Pharmacovigilance –Specific SOP Master List with Explanatory Notes

Pharmacovigilance Quality Management System (QMS) Documents
• Description of the company's Pharmacovigilance / Vaccine safety Drug Safety Policy • Description of the Pharmacovigilance / Risk Management System (Pharmacovigilance System Master File PSMF)   ○ Working Instruction on the generation of a PSMF as appendix
• Pharmacovigilance (Vaccine Safety) Quality Manual:

1. ICSR Management:
The purpose of the SOP is to describe the process for handling individual case safety reports (ICSRs) including special situation reports (e.g., pregnancy reports) coincident with the use of a marketed product (i.e., post-licensure) or a development compound (i.e., pre-licensure) for which the company's PV department bears reporting responsibility:
  ○ Case intake, duplicate search, case triage, data entry
  ○ Quality control and medical review (case assessment)
  ○ Reclassification
  ○ Unblinding of ICSRs from blinded clinical trials for regulatory reporting
  ○ Case finalization and case distribution
  ○ Performing follow-up (pre-licensure / post-licensure)
  ○ Handling of other important safety information OISI (e.g., urgent safety measures pre-and post-licensure, HHE, SAE)
  ○ Analysis of similar events (i.e., for SAE / IND safety reporting in Clinical Trials)
  ○ Handling of "not a case"
  ○ Case deletion
  ○ Case archival
  ○ Compliance monitoring
 	
Ideally to be combined with a User Manual which is an uncontrolled document

2. Product Complaint Handling The purpose of this SOP is to describe the procedure for the receipt, documentation, investigation, and monitoring of ICSRs due to quality defects and includes counterfeit drugs/vaccines, falsified medicinal products and clinical trial material complaints)

3. Generation of aggregate / Periodic Reports (DSURs, PSURs, PBRERs)
 	
Periodic Safety Update repots (PSURs) / Periodic Benefit Risk Evaluation Report (PBRER): The purpose of the SOP is to describe the responsibilities and processes associated with the handling of PSURs / PBRERs. Processes on preparing Summary Bridging Reports / Addendum Reports – if still accepted / required by NRA to be added.
  ○ Overall Planning
  ○ Initiation and Preparation
  ○ Quality Control
  ○ Review of document

- Finalization of document
- Distribution, submission, and archiving
- Compliance monitoring
- Assessment reports

Development Safety Update Report (DSURs) / Annual Reports:
The purpose of the SOP is to describe the responsibilities and processes associated with the handling of DSURs / annual reports. This SOP can be a stand-alone document or the specific DSUR processes can be integrated into the PSUR SOP.

Ideally to be combined with a User Manual, an uncontrolled document.

4. Literature Search (safety relevant) and Analysis for safety reporting:
The purpose of the SOP is to describe the review of scientific and medical literature (e.g., published case reports, clinical trials, conference abstract, posters, presentations) including weekly search of worldwide literature with identification, tracking of potential case reports from solicited / unsolicited literature and the creation of ICSRs to be included in the company's safety database. The process includes subsequent medical review of any identified ICSR associated with a company's medicinal product (if not included in the ICSR management SOP).
The process begins with the establishment of search parameters and ends with the receipt of an article / abstract ready to be processed.

5. Set-up and maintenance of inventory of regulatory requirements:
The purpose of the SOP is to describe regulatory intelligence with respective procedures to screen and assess new or updated PV, Clinical and Regulatory policy documents / guidelines on a regular basis for potential impact on company procedures, and to maintain oversight over Pharmacovigilance laws and regulations.

The document may be a subset of R&D relevant SOPs, however due to the country specific PV requirements, a PV stand-alone SOP is highly recommended):

6. Interaction and communication with Regulatory Authorities:
The purpose of the SOP is to describe the procedure to receive / initiate, store, and disseminate information resulting from communications with regulatory authorities.

7. Communication with other stakeholders (press releases require a corporate SOP)
The purpose of the SOP is to describe the procedure and roles and responsibilities to inform relevant stakeholders (e.g., patients, physicians, investigators, ECs / IRBs) on new and / or changed safety information (e.g., DHCP communication, SAE information for EC / IRB, investigators).

8. Generation / Maintenance of Risk Management Plans
The purpose of the SOP is to describe the steps in developing, reviewing, approving, updating / Revising, and storing the PV Risk Management plan RMP. The SOP can also describe the RMP implementation, and evaluation of the effectiveness of risk minimization activities, as applicable:
   - Preparing the first RMP for a compound in development (DRMP)
   - Preparing the Core RMP
   - Preparing /updating the Core RMP
   - Preparing Regional RMPs
   - Evaluation of Risk Minimization Measures and PV activities

- Periodic / ad hoc review of the RMP

9. Design, Conduct of Risk Minimization Programs / REMS, and their evaluation:
   Procedures can be integrated in the 8. and 11.

10. Signal Detection and Investigation
    The purpose of the SOP is to describe the standard procedures for proactive safety signal detection, signal evaluation efforts and appropriate communication of safety issues:
    - Definition of a signal
    - Detection of key events (e.g., vaccine – specific AESIs, etc.)
    - Frequency of signal detection activities
    - Evaluation of signals – Evidence of causality
    - Overall assessment of signal impact
    - Signal documents and actions

11. Design and Conduct of PASS
    The purpose of the SOP is to describe the roles and responsibilities in performing post-authorization studies (interventional or non-interventional / observational), imposed, or not imposed, including e.g., guidance on structure, requirements, reporting obligations (according to GVP Module VIII).

12. *Collection of safety information in patient support programs and market research programs (or part of the Design and Conduct of PSPs and MR programs) -may not be applicable for pure vaccine companies*

13. Safety Issue Management
    Can be integrated in to "Handling of Urgent safety measure

14. Crisis Management (Corporate SOP) – PV Business Continuity Plan (BCP) is a PV specific Guidance document:
    The purpose of the BCP Guidance is to describe specific PV related recommendations to consider for business continuity in case of a crisis. The BCP must include PV components to ensure that essential business operations and processes are protected and compliance with regulatory PV requirements are maintenance.

15. Safety Governance
    Ideally described by a Charter:
    The purpose of a Safety Governance Charter is to describe the scope, role, responsibilities, and procedures of the Company's Safety Governance (e.g., Safety Board, Safety Management Team) to review the safety data for all development compounds at pre-defined time points and before FIH and to address important safety issues emerging from clinical trials and post-licensure safety information (ICSRs, PSURs, media, etc.). Recommended safety measures are to be taken and implemented.

16. Management of internal safety databases
    The purpose of the SOP is to describe the roles and responsibilities for handling the company Safety Database.

17. Access and analysis of external databases
    The purpose of the SOP is to describe the roles and responsibilities for searching safety information in external databases (i.e., VigiBase; VAERs, other publicly accessible safety databases).

18. Safety Data Exchange Agreements and management of safety relevant business partnerships: The purpose of the SOP is to describe the responsibilities and procedures for developing, reviewing, updating, approving, terminating, and filing Safety Data Exchange Agreement (SDEA) / Pharmacovigilance Agreements (PVAs) with Partners with whom the company is negotiating or has a license or development / co-development agreement. This SOP also describes the signature requirements for SDEAs / PVAs. ○ Reviewing license agreements ○ SDEA / PVA – marketed products ○ SDEA / PVA – compounds under development or co-development ○ Periodic review and update of the agreements ○ Auditing ○ Signatures and training ○ Termination ○ Archiving and filing ○ Version Control
19. Generation and maintenance of the reference safety information (RSI): The purpose of the SOP is to describe the procedure and roles and responsibilities for developing, reviewing, updating, approving the Company Core Safety Information CCSI. The CCSI is the safety section of the Company Core Data Sheet (CCDS) and serves as the basis for safety labeling / RSI. Note: For Clinical Trials may include the procedure to develop the safety section for the Informed Consent Form (ICF) and the safety section of the Investigator Brochure (IB)
20. Generation and maintenance of integrated summaries of safety (ISS) / safety profiles The respective procedures are within Stats; PV ensures the safety analyses and implementation of integrated safety summaries in the PV respective documents.
21. Benefit-Risk Assessments / generation of clinical expert statements The purpose of the SOP is to describe the procedures and roles and responsibilities in continuously assessing the benefit risk profile of compounds in development, at filing / registration and of the marketed medicinal products.
22. Vaccine Safety and Risk Management Training: The purpose of the SOP is to ensure the establishment and execution of training requirements to ensure the staff involved in PV activities is adequately trained, including Company Training Matrix
23. The QPPV and local / EU QPPV as applicable The purpose of the SOP is to describe the role and responsibilities of the QPPV and Deputy.
24. MedDRA maintenance and coding principles – MedDRA Coding rules: The purpose of the SOP is to ensure consistent and medically accurate MedDRA coded data throughout the company to facilitate reliable data retrieval from the PV database essential for research, safety monitoring, exchange of clinical information and regulatory submissions. The document should be modeled on the MedDRA Term Selection Points to Consider and on the MSSO Guidance (updates) and include coding conventions.

25. Vaccine safety Quality management planning, conduct and compliance monitoring The purpose of the SOP is to describe the management of all suspected or confirmed quality issues that occur within GCP / PV research and development and pharmacovigilance (pre-licensure and post-licensure) ○ Describes the process of identification, evaluation, escalation, investigation, analysis, and documentation for all quality issues, as well as the periodic review to ensure the processes are in compliance with all applicable regulations. ○ Includes the development, implementation, and management of Corrective and Preventive Actions (CAPA).
26. Management of Safety Advisory Boards / Drug Safety Monitoring Committees: Based on a SOP a Committee Charter to be prepared to include the Mission, Membership / Composition, Conflict of Interest, Roles and Responsibilities, and Confidentiality.
27. Reconciliation of data sources with safety information: The purpose of the SOP is to describe the procedure for reconciling Serious Adverse Events (SAEs) between the clinical database and the Pharmacovigilance Database: NOTE: SAEs from clinical trials are included in the PV database and follow the ICSR management SOP.
28. Health hazard assessments / evaluations (HHE): The purpose the SOP is to describe the responsibilities and procedures for Health Hazard Evaluation (HHE) Report initiation, preparation, approval, distribution, and document retention:
29. First in Human (FIH) in Clinical Trials The purpose of the SOP is to provide the process for preparing a non-clinical safety data information package for assessment by a Safety Board or equivalent to warrant endorsement to proceed with clinical development activities for FIH clinical trials.

July 11 / KH