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3 Guideline on good pharmacovigilance practices (GVP)

4 Module I – Pharmacovigilance systems and their quality systems

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I.A. Introduction

This Module contains guidance for the establishment and maintenance of quality assured pharmacovigilance systems for marketing authorisation holders, competent authorities of Member States and the Agency. How the systems of these organisations interact while undertaking specific pharmacovigilance processes is described in each respective Module of GVP.

The definition of a pharmacovigilance system is provided in Article 1 of Directive 2001/83/EC as a system used by the marketing authorisation holder and by Member States to fulfil the tasks and responsibilities listed in Title IX and designed to monitor the safety of authorised medicinal products and detect any change to their risk-benefit balance. The Agency likewise maintains a pharmacovigilance system to fulfil its pharmacovigilance activities.

For performing their pharmacovigilance activities, marketing authorisation holders, competent authorities of Member States and the Agency shall establish and follow quality systems that are adequate and effective for this performance. The legal requirement for quality systems was introduced by Directive 2010/84/EU amending Directive 2001/83/EC and Regulation (EU) No 1235/2010 amending Regulation (EC) No 726/2004 to strengthen pharmacovigilance in the EU. The minimum requirements of these quality systems are set out in the Commission Implementing Regulation on the Performance of Pharmacovigilance Activities Provided for in Regulation (EC) No 726/2004 and Directive 2001/83/EC.

The guidance on quality systems in this Module is consistent with the general principles of the ISO 9000 Standards on quality management issued by the International Organization for Standardization (ISO). The general application of quality management to pharmacovigilance systems is described under I.B. and requirements specific to the operation of the EU network in I.C..

In this Module, all applicable legal requirements are referenced in the way explained in the GVP Introductory Cover Note and are usually identifiable by the modal verb “shall”. Guidance for the implementation of legal requirements is provided using the modal verb “should”.

I.B. Structures and processes

I.B.1. Pharmacovigilance system

A pharmacovigilance system is defined as a system used by an organisation to fulfil its legal tasks and responsibilities in relation to pharmacovigilance and designed to monitor the safety of authorised medicinal products and detect any change to their risk-benefit balance [DIR Art 1(28d)].

A pharmacovigilance system, like any system, is characterised by its structures, processes and outcomes. For each specific pharmacovigilance process, including its necessary structures, a dedicated Module is included in GVP.

I.B.2. Quality, quality objectives, quality requirements and quality system

For the purpose of GVP, which provides guidance on structures and processes of a pharmacovigilance system, the quality of a pharmacovigilance system can be defined as all the characteristics of the system which are considered to produce, according to estimated likelihoods, outcomes relevant to the objectives of pharmacovigilance.

In general terms, quality is a concept that can be understood as a degree subject to measurement. Measuring if the required degree of quality has been achieved necessitates pre-defined quality

requirements. Quality requirements are those characteristics of a system that are likely to produce the desired outcome, or quality objectives. Activities focussing on fulfilling quality requirements while conducting given tasks or responsibilities are called quality control. Activities focussing on providing confidence that quality requirements will be fulfilled are called quality assurance.

The overall quality objectives for pharmacovigilance systems are provided under I.B.4..

Specific quality objectives and quality requirements for the specific structures and processes of the pharmacovigilance systems are provided in each Module of GVP as appropriate.

The quality system shall be an integral part of the pharmacovigilance system [IM Art 12, Art 17(1)] and consists of its own structures and processes. It shall cover organisational structure, responsibilities, procedures, processes and resources of the pharmacovigilance system and shall include appropriate resource management, compliance management and record management [IM Art 10(2)].

I.B.3. Quality cycle

The quality system shall follow a cycle of:

- establishing structures and planning integrated and consistent processes (quality planning);
- carrying out the tasks and responsibilities (quality control);
- monitoring and evaluating how effectively the structures and processes have been established and how effectively the processes are being carried out (quality assurance); and
- correcting and improving the structures and processes and the carrying out of those processes as necessary (quality improvements) [IM Art 10(3)].

I.B.4. Overall quality objectives for pharmacovigilance

The overall quality objectives of a pharmacovigilance system are:

- complying with the legal requirements for pharmacovigilance tasks and responsibilities;
- preventing harm from adverse reactions in humans arising from the use of authorised medicinal products within or outside the terms of marketing authorisation or from occupational exposure;
- promoting the safe and effective use of medicinal products, in particular through providing timely information about the safety of medicinal products to patients, healthcare professionals and the public; and
- contributing to the protection of patients' and public health.

I.B.5. Principles for good pharmacovigilance practices

With the aim to fulfil the overall quality objectives in I.B.4., the following principles should guide the design of all structures and processes as well as the conduct of all tasks and responsibilities:

- The needs of patients, healthcare professionals and the public in relation to the safety of medicines should be met.
- Higher management should provide leadership in the implementation of the quality system and motivation for all staff members in relation to the quality objectives.

- All persons within the organisation should be involved in and support the pharmacovigilance system on the basis of task ownership and responsibility.
- All persons involved with the organisation should engage in continuous quality improvement following the quality cycle in I.B.3..
- Resources and tasks should be organised as structures and processes in such a way as to support the proactive, risk-proportionate, continuous and integrated conduct of pharmacovigilance.
- All available evidence on the risk-benefit balance of medicinal products should be sought and all relevant aspects, which could impact on the risk-benefit balance and the use of a product, should be considered for decision-making.
- Good cooperation should be fostered between marketing authorisation holders, competent authorities, public health organisations, patients, healthcare professionals, learned societies and other relevant bodies in accordance with the applicable legal provisions.

I.B.6. Responsibilities for the quality system within an organisation

The quality system shall be recognised as being the responsibility of all persons involved in the relevant processes of an organisation, so as to ensure a systematic approach towards quality and the implementation and maintenance of the quality system [IM Art 12, Art 17(1)]. A sufficient number of competent and appropriately qualified and trained personnel shall be available for the performance of pharmacovigilance activities [IM Art 13(1), Art 18(1)]. Their responsibility should include adherence to the principles defined in I.B.5..

For marketing authorisation holders, the systematic approach shall be ensured by management [IM Art 12].

For the purpose of a systematic approach towards quality in accordance with the quality cycle (see I.B.3.), managerial staff should be responsible for:

- ensuring that the organisation documents the quality system as described in I.B.11.;
- ensuring that changes to the pharmacovigilance system and its quality system are adequately controlled and clearly documented;
- ensuring that adequate resources are available and that training is provided (see I.B.7.);
- ensuring that suitable and sufficient premises, facilities and equipment are available (see I.B.8.);
- reviewing the pharmacovigilance system including its quality system at regular intervals to verify its effectiveness (see I.B.12.) and introducing corrective and preventive measures if deemed necessary;
- ensuring that mechanisms exist for timely and effective communication, including escalation processes of safety concerns relating to medicinal products within an organisation;
- investigating any concern arising within an organisation regarding suspected non-adherence to the requirements of the quality and pharmacovigilance systems and taking corrective, preventive and escalation action as necessary;
- ensuring that audits are performed (see I.B.12.).

In relation to the management responsibilities described above, higher management within an organisation should provide leadership through:

- motivating all staff members, based on shared values, trust and freedom to speak and act with responsibility and through recognition of staff members' contributions within the organisation; and
- assigning roles, responsibilities and authorities to staff members according to their competencies and communicating and implementing these throughout the organisation.

I.B.7. Training of personnel for pharmacovigilance

Achieving the required quality for the conduct of pharmacovigilance processes and their outcomes is intrinsically linked with the availability of a sufficient number of competent and appropriately qualified and trained personnel (see I.B.6.).

All personnel involved in the performance of pharmacovigilance activities shall be provided with appropriate instructions on critical processes, including business continuity [IM Art 13(3), Art 18(3)]. They shall receive initial and continued training in order to maintain and develop their competencies in accordance with training plans (see I.B.11.) [IM Art 13(2), Art 18(2)]. For marketing authorisation holders, initial and continued training relates specifically also to the roles and responsibilities of personnel [IM Art 13(2)].

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

There should be a process in place within the organisation to check that training results in the appropriate levels of understanding and conduct of pharmacovigilance activities for the assigned tasks and responsibilities, and in line with agreed professional development plans.

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

I.B.8. Facilities and equipment for pharmacovigilance

Achieving the required quality for the conduct of pharmacovigilance processes and their outcomes is also intrinsically linked with the appropriate control of facilities and equipment used to support the processes.

Facilities and equipment should be located, designed, constructed, adapted and maintained to suit their intended purpose in line with the quality objectives for pharmacovigilance (see I.B.4.). Facilities, equipment and their functionalities which are critical for the conduct of pharmacovigilance (see I.B.11.3.) should be subject to appropriate checks, qualification and/or validation activities to prove their suitability for the intended purpose. Documented risk assessment should be used to determine the scope and extent of checks, qualification or validation activities. This risk management approach should be applied throughout the lifecycle of the facilities and equipment taking into account such factors as impact on patient safety and data quality as well as the complexity of the concerned facilities and equipment.

I.B.9. Specific quality system processes

I.B.9.1. Compliance management by marketing authorisation holders

For the purpose of compliance management, marketing authorisation holders shall have specific quality system processes in place in order to ensure that:

- pharmacovigilance data are continuously monitored, that options for risk minimisation and prevention are considered and that appropriate measures are taken as necessary, whereby the marketing authorisation holder shall follow-up such information, as appropriate, independent of its source, including information spontaneously reported by patients or healthcare professionals, published in medical literature, or arising in the context of a post-authorisation study [IM Art 14(1)(a)] (see Modules VI, VIII and XII);
- all information on the risks of medicinal products as regards patients' or public health, including information on adverse reactions in human beings arising from use of the product within or outside the terms of the marketing authorisation or associated with occupational exposure, is evaluated scientifically [IM Art 14(1)(b)] (see Modules VI and XII);
- data on serious and non-serious adverse reactions are submitted to the EudraVigilance database in accordance with the legal requirements, whereby the marketing authorisation holder shall establish operating procedures in order to obtain accurate and verifiable data and processes that ensure the quality, integrity and completeness of the information submitted, including processes to avoid duplicate submissions and to validate signals [IM Art 14(1)(c)] (see Modules VI and IX) ;
- effective communication with competent authorities, including communication on new or changed risks (see Module XII), the pharmacovigilance system master file (see Module II), risk management systems (see Module V), risk minimisations measures (see Modules V and XVI), periodic safety update reports (see Module VII), corrective and preventive actions (see Modules II, III and IV) and post-authorisation safety studies (see Module VIII) [IM Art 14(1)(d];
- product information is kept up-to-date with the current scientific knowledge [IM Art 14(1)(e)] (see Module XII);
- appropriate communication of relevant safety information to healthcare professionals and patients (see Module XV) [IM Art 14(1)(f)].

I.B.9.2. Compliance management by competent authorities

For the purpose of compliance management, competent authorities shall have specific quality system processes in place in order to:

- ensure the evaluation of the quality, including completeness, of pharmacovigilance data submitted [IM Art 19(1)(a)];
- ensure the assessment of pharmacovigilance data and its processing in accordance with the legal timelines [IM Art 19(1)(b)];
- guarantee independence in the performance of pharmacovigilance activities [IM Art 19(1)(c)];
- ensure effective communication with patients, healthcare professionals, marketing authorisation holders and the general public [IM Art 19(1)(d)];
- conduct inspections, including pre-authorisation inspections [IM Art 19(1)(f)].

Independence in the performance of pharmacovigilance activities is interpreted in the sense that all regulatory decisions on medicinal products should be taken in the sole interest of patients' and public health.

I.B.10. Record management

As part of the quality system, a record management system shall be maintained for all documents used for pharmacovigilance activities, ensuring their retrievability as well as traceability of how safety concerns have been investigated, the timelines for these investigations and how and when decisions have been taken [IM Art 15(1), Art 20(1)].

The record management system should support:

- the management of the quality of pharmacovigilance data, including their completeness, accuracy and integrity;
- effective internal and external communication; and
- the retention of documents relating to the pharmacovigilance systems and the conduct of pharmacovigilance for individual medicinal products, in accordance with the applicable retention periods.

In addition, marketing authorisation holders shall record, handle and store all pharmacovigilance information so as to allow accurate reporting, interpretation and verification of the information [IM Art 15(1)]. Further, marketing authorisation holders shall establish mechanisms enabling the traceability and follow-up of adverse reaction reports while complying with data protection legislation [IM Art 15(1)].

As part of a record management system, measures shall be taken at each stage in the storage and processing of pharmacovigilance data to ensure data security and confidentiality. This shall involve strict limitation of access to documents and to databases to authorised personnel respecting the medical and administrative confidentiality of the data. In this context, it shall be ensured that the fundamental right to personal data protection is fully and effectively guaranteed in all pharmacovigilance activities in conformity with legal provisions. The processing of personal data may be justified if identifiable health data are processed only when necessary and only when the parties involved assess the necessity at every stage of the pharmacovigilance process [IM Art 15(2), Art 20(2)].

There should be appropriate structures and processes in place to ensure that pharmacovigilance data and records are protected from destruction.

I.B.11. Documentation of the quality system

All elements, requirements and provisions adopted for the quality system shall be documented in a systematic and orderly manner in the form of written policies and procedures, such as quality plans, quality manuals and quality records [IM Art 10(4)].

A quality plan documents the setting of quality objectives and sets out the processes to be implemented to achieve them. A procedure is a specified way to carry out a process and may take the format of a standard operating procedure and other work instruction or quality manual. A quality manual documents the scope of the quality system, the processes of the quality system and the interaction between the two. A quality record is a document stating results achieved or providing evidence of activities performed.

In order to have a systematic approach, the organisation should define in advance:

- quality objectives specific to their organisations in accordance with the overall quality objectives provided under I.B.4. and the structure- and process-specific quality objectives in accordance with each Module of GVP; and
- methods for monitoring the effectiveness of the pharmacovigilance system (see I.B.12.).

The quality system shall be documented by:

- documents on organisational structures and assignments of tasks to personnel (see I.B.11.1. and I.B.11.2.);
- training plans and records [IM Art 13(1)] (see I.B.7.)[IM Art 13(2), Art 18(2)];
- instructions for the compliance management processes (see I.B.9.) [IM Art 14(1), Art 19(1)];
- appropriate instructions on critical pharmacovigilance processes, including business continuity (see I.B.11.3.) [IM Art 13(3), Art 18(3)];
- performance indicators where they are used to continuously monitor the good performance of pharmacovigilance activities [IM Art 11(1)];
- reports of quality audits and follow-audits, including their dates and results [IM Art 16(2), Art 21(1)].

Training plans and records shall be kept and made available for audit and inspection [IM Art 13(2), Art 18(2)].

It is recommended that the documentation of the quality system also includes:

- the methods of monitoring the efficient operation of the quality system and, in particular, its ability to fulfil the quality objectives;
- records created as a result of pharmacovigilance processes which demonstrate that all steps required by the defined procedures have been taken;
- records and reports relating to the facilities and equipment including functionality checks, qualification and validation activities which demonstrate that all steps required by the applicable requirements, protocols and procedures have been taken;
- records to demonstrate that deficiencies and deviations from the established quality system are monitored, that corrective and preventive actions have been taken, that solutions have been applied to deviations or deficiencies and that the effectiveness of the actions taken has been verified.

I.B.11.1. Additional quality system documentation by marketing authorisation holders

In addition to the quality system documentation in accordance with I.B.11., marketing authorisation holders shall document:

- their resource management [IM Art 13(4)];
- job descriptions defining the duties of the managerial and supervisory staff [IM Art 13(1)];
- an organisation chart defining the hierarchical relationships of managerial and supervisory staff [IM Art 13(1)]; and

- their arrangements for record management for the documentation of the pharmacovigilance system including its quality system as well as for pharmacovigilance data and documents relating to authorised medicinal products, including the location of the records [Art 15(5)].

It is recommended that the documentation of the quality system additionally includes the organisational structures and assignments of tasks, responsibilities and authorities to all personnel.

For the requirements of documenting the quality system in the pharmacovigilance system master file (PSMF) or its annexes, see Module II.

I.B.11.2. Additional quality system documentation by competent authorities

In addition to the quality system documentation in accordance with I.B.11., competent authorities shall clearly determine, and to the extent necessary, keep accessible the organisational structures, assignment of tasks and responsibilities as well as contact points to facilitate interaction between competent authorities, marketing authorisation holders and persons reporting information on the risks of medicinal products as regards patients' or public health [IM Art 18(1)].

It is recommended that the documentation of the quality system additionally includes the organisational structures and assignments of tasks, responsibilities and authorities to all personnel.

I.B.11.3. Critical pharmacovigilance processes

Appropriate instructions, including those ensuring business continuity, shall be available for critical pharmacovigilance processes [IM Art 13(3), Art 18(3)].

Pharmacovigilance processes considered as critical include:

- continuous safety profile monitoring and benefit-risk evaluation of authorised medicinal products;
- establishing, assessing and implementing risk management systems and evaluating the effectiveness of risk minimisation;
- collection, processing, management, quality control, follow-up for missing information, coding, classification, duplicate detection, evaluation and timely electronic transmission of individual case safety reports (ICSRs) from any source;
- detection, investigation and evaluation of signals;
- scheduling, preparation (including data evaluation and quality control), submission and assessment of periodic safety update reports;
- meeting commitments and responding to requests from competent authorities, including provision of correct and complete information;
- interaction between the pharmacovigilance and quality defect systems;
- communication about safety concerns between marketing authorisation holders and competent authorities, in particular notifying changes to the risk-benefit balance of medicinal products;
- communicating information to patients and healthcare professionals about changes to the risk-benefit balance of products for the aim of safe and effective use of medicinal products;
- keeping product information up-to-date with the current scientific knowledge, including the conclusions of the assessment and recommendations from the applicable competent authority;

- implementation of variations to marketing authorisations for safety reasons according to the urgency required.

Business continuity plans should include:

- provisions for events that could severely impact on the organisation's staff and infrastructure in general or on the structures and processes for pharmacovigilance in particular; and
- back-up systems for urgent exchange of information within an organisation, amongst organisations sharing pharmacovgilance tasks or between marketing authorisation holders and competent authorities.

I.B.12. Monitoring of the performance and effectiveness of the pharmacovigilance system and its quality system

Processes to monitor the performance and effectiveness of a pharmacovigilance system and its quality system should include:

- reviews of the systems by those responsible for management;
- audits;
- compliance monitoring;
- inspections;
- evaluating the effectiveness of actions taken with medicinal products for the purpose of minimising risks and supporting their safe and effective use in patients.

For monitoring purposes, the respective organisation should define in advance indicators demonstrating the effectiveness in operating the pharmacovigilance system in relation to the quality requirements. The quality requirements for each pharmacovigilance process are provided in each Module of GVP as appropriate.

The requirements for the quality system itself are laid out in this Module and its effectiveness should be monitored by managerial staff, who should review the documentation of the quality system (see I.B.11.) at regular intervals. Pre-defined programmes for the review of the system should therefore be in place. Reviews of the quality system should include the review of standard operating procedures and work instructions, deviations from the established quality system, audit and inspections reports as well as the use of the indicators referred to above.

Risk-based audits of the quality system shall be performed at regular intervals to assure that it complies with the established quality requirements and to determine its effectiveness [IM Art 16(1), Art 21(1)]. Audits of the quality system should include audit of the pharmacovigilance system which is covered by the quality system. The audits shall be conducted by individuals who have no direct involvement in or responsibility for the matters or processes being audited [IM Art 16(1), Art 21(1)]. The methods and processes for the audits are described in Module IV. In relation to the pharmacovigilance system of a marketing authorisation holder, a report shall be made of the results of each quality audit and any follow-up audits carried out and be reviewed by the management responsible for the matters audited [IM Art 16(2)].

As a consequence of the monitoring of the performance and effectiveness of a pharmacovigilance system and its quality system (including the use of audits), corrective and preventive measures should be taken when deemed necessary. In particular as a consequence of audits, corrective action(s), including a follow-up audit of deficient matters, shall be taken when necessary [IM Art 16(2), Art 21(2)].

Additionally, the competent authorities should have in place arrangements for monitoring the compliance of marketing authorisations holders with legally required pharmacovigilance tasks and responsibilities. They shall further ensure compliance with the legal requirements by means of conducting inspections of marketing authorisation holders [DIR Art 111(1)] (see Module III). Guidance on compliance monitoring for each pharmacovigilance process is provided in each Module of GVP as appropriate.

Requirements and methods for evaluating the effectiveness of actions taken upon medicinal products for the purpose of minimising risks and supporting the safe and effective use of medicines in patients are described in Module XVI.

I.B.13. Preparedness planning for pharmacovigilance in public health emergencies

Any pharmacovigilance system should be adaptable to public health emergencies and preparedness plans should be developed as the need arises. For preparedness planning in the EU, see I.C.4..

I.C. Operation of the EU network

I.C.1. Overall pharmacovigilance responsibilities of the applicant and marketing authorisation holder in the EU

The marketing authorisation holder in the EU is responsible for the respective pharmacovigilance tasks and responsibilities laid down in Directive 2001/83/EC, Regulation (EC) No 726/2004 and the Commission Implementing Regulation on the Performance of Pharmacovigilance Activities Provided for in Regulation (EC) No 726/2004 and Directive 2001/83/EC in order to assure responsibility and liability for its authorised medicinal products and to ensure that appropriate action can be taken, when necessary.

For this purpose, the marketing authorisation holder shall operate a pharmacovigilance system [DIR 104(1)] and shall establish and follow a quality system that is adequate and effective for performing its pharmacovigilance activities [IM Art 10(1)].

There may be circumstances where a marketing authorisation holder may establish more than one pharmacovigilance system, e.g. specific systems for particular types of products (e.g. vaccines, products available without medical prescription).

A description of the pharmacovigilance system shall be developed by the applicant for a marketing authorisation in the format of a pharmacovigilance system master file (PSMF) and be maintained by the marketing authorisation holder after the marketing authorisation has been granted (see Module II). The applicant or the marketing authorisation holder is also responsible for developing and maintaining risk management systems (see Module V).

Guidance on the structures and processes on how the marketing authorisation holder should conduct the pharmacovigilance tasks and responsibilities is provided in GVP.

I.C.1.1. Responsibilities of the marketing authorisation holder in relation to the qualified person responsible for pharmacovigilance in the EU

As part of the pharmacovigilance system, the marketing authorisation holder shall have permanently and continuously at its disposal an appropriately qualified person responsible for pharmacovigilance in the EU (QPPV) [DIR Art 104(3)(a)].

The marketing authorisation holder shall submit the name and contact details of the QPPV to the competent authorities in Member States and the Agency [DIR Art 104(3) last paragraph]. Changes to this information should be submitted in accordance with Regulation (EC) No 1234/2008 on variations to the terms of marketing authorisation and the Communication from the Commission - Guideline on the Details of the Various Categories of Variations to the Terms of Marketing Authorisations for Medicinal Products for Human Use and Veterinary Medicinal Products[1].

The duties of the QPPV shall be defined in a job description [IM Art 13(1)].

Information relating to the QPPV shall be included in the pharmacovigilance systems master file (PSMF) [IM Art 4(1)(a)] (see Module II).

Each pharmacovigilance system can have only one QPPV. A QPPV may be employed by more than one marketing authorisation holder, for a shared or for separate pharmacovigilance systems or may fulfil the role of QPPV for more than one pharmacovigilance system of the same marketing authorisation holder, provided that the QPPV is able to fulfil all obligations.

In addition to the QPPV, competent authorities in Member States are legally provided with the option to request the nomination of a pharmacovigilance contact person at national level reporting to the QPPV. Reporting in this context relates to pharmacovigilance tasks and responsibilities and not necessarily to line management. A contact person at national level may also act as the QPPV.

The marketing authorisation holder shall ensure that the QPPV has sufficient authority to influence the performance of the pharmacovigilance activities and the quality system [IM Art 13(1)]. The marketing authorisation holder should therefore ensure that the QPPV has access to the pharmacovigilance system master file (PSMF) as well as authority over it and is notified of any changes to it. The authority over the pharmacovigilance system and the PSMF should allow the QPPV to implement changes to the system and to provide input into risk management plans (see Module V) as well as into the preparation of regulatory action in response to emerging safety concerns (see Module XII).

Overall, the marketing authorisation holder should ensure that structures and processes are in place, so that the QPPV can fulfil the responsibilities listed in I.C.1.3.. In order to do this, the marketing authorisation holder should ensure that mechanisms are in place so that the QPPV receives all relevant information and that the QPPV can access all information the QPPV considers relevant, in particular on:

- emerging safety concerns and any other information relating to the benefit-risk evaluation of the medicinal products covered by the pharmacovigilance system;
- ongoing or completed clinical trials and other studies the marketing authorisation holder is aware of and which may be relevant to the safety of the medicinal products;
- information from sources other than from the specific marketing authorisation holder, e.g. from those with whom the marketing authorisation holder has contractual arrangements; and
- the procedures relevant to pharmacovigilance which the marketing authorisation holder has in place at every level in order to ensure consistency and compliance across the organisation.

The outcome of the regular reviews of the quality system referred to in I.B.6. and I.B.12. and the measures introduced should be communicated by the managerial staff to the QPPV.

Compliance information should be provided to the QPPV on a periodic basis. Such information may also be used to provide assurance to the QPPV that commitments in the framework of risk management plans and post-authorisation safety systems are being adhered to.

[1] See Volume 2C of the Rules Governing Medicinal Products in the EU; http://ec.europa.eu/health/documents/eudralex/vol-2/index_en.htm

The managerial staff should also inform the QPPV of scheduled pharmacovigilance audits. The QPPV should be able to trigger an audit where appropriate. The managerial staff should provide the QPPV with a copy of the corrective and preventive action plan following each audit, so that the QPPV can assure that appropriate corrective actions are implemented.

In particular with regard to its adverse reaction database (or other system to collate adverse reaction reports), the marketing authorisation holder should implement a procedure to ensure that the QPPV is able to obtain information from the database, for example, to respond to urgent requests for information from the competent authorities or the Agency, at any time. If this procedure requires the involvement of other personnel, for example database specialists, then this should be taken into account in the arrangements made by the marketing authorisation holder for supporting the QPPV outside of normal working hours.

When a marketing authorisation holder intends to expand its product portfolio, for example, by acquisition of another company or by purchasing individual products from another marketing authorisation holder, the QPPV should be notified early in the due diligence process in order that the potential impact on the pharmacovigilance system can be assessed and the system be adapted accordingly. The QPPV may also have a role in determining what pharmacovigilance data should be requested from the other company, either pre- or post-acquisition. In this situation, the QPPV should be made aware of the sections of the contractual arrangements that relate to responsibilities for pharmacovigilance activities and safety data exchange and have the authority to request amendments.

I.C.1.2. Qualifications of the qualified person responsible for pharmacovigilance in the EU

It shall be ensured that the QPPV has acquired adequate theoretical and practical knowledge for the performance of pharmacovigilance activities [IM Art 13(1)]. The QPPV should have skills for the management of pharmacovigilance systems as well as expertise or access to expertise in relevant areas such as medicine, pharmaceutical sciences as well as epidemiology and biostatistics. If the QPPV has not completed basic medical training in accordance with Article 24 of Directive 2005/36/EC, access to a medically trained person (i.e. in accordance with Article 24 of Directive 2005/36/EC) shall be available [IM Art 13(1)] and this access should be documented in the pharmacovigilance system master file (PSMF) (see Module II).

The expectation is that the applicant or marketing authorisation holder will assess the qualification of the QPPV prior to appointment by, for example, reviewing university qualifications, knowledge of EU pharmacovigilance requirements and experience in pharmacovigilance.

The applicant or marketing authorisation holder should provide the QPPV with training in relation to its pharmacovigilance system, which is appropriate for the role prior to the QPPV taking up the position and which is appropriately documented.

I.C.1.3. Role of the qualified person responsible for pharmacovigilance in the EU

The qualified person responsible for pharmacovigilance in the EU (QPPV) is a natural person.

The QPPV appointed by the marketing authorisation holder shall be appropriately qualified (see I.C.1.2.) and shall be at the marketing authorisation holder's disposal permanently and continuously (see I.C.1.1.) [DIR Art 104 (3)(a)]. The QPPV shall reside and operate in the EU [DIR Art 104 (3) last paragraph]. Following European Economic Area (EEA) agreements, the QPPV may also reside and operate in Norway, Iceland or Liechtenstein. Back-up procedures in the case of absence of the QPPV

should be in place, accessible through the QPPV's contact details. The QPPV is expected to ensure that the back-up person has all necessary information to fulfil the role.

The QPPV shall be responsible for the establishment and maintenance of the marketing authorisation holder's pharmacovigilance system [DIR Art 104 (3) last paragraph] and therefore shall have sufficient authority to influence the performance of the pharmacovigilance activities and the quality system [IM Art 13(1)] and to promote, maintain and improve compliance with the legal requirements [IM Art 1(a)(1)]. Hence, the QPPV should have authority and responsibility over the pharmacovigilance system master file (PSMF) (see Module II), in order to promote, maintain and improve compliance with the EU legal requirements.

In relation to the medicinal products covered by the pharmacovigilance system, specific additional responsibilities of the QPPV should include:

- having an overview of medicinal product safety profiles and any emerging safety concerns;
- having awareness of any conditions or obligations adopted as part of the marketing authorisation and other commitments relating to safety or the safe use of the product;
- having awareness of risk minimisation measures;
- being involved in the review and sign-off of protocols of post-authorisation safety studies;
- having awareness of post-authorisation safety studies requested by a competent authority including the results of such studies;
- providing input into risk management plans;
- ensuring conduct of pharmacovigilance and submission of all pharmacovigilance-related documents in accordance with the legal requirements and GVP;
- ensuring the necessary quality, including the correctness and completeness, of pharmacovigilance data submitted to the competent authorities in Members States and the Agency;
- ensuring a full and prompt response to any request from the competent authorities in Members States and from the Agency for the provision of additional information necessary for the evaluation of the benefits and risks of a medicinal product;
- providing any other information relevant to the benefit-risk evaluation to the competent authorities in Members States and the Agency;
- providing input into the preparation of regulatory action in response to emerging safety concerns (e.g. variations, urgent safety restrictions, and communication to patients and healthcare professionals);
- acting as a single pharmacovigilance contact point for the competent authorities and the Agency on a 24-hour basis and also as a contact point for pharmacovigilance inspections.

This responsibility for the pharmacovigilance system means that the QPPV has oversight over the functioning of the system in all relevant aspects, including its quality system (e.g. standard operating procedures, contractual arrangements, database operations, compliance data regarding quality, completeness and timeliness of expedited reporting and submission of periodic update reports, audit reports and training of personnel in relation to pharmacovigilance). Specifically for the adverse reaction database, if applicable, the QPPV should be aware of the validation status of the database, including any failures that occurred during validation and the corrective actions that have been taken to address the failures. The QPPV should also be informed of significant changes that are made to the database (e.g. changes that could have an impact on pharmacovigilance activities).

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

I.C.1.4. Specific quality system processes of the marketing authorisation holder in the EU

In applying the requirements set out in I.B.9.1. in the EU, the marketing authorisation holder shall put in place the following additional specific quality system processes for ensuring:

- the submission of adverse reaction data to EudraVigilance within the legal timelines [IM Art 14(c)];
- monitoring the use of terminology, with data entry staff being instructed in the use of terminology and their proficiency verified [IM Art 15(3)];
- the retention of essential documents describing the pharmacovigilance system as long as the system described in the pharmacovigilance system master file (PSMF) exists and for at least further 5 years after it has ceased to exist [IM Art 15(4)];
- the retention of pharmacovigilance data and documents relating to authorised medicinal products as long as the marketing authorisation exists and for at least further 10 years after the marketing authorisation has ceased to exist [IM Art 15(4)];
- that the product information is kept up-to-date with current scientific knowledge, including the assessments and recommendations made public via the European medicines web-portal. To this end, the marketing authorisation holder shall continuously check the European medicines web-portal for any relevant updates, including consultations and notifications of procedures [IM Art 14(1)(e)].

The retention periods above apply unless longer periods are required by applicable regulatory requirements or national law [IM Art 15(4)].

During the retention period, retrievability of the documents should be ensured.

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

Documents transferred in situations where the business of the marketing authorisation holder is taken over by another organisation should be complete.

In addition to the quality system documentation in accordance with I.B.11. and I.B.11.1, the marketing authorisation holders shall define the duties of the QPPV in a job description [IM Art 13(1)].

I.C.1.5. Quality system requirements for pharmacovigilance tasks delegated by the marketing authorisation holder

The marketing authorisation holder may transfer any or all of the pharmacovigilance tasks, including the role of the QPPV, to another organisation or person (where the same requirements apply to a person as for an organisation). The ultimate responsibility for the fulfilment of all pharmacovigilance tasks and responsibilities and the quality and integrity of the pharmacovigilance system, however, always remains with the marketing authorisation holder.

Where certain tasks of the pharmacovigilance activities are delegated by a marketing authorisation holder to another organisation, the marketing authorisation holder shall retain responsibility that an effective quality system is applied in relation to those tasks [IM Art 14(2)]. All guidance provided in GVP is also applicable to the other organisation to which the tasks have been delegated.

When delegating tasks to another organisation, the marketing authorisation holder should ensure that detailed, up-to-date and clearly documented contractual arrangements between the marketing authorisation holder and the other organisation are in place, describing arrangements for delegation and the responsibilities of each party. A description of the delegated activities and/or services shall be included in pharmacovigilance system master file (PSMF) [IM Art 4(1)(f)] and a list of the contractual arrangements be included in an annex to the PSMF [Art 4(2)(b)] (see Module II). The other organisation may be subject to inspection at the discretion of the competent or supervisory authority in the relevant Member State.

Contractual arrangements should be prepared with the aim of enabling compliance with the legal requirements by each party involved. When preparing contractual arrangements, the marketing authorisation holder should include sufficiently detailed descriptions of the delegated tasks, the related interactions and data exchange, together with, for example, agreed definitions, tools, assignments and timelines. The contractual arrangements should also contain clear information on the practical management of pharmacovigilance as well as related processes, including those for the maintenance of pharmacovigilance databases. Further, they should indicate which processes are in place for checking whether the agreed arrangements are being adhered to on an ongoing basis. In this respect, regular audits of the other organisation by the marketing authorisation holder or introduction of other methods of control and assessment are recommended.

With respect to centrally authorised products, contractual arrangements between different marketing authorisation holders should also be in place in relation to separately authorised medicinal products with the application of Article 82(1) of Regulation (EC) No 726/2004 in order to ensure conduct of pharmacovigilance on the basis of complete worldwide data sets. Article 82(1) of Regulation (EC) No 726/2004 states that the use of two or more commercial designs for a given medicinal product covered by a single marketing authorisation is not prohibited by the Regulation. Such products are called duplicates.

I.C.2. Overall pharmacovigilance responsibilities within the EU regulatory network

The competent authorities in Member States and the Agency are responsible for the respective pharmacovigilance tasks and responsibilities imposed on them by Directive 2001/83/EC, Regulation (EC) No 726/2004 and the Commission Implementing Regulation on the Performance of Pharmacovigilance Activities Provided for in Regulation (EC) No 726/2004 and Directive 2001/83/EC in order to ensure that appropriate action can be taken, when necessary.

For this purpose each competent authority in a Member State as well as the Agency shall operate a pharmacovigilance system [DIR 101(1)] and shall establish and follow an adequate and effective quality system for performing their pharmacovigilance activities [IM Art 10(1)].

The Agency and the Member States shall cooperate to continuously develop pharmacovigilance systems capable of achieving high standards of public health protection for all medicinal products, regardless of the routes of marketing authorisation, including the use of collaborative approaches, to maximise use of resources available within the EU [REG Art 28e].

The requirement in I.B.11.2 according to which competent authorities shall clearly determine, and to the extent necessary, keep accessible the organisational structures, assignment of tasks and

responsibilities as well as contact points, relates to the interaction between competent authorities in Member States, the Agency, the European Commission, marketing authorisation holders and persons reporting information on the risks of medicinal products [IM Art 18(1)].

To facilitate the interaction between competent authorities in Member States, the Agency, marketing authorisation holders and person reporting pharmacovigilance information, contact points shall be established [IM Art 18(1)].

Guidance on the structures and processes to enable the competent authorities in Member States and the Agency to conduct the pharmacovigilance tasks and responsibilities is provided in the respective Modules of GVP.

I.C.2.1. Role of the competent authorities in Member States

Each Member State shall designate a competent authority for the performance of pharmacovigilance [DIR Art 101(3)]. This authority is usually the same as the competent authority responsible for granting national marketing authorisations.

Each competent authority in a Member State must operate a pharmacovigilance system for the fulfilment of their pharmacovigilance tasks and their participation in EU pharmacovigilance activities [DIR Art 101(1)]. In this context, the competent authority in a Member State is responsible for the safety monitoring of each medicinal product, independent of its route of authorisation, in the territory of that Member State. In particular, the competent authority in a Member State shall monitor data originated in their territory [IM Art 25(3)].

For nationally authorised products, including those authorised through the mutual recognition or the decentralised procedure, the competent authority in a Member State is responsible for granting, varying, suspending and revoking a marketing authorisation. The pharmacovigilance tasks and responsibilities of competent authorities in Member States for each process in relation to such products, are detailed in the respective Modules of GVP.

For products authorised through the mutual recognition or the decentralised procedure, one Member States acts as the Reference Member State. For practical reasons, the competent authority of the Reference Member State should coordinate communication with the marketing authorisation holder on pharmacovigilance matters and monitor the compliance of the marketing authorisation holder with legal pharmacovigilance requirements. These arrangements do not replace the legal responsibilities of the marketing authorisation holder with respect to individual competent authorities and the Agency.

Nationally authorised products, including those authorised through the mutual recognition or the decentralised procedure, may become subject to regulatory procedures at EU level on pharmacovigilance grounds. If a Commission Decision for a nationally authorised product exists as an outcome of such a regulatory procedure, the competent authorities in Member States are responsible for the implementation of the Commission Decision and also for its follow-up, unless exceptionally further action by the Agency and Commission has been foreseen in the Commission Decision reflecting the outcome of the regulatory procedure (see Module XIV).

The pharmacovigilance tasks and responsibilities of competent authorities in Member States in relation to centrally authorised products are also detailed in the respective Modules of GVP. They include the collaboration in signal detection (see Module IX) and implementation of Commission Decisions regarding risk management of centrally authorised products addressed to Member States (see Module V). Where urgent action is essential to protect human health or the environment, the competent authority in a Member State, on its own initiative or at the European Commission's request, may suspend the use of a centrally authorised product in its territory (see Modules XII and XIV).

Competent authorities in Member States are responsible for pharmacovigilance inspections of organisations in their territory in relation to medicinal products. This is independent of the route of marketing authorisation as well as which competent authority granted the marketing authorisation for the respective medicinal product (see Module III).

In relation to the various aspects of the role described above, each Member State's competent authority should ensure that all pharmacovigilance data are shared between competent authorities in other Member States, the European Commission and the Agency for each process in accordance with the legislation and the guidance in the respective GVP Modules.

I.C.2.2. Role of the European Commission

The European Commission is the competent authority for medicinal products authorised through the centralised procedure and is responsible for granting, varying, suspending and revoking their marketing authorisations by adoption of Commission Decisions on the basis of Opinions adopted by the Committee for Medicinal Products for Human Use (CHMP) (see I.C.2.3.3.).

Further, the European Commission adopts Commission Decisions in relation to nationally authorised medicinal products subject to regulatory procedures at EU level, including on pharmacovigilance grounds. The European Commission may also initiate such procedures (see Module XIV).

I.C.2.3. Role of the European Medicines Agency

I.C.2.3.1. General role of the Agency and the role of the Agency's secretariat

The role of the Agency is to coordinate the monitoring of medicinal products for human use authorised in the EU and to provide advice on the measures necessary to ensure their safe and effective use, in particular, by coordinating the evaluation and implementation of legal pharmacovigilance requirements and the monitoring of such implementation. The tools established and maintained by the Agency for the coordination are presented in the GVP Modules for each process.

The Agency provides coordination and technical, scientific and administrative support to the Pharmacovigilance Risk Assessment Committee (PRAC) (see I.C.2.3.2.) and the Committee for Medicinal Products for Human Use (CHMP) (see I.C.2.3.3.) and coordination and technical and administrative support to the Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh), as well as coordination between the committees and the CMDh (see I.C.2.3.4.).

Pharmacovigilance for centrally authorised products is conducted by the Agency with the involvement of the Rapporteur, the PRAC and the CHMP. The Agency should take the lead for communicating with the marketing authorisation holders of centrally authorised products. The respective responsibilities for each pharmacovigilance process are detailed in the GVP Modules.

For nationally authorised products, the Agency coordinates regulatory procedures at EU level on pharmacovigilance grounds through providing support to the CMDh and CHMP (see Module XIV).

The Agency also cooperates with other EU bodies as necessary.

Specific pharmacovigilance tasks of the Agency include:

- running the EudraVigilance database [REG Art 57(d)];
- monitoring selected medical literature for reports of suspected adverse reactions to medicinal products containing certain active substances [REG Art 27] (see Module VI);

- running processes for the EU coordination of the assessment of periodic safety update reports (see Module VII) and oversight of post-authorisation safety studies (see Module VIII);
- tasks relating to signal detection [REG Art 28a(1)(c), IM Art 22-28] (see Module IX);
- tracking of follow-up of safety concerns and other pharmacovigilance matters at EU level (see Module XII);
- assisting Member States with the rapid communication of information on safety concerns to healthcare professionals and coordinating the safety announcements of the national competent authorities [REG Art 57(e)] (see Module XV);
- distributing appropriate information on safety concerns to the general public, in particular by setting up and maintaining the European medicines web-portal [REG Art 57(f)] (see Module XV);
- coordination of safety announcements between national competent authorities for active substances contained in medicinal products authorised in more than one Member State, including providing timetables for the publication of information [DIR 106a(3)] (see Module XV);

and specifically in relation to centrally authorised products:

- assessing updates to risk management systems [REG Art 28a(1)(b)] (see Module V);
- monitoring the outcome of risk minimisation measures [REG Art 28a(1)(a)] (see Module XVI).

I.C.2.3.2. Role of the Pharmacovigilance Risk Assessment Committee (PRAC)

The Pharmacovigilance Risk Assessment Committee (PRAC) is responsible for providing recommendations to the Committee for Medicinal Products for Human Use (CHMP) and the Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh) on any question relating to pharmacovigilance activities in respect of medicinal products for human use and on risk management systems, including the monitoring of the effectiveness of those risk management systems [REG Art 56(1)(aa)]. Details on the responsibilities for each process are presented in the respective GVP Modules. The Mandate and Rules of Procedure of the PRAC are published on the Agency's website[2].

I.C.2.3.3. Role of the Committee for Medicinal Products for Human Use (CHMP)

The Committee for Medicinal Products for Human Use (CHMP) is responsible for evaluating applications and formulating Opinions serving as a basis for granting, varying, suspending or withdrawing marketing authorisations for centrally authorised products. The CHMP also prepares Opinions on safety concerns emerging after a marketing authorisation has been granted for centrally authorised products or, for nationally authorised products, including those through the mutual recognition or the decentralised procedure, in the framework of Union procedures in which at least one centrally authorised product is involved (see Module XIV), procedures for the assessment of periodic safety update reports (PSURs) (see Module VII) and procedures for post-authorisation safety studies (see Module VIII). For questions related to pharmacovigilance activities and risk management systems, the CHMP relies on the recommendations from the Pharmacovigilance Risk Assessment Committee (PRAC). The specific responsibilities of each party for each pharmacovigilance process are described in the GVP Modules. The Rules of Procedure of the CHMP are published on the Agency's website[3].

[2] http://www.ema.europa.eu
[3] http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000095.jsp&murl=menus/about_us/about_us.jsp&mid=WC0b01ac0580028c7a

I.C.2.3.4. Role of the Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh)

The Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh) is responsible for examining any question relating to marketing authorisations for medicinal products authorised through the mutual recognition or the decentralised procedure and questions on the variation of marketing authorisations granted by the Member States as well as questions arising for nationally authorised products from assessments of periodic safety update reports (see Module VII), post-authorisation safety studies (see Module VIII) and during the Union procedures. The CMDh shall reach a position on the basis of a PRAC recommendation in safety referral and Urgent Union procedures when only nationally authorised products, including those authorised through the mutual recognition or the decentralised procedure, are involved [DIR Art 107k](see Module XIV). The responsibilities of the CMDh for each pharmacovigilance process are described in the respective GVP Modules. The Rules of Procedure of the CMDh and the Functions and Tasks for CMDh are published on the HMA website[4].

I.C.2.4. Specific quality system processes of the quality systems of competent authorities in Member States and the Agency

In applying the requirements set out in I.B.9.2. in the EU, the competent authorities in Member States and the Agency shall put in place the following additional specific quality system processes for:

- monitoring and validating the use of terminology, either systematically or by regular random evaluation, with data entry staff being instructed in the use of terminology and their proficiency verified [IM Art 20(4)];
- assessing and processing pharmacovigilance data in accordance with the timelines provided by legislation [IM Art 19(1)(b)];
- ensuring effective communication within the EU regulatory network [IM Art 19(1)(d)];
- guaranteeing that, unless urgent public announcements are required for the protection of public health, competent authorities in Member States and the Agency inform each other and the European Commission not less than 24 hours prior to public announcements relating to information on pharmacovigilance concerns to allow for coordination of the content of safety announcements in case of a medicinal product or an active substance contained in medicinal products authorised in more than one Member State (see Modules XII and XV) [IM Art 19(1)(e)];
- ensuring that essential documents describing their pharmacovigilance systems are kept as long as the system exists and for at least further 5 years after they ceased to exist [IM Art 20(5)];
- ensuring that pharmacovigilance data and documents relating to authorised medicinal products are retained as long as the marketing authorisation exists or for at least further 10 years after the marketing authorisation has ceased to exist [IM Art 20(5)].

In this context, documents relating to a medicinal product include documents of a reference medicinal product where this is applicable.

The retention periods above apply unless longer periods are required by applicable regulatory requirements or national law [IM Art 20(5)].

During the retention periods referred to above, retrievability of the documents should be ensured.

[4] http://www.hma.eu/205.html

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

In addition to the above, competent authorities in Member States shall have specific quality system processes for collecting and recording all suspected adverse reactions that occur in their territory (see Module VI) [IM Art 19(2)].

In addition to the above, the Agency shall have specific quality system processes for literature monitoring in accordance with Article 27 of Regulation (EC) No 726/2004 (see Module VI) [IM Art 19(3)].

In addition to the quality system documentation in accordance with I.B.11. and I.B.11.2., competent authorities in Member States and the Agency shall clearly determine, and to the extent necessary, keep accessible the organisational structures, assignment of tasks and responsibilities and contact points to facilitate interaction between competent authorities in Member States, the Agency, marketing authorisation holders and persons reporting information on the risks of medicinal products as regards patients' or public health [IM Art 18(1)].

Quality audits of the Member States' and Agency 's pharmacovigilance systems (see I.B.12.) shall be performed according to a common methodology [IM Art 21(1)]. The results of audits shall be reported by competent authorities in Member States in accordance with Article 101(2) of Directive 2001/83/EC and by the Agency in accordance with Article 28f of Regulation (EC) No 726/2004 [IM Art 21(3)] (see Module IV).

I.C.2.5. Quality system requirements for pharmacovigilance tasks delegated by competent authorities in Member States

A competent authority in a Member State may delegate any pharmacovigilance task to another Member State subject to a written agreement of the latter Member State [DIR Art 103]. The written agreement should be reflected by exchange of letters, defining the scope of the delegation.

A competent authority in a Member State may transfer any or all of the pharmacovigilance tasks to another organisation, but the ultimate responsibility for the fulfilment of all pharmacovigilance tasks and responsibilities and the quality and integrity of the pharmacovigilance system always remains with the competent authority in a Member State.

Where tasks are delegated to another organisation, the competent authority in a Member State should ensure that the tasks are subject to a quality system compliant with the legal requirements applicable to their own organisation.

I.C.2.6. Transparency of the quality system of the EU regulatory network

The European Commission (EC) shall publish every three years a report on the performance of pharmacovigilance based on the reports submitted by the competent authorities in Member States (first EC report due on 21 July 2015) and by the Agency (first EC report due on 2 January 2014) on the results of their regular pharmacovigilance system audits (see Module IV) [DIR Art 101(2), Art 108b, REG Art 28f, Art 29].

I.C.3. Data protection in the EU

For the record management described in I.B.10., EU provisions for the protection of personal data, such as Directive 95/46/EC, apply [IM Art 15(2), Art 20(2)].

In addition, pharmacovigilance data processed by the Agency shall be subject to Regulation (EC) No 45/2001 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data [IM Art 20(4)].

I.C.4. Preparedness planning in the EU for pharmacovigilance in public health emergencies

The pharmacovigilance systems of marketing authorisation holders, competent authorities in Member States and the Agency should be adaptable to public health emergencies. Preparedness plans should be developed as the need arises (see I.B.13.).

A public health emergency is a public health threat duly recognised either by the World Health Organization (WHO) or the Community in the framework of Decision No. 2119/98/EC of the European Parliament and of the Council.

Pharmacovigilance requirements for public health emergencies should be considered by the competent authorities in Member States, the European Commission and the Agency on a case-by-case basis and appropriately notified to marketing authorisation holders and the public. The Agency publishes its notifications on the Agency's website.