The EU Pharmacovigilance System

3

This chapter introduces pharmacovigilance in the European Union (EU); due to the multi-level nature of the EU, pharmacovigilance is described both at the European and the national level. Both levels are linked through multiple inter-institutional relations and, in combination, the European and national levels make up the EU's pharmacovigilance system.

A simplified visual representation of the system is shown in Fig. 3.1, illustrating the main connections of the most important players of the system discussed in this chapter. Depending on the regulatory procedure and the life cycle of the medicine, these actors are connected in varying networks.

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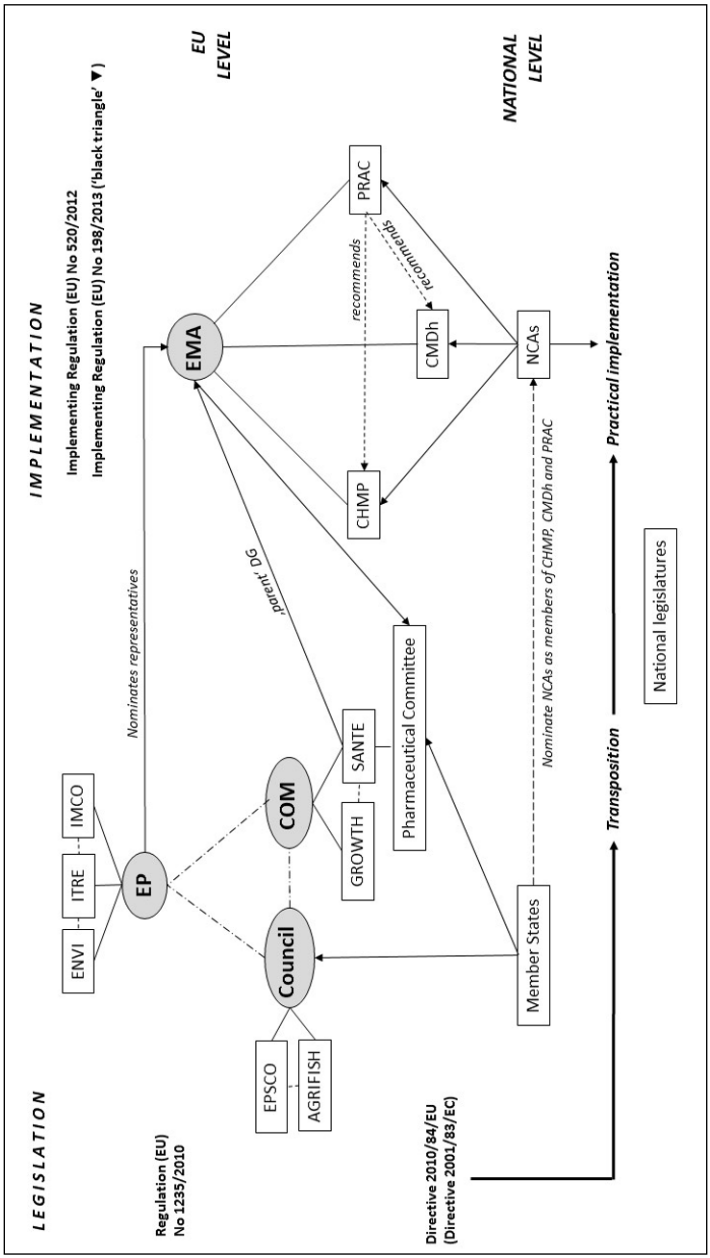
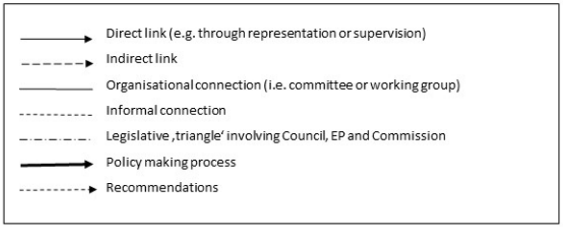


Fig. 3.1 The pharmacovigilance network on the European level

Abbreviations

- **EP** **European Parliament**
  - ENVI Environment, Public Health and Food Safety
  - ITRE Industry, Research and Energy
  - IMCO Internal Market and Consumer Protection
- **Council**
  - EPSCO Employment, Social Policy, Health and Consumer Affairs
  - AGRIFISH Agriculture and Fisheries
- **COM** **European Commission**
  - SANTE DG Health and Food Safety (‚parent' DG)
  - GROWTH DG Internal Market, Industry, Entrepreneurship and SMEs
- **EMA** **European Medicines Agency**
  - CMHP Committee for Medicinal Products for Human Use
  - PRAC Pharmacovigilance Risk Assessment Committee
  - CMDh Co-ordination Group for Mutual Recognition and Decentralised procedures – Human
- **NCAs** **National Competent Authorities**



In the past, EU pharmaceuticals regulation only included the efficient authorisation of medicinal products. The regulation continues to serves a dual objective, namely the free movement of medicinal products in the EU and the protection of public health. Marketing authorisation can be obtained through a decentralised procedure by Member States or in a centralised procedure by the European Medicines Agency (EMA).[3] During the course of these procedures, medicinal products undergo risk assessment to test their quality, safety and efficacy. Thus, the assessment of risks and benefits before marketing is the cornerstone of authorisation.

Hence, the emphasis was traditionally put on the risk assessment before marketing, and the continuous assessment of authorised products used to be neglected (see Abraham and Lewis 2000). In the 1990s, this began to change when the EU passed a series of legislations dedicated to pharmacovigilance. Today, EU regulation covers the whole life cycle of medicinal products: drug development and manufacturing, clinical trials, marketing authorisation and pharmacovigilance (see Scholz 2015). This includes not only the spontaneous reporting of adverse drug reactions (ADRs), but also systematic reporting through risk management plans (Moore and Begaud 2010).

In this chapter, we give an overview of the pharmacovigilance system in the EU. First, we introduce the main legislative and executive institutions in the EU, namely the European Commission (Commission), the Council of Ministers (Council) and the European Parliament (EP) as well as the actors responsible for implementing pharmacovigilance policy. We then give a brief overview of pharmacovigilance legislative developments, notably Directive 2001/83/EC and the subsequent reform through Directive 2010/84/EU and conclude by presenting the most important changes brought about by the reform Directive and discussing the ADR provisions in the Directive.

3 Pharmaceuticals authorised through the centralised procedure can be marketed throughout the entire EU. For some medicinal products, such as those derived from biotechnology processes, the centralised procedure is mandatory. For medicinal products outside of the scope of the centralised procedure, pharmaceutical companies can opt for decentralised procedures, whereby these products can then only be marketed in a few Member States.

3.1 EU Institutions and Pharmacovigilance Actors

For a better understanding of the EU system of pharmacovigilance, it is important to distinguish between two sets of actors. The first set of actors comprises the EU institutions which pass pharmaceutical regulations and set the policy framework for pharmacovigilance. The Commission, the Council and the EP are the institutions with legislative and executive tasks in the EU. Together, they can be conceived of as a legislative triangle.

The European Commission performs a variety of functions and is the institution which is supposed to represent European interests. Varying policy issues are dealt with by so-called Directorate Generals (DGs); DG Health and Food Safety (SANTE) handles the pharmaceuticals regulation. DG SANTE is also the "parent" DG of EMA, which means that representatives of this DG are important points of reference for the day-to-day activities of the agency. However, representatives of both DGs are members of the EMA Management Board which is the main steering body of the agency. Among its many functions, the initiation of legislation is a key task of the Commission. In addition, EU legislation can only be adopted based on proposals by the Commission. Regarding its executive functions, the Commission is supported by an expert group, the Pharmaceutical Committee, which was established in 1975; this committee consists of representatives of the Member States and EMA. Its main tasks relate to the implementation of pharmaceuticals legislation and particularly Directive 2001/83/EC, and it is supervised by DG SANTE.

The Council of Ministers has primarily legislative functions and is the institution which represents the Member States. Depending on the policy subject at stake, the Council convenes and negotiates in varying configurations with different national ministers present at meetings. Regarding the revision of Directive 2001/83/EC, the Council convened in two different configurations: the Employment, Social Policy, Health and Consumer Affairs (EPSCO) group as well as Agriculture and Fisheries (AGRIFISH). Together with the EP, the Council passes legislative acts such as the aforementioned pharmacovigilance legislation.

The European Parliament (EP) representing the people of Europe is, together with the Council, the legislature of the EU. Legislative proposals initiated by the Commission are dealt with by one or more parliamentary committees. Directive 2001/83/EC, for instance, was handled by the Environment, Public Health and Food Safety (ENVI) committee with two other committees providing further opinions on the legislative proposal.[4] The EP is entitled to send two representatives to the

4 Internal Market and Consumer Protection (IMCO) and Industry, Research and Energy (ITRE).

EMA Management Board. Usually, scientific experts are sent to represent the EP. As part of the legislature, the EP also plays an important role regarding budgetary oversight and control of EMA. However, the EP plays a limited role regarding the practical implementation of pharmacovigilance policies.

The second set of actors is responsible for implementing pharmacovigilance policy at the EU and national levels, based on the legislation passed by the EU institutions. As will be explained in Chapter 4, national legislatures have to transpose EU directives into national law. In addition, implementing legislation is adopted by the EU at the EU level. Yet this set also comprises the EMA, the national competent authorities, and pharmaceutical companies and other stakeholders.

The main task of the European Medicines Agency (EMA) is to coordinate the evaluation of medicinal products and to advise the EU institutions and the Member States on any issue relating to pharmaceuticals regulation. Since it began operating in 1995, the agency has become a central actor regarding various aspects of pharmaceuticals regulation and has a crucial role in providing the infrastructure for EU pharmacovigilance. For its scientific assessments, the agency relies on a number of committees, including the Committee for Medicinal Products for Human Use (CMPH), which issues recommendations to the Commission regarding the centralised authorisation procedure. In addition, since 2012, the Pharmacovigilance Risk Assessment Committee (PRAC) assesses and monitors the safety of medicinal products. PRAC issues opinions and recommendations about centralised and decentralised authorisation procedures.

The EMA's EudraVigilance database is an internet-based information system where reports of suspected adverse reactions are collected. It is legally required that ADRs occurring in the EU must be included in the database by the Member States and marketing authorisation holders.

Furthermore, the pharmacovigilance system of the EU relies heavily on the Member States and their national competent authorities. As can be seen in Fig. 3.1, Member State actors are involved in almost all pharmacovigilance activities. Drawing on national expertise and resources, the national competent authorities are at the centre of pharmacovigilance implementation and enforcement activities (see European Commission 2016a). These authorities are not only at the centre of practical implementation at the national level, but also represented at the EU level in the various EMA committees dealing with authorisation and pharmacovigilance.

At the EU level, the Co-ordination Group for Mutual Recognition and Decentralised Procedures (CMDh) is in charge of decision-making when medicinal products are marketed through the decentralised procedure. In addition, the Strengthening Collaboration for Operating Pharmacovigilance in Europe (SCOPE) Joint Action initiative supports the operation of EU pharmacovigilance

by delivering training, tools and templates to support best practices (European Commission 2015). The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) also aims to improve the science and practice of pharmacovigilance.

At the national level, the national competent authorities are the central bodies supervising the collection of information about suspected ADRs submitted by healthcare professionals, marketing authorisation holders and patients. By doing so, these authorities provide for resources, knowledge and expertise regarding causality assessment and signal detection (European Commission 2016b).

Pharmacovigilance is based on the EMA's close connections with the pharmaceutical industry (see Wiktorwowicz et al. 2012) and include risk management plans and post-authorisation safety studies which are important elements of the authorisation procedure and product surveillance after marketing. Regarding pharmacovigilance, marketing authorisation holders have to comply with a number of stipulations laid down in EU legislation. For instance, they have to appoint a responsible person in charge of pharmacovigilance who serves as the main contact point for regulatory authorities. In addition, marketing authorisation holders are also legally obligated to report ADRs.

Finally, some additional stakeholders are significant in the proper implementation of the EU pharmacovigilance legislation.

Regulation (EC) No 726/2004 explicitly mentions the participation of stakeholders in EU pharmaceuticals regulation. In the framework of EMA, a network of European patient and consumer organisations as well as a Patients' and Consumers' Working Party have been established.

The reform of the pharmacovigilance system by Directive 2010/84/EU has introduced the possibility for patients to report suspected side effects directly, either to the national competent authorities or the marketing authorisation holders. As explained below, the Directive also aims to simplify and facilitate individual reporting by patients.

3.2 Legislative Developments

Although pharmaceuticals regulation in the EU dates back to the 1960s, pharmacovigilance was neglected until the 1990s, when the EU began to pass a series of legislations dedicated to pharmacovigilance (see Abraham and Lewis 2000). Already, Directive 93/39/EEC stated that Member States must establish pharmacovigilance systems and encourage healthcare professionals to report ADRs. Marketing au-

thorisation holders were also requested to appoint a qualified person responsible for pharmacovigilance.

At that time, EU pharmaceuticals regulation consisted of various pieces of legislation that were interconnected in complex ways. Hence, with a view to simplification, the various pieces were codified in a single text, leading to Directive 2001/83/EC. This Directive is the legal basis of the EU legislation on pharmacovigilance and has been amended 10 times. Compared with Directive 93/39/EEC, the requirements for Member States and marketing authorisation holders to set up and maintain pharmacovigilance systems did not change substantially. Hence, the relevant provisions, introduced in essence in the early 1990s, were merely consolidated in Title IX of Directive 2001/83/EC which was dedicated to pharmacovigilance.

In 2006, the Commission initiated a public consultation with a view to reform the pharmacovigilance system. The goals stated by the Commission included clarifying stakeholder responsibility, ensuring the involvement of varying stakeholders (including healthcare professionals and stakeholders), and clarifying duplications and responsibilities. The public consultation was accompanied by an assessment report, which found "disparities and inconsistencies resulting from a non-optimal compliance of both national law and practice with the EC regulations" (European Commission 2006).

Based on the consultation, the Commission issued a legislative proposal in December 2008. In this proposal, the Commission explained that it was aiming at the following objectives: better protection of public health, proper internal market functioning, and a simplification of the current rules and procedures (European Commission 2008).

The proposal was then discussed by the Member States in the respective Council working group throughout the next year. After beginning preparatory talks in late 2009, the Council and the EP engaged in a series of informal meetings (so-called trialogues) with a view to ensuring the quick adoption of the Directive (Council of the European Union 2010). In September 2010, the EP passed Directive 2010/84/EU with a majority, thus concluding the legislative procedure.

Additional legislation is important to maintain the EU pharmacovigilance system. While Directive 2010/84/EU covers pharmacovigilance regarding decentralised authorisation, Regulation (EU) No 1235/2010 covers the centralised authorisation procedure. Operational aspects for these legislations were adopted through Commission Implementing Regulation No 520/2012. For instance, the regulation stipulates that individual case safety reports concerning biologicals must contain the batch numbers. Furthermore, Implementing Regulation No 198/2013 introduces the "black triangle" (▼). The recital of the Regulation is as follows:

Some medicinal products for human use are subject to additional monitoring because of their specific safety profile, including medicinal products with a new active substance, biological medicinal products and products for which post-authorisation data are required (see also James 2014). As the Commission explains on its website, the black triangle (▼) aims to highlight to patients the importance of reporting suspected side effects stemming from the medicines they are taking, improving their safety.

A product which is subject to additional monitoring is included in an online up-to-date list which is publicly available on the EMA homepage. All products on this list must display an inverted black triangle symbol (▼) and include a standardised explanatory sentence in both their summary of product characteristics and in the package leaflet (European Commission 2014: 15). This additional list was launched by the EMA in April 2013 and draws attention to and increases transparency for patients in order to encourage the reporting of suspected adverse effects.

Finally, Regulation (EU) No 1027/2012 and Directive 2012/26/EU amended the legislation due to the withdrawal of a medicine called Mediator (benfluorex) (cf. Box 5.4 in Chapter 5.4). These amendments require a marketing authorisation holder to notify the competent authority of that Member State when a medicine is withdrawn from the market.

Complementing legislation, the EU system of pharmacovigilance comprises a set of technical principles described in respective guidance documents. These principles ensure that the requirements of pharmaceuticals regulation are applied in a uniform manner. These principles include good manufacturing practice (GMP), good distribution practice (GDP) and good pharmacovigilance practice (GVP). The GVP guidance documents aim to facilitate pharmacovigilance in the EU and cover medicines authorised through both the centralised and the decentralised procedure.

3.3 The Pharmacovigilance Reform: Directive 2010/84/EU and Article 102

The aim of the new pharmacovigilance Directive 2010/84/EU is "to improve the operation of Union law on the pharmacovigilance of medicinal products" (Recital 3). In summary, the new legislation brought about the following changes to the EU system of pharmacovigilance:

- Extension of the scope for additional monitoring (e.g. of biologicals)
- Competent authorities may require additional monitoring for products that are subject to studies after marketing
- Medicinal products subject to additional monitoring are required to be identified by the black triangle (▼) and to be included in a publicly available list
- Patients are encouraged to report ADRs directly to the competent authorities
- ADRs are extended to include medication errors and overdose

The reform of the EU pharmacovigilance system aimed at facilitating ADR reporting with a specific emphasis on the identification of biologicals (European Commission 2007). To this end, the Commission enhanced Articles 101 and 102 which laid down provisions in this respect (Box 3.1). In these articles, three elements can be identified: 1) Member States must take measures to encourage healthcare professionals to report ADRs; 2) Member States may impose specific requirements to do so; 3) Member States must establish a pharmacovigilance system. The revision of these provisions through Directive 2010/84/EU mainly extends the latter element, whereas the former two elements were retained as described.

The extension of these provisions proved to be a controversial subject with Member States. Based on the initial provision of the Commission proposal, Article 102 alone sparked 14 comments, with nine Member States requesting changes (Council of European Union 2009). Throughout the legislative procedure, the exact wording of these provisions was subject to much discussion among Member States.

In total, the parliamentary committees dealing with the Commission proposal tabled more than 70 amendments. Throughout the informal trialogue meetings with the Council, a compromise text was developed which did not retain all amendments in the proposed wording, but which maintained key stipulations included by the EP.

Pharmacovigilance provisions in Article 102 of Directive 2010/84/EU were adopted as follows (Box 3.1):

The Member States shall:

a. take all appropriate measures to encourage patients, doctors, pharmacists and other healthcare professionals to report suspected adverse reactions to the national competent authority; for these tasks, organisations representing consumers, patients and healthcare professionals may be involved as appropriate;

In the Commission proposal and in the Council discussions, patients were not originally included. The inclusion of patients in this stipulation is due to the amendment of the EP which was eventually retained in the compromise text; in the literature,

there is no agreement on whether patients' inclusion improves pharmacovigilance by extending the scope of actors reporting ADRs or whether such inclusion leads to information overload and a diminution of the quality of the reports (see e.g. de Langen et al. 2008). The inclusion of consumer and patients' organisations is also due to the parliamentary amendment; their role, however, was diminished in the compromise text.

b. facilitate patient reporting through the provision of alternative reporting formats in addition to web-based formats;

In connection with the general inclusion of patients in ADR reporting in point a), this stipulation was also included due to parliamentary amendment.

c. take all appropriate measures to obtain accurate and verifiable data for the scientific evaluation of suspected adverse reaction reports;

d. ensure that the public is given important information on pharmacovigilance concerns relating to the use of a medicinal product in a timely manner through publication on the web portal and through other means of publicly available information as necessary;

The wording of point c) was subject to much discussion among Member States. In contrast to the original stipulation of the Commission proposal, the Council added the provision relating pharmacovigilance to scientific evaluation. This was absent in the proposal which only spoke of "high quality information". A parliamentary amendment extending this "quality" stipulation to not only reports but also databases was not included in the compromise text. However, the stipulation on risk communication due to ADR reporting in point d) was included by the EP and retained in the final text.

e. ensure, through the methods for collecting information and where necessary through the follow-up of suspected adverse reaction reports, that all appropriate measures are taken to identify clearly any biological medicinal product prescribed, dispensed, or sold in their territory which is the subject of a suspected adverse reaction report, with due regard to the name of the medicinal product, in accordance with Article 1(20), and the batch number;

Based on the Commission proposal, the exact wording regarding the identification of biologicals was also the subject of much discussion among the Member States.

However, a substantial amendment was made by the EP. First, the EP extended the scope of the stipulation to suspected adverse reaction reports. Second, in contrast to the original stipulation, the EP explicitly included the name of the medicinal product, the international non-proprietary name, the name of the marketing authorisation holder and the batch number. The members of the respective committee justified the amendment with the concern that the Commission proposal lacked details on how to identify biologicals. According to this view, a lack of details would lead to different national pharmacovigilance approaches for medicinal products subject to centralised authorisation. In the compromise text, the elements of reporting, including the batch number, were maintained. In addition, the wording of the stipulation was softened and the references to EudraVigilance and standard reporting formats were deleted.

f. take the necessary measures to ensure that a marketing authorisation holder who fails to discharge the obligations laid down in this Title is subject to effective, proportionate and dissuasive penalties.

For the purposes of point (a) and (e) of the first paragraph the Member States may impose specific obligations on doctors, pharmacists and other healthcare professionals.

In the original stipulation of the Commission proposal and the various versions of the Council discussions, the imposition of specific obligations were only foreseen for point (a), hence the general reporting requirements. In its amendment, the EP extended the possibility of imposing obligations to point (e), hence the reporting details regarding biologicals. The Commission also included the following stipulation: "Reporting of suspected adverse reactions due to medication errors should be on a 'no blame' basis, and should be legally privileged" (European Parliament 2010).[5]

Relating to the justification regarding the specific elements of reporting in point (e), the EP reasoned that this amendment would not only increase the clarity of the provision, but would also strengthen the legal basis for requesting from health professionals requirements regarding the identification of biologicals. While the extension of specific obligations to point (e) was retained, the latter amendment was not included in the compromise text.

5 During the parliamentary committee discussions, an additional amendment was proposed whereupon medication errors could have been reported anonymously. However, this amendment was not included by the responsible rapporteur in the EP report on amendments.

Tab. 3.1 Development of Article 102 of Directive 2010/84/EU

Commission proposal 12/2008	**Council 03/2010**	**Council 04/2010**	**EP amendments 06/2010**	**Council 06/2010**
The Member States shall:				
(1) take all appropriate measures to encourage doctors, pharmacists and other healthcare professionals to report suspected adverse reactions to the national competent authority or the marketing authorisation holder;	(1) take all appropriate measures to encourage doctors, pharmacists and other healthcare professionals to report suspected adverse reactions to the national competent authority or the marketing authorisation holder;	(1) take all appropriate measures to encourage doctors, pharmacists and other healthcare professionals to report suspected adverse reactions to the national competent authority or the marketing authorisation holder;	(1) take all appropriate measures to encourage patients, doctors, pharmacists and other healthcare professionals to report suspected adverse reactions to the national competent authority; *or the marketing authorisation holder; these measures shall include training for health professionals and a public information campaign for patients. Patients' and consumer organisations shall be involved in providing information to patients and in developing public information campaigns in cooperation with regulatory bodies.* *(1a) facilitate direct patient reporting through the provision of alternative reporting formats in addition to web-based formats;*	(1) take all appropriate measures to encourage <u>patients</u>, doctors, pharmacists and other healthcare professionals to report suspected adverse reactions to the national competent authority or the marketing authorisation holder; <u>for these tasks, consumer organisations, patients organisations and healthcare professionals organisations</u> scientific societies may be involved as appropriate. <u>(1a) facilitate patient reporting through the provision of alternative reporting formats in addition to web-based formats;</u>

Commission proposal 12/2008	Council 03/2010	Council 04/2010	EP amendments 06/2010	Council 06/2010
(2) ensure that adverse reaction reports contain the highest-quality information possible;	(2) ensure that all appropriate measures are taken to obtain accurate and verifiable data for the scientific evaluation of adverse reaction reports and that they contain the highest-quality information possible	(2) ensure that all appropriate measures are taken to obtain accurate and verifiable data for the scientific evaluation of adverse reaction reports and that they contain the highest-quality information possible	(2) ensure that adverse reaction reports *and databases* contain the highest-quality information possible;	(2) ensure that all appropriate measures are taken to obtain accurate and verifiable data for the scientific evaluation of suspected adverse reaction reports and that they contain the highest-quality information possible;
			(2a) ensure that the public is given important information in good time on pharmacovigilance concerns relating to the use of a medicinal product through publication on the web portal and through other means of public information as necessary;	(2a) ensure that the public is given important information in good time on pharmacovigilance concerns relating to the use of a medicinal product through publication on the web portal and through other means of public information as necessary;

Commission proposal 12/2008	Council 03/2010	Council 04/2010	EP amendments 06/2010	Council 06/2010
(3) through the methods of collecting information and where necessary through the follow-up of adverse reaction reports, ensure that any biological medicinal product prescribed, dispensed or sold in their territory which is the subject of an adverse reaction report is identifiable;	(3) through the methods of collecting information and where necessary through the follow-up of adverse reaction reports, ensure that any biological medicinal product prescribed, dispensed or sold in their territory which is the subject of an adverse reaction report is identifiable;	(3) make sure, through the methods of collecting information and where necessary through the follow-up of adverse reaction reports, ensure that all appropriate measures are taken to identify any biological medicinal product prescribed, dispensed or sold in their territory which is the subject of an adverse reaction report is identifiable;	(3) ensure that any biological medicinal product prescribed, dispensed or sold in their territory which is the subject of *a report on a suspected* adverse reaction is identifiable *by, where available, the name of the MAH, the INN, the name of the medicinal product and the batch number, using the standard forms and procedures developed in accordance with Article 25(1) of the Regulation (EC) No 726/2004 and taking due account of the developments within the EudraVigilance system.*[1]	(3) make sure, through the methods of collecting information and where necessary through the follow-up of suspected adverse reaction reports, ensure that all appropriate measures are taken to identify any biological medicinal product prescribed, dispensed or sold in their territory which is the subject of an suspected adverse reaction report is identifiable; with due regard to the name of the medicinal product (in accordance with Article 1(20)) and the batch number.
(4) take the necessary measures to ensure that a marketing authorisation holder who fails to discharge the obligations laid down in this Title is subject to effective, proportionate and dissuasive penalties.	(4) take the necessary measures to ensure that a marketing authorisation holder who fails to discharge the obligations laid down in this Title is subject to effective, proportionate and dissuasive penalties.	(4) take the necessary measures to ensure that a marketing authorisation holder who fails to discharge the obligations laid down in this Title is subject to effective, proportionate and dissuasive penalties.	(4) take the necessary measures to ensure that a marketing authorisation holder who fails to discharge the obligations laid down in this Title is subject to effective, proportionate and dissuasive penalties.	(4) take the necessary measures to ensure that a marketing authorisation holder who fails to discharge the obligations laid down in this Title is subject to effective, proportionate and dissuasive penalties.

Commission proposal 12/2008	Council 03/2010	Council 04/2010	EP amendments 06/2010	Council 06/2010
For the purposes of point (1) of the first paragraph the Member States may impose specific requirements on doctors, pharmacists and other healthcare professionals respecting the reporting of suspected serious or unexpected adverse reactions.	For the purposes of point (1) of the first paragraph the Member States may impose specific requirements on doctors, pharmacists and other health-care professionals respecting the reporting of suspected serious or unexpected adverse reactions.	For the purposes of point (1) of the first paragraph the Member States may impose specific requirements on doctors, pharmacists and other healthcare professionals respecting the reporting of suspected serious or unexpected adverse reactions.	For the purposes of *points (1) and (3)* of the first paragraph the Member States may impose specific requirements on doctors, pharmacists and other healthcare professionals. *Reporting of suspected adverse reactions due to medication errors should be on a 'no blame' basis, and should be legally privileged* [not to be used in court proceedings].	For the purposes of point (1) and (3) of the first paragraph the Member States may impose specific requirements on doctors, pharmacists and other healthcare professionals respecting the reporting of suspected serious or unexpected adverse reactions.

[1] Justification: The present proposal lacks details about how to clearly identify biological medicinal products and creates the risk of 27 different approaches (…) providing a number of identifiers for biologicals and is linked to an amendment to Article 25 of the Regulation (EC) No 726/2004, which assigns to the European Medicines Agency (EMA) the task of developing forms for adverse event reporting for biological medicinal products (…) ensure that a legal basis is created to request from healthcare professionals and pharmacists requirements relating specifically to the identification of biologics.

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