Responsibilities of Pharmacovigilance (PV) System Stakeholders Policy Summary

This policy aims to establish a clear understanding that all personnel are part of the Pharmacovigilance System (PV System) and that the PV System performance depends on all stakeholders being aware of and contributing to pharmacovigilance activities. This policy defines the deliverables for each group.

Pharmacovigilance is a company-wide global concept spanning the whole life-cycle of a product. The legislative requirement for pharmacovigilance is the responsibility of all personnel of the marketing authorization holder (MAH). Staff performing certain functions will be more involved than others, although any individual may learn about pharmacovigilance-relevant information relating to the products for which the company holds a marketing authorization.

Affiliate organizations are responsible to:

- Implement an affiliate PV System that is compliant with local legislation and PSRM systems, procedures and standards; and
- Implement medical information services including managing reports of adverse events and Special Situations reported to the medical information function.

Global Clinical Research is responsible to:

- Implement systems, procedures, and standards to ensure sponsored interventional clinical trials meet Good Clinical Practice (GCP) standards;
- Implement an up-to-date inventory for interventional clinical trials that address PV-oversight needs; and
- Contribute data relating to interventional clinical trials to PV-deliverables, such as (but not limited to), Pharmacovigilance System Master File (PSMF), Periodic Safety Update Reports (PSUR) and Development Safety Update Reports (DSUR).

Global Operations Auditing:

- Implement a risk-proportionate audit program for the PV System, which should cover all departments that may receive adverse reaction reports or that are involved in pharmacovigilance activities including, but not limited to, PSRM, affiliates, product quality, medical affairs, regulatory affairs and third parties;
- Produce the audit outcome report and approve it;

- Request a corrective and preventive action (CAPA) plan from the auditee and approve the CAPA plan; and
- Provide an overview on audits conducted and their respective outcomes for the PSMF on a regular basis.

Legal is responsible to:

- Forward information about customer complaints and claims relating to a potential adverse event and or Special Situation to the PV function (PSRM or affiliate PV, as applicable) for processing and evaluation.

Medical Affairs is responsible to:

- Implement systems, procedures and standards which ensure that interventional and noninterventional clinical studies and programs sponsored by Medical Affairs or supported by Medical Affairs (the latter referring to investigator-initiated interventional and noninterventional clinical studies and programs) comply with PV requirements;
- Implement up-to-date inventory(ies) that address PV-oversight needs for interventional and noninterventional clinical studies and programs under the auspices of Medical Affairs, including patient support programs (PSP) and/or market research programs (MRP).
- Contribute data relating to interventional and non-interventional clinical studies and programs under the auspices of Medical Affairs to PV deliverables, such as (but not limited to), PSMF, PSURs and RMPs.

Global Digital Marketing is responsible to:

- Implement up-to-date inventory(ies) that address PV-oversight needs;
- Screening of social media project content for product safety related information and forwarding all relevant hits to the affiliate PV-function;
- Contribute data relating to social media activities to PV-deliverables, such as (but not limited to), PSMF, PSURs and RMPs.

Product Safety and Risk Management (PSRM) is responsible to:

- Coordinate the PV System to fulfil its legal tasks and responsibilities in relation to pharmacovigilance and designed to monitor the safety of authorized medicinal products and detect any change to their risk-benefit balance;
- Ensure basic PV-training to all employees and ensure refresher training on an annual basis;

- Develop and maintain the Pharmacovigilance System Master File (PSMF) in accordance with the Guideline on good pharmacovigilance practices: Module II – Pharmacovigilance system master file;
- Develop and maintain Risk Management Plans, as applicable;
- Manage and report adverse reactions and other PV-relevant information in accordance with regulatory requirements;
- Produce periodic safety reports, such as (including but not limited to) PSURs, PBRERs, PADERs, DSURs;
- Oversee and contribute to Post-authorization Safety Studies (PASS);
- Evaluate post-marketing reports for safety signals, an activity that encompasses signal detection, validation, prioritization, assessment and reporting of signals;
- Collaborate with relevant stakeholders in minimizing medicinal product risks relating to individual patients and public health;
- Negotiate and establish Pharmacovigilance Agreements (PVA) with Third Parties, such as (including but not limited to), commercial partners and service providers with whom safety information on medicinal products must be exchanged;
- Monitor and enhance the performance of the PV System in collaboration with all PV System stakeholders;
- Implement systems, procedures and standards that ensure business continuity in case of major business disruption;
- Track and verify implementation of CAPAs against objective evidence; and
- Provide status on CAPA implementation for inclusion into PSMF.

Global Quality Operations is responsible to:

- Implement systems, procedures and standards which ensure that product quality complaints relating to medicinal products are documented and captured;
- Set-up of a mechanism which ensures the transfer of product quality complaints associated with adverse events to the affiliate PV-function, as well as a reconciliation mechanism to ensure all adverse events have been transferred;
- Cross-reference the ID of the product quality complaint (PQC) record in the PQC-database with the ID of the adverse event record in the PV-database, if a report contains both a product quality complaint and an adverse event;
- Notify PSRM if during analysis of a product quality complaint, a critical safety concern is detected (e.g., incorrect amount of an active ingredient) and urgent action may be required; and
- Collaborate with PSRM regarding Medical Risk Assessment and/or product recalls.

PV System Oversight Committee (PSOC) is responsible to:

- Meet in appropriate intervals or ad hoc, if needed, to review the performance of the PV System and, if applicable, to decide on measures to ensure good performance.

Regulatory Affairs is responsible to:

- Notify PSRM of Health Authority requests related to safety aspects of products, including Health Authority PSUR assessment reports;
- Notify PSRM of safety-related label changes;
- Submit safety-related label changes as per local or regional requirements; • Provide Regulatory information related to PV-deliverables, such as (but not limited to), PSMF and PSURs; and
- Maintain the following information on changes to Marketing Authorizations within Regulatory Databases, which PSRM may access:
  - Approvals;
  - Suspensions or Withdrawals due to safety reasons; and
  - Loss of Marketing Authorization due to “Sunset Clause” or divestment, change in MAH name, as well as voluntary revocation of marketing authorizations.

Sales and Marketing is responsible to:

- Train medical sales representatives on pharmacovigilance aspects so that they are able to recognize and capture safety information appropriately, since Health Care Professionals may report a problem with a medicinal product to a medical sales representative rather than contacting their medical information or pharmacovigilance department;
- Medical sales representatives shall transmit safety-related information to the affiliate PV-function within 24 hours of becoming aware of it;
- Contribute exposure data (or sales volume as a surrogate) to PV deliverables, such as (but not limited to), PSURs and RMPs;
- If applicable, implement risk-minimization measures, e.g., educational material, in accordance with the provision laid out in the Risk Management Plan for a given product;
- Keep inventory(ies) on market research programs and patient support programs;
- Implement systems, procedures and standards that ensure documentation of received safety related information and its transfer to the PV-function (PSRM or affiliate PV, as applicable) for market research programs and patient support programs initiated by Sales and Marketing;
- Ensure reconciliation of all relevant safety information; and

- If applicable, ensure, in collaboration with pharmacovigilance, that vendor contracts have PV provisions included, and relevant vendor staff is appropriately trained on PV-obligations

Head of Global Product Safety and Risk Management is responsible to:

- Promote awareness and understanding of the MAH's responsibilities for pharmacovigilance;
- Provide appropriate guidance, as necessary, when a serious safety issue is identified that may require actions such as a recall, suspension or withdrawal (including briefing of personnel that deals with the press); and
- Ensure availability of appropriate personnel, systems and support so that legal pharmacovigilance obligations are fulfilled.

Management of all PV System stakeholder functions is responsible to:

- Ensure appropriate training as specified in the Cross-functional Training Matrix.

It is the responsibility of all employees to complete their required PV training, which includes the definition of adverse events and how to appropriately report them.