PHARMA DEVILS

PHARMACOVIGILANCE DEPARTMENT

STANDARD OPERATING PROCEDURE	
Department: Pharmacovigilance	**URS No.:**
Title: Implementation of Safety Variations in Products Labeling Documents	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

1.0 OBJECTIVE:

To lay down a procedure for Implementation of Safety Variations in ……. products'labeling documents i.e. Package Inserts (PI)/ Patient Information Leaflet (PIL) Summary of Product Characteristics (SPC or SmPC).

2.0 SCOPE:

This Standard procedure is applicable to …….. including all subsidiaries.

3.0 RESPONSIBILITY:

3.1 Pharmacovigilance (PV) Department:

Preparation of this SOP, to assist in implementation of safety variations in PI's/PIL's/SPC's. Distribution, Retrieval and Destruction of this SOP.

3.2 Pharmacovigilance Officer In-charge (PvOI):

Review, training and effective implementation of this SOP. Ensure proper systematic implementation of this SOP.

To ensure proper implementation of safety variations in PI's/PIL's/SPC's.

Review and approve the safety variations in PI's/PIL's/SPC's for …. product.

3.3 Drug Regulatory Affairs Department

To support PV department on restrictions and/or urgent safety variations.

3.4 Quality Assurance (QA) Department

To support PV department on restrictions and/or urgent safety variations from product recall or withdrawal perspective.

4.0 ACCOUNTABILITY:

Pharmacovigilance officer in charge.

5.0 PROCEDURES:

5.1. Responsibilities of Pharmacovigilance Department:

5.1.1. Evaluate the need for urgent safety restrictions, safety variations and product withdrawal related to safety issues for regulatory authorized products, as well as the severity and urgency of the situation.

5.1.2. Discuss any withdrawal measure with regulatory authority from safety point.

5.1.3. Inform the regulatory authority regarding the need for urgent safety restrictions, safety variations and product withdrawal.

5.1.4. Inform HCP's and Patients/the public for regulatory authorized products, as appropriate.

5.1.5. Inform contract partners/distributors (if applicable) of the need for urgent safety restrictions, safety variations and product withdrawal within their concerned territory.

5.1.6. Render support to Head QA in supervision and ensuring the resolution of issues related with restrictions and/or urgent safety variations and product withdrawal involving a product for which …… holds a

Marketing Authorization as per Procedure for Recall and Withdrawal".

5.1.7. Prepare "Direct Healthcare Professional Communications" and "Risk Management Plan".

5.2. Responsibilities of Third parties (e.g. Contract Partners or distributor or agents etc.) [If applicable]:

Inform immediately to ……..PV department of any incoming safety related issue related with restrictions and/or urgent safety variations and product withdrawal for safety reasons involving a product for which …….. holds a Marketing Authorization.

5.2.1. Discuss any withdrawal measure with regulatory authority.

5.2.2. Inform HCP's and Patients/the public as appropriate.

5.2.3. Inform the regulatory authority regarding the need for urgent safety restrictions, safety variations and product withdrawal (if required).

5.2.4. Track the evolution of the issues related with restrictions and/or urgent safety variations and product withdrawal and maintain …….. PV department informed of the status of the situation.

5.2.5. Inform healthcare professionals/patients, if applicable and whenever necessary.

5.3. Responsibilities of QA Department:

5.3.1. QA Department shall support PV department on restrictions and/or urgent safety variations for safety reasons.

5.3.2. QA shall inform PV department the evolution and the implementation date of the restrictions and/or urgent safety variations.

5.3.3. Define, implement and supervise the withdrawal process.

5.3.4. Head QA shall inform PV department of the evolution and the ending date of product recall.

5.4. Responsibilities of Drug Regulatory Affairs (DRA) Department:

5.4.1. DRA Department along with QA shall support PV department on restrictions and/or urgent safety variations for safety reasons.

5.4.2. Implement the restrictions and/or urgent safety variations process, such as submission of safety variations applications.

5.4.3. Supervise the withdrawal process from regulatory affairs perspective. It is recognized that at the time of authorization, information on the safety of a medicinal product is relatively limited. A medicinal product is authorized on the basis that in the

5.4.4. Specified indication(s), at the time of authorization, the risk-benefit is judged positive for the target population. However, not all actual or potential risks shall have been identified when an initial authorization is sought. In the event that the overall risk-benefit balance is considered to have changed it probably requires major changes in the marketing authorization, such as:

- Marketing authorization withdrawal, revocation, suspension.
- The need to inform Healthcare Professionals (e.g. through DHPC's) and Patients/the public about an identifiable risk.
- PI/PIL/SPC variations (e.g. inclusion of new information on contraindications, changes on posology, etc.).

- Restrictions on distribution.
- Failure to obtain a marketing authorization renewal. Clinical trial suspension.
- Dosage modification.
- Changes in target population or indications.
- Formulation changes.
- Urgent safety restrictions.
- Risk Management Plan implementation.

5.5. Safety Signal Identification:

The Marketing Authorization Holder (MAH) shall inform the regulatory authority in the event of new risks or risks that have changed or changes to the risk-benefit balance being detected.

5.6. Submission of safety variations:

5.6.1. As with responding to requests for information from regulatory authority, deadlines for submission of safety variations shall depend on the urgency and potential public health impact of the Pharmacovigilance issue.

5.6.2. The regulatory authority shall ensure that requests for safety variations have a clearly stipulated deadline and this deadline shall be appropriate to the complexity and urgency of the issue. The regulatory authority shall liaise with …… regarding the appropriate deadline, as required.

5.6.3. Failure of …….. to submit the variation application within the deadline is considered as non-compliance.

5.7. Direct Healthcare Professional Communications (DHPC):

Where the …….. as the MAH proposes or is requested by the regulatory authority to disseminate a DHPC, the regulatory authority shall be provided with:

5.7.1. The proposed communication plan; including.

5.7.2. The proposed communication text of the DHPC.

5.7.3. The proposed texts of any related communication documents.

5.8. Risk Management Plan (RMP):

5.8.1. The description of a risk management system shall be submitted in the form of an RMP. The RMP is submitted whenever additional risk minimization activities are though necessary.

5.8.2. The regulatory authority may impose an obligation on a MAH to operate a risk management system if there are concerns about the risks affecting the risk-benefit balance of an authorized medicinal product. In that context, the regulatory authority shall also oblige the MAH to submit a detailed description of the risk management system which he intends to introduce for the medicinal product concerned.

5.8.3. The imposition of such obligations shall be duly justified, notified in writing and shall include the timeframe for submission of the detailed description of the risk management system.

5.8.4. The need for a RMP or an update to the RMP shall be discussed with the regulatory authority as appropriate, well in advance of the submission of an application involving a significant change to an existing marketing authorization.

5.8.5. An updated RMP shall always be submitted if there is a significant change to the benefit- risk balance of one or more medicinal products included in the RMP. When the RMP is updated, the risk minimization plan

shall include an evaluation of the impact of routine and/or additional risk minimization activities as applicable.

6.0 DISTRIBUTION:

Not Applicable

7.0 REFRENCE:

Not Applicable

8.0 ANNEXURES:

Not Applicable

9.0 ABBREVIATIONS:

DHPC	Direct Healthcare Professional Communication
DRA	Drug Regulatory Affairs
HCP	Health Care Professional
MAH	Marketing Authorization Holder
PI	Package Insert
PIL	Patient Information Leaflet
PVOI	Pharmacovigilance Pharmacovigilance Officer In-charge
RMP	Risk Management Plan
SPC	Summary of Product Characteristics
SOP	Standard Operating Procedure

10.0 REVISION HISTORY:

Revision No.	Effective Date	Reason for Revision	Change Control No.
00		New SOP	NIL