

I. PURPOSE

This Standard Operating Procedure (SOP) describes the procedure for swift response to identified/received Emerging Safety Issue (ESI) and Significant Safety Issue (SSI) at Pharmexpert LLC (Pharmex).

II. SCOPE

This procedure shall apply to Pharmex's staff involved in Pharmacovigilance (PV) processes.

III. RESPONSIBILITIES

Role	Responsibility
PV Specialists	<ul style="list-style-type: none"> • Swift response to identified/received ESI/SSI • Safety communication to MAH's QPPV/RA
Marketing Authorization Holder's Qualified Person responsible for PV (MAH's QPPV)	<ul style="list-style-type: none"> • Initiation/ review and approval of USR procedure • Providing necessary documents • Implementation of RA decision
Quality Assurance Manager (QAM)	<ul style="list-style-type: none"> • Compliance monitoring

IV. DEFINITIONS

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

Emerging safety issue – a safety issue considered by a MAH to require urgent attention by the Regulatory Authority (RA) because of the potential major impact on the risk-benefit balance of the medicinal product (MP) and/or on patients' or public health, and the potential need for prompt regulatory action and communication to patients and healthcare professionals.

Examples include:

- major safety issues identified in the context of ongoing or newly completed studies, e.g. an unexpectedly increased rate of fatal or life-threatening adverse events;
- major safety issues identified through spontaneous reporting or published in the scientific literature, which may lead to considering a contra-indication, a restriction of use of the MP or its withdrawal from the market;
- major safety-related regulatory actions outside the EU, e.g. a restriction of the use of the MP or its suspension.

Urgent safety restriction (USR) – means an interim change in terms of marketing authorisation due to new information having a bearing on the safe use of the MP.

Risk-benefit balance – an evaluation of the positive therapeutic effects of the MP in relation to the risks,