Guideline on Good Pharmacovigilance Practices

Module V- Pharmacovigilance System Master File

Turkish Medicines and Medical Devices Agency
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CHAPTER I

1.1. Introduction

This guideline provides guidance regarding the requirements for the Pharmacovigilance System Master File (PSMF). Marketing authorization holders are legally required to create and maintain a PSMF and make it available to the Agency upon request, according to Article 5, Paragraph 5, Subparagraph (e) of the Regulation on the Safety of Medicinal Products. The PSMF definition is provided in Article 4, Paragraph 1, Subparagraph (h) of the above Regulation, and the minimum requirements for its contents and maintenance are set out in chapter three.

The PSMF, detailing the current pharmacovigilance system, will be located at the site in Turkey where the main pharmacovigilance activities of the marketing authorization holder are performed. Information about elements of the system to be implemented in the future may be included in the PSMF, but these should be clearly described as planned, rather than established activities. The content of the PSMF should reflect global availability of safety information for medicinal products authorized in Turkey.

It is a requirement of the marketing authorization application that summary information about the pharmacovigilance system is submitted to the Agency. Applicants are required, at the time of initial marketing authorization application, to have in place a description of the pharmacovigilance system that will be in place and functioning at the time of grant of the marketing authorization. The PSMF will not be routinely requested during the assessment of new marketing authorization applications, but may be requested particularly if a new pharmacovigilance system is being implemented, or if product specific safety concerns arise with compliance with pharmacovigilance requirements.

There is no requirement for variations for changes in the content of the PSMF, but the marketing authorization holder will notify the Agency when the qualified person responsible for pharmacovigilance and related contact details change or when the location of the PSMF changes.

CHAPTER II
Structures and Processes

2.1. Objectives

The PSMF will describe the pharmacovigilance system and support and document its compliance with the requirements. As well as fulfilling the requirements for a PSMF laid down in the Regulation and the GVP Modules, it will also contribute to the appropriate planning and conduct of audits by the applicant or marketing authorizations holders, the fulfillment of supervisory responsibilities of the qualified person responsible for pharmacovigilance, and compliance with regulatory requirements. The PSMF provides an overview of the pharmacovigilance system, which may be requested and assessed by the Agency during marketing authorization applications or the post-authorization phase.

Through the production and maintenance of the PSMF, the marketing authorization holder

and the qualified person responsible for pharmacovigilance will be responsible 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.

The use of this information should contribute to the appropriate management and development of the pharmacovigilance system.

2.2. Registration and maintenance

2.2.1. Summary of the applicant's pharmacovigilance system

Article 9, Paragraph 1 of the Regulation on the Safety of Medicinal Products requires the applicants to include a summary of the applicant's pharmacovigilance system in the marketing authorization application, which must include the following elements:

- documentation that the applicant has at his disposal a qualified person responsible for pharmacovigilance;
- the contact details of the qualified person responsible for pharmacovigilance;
- a statement signed by the applicant to the effect that the applicant has the necessary means to fulfill the tasks and responsibilities related to pharmacovigilance;
- a statement that a PSMF for the medicinal product is available.

2.2.2. Transfer of responsibilities for the PSMF

The pharmacovigilance system may change over time. Transfer or delegation of responsibilities and activities concerning the master file should be documented (see 2.4.2. and 2.4.8.) and managed to ensure that the marketing authorization holder fulfils their responsibilities. Since the qualified person responsible for pharmacovigilance has responsibility for the pharmacovigilance system, changes to the PSMF should also be notified to the qualified person responsible for pharmacovigilance in order to support their authority to make improvements to the system. The types of changes that should be routinely and promptly notified to the qualified person responsible for pharmacovigilance are:

- Updates to the PSMF or its location that are notified to the Agency;
- The addition of corrective and/or preventative actions to the PSMF (e.g. following audits and inspections). The qualified person responsible for pharmacovigilance should also be able to access information about deviations from the processes defined in the quality management system for pharmacovigilance;
- Changes to content that fulfill the criteria for appropriate oversight of the pharmacovigilance system (in terms of capacity, functioning and compliance);
- Changes in arrangements for the provision of the PSMF to the Agency;
- Transfer of significant services for pharmacovigilance to a contract organization;
- Addition of products to the pharmacovigilance system for which the qualified person responsible for pharmacovigilance is responsible;

- Changes for existing products which may require a change or increased workload in relation to pharmacovigilance activity e.g. new indications, studies.

The qualified person responsible for pharmacovigilance should be in a position to ensure and to verify that the information contained in the PSMF is an accurate and up-to-date reflection of the pharmacovigilance system under his or her responsibility.

2.3. The representation of pharmacovigilance systems

The PSMF will 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 such system will be described in a PSMF. Those files will cumulatively cover all medicinal products of the marketing authorization holder for which a marketing authorization has been issued.

- It is anticipated that there will be circumstances where a single marketing authorization holder may establish more than one pharmacovigilance system e.g. specific systems for particular types of products (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 specific PSMF will be in place to describe each system.
- A single qualified persons responsible for pharmacovigilance will be appointed to be responsible for the establishment and maintenance of the pharmacovigilance system described in the PSMF.
- Where a pharmacovigilance system is shared by several marketing authorization holders each marketing authorization holder is responsible for ensuring that a PSMF exists that describes the pharmacovigilance system applicable for their products. For a particular products the marketing authorization holder may delegate through written agreement a part or all of the pharmacovigilance activity for which the marketing authorization holder is responsible. In this case the pharmacovigilance system master file of the marketing authorization holder may cross refer to all or part of the PSMF managed by the system of the party to whom the activity has been delegated, subject to agreement by and between the marketing authorization holder and the Agency on access to that system's information. The marketing authorization holder should be able to assure the content of the referenced files in relation to the pharmacovigilance system applicable to their products. Activities for maintaining the PSMF in a current and accessible state can be delegated to a contract organization for pharmacovigilance (COPV).
- Where applicable, a list of all PSMFs held by the same marketing authorization holder will be provided in the annex (see 2.4.8.) [Regulation on the Safety of Medicinal Products, Article 12(1)d]; this includes the details of the qualified persons responsible for pharmacovigilance and the relevant products.
- Submission of summary information to the Agency cannot contain multiple addresses for a single PSMF. This address may be different to that of the applicant/marketing authorization holder (for example, a different office of the marketing authorization holder or when a contract organization for pharmacovigilance undertakes the main activities).

- 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 PSMF location, maintenance of the file and its provision to the Agency upon request [Regulation on the Safety of Medicinal Products, Article 5(5)]. Detailed written agreements describing the roles and responsibilities for PSMF content, submissions and management, as well as to govern the conduct of pharmacovigilance in accordance with the legal requirements, should be in place.
- When a pharmacovigilance system is shared by multiple marketing authorization holders, it is advised that the partners agree on how to mutually maintain the relevant sections within their own PSMFs. Accessibility of the pharmacovigilance system master file to all the applicable marketing authorization holders, and its provision to the Agency should be defined in written agreements. It is vital that marketing authorization holders can gain assurance that the pharmacovigilance system used for their products is appropriate and compliant.

2.4. Information to be contained in the PSMF

The PSMF will include documents to describe the pharmacovigilance system. The content of the PSMF should reflect the global availability of safety information for medicinal products authorized in Turkey. The content will be indexed to allow for efficient navigation around the document and the annex headings described in 2.6.1. While building the structure of the content of the PSMF, it should be ensured 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 should be referred to and contained in the annexes. The control associated with change of content is described in section 2.5.

2.4.1. PSMF section on qualified person responsible for pharmacovigilance

The contact details of the qualified person responsible for pharmacovigilance will be provided in the marketing authorization application [Regulation on the Safety of Medicinal Products, Article 9(1)].

The information relating to the qualified person responsible for pharmacovigilance provided in the PSMF [Regulation on the Safety of Medicinal Products, Article 11(1)] will include:

- A description of the responsibilities guaranteeing that the qualified person has sufficient authority over the pharmacovigilance system in order to promote, maintain and improve compliance;
- a summary curriculum vitae with the key information on the role of the qualified person responsible for pharmacovigilance, including proof of registration with the database maintained by the Risk Management Office;
- contact details of the qualified person responsible for pharmacovigilance, including the name, mailing address, telephone and fax numbers and e-mail address of the qualified person responsible for pharmacovigilance;
- details of back-up arrangements to apply in the absence of the qualified person responsible for pharmacovigilance.

2.4.2. PSMF section on the organizational structure of the marketing authorization holder

A description of the organizational structure of the marketing authorization holder relevant to the pharmacovigilance system must be provided. The description should provide a clear overview of the companies involved, the main pharmacovigilance departments and the relationships between organizations and operational units relevant to the fulfillment of pharmacovigilance obligations. This should include third parties.

Specifically, the PSMF will describe:

- The organizational structure of the marketing authorization holder, showing the position of the qualified person responsible for pharmacovigilance in the organization.
- The sites where the pharmacovigilance functions are undertaken covering individual case safety report (ICSR) collection, evaluation, safety database case entry, periodic safety update report production, signal detection and analysis, risk management plan management, pre- and post-authorization study management, and management of safety variations.

Diagrams may be preferable; the name of the department or third party should be also indicated.

Delegated activities

The PSMF, where applicable, will contain a description of the delegated activities and/or services relating to the fulfillment of pharmacovigilance obligations [Regulation on the Safety of Medicinal Products, Article 11(6)].

Links with other organizations, such as co-marketing agreements and contracting of pharmacovigilance activities should be outlined. A description of the location and nature of contracts and agreements relating to the fulfillment of pharmacovigilance obligations should be provided. This may be in the form of a list and/or table to show the parties involved, the roles undertaken and the concerned medicinal product(s) and territories. The list should be organized according to; service providers (e.g. medical 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 will be made available at the request of the Agency or during inspection and audit, and the list provided in the annexes (see 2.4.8).

2.4.3. PSMF section the sources of safety data

The description of the main units for safety data collection should include all parties responsible, on a global basis, for solicited and spontaneous case collection for products authorized in Turkey. This should include medical information sites as well as affiliate offices and may take the form of a list describing the country, nature of the activity and the products, if the activity is product specific, and providing a contact point (address, telephone and e-mail) for the site. The list may be located in the Annexes of the PSMF. Information about third parties (local distribution/marketing arrangements) should also be included in the section describing contracts and agreements (see 2.4.2. and 2.4.8.).

Flow diagrams indicating the main stages, timeframes and parties involved may be used. However represented, the description of the process for ICSRs from collection to

reporting to the Agency should indicate the departments and/or third parties involved.

Marketing authorization holders should be able to produce and make available a comprehensive list of sources (e.g. data from any studies, registries, surveillance or support programs sponsored by the marketing authorization holder through which ICSRs could be reported) to support inspection, audit and oversight by the qualified person responsible for pharmacovigilance. The list should describe, on a worldwide basis, the status of each study/program, the applicable countries, the products and the main objective. It should distinguish between interventional and non-interventional studies and should be organized per active substance. The list should cover all studies/programs ongoing as well as completed in the last two years. This list may be located in an annex or provided separately.

2.4.4. PSMF section on computerized systems and databases

The location, functionality and operational responsibility for computerized systems and databases used to receive, collate, record and report safety information and an assessment of their fitness for purpose shall be described in the PSMF, including a description of the operational responsibilities associated with each [Regulation on the Safety of Medicinal Products, Article 11(3)].

Where multiple computerized systems/databases are used, the applicability of these to pharmacovigilance activities should 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 computer system functionality should also be described; the change control, nature of testing, back-up procedures and electronic data repositories vital to pharmacovigilance compliance should be included in summary, and the nature of the documentation available described. For paper-based documents, 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, should be described.

2.4.5. PSMF section on pharmacovigilance processes

The availability of clear written procedures is an essential element of any pharmacovigilance system. Module 4 describes the required minimum set of written procedures for pharmacovigilance. A description of the procedural documentation available (standard operating procedures, manuals, at a 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) should be provided in the PSMF.

A description of the process, data handling and records for the performance of pharmacovigilance, covering the following aspects will be included in the PSMF:

- Continuous monitoring of risk-benefit profiles and the result of evaluation and the decision making process for taking appropriate measures (this should include signal generation, detection and evaluation). This may also include several written procedures and instructions concerning safety database outputs, interactions with clinical departments etc.
- Risk management system(s) and monitoring of the outcome of risk minimization measures (several departments may be involved in this area and interactions should be defined in written procedures or agreements).

- ICSR collection, collation, follow-up, assessment and reporting (the procedures applied to this area should clarify what are local and what are global activities).
- Periodic risk/benefit assessment report planning, creation and submission (see Module III).
- Communication of safety concerns to consumers, healthcare professionals and the Agency;
- Implementation of safety variations to the summary of product characteristics and package leaflets (procedures should cover both internal and external communications) [Regulation on the Safety of Medicinal Products, Article 11(4)].

In each area, the marketing authorization holder should be able to provide evidence of a system that supports appropriate and timely decision making and action.

The description must be accompanied by the list of processes referred to in Article 27, Paragraph 1 of the Regulation on the Safety of Medicinal Products, as well as interfaces with other functions. Interfaces with other functions include, but are not limited to, the roles and responsibilities of the qualified person responsible for pharmacovigilance, responding to the Agency's requests for information, literature searching, safety database change control, safety data exchange agreements, safety data archiving, pharmacovigilance auditing, quality control and training. The list, which may be located in the annexes, should comprise the procedural document reference number, title, effective date and document type (for all standard operating procedures, work instructions, manuals etc.). Procedures belonging to service providers and other third parties should be clearly identified. Documents relating to specific local/country procedures need not be listed, but a country-specific list may be requested. If no or only some countries use specific local procedures, this should be indicated (and the names of the applicable countries provided).

2.4.6. PSMF section on pharmacovigilance system performance

The PSMF should contain evidence of the ongoing monitoring of performance of the pharmacovigilance system, including compliance of the main outputs of pharmacovigilance. The PSMF should include a description of the monitoring methods applied and contain as a minimum:

- An explanation of how the correct reporting of ICSRs is assessed. In the annex, figures/graphs should be provided to show the timings of 15-day reporting over the past year;
- A description of any metrics used to monitor the quality of submissions and performance of pharmacovigilance. This should include information provided by the Agency regarding the quality of ICSR reporting, periodic risk/benefit assessment reports or other submissions;
- An overview of the time schedules of periodic risk/benefit assessment reporting to the Agency (the annex should reflect the latest figures used by the marketing authorization holder to assess compliance);
- 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;

- Where applicable, an overview of adherence to risk management plan commitments, or other obligations or conditions relevant to pharmacovigilance.

Targets for the performance of the pharmacovigilance system will be described and explained. A list of performance indicators must be provided in the annex to the PSMF alongside the results of actual performance measurements.

2.4.7. PSMF section on the quality system

A description of the quality management system should be included in the PSMF, in terms of the structure of the organization and the application of the quality criteria to pharmacovigilance. This will include:

Document and Record Control

A description of the archiving arrangements for electronic and/or hardcopy versions of the PSMF should be provided, as well as an overview of the procedures applied to other quality system and pharmacovigilance records and documents (see Module IV).

Procedural documents

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

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 section (see section 2.4.5) [Regulation on the Safety of Human Medicinal Products, Article 11(5)(a)].

Training

- A description of the resource management for the performance of pharmacovigilance activities: the organizational chart giving the number of people (full time employees) involved in pharmacovigilance activities (this may be provided in the section describing the organizational structure) (see 2.4.3).
- Information about sites where the personnel are located (this is described under sections 2.4.2 and 2.4.3) 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 (a description should be provided in order to explain the training organization in relation to the personnel and site information).
- A summary description of the training concept: staff should be appropriately trained for performing pharmacovigilance related activities and this includes not only staff within pharmacovigilance departments but also any individual that may receive safety reports.

Auditing

Information about quality assurance auditing of the pharmacovigilance system should be included in the PSMF. A description of the approach used to plan audits of the pharmacovigilance system and the reporting mechanism and timelines should be provided, with a current list of the scheduled and completed audits concerning the pharmacovigilance system maintained in the annex referred to in 2.4.8. [Regulation on the Safety of Medicinal Products, Article 12(1)ç]. This list should describe the dates of audits, (ongoing or completed), scope and completion status of audits of service providers, specific pharmacovigilance activities or sites undertaking pharmacovigilance and their operational interfaces relevant to the fulfillment of the obligations in the Regulation on the Safety of Medicinal Products, and cover a period of five years.

The PSMF will also contain a note associated with any audit where significant findings are raised. This means that the presence of findings that fulfill the criteria for major or critical findings must be indicated. The audit report must be documented within the quality system; in the PSMF, it is sufficient to include a brief description of the corrective and/or preventative 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 preventative action plan(s). In the annex, in the list of audits conducted, those associated with unresolved notes in the PSMF, should be identified. The note and associated corrective and preventative action(s), shall be documented in the PSMF until the corrective and/or preventative 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 [Regulation on the Safety of Medicinal Products, Article 5(4)]. The addition, amendment or removal of the notes must therefore be recorded in the logbook.

As a means of managing the pharmacovigilance system, and providing a basis for audit or inspection, the PSMF should also describe the process for recording, managing and resolving deviations from the quality system. The master file will also document deviations from pharmacovigilance procedures, their impact and management until resolved [Regulation on the Safety of Medicinal Products, Article 13(3)]. This may be documented in the form of a list referencing a deviation report, and its date and the procedure concerned.

2.4.8. Annex to the PSMF

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

- A list of medicinal products covered by the PSMF including the name of the active substances [Regulation on the Safety of Medicinal Products, Article 12(1)a]. The list of medicinal products authorized in Turkey should also include information on the market availability of the product in Turkey and on other countries where the product is authorized or on the market.

The list should be organized per active substance and, where applicable, should indicate what type of product specific safety monitoring requirements exist (for example risk minimization measures contained in the risk management plan or laid down as conditions of the marketing authorization, non-standard periodic risk/benefit assessment reporting periodicity). The monitoring information may be provided as a secondary list.

For marketing authorizations that are included in a different pharmacovigilance system,

for example, because the marketing authorization holder has more than one pharmacovigilance system or there are third parties sharing the system, reference to the additional pharmacovigilance system master file(s) should also be provided as a separate list in the annexes, such that, for a marketing authorization holder, the entire product portfolio can be related to the set of PSMFs.

- Where pharmacovigilance systems are shared, all products that utilize the pharmacovigilance system should be included, so that the entire list of products covered by the file is available. The products lists may be presented separately, organized per marketing authorization holder. Alternatively, a single list may be used, which is supplemented with the name of the marketing authorization holder for each product, or a separate note can be included to describe the product and the marketing authorization holder covered.
- A list of written policies and procedures for the purpose of complying with Article 27(1) of the Regulation on the Safety of Medicinal Products;
- A list of contractual agreements covering the activities delegated to third parties, including the names of the medicinal products;
- A list of tasks that have been delegated by the qualified person responsible for pharmacovigilance;
- A list of all completed audits, for a period of five years, and a list of audit schedules;
- Where applicable, a list of performance indicators;
- Where applicable, a list of other PSMFs held by the same marketing authorization holder. This list should include the PSMF numbers, and the name of the marketing authorization holder of the qualified person responsible for pharmacovigilance system. If the pharmacovigilance system is managed by a COPV, the name of this organization should also be included.

A logbook in accordance with Article 14(4) of the Regulation on the Safety of Medicinal Products and other change control documentation should be included as appropriate. Documented changes will include at least the date, person responsible for the change and the nature of the change.

2.5 Change control, logbook, versions and archiving

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 PSMF accordingly. The Agency may solicit information about important changes to the pharmacovigilance system, such as, but not limited to:

- Changes to the pharmacovigilance safety databases, 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;
- Changes in the provision of significant services for pharmacovigilance, especially major contractual arrangements concerning the reporting of safety data;
- Organizational changes, such as takeovers, mergers, the sites at which pharmacovigilance is conducted or the delegation/transfer of PSMF management.

In addition to these changes being documented in the pharmacovigilance system master

file for the purpose of change control (in the logbook), the qualified person responsible for pharmacovigilance should be always kept informed of these changes.

Changes to the PSMF should be duly recorded to enable keeping track of the history of changes (specifying the date and the nature of the change). Descriptive changes to the content of the master file must also be recorded in the logbook.

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 updates; 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 PSMF content itself, provided that the history of changes is maintained and available to the Agency on request. If the PSMF 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 authorizations holders need to ensure that the obligations concerning the timely provision of the pharmacovigilance system master file can be met. It must be also ensured that the qualified person responsible for pharmacovigilance is able to gain access to current and accurate information about the pharmacovigilance system, including the information contained in the annexes (either via the PSMF itself or via access to the systems used to generate the annex content).

Marketing authorization holders should be able to justify their approach and have document control procedures in place to govern the maintenance of PSMF. As a basis for audit and inspections, the PSMF provides a description of the pharmacovigilance system at present, but the functioning and scope of the pharmacovigilance system in the past should be also understood.

Changes to the PSMF should 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 qualified person responsible for pharmacovigilance and relevant third parties should be kept in order to ensure that change control is fully implemented.

The PSMF system master file should be retained in a manner that ensures its legibility and accessibility.

2.6. PSMF presentation

The PSMF will be continuously accessible to the qualified person responsible for pharmacovigilance and the Agency on request. 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.

Although provision of the document within 7 days at the request of the Agency is required [Regulation on the Safety of Medicinal Products, Article 8(12)], marketing authorization holders should be aware that prompt access to the PSMF may also be required

by the Agency, at the stated PSMF location.

2.6.1. Format and layout

The PSMF may be in electronic form on condition that a printed copy can be made available to the Agency if requested. In any format, the PSMF should be legible, complete, provided in a manner that ensures all documentation is accessible and allow full traceability of changes. Therefore, it may be appropriate to restrict access to the PSMF in order to ensure appropriate control over the content and to assign specific responsibilities for the management of the PSMF in terms of change control and archiving.

The PSMF must be written in Turkish. However, global PSMFs written in English may be acceptable, to the extent that they include a specific section covering Turkey. The PSMF should be indexed in a manner consistent with the headings described in this module, and 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 should be included as appendices and described in the index.

The documents and particulars of the PSMF will be presented with the following headings and, if hardcopy, in the order outlined:

The Cover Page will include:

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- The name of the marketing authorization holder and the qualified person responsible for pharmacovigilance, responsible for the pharmacovigilance system described, as well as the relevant qualified person responsible for pharmacovigilance working for the marketing authorization holder at the COPV, if applicable.
- The names of other marketing authorization holders sharing the same pharmacovigilance system.
- The list of pharmacovigilance system master files for products with a different pharmacovigilance system.
- The date of issue / last update.

The headings used in 2.4 should be used for the main content of the PSMF. The minimum required content of the annexes is outlined in 2.4.8, and additional information may be included in the annexes, depending on the requirements in the content of main sections. The positioning of content in the annexes is outlined below, with the descriptions of possible content in a bulleted list:

The qualified person responsible for pharmacovigilance, Annex A:

- The list of tasks that have been delegated by the qualified person responsible for pharmacovigilance, or the applicable procedural documents
- The curriculum vitae of the qualified person responsible for pharmacovigilance and associated documents
- Contact details.

The organizational structure of the marketing authorization holder, Annex B:

- The lists of contracts and agreements.

Sources of safety data, Annex C:

- Lists associated with the description of sources of safety data (e.g. affiliates and third parties).

Computerized systems and databases, Annex D:

Pharmacovigilance process, and written procedures, Annex E:

- Lists of procedural documents.

Pharmacovigilance System Performance, Annex F:

- Lists of performance indicators
- Current results of performance assessment in relation to the indicators.

Quality System, Annex G:

- Audit schedules
- List of audits conducted and completed

Medicinal Products, Annex H:

- List(s) of medicinal products covered by the pharmacovigilance system
- Any notes that the marketing authorization holder may wish to highlight per medicinal product

Document and Record Control, Annex I:

- Logbook
- Documentation of history of changes for annex contents, indexed according to the Annexes A to H and their content if not provided within the relevant annex itself
- Documentation to support notifications and signatures concerning the PSMF, 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 should still be named according to the format described. For example, Annex E should not be renamed to Annex D in circumstances where no Annex concerning computerized systems and databases is used, Annex D should simply be described as ‘unused’ in the indexing, in order that recipients of the pharmacovigilance system master file are assured that missing content is intended.