TABLE OF CONTENTS

I. PURPOSE

This Standard Operating Procedure (SOP) describes the procedure of acting as a Local Contact Person responsible for Pharmacovigilance (LCPPV) in order to ensure compliance of Pharmacovigilance (PV) system of Marketing Authorization Holders (MAH) with valid regulatory requirements for the concerned Medicinal Products (MP) in the authorized countries.

II. SCOPE

This procedure shall apply to activity of LCPPVs managed by PharmExpert LLC (Pharmex) in the countries of responsibility.

III. RESPONSIBILITIES

Role	Responsibility
Pharmex	• Management of LCPPVs • Providing Local PV processes with necessary resources
LCPPV/LCPPV back-up/ Designee/HPVD	• Fully adhere to this SOP
Quality Assurance Manager (QAM)	• Compliance monitoring

IV. DEFINITIONS

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

Abuse – this corresponds to the persistent or sporadic, intentional excessive use of MP, which is accompanied by harmful physical or psychological effects.

Adverse event (AE) – Any untoward medical occurrence in a patient to whom a MP is administered and which does not necessarily have a causal relationship with this treatment.

An adverse event can therefore be any unfavourable and unintended sign (e.g. an abnormal laboratory finding), symptom, or disease temporally associated with the use of a MP, whether or not considered related to this MP.

Adverse reaction (AR) – A response to a MP which is noxious and unintended. Response in this contest means that a causal relationship between a MP and an AE is at least a reasonable possibility.

Aggregate reports

Reports of a set of cases, meant for RAs.

- Annual Safety Report (ASR): In clinical trials, an annual report of all newly available safety information. An ASR includes a global analysis for all trials with the same Investigational Medicinal Product (IMP)
- Development Safety Update Report (DSUR)
- Periodic Safety Update Report (PSUR): Also called PBRER (Periodic Benefit Risk Evaluation Report)

Day 0 (zero) – the clock for the submission of a valid ICSR starts as soon as the information containing the minimum criteria has been brought to the attention of the personnel of the MAH, including medical representatives and contractors. This date should be considered as day zero. It is the first day when the MAH gets knowledge of a valid ICSR, irrespective of whether the information is received during a weekend or public holiday. The timelines for submission are based on calendar days.

Contract Party (CP) – CP for Designee (SPVS/PVS) means MAH or Third party; CP for LCPPV who is staff of Pharmex means Pharmex; CP for outsourced LCPPV means Pharmex or MAH or Third party.

Individual Case Safety Report (ICSR) – refers to the format and content for the submission of an individual report of suspected ARs in relation to a MP that occur in a single patient at a specific point of time.

Marketing Authorization Holder (MAH) – the pharmaceutical company that has filed and obtained the marketing authorization submissions for the product.

Medicinal product (MP)

Any substance or combination of substances

- presented as having properties for treating or preventing disease in human beings; or
- which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.

Misuse – this refers to situations where the MP is intentionally and inappropriately used not in accordance with the authorized product information.

Occupational exposure – this refers to the exposure to a MP, as a result of one's professional or non-professional occupation.

Off-label use – this relates to situations where the MP is intentionally used for a medical purpose not in accordance with the authorized product information.

Pharmacovigilance (PV) – science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem (see WHO13).

In line with this general definition, underlying objectives of PV in accordance with the applicable EU legislation for are:

- preventing harm from ARs in humans arising from the use of authorized MPs within or outside the terms of marketing authorization or from occupational exposure; and
- promoting the safe and effective use of MPs, in particular through providing timely information about the safety of MPs to patients, healthcare professionals and the public.

Pharmacovigilance is therefore an activity contributing to the protection of patients' and public health.

Third party – the company partially/completely responsible for MAH's PV system or participate in the chain of functioning of PV system and directly/indirectly reports to MAH's QPPV (Qualified Person responsible for PV).

Overdose – this refers to the administration of a quantity of a MP given per administration or cumulatively, which is above the maximum recommended dose according to the authorized product information. Clinical judgement should always be applied.

Periodic Safety Update Report (PSUR) – a report prepared by the MAH describing the worldwide safety experience with a medicine at a defined time after its authorization.

Serious ICSR – a serious AR corresponds to any untoward medical occurrence that at any dose results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability or incapacity, or is a congenital anomaly/birth defect.

Signal – information arising from one or multiple sources, including observations and experiments, which suggests a new potentially causal association, or a new aspect of a known association between an intervention and an event or set of related events, either adverse or beneficial, that is judged to be of sufficient likelihood to justify verification action.

Standard Operating Procedure (SOP) – a set of step-by-step instructions compiled by an organization to help workers carry out routine operations.

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

V. PROCEDURE

A. General Specification

1. MAH's Responsibility

As part of the PV system, the MAH shall have permanently and continuously at his disposal, an appropriately QPPV:

- Reside and operate in the European Union (EU)/ European Economic Area (EEA)/ Eurasian Economic Union (EEU)/other applicable territories
- In addition, local RA may request the nomination of a LCPPV for PV issues at national level reporting to the QPPV