Annex 11
of Pharmacovigilance Procedure
(item 4 of chapter 1 of section V)

STRUCTURE
of applicant's pharmacovigilance system master file

Cover page.

Description of pharmacovigilance system by sections:

I. Information on qualified person responsible for pharmacovigilance

II. Information on organizational structure of applicant/registration certificate holder

III. Information on sources of safety data

IV. Information on computerized systems or databases

V. Information on pharmacovigilance processes

VI. Information on pharmacovigilance system performance

VII. Information on quality system in pharmacovigilance

Annexes.

REQUIREMENTS FOR COMPLETING

the master file

Cover page shall include the following information:

the unique number;

name of applicant/registration certificate holder;

full name of qualified person responsible for the pharmacovigilance system described;

name of third person/other applicants/registration certificate holders (if any), sharing pharmacovigilance system;

full name of qualified person responsible for the pharmacovigilance system described, third person/ other applicants/registration certificate holders (if any), sharing pharmacovigilance system;

list of pharmacovigilance system master files (hereinafter - PSMF) for applicant/registration certificate holder (concerning medicinal products, vaccines, tuberculin (hereinafter - medicinal products), which have different pharmacovigilance systems);

Date of preparation or last update.

Description of pharmacovigilance system by sections:

I. Information on qualified person responsible for pharmacovigilance

Information on QPPV shall be provided including his/her contact details, qualification and experience, CV with key information on the role of QPPV, a list of the responsibilities guaranteeing that the QPPV has sufficient authority pertinent to development of pharmacovigilance system, maintenance and improvement its functioning, including in Ukraine, details of back-up arrangements to apply in the absence of QPPV; and information relating to the CPPV, including in Ukraine, if different from QPPV, including his/her contact details, data about qualification and experience; information on fulfilling obligations of QPPV/CPPV, if absent (illness/vacation) and other information, if available.

II. Information on organizational structure of applicant/registration certificate holder

A description of the organisational structure of the registration certificate holder/applicant including related to the pharmacovigilance must be provided, which should include information on enterprises, institutions, organisations involved, irrespective of form of ownership and the relationship(s) between them, as well as on third persons involved in activity related to the pharmacovigilance. Specifically, the PSMF shall describe:

the organisational structure of the registration certificate holder(s), showing the position of the QPPV in the organisation;

the site(s) where the pharmacovigilance functions are undertaken covering adverse reaction reports collection, their evaluation, safety database case entry, PSUR production, signal detection and analysis, risk management plan development and fulfilment, clinical and non-interventional study management, introduction of changes related to safety of medicinal products and/or pharmacovigilance system in registration materials.

Information may be in the form of a list/table to show the parties involved, their obligations and the concerned medicinal product(s) and countries. The list should be organised according to service providers (e.g. medical information, auditors, patient support programme providers, study data management etc.), contractual relations (distributors, partners, co-marketing etc.) and other technical providers (hosting of computer systems etc.). Contracts in part of subject matter shall be made available at the request or during inspection and audit, and the list of contracts provided in the Annexes.

III. Information on sources of safety data

The description of the main units for safety data collection shall be provided, which includes all parties responsible for solicited and spontaneous safety data collection for medicinal products in place of pharmacovigilance activity arrangement. Sources of safety data include data of any studies, registries, surveillance or support programmes sponsored by the registration certificate holder through which data about adverse reactions, lack of efficacy or any other information related to safety and efficacy of medicinal product could be reported. The list of sources of safety data should be comprehensive and should include all ongoing studies/programmes as well as studies/programmes completed in the last two years and may be located in an Annex or provided separately.

IV. Information on computerised systems and databases

The location, functionality and operational responsibility for computerised systems and/or databases used to receive, collate, record and report safety information and an assessment of their fitness for performing pharmacovigilance by the applicant shall be described.

Where multiple computerised systems and/or databases are used, the applicability of these to pharmacovigilance activities should be described taking in account the extent of computerisation within the pharmacovigilance system. The validation status of databases should also be described. Information about change control procedure, nature of testing, back-up procedures and electronic data repositories vital to pharmacovigilance compliance should be included in summary. In addition the nature of the documentation available shall be described. For paper-based systems (where an electronic system may only be used for expedited reports about adverse reactions), 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 reactions to medicinal products, should be described.

V. Information on pharmacovigilance processes

A description of data handling and records for the performance of pharmacovigilance, covering the following aspects shall be included (but not limited to):

continuous monitoring of medicinal product risk-benefit profile(s), result of evaluation, decision making process for taking appropriate measures; signal generation, its detection and evaluation, list of standard operating procedures (hereinafter- SOP), instructions, working instructions concerning safety database outputs, interactions with other organization departments of the applicant, etc;

risk management system(s) and monitoring of the outcome of risk minimisation measures. Several organization departments of the applicant may be involved in this area and interactions should be defined in SOP or agreements;

ICSR collection, collation, follow-up, assessment and reporting. The procedures applied to this area should clarify what are central and what are local activities;

PSUR scheduling, production and submission;

communication of safety concerns to consumers, healthcare professionals and the authorized body;

implementation of safety variations to the instruction for medical use. Procedures should cover both internal and external communications on safety issues.

The description must be accompanied by the list of SOPs, instructions, working instructions related to compliance management, as well as interfaces with other functions, which include (but are not limited to) the roles and responsibilities of the QPPV/CPPV, responding to authorized body requests for information, scientific and medical 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 reference number, title, effective date and document type (for all SOP, instructions, work instructions etc.). Procedures belonging to service providers and other third parties should be clearly identified. Documents relating to specific legal requirement of country, where the medicinal product covered by this pharmacovigilance system has been registered, need not be listed, but their list may be requested on legal level of countries, where the medicinal products covered by this system have been registered. If no or only some countries use specific local procedures, this should be indicated, and the names of the applicable countries, where the medicinal products covered by this system have been registered, provided.

VI. Information on pharmacovigilance system performance

A description of monitoring of performance of the pharmacovigilance system of registration certificate holder/applicant, which is used, shall be provided. Targets for the performance of the pharmacovigilance system shall 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. Such information may be provided as figures/graphs to show and to prove the performance of pharmacovigilance system. The PSMF should include a description of the monitoring methods applied and contain as a minimum:

a description of procedure for evaluating the correct reporting of ICSRs. In the annex, figures/graphs should be provided to show and to prove the compliance with terms and timeliness of reporting ICSRs over the past year;

general records about submitting PSUR to regulatory authorities (the annex should contain the latest data used by the registration certificate holder/applicant to assess compliance of timeliness of such reporting);

a concise description of the methods used to ensure timeliness of safety variation submissions compared to internal and envisaged by legislation deadlines, including tracking and description of required safety variations pertinent to which applications have not been submitted;

where applicable, generalized data of adherence to risk management plan commitments, or other obligations or conditions of registration certificate(s) relevant to pharmacovigilance shall be provided.

VII. Information on quality system in pharmacovigilance

A description of the quality management system should be provided, in terms of the structure of the organisation and the application of the quality system to pharmacovigilance. This description shall include information about:

document and record control (a description of the archiving arrangements for electronic and/or hardcopy versions of the PSMF, ICSR, PSUR, RMP should be provided, as well as other pharmacovigilance records and documents);

procedural documents (a general description of documents used in pharmacovigilance (SOP, instructions, work instructions etc), the applicability of the various documents within the enterprises, institutions, organisations irrespective of form of ownership 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 should be provided);

training (a description of the resource management for the performance of pharmacovigilance activities (the organisational chart giving the number of applicant’s people involved in pharmacovigilance activities should be provided. These data may be given in the section describing the organisational structure); a summary description of the staff training concept (not only staff within pharmacovigilance departments but also any individual that may receive ICSR) including a reference to the location training files should be provided);

auditing (information about quality assurance auditing of the pharmacovigilance system should be included. A description of the approach used to plan audits of the pharmacovigilance system and the reporting mechanism and timelines, with a current list of the scheduled and completed audits concerning the pharmacovigilance system maintained in the annex should be provided. This list

should describe the date(s) of audit conduct and of report, scope and information about audits of third parties according to contractual relations, specific pharmacovigilance activities or sites undertaking pharmacovigilance and their operational interfaces with other organizational departments relevant to the fulfilment of the pharmacovigilance obligations and cover a rolling 5 year period.

The PSMF shall also contain a concise information about all audits where significant and critical inconsistencies are revealed with a brief description of the corrective and/or preventative action(s) associated with such inconsistencies, 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 audits, information about which is contained in PSMF, should be identified. The concise information about audits where critical data are revealed with the brief description of the corrective and preventative action(s) should be documented in the PSMF until positive result is achieved after taking the corrective action(s) and/or sufficient improvement has been independently verified. The addition, amendment or removal of information about audits in the PSMF must be recorded in the logbook.

As a means of managing the pharmacovigilance system, and providing a basis for audit the PSMF should also describe the process for recording, managing and resolving deviations from the quality system and also document deviations from pharmacovigilance procedures, their impact and management until resolved. The deviation may be documented in the form of a list referencing a deviation report, and its date and procedure concerned.

The description of pharmacovigilance system envisages the availability of references to legislation on which basis the pharmacovigilance system was developed and functions and a brief description of registration certificate holder/applicant.

Information in PSMF should be provided according to annexes structure and content. Annex E should not be renamed to Annex D in circumstances where no Annex concerning computerised systems and databases is used, Annex D should simply be described as ‘unused’ in the indexing of PSMF, in order that recipients of the PSMF are assured that missing content is intended.

Information in annexes to PSMF shall be provided according to it sections where there is reference to appropriate annex and contain the following data (but not limited to):

Annex A to section I. Information on the qualified person responsible for pharmacovigilance;

Annex B to section II. Information on the organisational structure of the applicant/registration certificate holder;

Annex C to section III. Information on sources of safety data;

Annex D to section IV. Information on computerised systems and databases;

Annex E to section V. Information on pharmacovigilance process (SOP lists, instructions, working instructions);

Annex F to section VI. Information on pharmacovigilance system performance (lists of performance indicators, current results of performance assessment in relation to the indicators);

Annex G to section VII. Information on quality system in pharmacovigilance (audit schedules, list of audits conducted and completed, information on measures applied);

Annex H to Description of pharmacovigilance system (List of medicinal products covered by the pharmacovigilance system);

Annex I. Document and Record Control (logbook, documentation of history of changes for contents (indexed accordingly) and description of such changes).