



National Agency for Food & Drug Administration & Control (NAFDAC)

Pharmacovigilance Directorate

NAFDAC Good Pharmacovigilance Practice (GVP) Guideline

CHAPTER 2: PHARMACOVIGILANCE SYSTEM MASTER FILE (PSMF)

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2.1. Purpose

The purpose of this Chapter is to establish the mandatory requirements for the preparation, content, structure, maintenance, and accessibility of the Pharmacovigilance System Master File (PSMF). It is intended to ensure that the pharmacovigilance system is fully documented in a manner that supports regulatory oversight, effective risk management, and compliance with applicable pharmacovigilance obligations.

This Chapter further aims to ensure that the PSMF provides a true, complete, and current representation of the pharmacovigilance system and enables the Qualified Person for Pharmacovigilance (QPPV) and the Authority to always verify its adequacy and performance.

2.2. Scope

This Chapter applies to all Marketing Authorization Holders (MAHs) required to maintain a pharmacovigilance system. It covers all pharmacovigilance systems, including those that are shared between multiple MAHs or where activities are delegated to third parties.

The provisions of this Chapter apply to the main body of the PSMF and its Annexes, including all supporting documentation, and shall be complied with in full. MAHs shall ensure that the PSMF is maintained in a manner that is accurate, complete, up to date, and readily accessible to the QPPV and the Authority always.

This Chapter is aligned with international best practices and makes reference to the *Guideline on Good Pharmacovigilance Practices (GVP) Module II: Pharmacovigilance System Master File (Revision 2) (EMA/816573/2011/Rev 2)*.

2.3. Definitions

For this Chapter, the following definitions shall apply:

2.3.1. Audit

A systematic, independent, and documented process for obtaining audit evidence and evaluating it objectively to determine the extent to which audit criteria are fulfilled.

2.3.2. Corrective and Preventive Action (CAPA)

Actions taken to eliminate the cause of an identified non-conformity, deviation, or other undesirable situation (corrective action), and actions taken to prevent the occurrence of potential non-conformities (preventive action).

2.3.3. Delegated Activity

Any pharmacovigilance activity or responsibility transferred by a Marketing Authorization Holder (MAH) to a third party through a documented contractual arrangement, while the MAH retains ultimate regulatory responsibility.

2.3.4. Deviation

A departure from an approved procedure, process, regulatory requirement, or established pharmacovigilance system requirement.

2.3.5. Good Pharmacovigilance Practice (GVP)

A set of measures designed to monitor the safety of medicinal products and detect, assess, understand, and prevent adverse effects or any other medicine-related problems.

2.3.6. Individual Case Safety Report (ICSR)

A structured report containing information describing one or more suspected adverse reactions in an individual patient.

2.3.7. Marketing Authorization Holder (MAH)

A person or legal entity in whose name a Certificate of Registration has been issued by NAFDAC and who is responsible for ensuring compliance with all regulatory obligations, including pharmacovigilance requirements.

2.3.8. Pharmacovigilance

The science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other medicine-related problem.

2.3.9. Pharmacovigilance System

A system used by a Marketing Authorization Holder to fulfil pharmacovigilance responsibilities and designed to monitor the safety of authorised medicinal products and detect any changes to their benefit-risk balance.

2.3.10. Pharmacovigilance System Master File (PSMF)

A detailed description of the pharmacovigilance system used by a Marketing Authorization Holder with respect to one or more authorised medicinal products, which serves as a reference document for the management, oversight, and inspection of the pharmacovigilance system.

2.3.11. Qualified Person for Pharmacovigilance (QPPV)

A suitably qualified and experienced person appointed by the Marketing Authorization Holder who is responsible for the establishment, maintenance, oversight, and continuous improvement of the pharmacovigilance system and for ensuring compliance with applicable pharmacovigilance requirements.

2.3.12. Quality Management System (QMS)

A formalized system comprising organizational structure, responsibilities, procedures, processes, and resources required to ensure that pharmacovigilance activities are conducted in accordance with regulatory requirements and quality standards.

2.3.13. Risk Management Plan (RMP)

A detailed description of the risk management system for a medicinal product, including activities and interventions designed to identify, characterize, prevent, or minimize risks relating to the product.

2.3.14. Periodic Safety Update Report (PSUR) / Periodic Benefit-Risk Evaluation Report (PBRER)

A pharmacovigilance document intended to provide an evaluation of the benefit-risk balance of a medicinal product at defined time points after authorization.

2.3.15. Safety Database

A validated computerized system used for the collection, storage, processing, management, retrieval, and reporting of pharmacovigilance data, including Individual Case Safety Reports (ICSRs).

2.3.16. Shared Pharmacovigilance System

A pharmacovigilance system that is used by more than one Marketing Authorization Holder and is managed under documented agreements defining roles, responsibilities, and oversight arrangements.

2.3.17. Signal

Information arising from one or multiple sources, including observations and experiments, suggesting a new potentially causal association or a new aspect of a known association between a medicinal product and an event that warrants further investigation.

2.3.18. Standard Operating Procedure (SOP)

A written instruction describing the steps to be followed to perform a specific pharmacovigilance activity consistently and in compliance with regulatory requirements.

2.3.19. Third Party

Any individual, organization, contractor, vendor, distributor, affiliate, or service provider engaged by the Marketing Authorization Holder to perform pharmacovigilance-related activities.

2.3.20. Validation

The documented process of demonstrating that a computerized system consistently performs according to its intended purpose and predefined specifications.

2.4. Introduction

2.4.1. The pharmacovigilance system master file provides an overview of the pharmacovigilance system put in place by the MAH and contributes to the appropriate management of and improvement(s) to the pharmacovigilance system. The PSMF shall reflect safety information for medicinal products authorized in Nigeria. The PSMF shall contribute to the planning and conduct of audits by the MAH, fulfilment of supervisory responsibilities of the QPPV and inspections by NAFDAC. PSMF provides an overview of the Pharmacovigilance system which may be requested and assessed by the Agency during marketing authorization application (s) or post authorization.

2.5. Objectives

2.5.1. PSMF enables the Marketing Authorization Holder and the Qualified Person for Pharmacovigilance (QPPV) to:

- gain assurance that a pharmacovigilance system has been implemented in accordance with the requirements;
- confirm aspects of compliance in relation to the system;
- obtain information about deficiencies in the system, or non-compliance with the requirements;
- obtain information about risks or actual failure in the conduct of specific aspects of pharmacovigilance.

2.5.2. This information will contribute to the appropriate management and improvement of the PV system.

2.6. Maintenance of the Pharmacovigilance System Master File

2.6.1. Marketing Authorization Holders in Nigeria are required to maintain a pharmacovigilance system master file and submit to the Agency during application for Certificate of Registration of a medicinal product, upon request, and upon update. The pharmacovigilance system master file shall be located either at the site in Nigeria where the Marketing Authorization Holder's main pharmacovigilance activities are performed, or at the site in Nigeria where the qualified person responsible for pharmacovigilance operates. Where the PSMF is stored in electronic form, the location stated must be a site where the data stored can be directly accessed.

2.6.2. Applicants for, and holders of, listings for traditional herbal medicinal products shall also be required to establish and maintain a Pharmacovigilance System Master File (PSMF).

2.6.3. Marketing Authorization Holders shall continue to ensure that information about QPPV, name and contact details (phone no and email address), and location of the PSMF are up to date.

2.6.4. When there is a change in the QPPV or location of the PSMF, the MAH shall notify NAFDAC no later than 30 calendar days.

2.7. Transfer of responsibility for the PSMF

2.7.1. Transfer or delegation of responsibilities and activities concerning the master file shall be documented (see sections 2.18. and 2.35) and managed to ensure that the Marketing Authorization Holder fulfils their responsibilities. Since a specific QPPV has responsibility for the pharmacovigilance system, changes to the pharmacovigilance system master file shall also be notified to the QPPV in order to support their authority to make improvements to the system. The types of changes that shall be routinely and promptly notified to the QPPV are:

- a. Updates to the PSMF or its location that are notified to the competent authorities.
- b. The addition of corrective and/or preventive actions to the pharmacovigilance system master file (e.g. following audits and inspections). The QPPV shall also be able to access information about deviations from the processes defined in the quality management system for pharmacovigilance.
- c. Changes to content that fulfil the criteria for appropriate oversight of the pharmacovigilance system (in terms of capacity, functioning, and compliance);
- d. Transfer of significant services for pharmacovigilance to a third party (e.g., outsourcing of PSUR/PBRER production);
- e. Inclusion of products into the pharmacovigilance system for which the QPPV is responsible.
- f. Changes for existing products which may require a change or increased workload in relation to pharmacovigilance activity, e.g., new indications or studies.
- g. Changes in arrangements for the provision of the PSMF to competent authorities

2.7.2. Any incoming QPPV must formally accept, in writing, the transfer of responsibility for the pharmacovigilance system. The QPPV shall also be able to ensure and verify that the Pharmacovigilance System Master File (PSMF) accurately and consistently reflects the current structure, processes, and activities of the pharmacovigilance system under his or her responsibility (see Chapter 1).

2.8. The Representation of Pharmacovigilance Systems

2.8.1. The pharmacovigilance system master file may describe the pharmacovigilance system for one or more medicinal products of the Marketing Authorization Holder. For different categories of medicinal products, the Marketing Authorization Holder may, if appropriate, apply separate pharmacovigilance systems. Each of such systems shall be described in a separate pharmacovigilance system master file. Those files shall cumulatively cover all medicinal products of the Marketing Authorization Holder for which a Certificate of Registration has been issued.

2.8.2. It is anticipated that there may be circumstances in which a single Marketing Authorization Holder may establish more than one pharmacovigilance system, e.g., specific systems for particular product types (vaccines, consumer health, etc.), or that the pharmacovigilance system may include products from more than one marketing authorization holder. In either case, a single and clearly defined specific system shall be in place to describe each system.

2.8.3. A single QPPV shall be appointed to be responsible for the establishment and maintenance of the pharmacovigilance system described in the pharmacovigilance system master file.

2.8.4. Where a pharmacovigilance system is shared by multiple Marketing Authorization Holders (MAHs), each MAH shall ensure that the system adequately covers its registered product(s) and shall retain full regulatory responsibility. Pharmacovigilance activities may be delegated through a written agreement; however, accountability shall not be transferred. The MAH's PSMF may cross-reference that of the delegated party, provided access is assured to the MAH and the Agency. The MAH shall ensure oversight and maintain the PSMF in a current and accessible state.

2.8.5. Where applicable, a list of all pharmacovigilance system master files held by the same Marketing Authorization Holder should be provided in the annex (see section 2.18); this includes:

- a. Their location(s),
- b. Details of the responsible QPPV(s) and
- c. The relevant product(s).

2.8.6. The address of the location of the pharmacovigilance system master file should be an office address which reflects either the site in Nigeria where the main pharmacovigilance activities of the Marketing Authorization Holder are performed or the site in Nigeria where the qualified person responsible for pharmacovigilance operates. This address may be different to that of the Marketing Authorization Holder, for example, a different office of the Marketing Authorization Holder or when a third party undertakes pharmacovigilance activities.

2.8.7. Similarly, the QPPV details aligned to a product may be those of contract QPPV responsible for the pharmacovigilance system for a particular medicinal product, and not necessarily a QPPV directly employed by the Marketing Authorization Holder.

2.8.8. When delegating any activities concerning the pharmacovigilance system and its master file, the Marketing Authorization Holder retains ultimate responsibility for the pharmacovigilance system, submission of information about the pharmacovigilance system master file location, maintenance of the pharmacovigilance system master file, and its provision to the Agency. Detailed written agreements describing the roles and responsibilities for pharmacovigilance system master file content, submissions, and management, as well as to govern the conduct of pharmacovigilance in accordance with the legal requirements, shall be in place.

2.8.9. When a pharmacovigilance system is shared, it is advised that the partners agree on how to mutually maintain the relevant sections within their own pharmacovigilance system master files. Accessibility of the pharmacovigilance system master file to all the applicable Marketing Authorization Holder(s), and its provision to the Agency shall be defined in written agreements. Marketing Authorization Holder(s) must have assurance that the pharmacovigilance system used for their products is appropriate and compliant.

2.9. Content of a Pharmacovigilance System Master File (PSMF)

2.9.1. The pharmacovigilance system master file shall include documents to describe the pharmacovigilance system. The content of the pharmacovigilance system master file shall have the headings used in sections 2.10 to 2.18 and shall reflect the global availability of safety information for medicinal products authorized in Nigeria. The content shall be indexed to allow for efficient navigation around the document.

2.9.2. The main principle for the structure of the content of the pharmacovigilance system master file is that the primary topic sections contain information that is fundamental to the description of pharmacovigilance system. Detailed information is required to fully describe the system, and, since this may change frequently, it shall be referred to and contained in the Annexes.

2.10. Qualified Person Responsible for Pharmacovigilance (QPPV)

2.10.1 The information relating to the QPPV provided in the PSMF shall include:

- a. A description of the responsibilities guaranteeing that the qualified person has sufficient authority over the pharmacovigilance system to promote, maintain, and improve compliance
- b. A summary curriculum vitae with the key information on the role of the qualified person responsible for pharmacovigilance;
- c. Contact details;

- d. Details of back-up arrangements to apply in the absence of the qualified person responsible for pharmacovigilance and
- e. Registrations relevant to pharmacovigilance (if any)
- f. A list of tasks that have been delegated by the qualified person for pharmacovigilance shall also be included in the Annexes (see section 2.18). This shall outline the activities that are delegated and to whom and include access to a medically qualified person if applicable (Chapter 1). This list may be supplied as a copy of a written procedural document, provided the required content is covered.

A list of tasks delegated by the Qualified Person for Pharmacovigilance (QPPV) shall be included in the Annexes (see Section 2.18). This list shall specify the delegated activities, the individuals or functions to whom the tasks are assigned, and, where applicable, arrangements for access to a medically qualified person (see Chapter 1). The list may be included in a written procedural document, provided that all required information is included.

g. The information relating to the Qualified Person for Pharmacovigilance (QPPV) shall include details of the QPPV's qualifications, relevant experience, and professional registrations in pharmacovigilance.

2.9.4. Contact details shall include the name, postal address, telephone number, and email address, reflecting the usual place of work of the QPPV, which may differ from that of the Marketing Authorization Holder.

2.9.5. Where the QPPV is employed by a third party, this shall be clearly indicated, and the name of the employing organisation shall be provided, irrespective of whether the QPPV's usual working address is that of the Marketing Authorization Holder.

2.11. Organizational Structure of the Marketing Authorization Holder

2.11.1. A description of the organizational structure of the Marketing Authorization Holder relevant to the pharmacovigilance system must be provided. The description shall provide a clear overview of the company(ies) involved, the main pharmacovigilance departments, and the relationship(s) between organizations and operational units relevant to the fulfilment of pharmacovigilance obligations. This shall include third parties. Specifically, the pharmacovigilance system master file shall describe:

- a. The organogram of the Marketing Authorization Holder(s), showing the position of the QPPV in the organization.
- b. The site(s) where the pharmacovigilance functions are undertaken covering individual case safety report collection, evaluation, safety database case entry, periodic safety update report production, signal detection and analysis, management of the risk management plan, pre- and

post-authorization study management, and management of safety variations to product particulars.

c. Flow charts may be particularly useful; the name of the department or third party shall be indicated.

2.12. Delegated activities

2.12.1 The pharmacovigilance master file, where applicable, shall contain a description of the delegated activities and/or services relating to the fulfillment of pharmacovigilance obligations. This includes arrangements with other parties in any country, worldwide and if applicable, to the pharmacovigilance system applied to products authorized in Nigeria.

2.12.2 Links with other organizations, such as co-marketing agreements and contracting of pharmacovigilance activities, shall be outlined. A description of the location and nature of contracts and agreements relating to the fulfilment of pharmacovigilance obligations shall be provided. This may be in the form of a list/table to show the parties involved, the roles undertaken, and the concerned product(s). The list shall be organized according to service providers (e.g., medicinal information, auditors, patient support program providers, study data management, etc.), commercial arrangements (distributors, licensing partners, co-marketing, etc.), and other technical providers (hosting of computer systems, etc.). Individual contractual agreements shall be made available at the request of the Agency or during inspection and audit and the list shall be provided in the Annexes.

2.13. Sources of Data

2.13.1 The description of the main units for safety data collection shall include all parties responsible on a global basis for solicited and spontaneous case collection for products authorized in Nigeria. This shall include medicinal information sites as well as affiliate offices and may take the form of a list describing the country, nature of the activity, and the product(s) (if the activity is product specific), and providing a contact point (address, telephone, and email) for the site. The list may be found in the PSMF annexes. The information about third parties (licensed partners or local distribution/marketing arrangements) shall also be included in the section describing contracts and agreements. (see sections 2.10 and 2.18)

2.13.2 The description of the main units responsible for safety data collection shall include all parties involved, on a global basis, in the collection of solicited and spontaneous reports for products authorised in Nigeria. This shall include medical information services, affiliate offices, and other relevant entities.

2.13.3 The information may be presented as a list indicating, for each site, the country, nature of the activity, applicable product(s) (where relevant), and a contact point, including address, telephone number, and email. Such a list may be included in the Annexes to the PSMF.

2.13.4 Information on third parties, including licensed partners and local distribution or marketing arrangements, shall also be included in the section describing contracts and agreements.

2.13.5 Flow diagrams may be used to illustrate the main stages, timelines, and parties involved in the process. Regardless of the format used, the description of the Individual Case Safety Report (ICSR) process from case collection to reporting to the Agency shall clearly identify the departments and/or third parties involved.

2.13.6 For inspection and audit of the pharmacovigilance system, sources of safety data shall include studies, registries, surveillance activities, or support programmes sponsored by the Marketing Authorisation Holder (MAH) from which Individual Case Safety Reports (ICSRs) may arise. The MAH shall maintain and make available a comprehensive list of such sources to support inspection, audit, and QPPV oversight.

2.13.7 The list shall be organized by active substance, distinguish between interventional and non-interventional studies, and include both ongoing studies/programs and those completed within the previous two (2) years. For each study or program, the list shall include the status, applicable country(ies), product(s) involved, and the primary objective. The list may be included in Annex C to the PSMF.

2.14 Computerized systems and databases

2.14.1 the location, functionality, and operational responsibility for computerized systems and databases used to receive, collate, record, and report safety information, as well as an assessment of their fitness for purpose, shall be described in the pharmacovigilance system master file (PSMF).

2.14.2 Where multiple computerized systems/databases are used, the applicability of these to pharmacovigilance activities shall be described in such a way that a clear overview of the extent of computerization within the pharmacovigilance system can be understood.

The validation status of key aspects of the computer system functionality shall also be described; the change control, nature of testing, back-up procedures, and electronic data repositories vital to pharmacovigilance compliance shall be included in the summary, and the nature of the available documentation shall be described.

For a paper-based system (where an electronic system may only be used for expedited submission of ICSRs), the management of the data, and mechanisms used to assure the integrity and accessibility of the safety data, and in particular, the collation of information about adverse drug reactions/ adverse events shall be described.

2.15 Pharmacovigilance processes

2.15.1 An essential element of any pharmacovigilance system is that there are clear written procedures in place. Chapter 1 describes the required minimum set of written procedures for pharmacovigilance. A description of the procedural documentation available (standard operating procedures, manuals, at global and/or national Level etc.), the nature of the data held (e.g. the type of case data retained for ICSRs) and an indication of how records are held (e.g. safety database, paper file at site of receipt) shall be provided in the pharmacovigilance system master file.

2.15.2 A description of the process, data handling and records for the performance of pharmacovigilance, covering the following aspects shall be included in the pharmacovigilance system master file:

- a. Continuous monitoring of product benefit-risk profile(s) applied and the result of evaluation and the decision-making process for taking appropriate measures; this shall include signal generation, detection and evaluation. This may also include several written procedures and instructions concerning safety database outputs, interactions with clinical departments etc.;
- b. Risk management system(s) and monitoring of the outcome of risk minimization measures; several departments may be involved in this area, and interactions shall be defined in written procedures or agreements.
- c. ICSR collection, collation, follow-up, assessment, and reporting; the procedures applied to this area shall clarify what is local and what are global activities.
- d. PSUR/PBRER scheduling, production and submission, if applicable (see Chapter 6);
- e. Communication of safety concerns to consumers, healthcare professionals and the Agency.
- f. Implementation of safety variations to the summary of product characteristics (SmPC) and patient information leaflets; procedures cover both internal and external communications.

2.15.3 In each area, the Marketing Authorization Holder (MAH) shall be able to provide evidence of a system that supports appropriate and timely decision-making and action.

2.15.4 The system description shall be accompanied by a list of processes relating to compliance management and interfaces with other relevant functions. These interfaces may include, but are not limited to, the roles and responsibilities of the QPPV, responses to requests for information from the Agency, literature searching, safety database change control, safety data exchange agreements, safety data archiving, pharmacovigilance auditing, quality control, and training.

2.15.3 The list of processes may be included in the Annexes and shall contain the procedural document reference number, title, effective date, and document type (e.g., standard operating procedures, work instructions, manuals). Procedures belonging to service providers or other third parties should be clearly identified.

2.16 Pharmacovigilance System Performance

2.16.1 The pharmacovigilance system master file shall contain evidence of the ongoing monitoring of performance of the pharmacovigilance system including compliance of the main outputs of pharmacovigilance. The pharmacovigilance system master file shall include a description of the monitoring methods applied and contain as a minimum:

- a. An explanation of how the correct reporting of ICSRs is assessed. In the annex, figures/graphs shall be provided to show the timeliness of 15-day and 90-day reporting over the past year;
- b. A description of any metrics used to monitor the quality of submissions and performance of pharmacovigilance. This shall include information provided by the Agency regarding the quality of ICSR reporting, PSUR/PBRERs or other submissions.
- c. An overview of the timeliness of PSUR/PBRER reporting to the Agency (the annex shall reflect the latest figures used by the Marketing Authorization Holder to assess compliance);
- d. An overview of the methods used to ensure timeliness of safety variation submissions including the tracking of required safety variations that have been identified but not yet been submitted;
- e. Where applicable, an overview of adherence to risk management plan commitments, or other obligations or conditions of Certificate of Registration(s) relevant to pharmacovigilance.

2.16.2 Targets for the performance of the pharmacovigilance system shall be described and explained.

2.16.3 A list of performance indicators must be provided in the Annex to the pharmacovigilance system master file, alongside the results of (actual) performance measurements.

2.17 Quality Management System

2.17.1 A description of the quality management system shall be provided, in terms of the structure of the organization and the application of the quality to pharmacovigilance. This shall include:

2.17.1.1 Document and Record Control

a. A description of the archiving arrangements for electronic and/or hardcopy versions of the pharmacovigilance system master file shall be provided, as well as an overview of the procedures applied to other quality system and pharmacovigilance records and documents (see also Chapter1).

2.17.1.2 Procedural documents

a. A general description of the types of documents used in pharmacovigilance (standards operating procedures, work instructions etc.), the applicability of the various documents at global, regional or local level within the organization, and the controls that are applied to their accessibility, implementation and maintenance.

b. Information about the documentation systems applied to relevant procedural documents under the control of third parties.

c. A list of specific procedures and processes related to the pharmacovigilance activities and interfaces with other functions, with details of how the procedures can be accessed, must be provided, and the detailed guidance for the inclusion of these is in sections 2.15.1 to 2.15.2.

2.17.1.3 Training

- a. A description of the resource management for the performance of pharmacovigilance activities;
- b. The organizational chart giving the number of people (full-time equivalents) involved in pharmacovigilance activities, which may be provided in the section describing the organizational structure (see sections 2.13.1 to 2.13.7)
- c. Information about sites where the personnel are located (sections 2.11 to 2.13.7) whereby the sites are provided in the PSMF in relation to the organization of specific pharmacovigilance activities and in the Annexes, which provide the list of site contacts for sources of safety data. However, a description shall be provided to explain the training organization in relation to the personnel and site information;
- d. A summary description of the training concept, including a reference to the location training files.
- e. Staff shall be appropriately trained in performing pharmacovigilance-related activities and this includes not only staff within pharmacovigilance departments but also any individual that may receive safety reports.

2.17.1.4 Auditing.

- a. Information about quality assurance auditing of the pharmacovigilance system shall be included in the pharmacovigilance system master file. A description of the approach used to plan audits of the pharmacovigilance system and the reporting mechanism and timelines shall be provided, with a current list of the scheduled and completed audits concerning the pharmacovigilance system maintained in the annex referred to in section 2.18. This list shall describe the date(s) (of conduct and of report), scope, and completion status of audits of service providers, specific pharmacovigilance activities or sites undertaking pharmacovigilance, and their operational interfaces relevant to the fulfilment of the obligations in the regulations and cover a period of 5 years.
- b. The pharmacovigilance system master file shall also contain a note associated with any audit where significant findings are raised. The audit report must be documented within the quality system; in the pharmacovigilance system master file it is sufficient to provide a brief description of the corrective and/or preventive action(s) associated with the significant finding, the date it was identified and the anticipated resolution date(s), with cross reference to the audit report and the documented corrective and preventive action plan(s). In the annex, in the list of audits conducted, those associated with unresolved notes in the pharmacovigilance system master file shall be identified. The note and associated corrective and preventive action(s) shall be documented in the pharmacovigilance system master file until the corrective and/or preventive action(s) have been fully implemented; that is, the note is only removed once corrective action and/or sufficient improvement can be demonstrated or has been independently verified. The addition, amendment, or removal of the notes must therefore be recorded in the logbook.
- c. The Pharmacovigilance System Master File (PSMF) shall contain a summary note for any audit that identifies significant findings. While the complete audit report shall be maintained within the Quality Management System, the PSMF shall include a concise description of the significant finding(s), the associated corrective and/or preventive action(s) (CAPAs), the date the finding was identified, the target completion date(s), and a cross-reference to the corresponding audit report and CAPA documentation.

In the Annex containing the audit inventory, audits associated with unresolved significant findings shall be clearly identified. Such findings and their related CAPAs shall remain documented in the PSMF until all actions have been fully implemented and their effectiveness has been demonstrated or independently verified. Any addition, modification, status update, or closure of these notes shall be documented in the PSMF logbook to ensure appropriate traceability and change control.

As a means of managing the pharmacovigilance system, and providing a basis for audit or inspection, the pharmacovigilance system master file shall also describe the process for recording, managing and resolving deviations from the quality system. The master file shall also

document deviations from pharmacovigilance procedures, their impact, and management until resolved. This may be documented in the form of a list referring to a deviation report, and its date and procedure concerned.

2.18 Annex to the PSMF

2.18.1 An annex to the pharmacovigilance system master file shall contain the following documents:

- a. List of Products Covered by the Pharmacovigilance System
The PSMF shall include a list of medicinal products covered by the pharmacovigilance system, indicating the product name, active substance(s), and the corresponding NAFDAC registration number.
- i. The list shall be organised by active substance and, where applicable, indicate any product-specific safety monitoring requirements, such as risk minimisation measures specified in the Risk Management Plan (RMP), conditions of the Marketing Authorization, or non-standard PSUR/PBRER submission schedules. Such monitoring requirements may be provided as a secondary list.
- ii. Where some Marketing Authorizations are covered by a different pharmacovigilance system (e.g., where the MAH operates more than one pharmacovigilance system or where activities are delegated to a third party), reference to the relevant PSMF(s) shall be provided in the Annexes to enable the complete product portfolio of the MAH to be linked to the appropriate pharmacovigilance system master files.
- iii. Where a pharmacovigilance system is shared by multiple MAHs, all products covered by the system shall be included. Product lists may be presented separately for each MAH or as a single consolidated list identifying the relevant MAH(s) for each product.
- a. A list of written policies and procedures;
- b. A list of contractual agreements covering delegated activities, including the medicinal products.
- c. A list of tasks that have been delegated by the qualified person for pharmacovigilance.
- d. A list of all completed audits, for a period of five years, and a list of audit schedules;
- e. Where applicable, a list of performance indicators.

f. Where applicable, the PSMF shall include a list of other pharmacovigilance system master files held by the same Marketing Authorization Holder (MAH). The list shall include the PSMF number(s), the name of the MAH, and the name of the QPPV responsible for each pharmacovigilance system. Where the system is managed by a third party, the name of the service provider shall also be provided.

g. A logbook and other change control documentation shall be included as appropriate. Documented changes shall include at least the date, person responsible for the change and the nature of the change.

2.19 Change control, logbook, versions, and archiving

2.19.1 It is necessary for Marketing Authorization Holders to implement change control systems and to have robust processes in place to continuously be informed of relevant changes in order to maintain the pharmacovigilance system master file accordingly. The Agency may request information about important changes to the pharmacovigilance system, such as, but not limited to:

- a. Changes to the pharmacovigilance safety database(s), which could include a change in the database itself or associated databases, the validation status of the database as well as information about transferred or migrated data.
- b. Changes in the provision of significant services for pharmacovigilance, especially major contractual arrangements concerning the reporting of safety data.
- c. Organizational changes, such as takeovers, mergers, the sites at which pharmacovigilance is conducted or the delegation/transfer of pharmacovigilance system master file management.

2.19.2 In addition to these changes being documented in the pharmacovigilance system master file for the purpose of change control (in the logbook), the QPPV shall always be kept informed of these changes.

2.19.3 Changes to the pharmacovigilance system master file shall be recorded, such that a history of changes is available (specifying the date and the nature of the change). Changes to the PSMF must be recorded in the logbook. Descriptive changes to the content of the master file must be recorded in the logbook.

2.19.4 Change history for the information contained in the annexes may be 'on demand', in which case the logbook would indicate the date of the revision of PSMF content and/or annex update(s), the history of changes for annex content would also be updated. Information that is being regularly updated and is contained in the annexes, such as product and standard operating procedure lists or

compliance figures, may include outputs from controlled systems (such as electronic document management systems or regulatory databases). The superseded versions of such content may be managed outside of the pharmacovigilance system master file content itself, provided that the history of changes is maintained and available to the Agency on request.

If the pharmacovigilance system master file has not been requested or has remained unchanged for a period of time (for example, if the changes in the content of annexes are managed outside of the pharmacovigilance system master file), it is recommended that a review is conducted periodically. Marketing Authorization Holders need to ensure that the obligations concerning the timely provision of the pharmacovigilance system master file can be met.

It is also noted that the QPPV must be able to gain access to current and accurate information about the pharmacovigilance system, hence permanent access to the pharmacovigilance system master file must be enabled, including the information contained in the annexes (either via the pharmacovigilance master file itself or via access to the systems used to generate the annex content).

2.19.5. Changes to information contained in the Annexes may be documented on demand. In such cases, the PSMF logbook shall record the date of revision to the PSMF or updates to the Annexes, while the detailed change history for Annex content shall be maintained accordingly.

Annex information that is regularly updated, such as product lists, standard operating procedure lists, or compliance metrics, may be generated from controlled systems (e.g., electronic document management systems or regulatory databases). Superseded versions of such information may be maintained outside the PSMF, provided that the change history is preserved and can be made available to the Agency upon request.

Where the PSMF has not been requested or remains unchanged for an extended period, periodic review is recommended to ensure accuracy and completeness. Marketing Authorization Holders shall ensure that the PSMF can be provided to the Agency in a timely manner when requested.

The QPPV shall have permanent access to current and accurate information on the pharmacovigilance system, including the PSMF and its Annexes, either directly through the PSMF or through access to the systems used to generate the Annex content.

2.19.6 Marketing Authorization Holders shall be able to justify their approach and have document control procedures in place to govern the maintenance of the pharmacovigilance system master file.

2.19.7 Changes to the pharmacovigilance system master file shall also account for shared pharmacovigilance systems and delegated activities. A record of the date and nature of notifications of the changes made available to the Agency, the QPPV and relevant third parties shall be kept to ensure that change control is fully implemented.

2.19.8 The pharmacovigilance master file shall be retained in a manner that ensures its legibility and accessibility.

2.20 Presentation

2.20.1 The pharmacovigilance system master file shall be continuously accessible to the QPPV and to the Agency. The information shall be succinct, accurate and reflect the current system in place, which means that whatever format is used, it must be possible to keep the information up to date and, when necessary, to revise to take account of experience gained, technical and scientific progress and amendments to the legislative requirements.

2.20.2 The Pharmacovigilance System Master File (PSMF) shall be continuously accessible to the QPPV and the Agency. The information contained in the PSMF shall be concise, accurate, and reflect the current pharmacovigilance system in place. The format used shall allow the PSMF to be readily updated and revised, as necessary, to incorporate operational experience, scientific and technical developments, and changes in regulatory requirements.

2.21 Format and layout

2.21.1 The pharmacovigilance system master file may be in electronic form on condition that a clearly arranged printed copy can be made available to the Agency. In any format, the pharmacovigilance system master file shall be legible, complete, provided in a manner that ensures all documentation is accessible and allows full traceability of changes.

2.21.2 Therefore, it may be appropriate to restrict access to the pharmacovigilance system master file to ensure appropriate control over the content and to assign specific responsibilities for the management of the pharmacovigilance system master file in terms of change control and archiving.

2.21.3 The pharmacovigilance system master file shall be indexed in a manner consistent to allow easy navigation to the contents. In general, embedded documents are discouraged. The use of electronic book-marking and searchable text is recommended. Documents such as copies of signed statements or agreements shall be included as appendices and described in the index.

2.21.4 The Pharmacovigilance System Master File (PSMF) shall be indexed to allow easy navigation of its contents. Embedded documents are generally discouraged. The use of electronic bookmarking and searchable text is recommended. Copies of signed statements, agreements, and similar documents shall be included as appendices and clearly referenced in the index.

2.21.5 The documents and particulars of the pharmacovigilance system master file shall be presented with the following headings and, if in hardcopy, in the order outlined:

2.21.6 Cover page

The cover page of the Pharmacovigilance System Master File (PSMF) shall include:

- a. The name of the Marketing Authorization Holder (MAH), the MAH of the QPPV responsible for the described pharmacovigilance system (if different), and the name of any third-party company providing QPPV services, where applicable.
- b. The name of any other MAH(s) sharing the pharmacovigilance system.
- c. A list of other PSMFs for the MAH covering products managed under different pharmacovigilance systems.
- d. The date of preparation or last update of the PSMF.

2.21.7 The headings referred to in section 2.9 shall be used for the main content of the pharmacovigilance system master file. The minimum required content of the annexes is outlined in section 2.18, and additional information may be included in the annexes, provided that the requirements for the main sections (2.10 to 2.17) are also met. The positioning of content in the Annexes is further outlined; the bullet points are descriptions of possible content (and not required headings):

2.21.8 The headings described in Section 2.15 shall be used for the main content of the Pharmacovigilance System Master File (PSMF). The minimum required content for the Annexes is outlined in Section 2.18; additional information may also be included, provided that the requirements for the main sections (Sections 2.10–2.17) are met. The placement of content within the Annexes is further described in the following bullet points, which represent examples of possible content and do not constitute mandatory headings:

Annex A: Qualified Person Responsible for Pharmacovigilance (QPPV)

- i. List of tasks delegated by the QPPV or the applicable procedural document
- ii. Curriculum vitae of the QPPV and supporting documentation
- iii. Contact details of the QPPV

Annex B: Organisational Structure of the Marketing Authorization Holder (MAH)

- i. List of relevant contracts and agreements

Annex C: Sources of Safety Data

- i. Lists related to sources of safety data, including affiliates and third-party contacts.

Annex D: Computerised Systems and Databases

Annex E: Pharmacovigilance Processes and Written Procedures

- i. List of pharmacovigilance procedural documents

Annex F: Pharmacovigilance System Performance
i. List of performance indicators
ii. Current results of performance assessments against the indicators

Annex G: Quality System
i. Audit schedules
ii. List of audits conducted and completed

Annex H: Products
i. List(s) of products covered by the pharmacovigilance system
ii. Notes identifying the relevant Marketing Authorization Holder (MAH) for each product, where applicable

Annex I: Document and Record Control
i. PSMF logbook

Annex J: Change History
Documentation of the history of changes for Annex contents, indexed according to Annexes A–H where such information is not already included within the respective Annex.

2.21.9 Documentation to support notifications and signatures concerning the pharmacovigilance system master file, as required. Where there is no content for an Annex, there is no need to provide blank content pages with headings; however, the Annexes that are provided shall still be named according to the format described. For example, Annex E shall not be renamed to Annex D in circumstances where no Annex concerning computerized systems and databases is used; Annex D shall simply be described as 'unused' in the indexing, so that recipients of the pharmacovigilance system master file are assured that missing content is intended.

2.21.10 Documentation shall be maintained to support notifications and signatures related to the Pharmacovigilance System Master File (PSMF) as required. Where an Annex contains no content, blank pages with headings are not necessary. However, all provided Annexes shall retain their designated format and numbering. For example, if Annex D (Computerised Systems and Databases) is not used, it shall not be renumbered; instead, it shall be indicated as “unused” in the index. This ensures that recipients of the PSMF understand that missing content is intentional.

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