	Yes No Not applicable	Yes No Not applicable	Yes No Not applicable

4. Patient's Relevant Medical History (Supplement attached Yes/No)

(E.g. Concomitant diseases, previous history of present condition, allergy, drug or alcohol abuse)

5. Concomitant Drugs

Drug Name (generic)	Dose/ Unit	Route	Frequency	Start date	Stop date	Ongoing	Causal relationship To event
							None Possible
	Indication:						
							None Possible
	Indication:						
							None Possible

6. Reporter Details

Name: Address: Country: Tel. No: Email:	Occupation:[ ]Physician[ ] Pharmacist[ ] Nurse[ ] Consumer[ ] Other, specify:…… Also reported to:[ ]Regulatory Authority [ ] Distributor[ ] None Date: DD/MM/YYYY, Signature:
7. Send this report to:	**8. To be filled by Manufacturer:**
…….	Date received by receiver: DD/MM/YYYY Name and sign of receiver: Safety Report ID:

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ANNEXURE II
CASE LOG

S.No.	Local tracking number	Country	Product	Source (Health authority, or Spontaneous reporter)	Information type (Single case, Safety finding from local literature review)