Pharmacovigilance Systems Master File (PSMF)

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Pharmacovigilance System Master File (PSMF)

A detailed description of the pharmacovigilance system used by the marketing authorisation holder with respect to one or more authorised medicinal products. *Article 1(28e) of Directive 2001/83/EC of the European Parliament*

Was introduced to harmonise and strengthen the conduct of pharmacovigilance activities

The PSMF is a legal requirement in many countries. Local regulatory requirements must be checked and followed

The content of PSMF should reflect global availability of safety information for medicinal products, presenting information on the pharmacovigilance system applied at global, regional and local levels.

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Objectives of PSMF

- ***Describe*** the pharmacovigilance (PV) system
- ***Support/document*** PV system's compliance with the requirements
- ***Provides***:
  - information on
    - aspects of compliance in relation to the system
    - deficiencies in the system, non-compliance with the requirements
    - risks or actual failure in the conduct of specific PV aspects and
    - the action/measure taken
- ***Contribute*** to:
  - the fulfilment of supervisory responsibilities of the qualified personnel for PV activities (QPPV),
  - planning and conduct of internal audits and
  - external inspections/verification of compliance by the national competent authorities (NCAs)
  - appropriate management of and improvement(s) to the pharmacovigilance system.

<u>Thereby, assuring PV system implementation and compliance.</u>

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How many PSMFs?

One MAH + One PV system = One PSMF

- One PSMF describes PV system **for one or more** medicinal products of one MAH

One MAH + Multiple PV system = Multiple PSMF

  - MAH may apply separate PV systems for different categories of products (vaccines, consumer health)
  - Describe each system in a separate PSMF
- **Multiple MAH = Multiple PSMF**
  - PV system may be shared by several MAH
    - each MAH responsible for a PSMF to describe PV system applicable for its product
  - MAH may delegate PV activity to contractor
    - PSMF of MAH may cross refer to all or part of the PSMF managed by the contractor's system
    - MAH retains ultimate responsibility for the PV system
  - Written agreement are mandatory.

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Structures and Process

Information to be contained

- Include documents to describe the PV system
- Content should reflect global availability of safety information
- Content should be indexed and follow modular system *(see local requirements, if applicable)*
- Primary topic sections:
    - Information that is fundamental to the description of PV system.
- Annexes:
    - Detailed and dynamic information to fully describe the system
- Change control, logbook and versioning should be maintained
- If no information available from the past, then descriptions of what will be implemented can be provided instead

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Contents of PSMF

- Indexed with appropriate sections for efficient navigation
- Partitioned
  - Sections:
    1. QPPV
    2. MAH's organisational structure
    3. Safety data sources
    4. Computerised systems and databases
    5. PV processes
    6. PV system performance and
    7. Quality system
  - Annexes

SECTIONS

1. Qualified Person Responsible for PV (QPPV)

- A **description of the responsibilities** ensuring sufficient authority over the PV system that
  - promotes,
  - maintains and
  - improves compliance
- A summary **curriculum vitae** with the key information on the role
- Description of the qualifications, **experience** and registrations relevant to PV
- **Contact details** including name, postal, telephone, fax and e-mail and the usual working address
- Details of **back-up** arrangements to apply in his/her absence

A list of delegated tasks with respect to the personnel whom it is assigned to be part of the Annexes

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2. MAH's Organisational Structure

- Clear overview of:
  - **company(ies**) involved,
  - the main **PV departments** and
  - the relationship(s) between organisations and operational units fulfilling PV obligations
- QPPV's position and sites for PV activities
- Details of the **links with other organisations**, such as contracting of PV activities and co-marketing agreements
- Description of any related contracts and agreements location and nature:
  - ***list/table*** - the parties involved, the **roles** undertaken and the concerned **product(s**) and **territories** and
  - ***organised*** according to
    - **service providers** (e.g. patient support programme providers, study data management etc.),
    - **commercial arrangements** (distributors, licensing partners, etc.) &
    - **other technical providers** (hosting of computer systems etc.)

At the request of NCAs and the Agency or during inspection and audit, the required information should be made available

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3. Safety Data Sources

- **Description** of all responsible parties on a global basis in the form of:
  - **List** (Annexed):
    - describes the country, nature of the activity
    - a contact point (address, telephone and e-mail) for the site
  - **Flow diagrams**:
    - indicating the main stages, timeframes and parties involved and
    - description of the departments and/or third parties involved
- List that:
  - describes (on a worldwide basis)
    - the product(s),
    - the applicable country(ies),
    - the status of each study/programme, including ongoing studies/programmes as well as studies/programmes completed in the last two years
  - distinguishes between interventional and non-interventional studies and organised as per active substance

4. Computerised Systems and Databases

- Description of the **location, functionality and operational responsibility** used to receive, collate, record and report safety information
- Description of the **validation status** of key functionality aspects
- Summary of the aspects vital to PV compliance e.g., **change control, nature of testing, back-up procedures and electronic data repositories**
- For paper-based systems (e-system used only for expedited submission of ICSRs), description on:
  - data management
  - mechanisms used to assure the integrity and accessibility of the safety data, and
  - the collation of adverse drug reactions (ADRs) information

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5. PV Process (1/2)

- Description of:
  - the available **procedural documentation** (SOPs, manuals, etc.)
  - the **nature of the data** held (e.g., the type of case data retained for ICSRs) and
  - the **records management** (e.g., safety database, paper file at site of receipt)

- Description of the process, but not limited to:
  - continuous monitoring of product's **risk-benefit** profile(s)
  - risk **management system(s**) and monitoring of the outcome of risk minimisation measures
  - procedures for **ICSR collection, collation, follow-up, assessment** and **reporting**
  - **PSUR** scheduling, production and submission, if applicable;
  - **communication of safety concerns** to consumers, healthcare professionals (HCPs) and the NCAs;
  - **implementation of safety variations** to the pack insert and patient information leaflets

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5. PV Process (2/2)

- The description should be accompanied with:
  - A list (annexed) of applicable processes and comprises:
    - the procedural document reference number and title
    - effective date and
    - document type
- Clear identification of procedures pertaining to **service providers** and other third parties
- System for supporting appropriate and **timely decision making** and action in each area
- Information pertaining to any specific local procedures

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6. PV System Performance

- Evidence of the ongoing monitoring and description of methods
- Information on:
  - the assessment methodology for ensuring correct reporting of ICSRs with figure/graphs showing the timeliness of reporting
  - description of the information provided by authorities regarding ICSR reporting quality, PSURs or other submissions
  - an overview of the methods used to ensure timeliness such as
    - PSUR reporting to the authorities
  - an overview of RMP* commitments adherence, or other obligations or conditions of authorisation(s) relevant to PV
- Description and explanation of PV system performance target with a list of performance indicators alongside the results of actual performance measurements in the annexure
- **Risk Management Plan*

7. Quality Systems (1/2)

- For document and record control
  - an overview of the procedures applied to other QS and PV records and documents
  - description of the arrangements for electronic and/or hardcopy versions archiving
- For procedural documents
  - A general description of
    - the types of documents such as SOP, manual etc.
    - the applicability of the various documents at global, regional or local level, and
    - the controls that are applied to their accessibility, implementation and maintenance
  - Information about the documentation systems applied to those under the control of third parties
- Pertaining to training:
  - a description of the resource management i.e., the organisational chart
  - description providing explanation for training organized in relation to the relevance, personnel and site information
  - a summary description of training concepts along with location for training files

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7. Quality Systems (2/2)

- Pertaining to audit,
  - a list of specific procedures and processes that provides:
    - information about quality assurance auditing of the PV system and
    - PV system audits with description of approach used to plan, reporting mechanism & timelines
  - for audit with significant findings provide associated note
    - brief description of CAPA* plan associated with the finding, anticipated resolution date(s)
  - In the annex, provide list of audits conducted (last 5 years) with clarity on the ones with and without unresolved notes

CAPA: Corrective and Preventive Actions

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8. Annexures

Annex A – QPPV
- The curriculum vitae of the QPPV and associated documents
- Contact details
- List of tasks delegated by QPPV

Annex B – The Organisational Structure of the MAH
- The lists of contracts and agreements

Annex C – Sources of safety data
- Lists associated with the description of sources of safety data e.g. affiliates and third party contacts

Annex D – Computerised systems and Databases

Annex E – PV Process, and written procedures
- Lists of procedural documents

Annex F – PV System Performance
- Lists of performance indicators
- Current results of performance assessment in relation to the indicators

Annex G – Quality Systems
- Audit schedules
- List of audits conducted and completed

Annex H – Products
- List(s) of products covered by the PV system and any notes concerning the MAH per product

Annex I – Document and Record Control
- Logbook
- Documentation of history of changes for Annex contents, indexed accordingly

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Change Control, Logbook, Versions and Archiving

- All changes should be documented in the PSMF for the purpose of change control
- Though PSMF provides a description of the current PV system, especially for audit or inspection, but past functioning and scope of the PV system also important
- Logbook
  - should be used for recording the changes to the PSMF
  - should be such that it provide a history of change(s) along with their respective date and the nature
- A periodic review of the PSMF should be conducted in case it has remained unchanged for a period of time

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How to prepare a good PSMF

- Planning
  - Why needed? which format?
  - Status of current PV system.
  - How can source data be obtained?
  - Stakeholders and resources available (human and technology)
  - SOP for PSMF (roles and responsibilities). Have formal process for review and update.
  - Restricted access to ensure appropriate control
- Accuracy and Clarity
  - Clear written procedures should be in place and accurately reflect information in the PSMF
  - For new setup, it may be good idea to wait till SOPs are developed. Draft PSMF can be developed in parallel
  - Diagrams may be particularly useful (e.g., org chart, flow of AEFI information)
  - Information should be succinct, accurate and reflect the current system in place (possible to keep the information up to date)
  - Documents should not be embedded in the electronic file
  - Electronic book-marking and searchable text is recommended

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PSMF: Take-home Points

- PSMF is an important document and regulatory requirement in many regions
- Can be a very useful tool for manufacturers even if it is not a regulatory requirement:
  - Simplification – uniform information describing the PV system is available for audit
  - Tool for QPPV to oversee and manage system (Should be reviewed and signed-off by QPPV)
  - Opportunity for manufacturer to use existing systems to maintain oversight and to generate content for submission when required
  - Generally, the first document requested by inspectors in regions where applicable
  - Be future ready as more regions/countries encourage use of this document
- SOP to develop and maintain PSMF is highly recommended
- Company's internal document. Only to be shared on request.
- Company may utilize formats available for development. The best format to use is the one required by local regulations
- Information should be accurate and kept up-to-date
- Limit access to the document; secure archiving and robust system to maintain are important

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Thank You