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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).

m) The «PV Tasks Tracker» completes and maintains by HPVD.

n) In order to comply with regulatory requirements and contractual obligations, setting up of reminders for LCPPV/Designee concerning timely performing of tasks are arranged by SA.

o) The columns «O, P» of the «PV Tasks Tracker» related email addresses keep actual by Designee.

p) The MAH name, contact details of QPPV (back-up), LCPPV (back-up), PSMF location address and expiry date of Power of Attorney are listed in the log «Summary of PV system» (R02T-SOP-PV-004), path: <RA>.

q) The log «Summary of PV system» for new MAHs completes by HPVD.

r) Further changes are maintained by Designee. Upon receiving information about the change, Designee will enter new information in the «Summary of PV system Log».

s) QAM on weekly basis performs compliance monitoring of activity of the LCPPV/Designee on defined Key Performance Indicators.

B. Process

1. Appointment of LCPPV

a) Upon request of MAH/Third party on appointment of LCPPV for specific country(s), Pharmex provides the CV/JD of the appropriate qualified LCPPV/LCPPV back-up.

b) After signing of the service agreement, QAM enters the service agreement details in the «SA Register» (R04T-SOP-PV-015).

c) HPVD:

- assigns responsible person (Designee) for the new company;
- enters new company details and outsourced tasks in the «PV Tasks Tracker»;
- saves the product list in the folder, path: <Product List/Country N/YYYY>;
- names the file: <Country Code_MAH name_DD-Mnn-YYYY>.

d) Designee sends the drafts of LCPPV authorization documents to the MAH/Third party.

Note. The required documents, submission route, format, language and applicable proof of submission (PS) are listed in the section «LCPPV» of the «RI Questionnaire» (R01T-SOP-PV-007).

e) The MAH/Third party may use its own draft of documents for authorization of LCPPV/LCPPV back-up (If applicable).

f) Duly signed and sealed documents in company letterhead of MAH are submitted to the respective country's RA by LCPPV/Designee within 3-7 business days.

g) PS is sent to the MAH/Third party and scan of documents are saved by Designee in the folder, path:

(if possible).

7. Foreign ICSR's

a) Where required, ICSRs received from CP occurred outside of the country resides LCPPV are submitted to local RA.

b) Upon receipt of the foreign ICSRs, LCPPV/Designee shall send ACK to CP and record the case details, ACK date/time in the «Local Case Tracker».

8. Regulatory Reporting

a) The LCPPV/Designee will receive processed local and foreign AE reports from the CP in CIOMS I/ICSR (pdf) or XML format forms.

b) The LCPPV/Designee is responsible for submission the expedited reports in line with the section «ICSRs» of «RI Questionnaire» and recoding in the «Local Case Tracker».

c) If local regulations require the report to be translated into local language or a different format, this shall be performed by the LCPPV and submitted with the report. The translation document should not replace the reports of CP, unless specifically stated in local regulations.

d) PS is sent to the CP within 1 day of submission along with the completed «Local Case Tracker».

e) All local and foreign ICSRs shall be stored by Designee in the SDB:

- Local ICSR: <Safety Database/Country N/YYYY/Country Code_Local ICSR/Country Code_ICSR/Company N>
- Foreign ICSR: < Safety Database/Country N/YYYY/Country Code_Foreign ICSR/Company N>

f) All source documents (including handwritten notes, translation, PS) related to AE/other safety related information shall be stored in the SDB:

- Primary documentation for spontaneous report (SR): <Safety Database/Country N/YYYY/Country Code_Local ICSR/Country Code_SR_Primary docs/Company N>
- Primary documentation for AE reports identified during LLS: <Safety Database/Country N/YYYY/Country Code_Local ICSR/Country Code_LS_Primary docs/Company N>

9. Special Situations

In line with applicable regulations, reports received regarding the following safety-related events (including, not limited to) occurring in respective country shall also be collected and processed according to the ¶ 6, even when no AE has been reported:

- Lack of Therapeutic Efficacy
- Product quality complaints
- Exposure during pregnancy or parental exposure and exposure during lactation.
- Accidental exposure / Occupational exposure

Dear Colleagues,

Please, find monthly reconciliation report for the month: XXXX. Country: XXXXXXX.

1.AEs/other safety related information received from:

- Daily monitoring (telephone, email) – <0> or <indicate result>
- Health/Regulatory Authorities – <0> or <indicate result>
- Local Literature Search – <0> or <indicate result> or <not applicable>

2.Safety information received from MAH/Third party – <0> or <indicate result>

3.Local Regulatory updates – <0> or <indicate result>

4.Regulatory Authority' requests – <0> or <indicate result>

5.Documents to/from RA:

- Submitted – <0> or <indicate result> (document name/outgoing number/submission date)
- Received – <0> or <indicate result> (document name/incoming number/submission date)

Please, confirm receipt.

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c) Designee may send reconciliation email for multiple country in the same email indicating data for each country separately (as list or table).

d) LCPPV/Designee may send the content of reconciliation email in Russian language.

e) In the projects where Designee reports to the MAH/Third party weekly LLS, RI results once a month, the «LS Tracker» (R02T-SOP-PV-006) and «RI Tracker» (R03T-SOP-PV-007) also will be attached to the monthly reconciliation email.

f) Designee saves:

- monthly reconciliation emails for the single country sent in line with the point b (column «K» of the «PV Tasks Tracker» with marking «Y» and «Mix») in the folder, path: <LCPPV Reports/Country N/YYYY/Country Code_Pharmex Reporting/Company N/Month>.
- monthly reconciliation emails for the multiple country sent in line with the point b (column «K» of the «PV Tasks Tracker» with marking «Y» and «Mix») in the folder, path: <LCPPV Reports/Multicountry/YYYY/Company N/Month>.
- All reports including the reconciliation reports prepared in the forms of MAH/Third party in the folder, path: <LCPPV Reports/Country N/YYYY/Country Code_Pharmex Reporting/Company N/Month>.