I. PURPOSE

This Standard Operating Procedure (SOP) describes the procedure for proposing changes to the product information (e.g. the summary of product characteristics (SmPC) or package leaflet (PL) of the medicinal products (MP) based on the new safety data in accordance with Good Pharmacovigilance Practices(GVP).

II. SCOPE

This procedure shall apply to the processes of proposing safety changes to the SmPC and PL by PharmExpert LLC (Pharmex).

III. RESPONSIBILITIES

Role	Responsibility
Senior Pharmacovigilance Specialist (SPVS)	• Proposing suggestions for making changes to the SmPC/PL • Registration of proposed changes to the SmPC/PL • Sending the draft to the MAH's QPPV • Informing MP circulation entities • Storage and archiving
Marketing Authorization Holder's Qualified Person responsible for Pharmacovigilance (MAH's QPPV)	• Review and approval of proposed safety changes to the SmPC/PL
Quality Assurance Manager	• Compliance monitoring

IV. DEFINITIONS

Abbreviations used in the text are spelled out on its first mention.

PL – the leaflet in every pack of MP that contains information on the medicine for end-users, such as patients and animal owners.

SmPC – a document describing the properties and the officially approved conditions of use of a MP. Summaries of product characteristics form the basis of information for healthcare professionals on how to use the medicine safely and effectively.

For other terms and definitions refer to the SOP-QA-003 «Pharmacovigilance Glossary».

V. PROCEDURE

A. Safety Changes

New safety data can be found during:

- regulatory intelligence monitoring;
- monitoring procedure of the medical-scientific literature;
- preparation of periodic safety update reports;
- preparation of Risk Management Plans;
- handling of signals;
- requests and reports of Regulatory Authorities (RA);
- adopting the SmPC/PL in accordance with the reference MP.

The required changes to the SmPC/PL can be including, but not limited to:

- new contra-indications;
- special warnings;
- new safety and/or efficacy data;
- interaction with other MPs;
- unexpected adverse drug reactions (ADR) or change of frequency of known ADRs;
- changes in dosage or frequency of use;
- inclusion and exclusion of indications in the PL.

B. Process

1. Proposing Safety Changes to the SmPC/PL

SPVS within 5 business days:

a) Fill the «Safety Changes Application Form» (R01F-SOP-PV-010).

b) If there is available an approved signal, check the SmPC/PL of MP and compare it with the SmPC/PL of the reference MP (sections «Contraindications»; «Undesirable effects»; «Special warnings and precautions for use»; «Interaction with other MPs and other forms of interaction»; «Fertility, pregnancy and lactation»; «Effects on ability to drive and use machines»).

c) Justify the differences (if any) and/or make changes to the SmPC/PL of MP in accordance with RA decisions.

d) Make these changes in all SmPC/PL of MPs with the same International Nonproprietary Names (INN).

e) Get approval of HPVD.

f) Send the «Safety Changes Application Form» to the MAH's QPPV.

2. Approval of Safety Changes to the SmPC/PL

MAH's QPPV within 5 business days:

a) Review the proposed safety changes to the SmPC/PL.