Guideline on Pharmacovigilance Systems and Quality Systems

THE NATIONAL MEDICINES REGULATORY AUTHORITY
NORIS CANAL ROAD, COLOMBO 10, SRI LANKA

Content

Pharmacovigilance Systems and their Quality Systems

1. Legal Background

The legal obligations for market authorization holders to fulfill pharmacovigilance requirements are set out in the National Medicines (Registration and Licensing of Medicine) Regulations, 2019, made under the National Medicines Regulatory Authority Act, No. 05 of 2015.

2. Overall Pharmacovigilance responsibilities of the marketing authorization holder

The marketing authorization holder shall operate a pharmacovigilance system and shall establish and use a quality system that is adequate and effective for performing its pharmacovigilance activities in order to assure responsibility and liability for its authorized medicinal products and to ensure that appropriate action can be taken, when necessary.

2.1. The basic pharmacovigilance system

A pharmacovigilance system is defined as the system used by the marketing authorization holder to fulfill 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.

Pharmacovigilance system of market authorization holder should consist at least of the following: -

i Collection and management of data on product safety, including individual ADR reporting;
ii An established system for signal detection of new or changing safety issues;
iii Data evaluation and decision making with regards to safety issues;
iv Pro-active risk management to minimize any potential risk associated with the use of a product;
v Action to protect public health (including regulatory action);
vi Communication with stakeholders and the public;
vii Audit, both of the outcomes of action taken and the key processes involved.

2.2. Qualified Person responsible for Pharmacovigilance

As a part of the pharmacovigilance system, every market authorization holder shall have permanently and continuously at its disposal an appropriately qualified person responsible for pharmacovigilance (QPPV); The QPPV shall be responsible for the establishment and maintenance of the marketing authorization holder's pharmacovigilance System and therefore shall have sufficient authority to influence the performance of the quality system and the pharmacovigilance activities and to promote, maintain and improve compliance with the legal requirements.

Each pharmacovigilance system can have only one QPPV. A QPPV may be employed by more than one marketing authorization holder (i.e. only in case of subcontracting to a third party organization), for a shared or for separate pharmacovigilance systems or may fulfill the role of QPPV for more than one pharmacovigilance system of the same marketing authorization holder, provided that the QPPV is able to fulfill all obligations. The ability of a QPPV to adequately oversight more than one pharmacovigilance system depends on several factors including but not restricted to the number of medicinal products covered by that system, the safety profile of these products and the complexity of the MAH organizational structure. Depending on these factors, it is NOT expected that a QPPV can adequately fulfill all the obligations for more than 1-5 MAHs in maximum.

2.2.1. Qualification and conditions of the QPPV

The appointed QPPV;

- should be a pharmacist or a medical doctor
- have adequate theoretical and practical knowledge for the performance of pharmacovigilance activities

  Note: Taking into consideration that pharmacovigilance practice and regulations are relatively new in Sri Lanka, thus having an experienced QPPV may be challenging for the MAHs. Accordingly, it is accepted by the NMRA ***that for only a transitional period*** *of 5 years of the since this guideline became into effect the qualifications on the nominated QPPV may be expressed in terms of his adequate pharmacovigilance training rather than his practical experience in pharmacovigilance. Under these circumstances, the MAH is responsible of providing him the unachieved PV trainings*

- have a basic training in epidemiology and biostatistics (desirable)

- should be knowledgeable on all applicable sections of this guideline and other referenced guidelines as well as the pharmacovigilance regulation in Sri Lanka
- should be a full time employee dedicated to pharmacovigilance duties
- should reside and operate in Sri Lanka

2.2.2. Responsibilities of the QPPV

The QPPV shall be responsible for the following duties;

- establishment and maintenance of the marketing authorization holder 's Pharmacovigilance System and having oversight over the functioning of all relevant aspects of the system, including its quality system;
- being responsible for all vigilance activities related to their medicinal products in Sri Lanka; having awareness of any conditions or obligations adopted as part of the marketing authorizations and other commitments relating to safety or the safe use of the products;
- establishing an effective system for collection, collation, processing, management and regulatory reporting of individual case safety reports (ICSRs)/AEFIs associated with the use of their medicinal products in Sri Lanka
- having sufficient authority over the content of risk management plans and ensuring the national implementation of the incorporated activities including the risk minimization measures and their effectiveness assessment;
- being involved in the review and sign-off of protocols of post-authorization safety studies conducted in Sri Lanka;
- having awareness of post-authorization safety studies requested by a NMRA including the results of such studies;
- ensuring conduct of pharmacovigilance and submission of all pharmacovigilance-related documents (e.g. Periodic Benefit-Risk Evaluation Reports (PBRER), post authorization study reports, Direct Healthcare professional communication, risk management plans and pharmacovigilance system master file) in accordance with the national legal requirements and guidelines;
- ensuring the necessary quality, including the correctness and completeness, of pharmacovigilance data submitted to the NMRA;
- ensuring a full and prompt response to any request from the NMRA for the provision of additional information necessary for the benefit-risk evaluation of a medicinal product;
- providing any other information relevant to the benefit-risk evaluation NMRA;

- having an overview of medicinal product safety profiles and any emerging safety concerns;
- providing input into the preparation of regulatory action in response to emerging safety concerns (e.g. variations and communication to patients and healthcare professionals);
- acting as a single pharmacovigilance contact point for the NMRA on a 24-hour basis and also as a contact point for pharmacovigilance inspections

The QPPV may delegate specific tasks, under supervision, to appropriately qualified or trained individuals, provided that the QPPV maintains system oversight and overview of the safety profiles of all products. Such delegation should be documented.

Back-up procedures in the case of absence of the QPPV shall be in place and should be accessible through the QPPV's contact details. The QPPV should ensure that the back-up person has all necessary information to fulfill the role.

2.2.3. Registration of the QPPV

The market authorization holder must provide the NMRA with the name and details of the QPPV (including full name, qualification, postal address, email address, telephone and fax numbers). The MNRA will keep electronic register for QPPV.

Any changes of these details should be promptly submitted to the NMRA. While the change of the QPPV should be submitted as variation

2.3. Subcontracting of pharmacovigilance activities

There may be situations where the MAH may subcontract certain activities of the PV system to third parties, i.e. to another organization. The MAH shall nevertheless retain full responsibility in ensuring the quality, efficacy, and integrity of the PV system and in ensuring that an effective quality system is applied in relation to those subcontracted tasks.

This guidance document also applies to the other organization to which the tasks have been subcontracted. The subcontracted organization may be subject to inspection at the discretion of the NMRA.

2.3.1. Vendor qualification assessment

Before subcontracting the organization, the MAH should conduct vendor assessment to ensure that it is adequately qualified in pharmacovigilance for example but not restricted to: availability of qualified staff in pharmacovigilance, needed resources, quality management system and appropriate pharmacovigilance process suitable to the delegated tasks.

This vendor qualification assessment should be documented.

2.3.2. Contractual agreements

When tasks are subcontracted to another organization, the MAH shall draw up detailed and up-to-date subcontracts e.g. Safety Data Exchange Agreements. These

- should clearly document the contractual arrangements between the MAH and the other organization, describing arrangements for delegation and the responsibilities of each party with the aim of enabling compliance with the legal requirements
- the MAH should include sufficiently detailed descriptions of the delegated tasks, the related interactions and data exchange, together with, for example, agreed definitions, tools, assignments and timelines and regulatory reporting responsibilities.
- Should specify the processes for exchange of safety information, including timelines and regulatory reporting responsibilities. Processes should be in place to avoid duplicate reporting to the NMRA.
- Should specify a confirmation and/or reconciliation process to ensure that all notifications are received concerning the exchange of safety information
- should also contain clear information on the practical management of pharmacovigilance as well as related processes, including those for the maintenance of pharmacovigilance databases.
- should indicate which processes are in place for checking whether the agreed arrangements are being adhered to on an ongoing basis. In this respect, regular risk-based audits of the other organization by the MAH or introduction of other methods of control and assessment are recommended.

2.3.3. Subcontracting pharmacovigilance for MAH represented by agent in Sri Lanka

Based on the requirements that in case of subcontracting the MAH shall retain full responsibility in ensuring the quality, efficacy, and integrity of the PV system as well as the compliance of the subcontracted organization; thus for Multinational or international MAH represented by an agent in Sri Lanka if subcontracting local pharmacovigilance tasks is decided; the whole subcontracting process should be done through and be under the control of the MAH and not the agent individually. Furthermore, a three parties contact between the MAH, agent and the subcontracted organization may be considered.

2.4. Training of Personnel for Pharmacovigilance

- Achieving the required quality for the conduct of pharmacovigilance processes and their outcomes by an organization is intrinsically linked with the availability of a sufficient number of competent and appropriately qualified and trained personnel.

- All personnel involved in the pharmacovigilance activities shall receive initial and continued training. For MAH, this training shall relate to the roles and responsibilities of the personnel.

- The organization shall keep training plans and records for documenting, maintaining and developing the competences of personnel. Training plans should be based on training needs assessment and should be subject to monitoring.

- The training should support continuous improvement of relevant skills, the application of scientific progress and professional development and ensure that staff members have the appropriate qualifications, understanding of relevant pharmacovigilance requirements as well as experience for the assigned tasks and responsibilities. All staff members of the organization should receive and be able to seek information about what to do if they become aware of a safety concern.

- There should be a process in place within the organization to check that training results in the appropriate levels of understanding and conduct of pharmacovigilance activities for the assigned tasks and responsibilities, or to identify unmet training needs, in line with professional development plans agreed for the organizations as well as the individual staff members.

- Adequate training should also be considered by the organization for staff members to whom no specific pharmacovigilance tasks and responsibilities have been assigned but whose activities may have an impact on the pharmacovigilance system or the conduct of pharmacovigilance. Such activities include but are not limited to activities related to clinical trials, technical product complaints, medical information, terminologies, sales and marketing, regulatory affairs, legal affairs and audits.

- Appropriate instructions on the processes to be used in case of urgency, including business continuity, shall be provided by the organization to their personnel.

2.5. Record retention

- The MAH shall ensure:

- the retention of documents of the pharmacovigilance system master file (PSMF) as long as the system described in the PSMF exists and for at least further 5 years after it has been formally terminated by the marketing authorization holder;

- the retention of pharmacovigilance data and documents relating to individual authorized medicinal products as long as the marketing authorization exists and for at least further 10 years after the marketing authorization has ceased to exist;

- During the retention period, retrievability of the documents should be ensured. Documents can be retained in electronic format, provided that the electronic system has been appropriately validated and appropriate arrangements exist for system security, access and back-up of data. If documents in paper format are transferred into an electronic format, the transfer process should ensure that all of the information present in the original format is retained in a legible manner and that the media used for storage will remain readable over time.

- Documents transferred in situations where the business of the marketing authorization holder is taken over by another organization should be complete

2.6. Specific quality system procedures and processes

For the purpose of compliance management by the marketing authorization holders, they shall have specific quality system procedures and processes in place in order to ensure compliance regarding the following critical pharmacovigilance processes:

- continuous safety profile monitoring and benefit-risk evaluation of authorized medicinal products;

- establishing, assessing and implementing risk management systems and evaluating the effectiveness of risk minimization;

- collection, processing, management, quality control, follow-up for missing information, coding, classification, duplicate detection, evaluation and timely electronic transmission of individual case safety reports (ICSRs) from any source;

- signal management;

- scheduling, preparation (including data evaluation and quality control), submission and assessment of periodic safety update reports;

- meeting commitments and responding to requests from NMRA, including provision of correct and complete information;
- interaction between the pharmacovigilance and product quality defect systems;
- communication about safety concerns between marketing authorization holders and NMRA, in particular notifying changes to the risk-benefit balance of medicinal products;
- communicating information to patients and healthcare professionals about changes to the risk-benefit balance of products for the aim of safe and effective use of medicinal products;
- keeping product information up-to-date with the current scientific knowledge, including the conclusions of the assessment and recommendations from the NMRA;
- implementation of variations to marketing authorizations for safety reasons according to the urgency required.
- effective communication by the marketing authorization holder with NMRA, including:
    - the pharmacovigilance system master file,
    - corrective and preventive actions in response to pharmacovigilance audit and inspection
    - and post-authorization safety studies;

For more guidance on the structure and process on pharmacovigilance system and quality management, refer to the *EMA Guideline on good pharmacovigilance practices (GVP) Module I*.