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ΕΙΔΙΚΟ ΑΡΘΡΟ

Η φαρμακοεπαγρύπνηση στην Ευρωπαική Ένωση

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ΠΕΡΙΛΗΨΗ

Το παρόν άρθρο στοχεύει στη διερεύνηση της φαρμακοεπαγρύπνησης στην Ευρωπαϊκή Ένωση (ΕΕ) και στον εντοπισμό των ρυθμιστικών πλαισίων στα κράτη μέλη. Στην ΕΕ, η Ευρωπαϊκή Επιτροπή, ο Ευρωπαϊκός Οργανισμός Φαρμάκων και οι αρχές κάθε κράτους μέλους είναι υπεύθυνες για τη φαρμακοεπαγρύπνηση. Η φαρμακοεπαγρύπνηση απαιτεί στενή και αποτελεσματική συνεργασία μεταξύ των κρατών μελών της ΕΕ, της φαρμακοβιομηχανίας, των μονάδων υγείας και ακαδημαϊκών μονάδων και μεμονωμένων επαγγελματιών υγείας και ασθενών. Εντός της ΕΕ, τα φάρμακα υπόκεινται σε αυστηρούς ελέγχους και αξιολόγηση της ποιότητας, της αποτελεσματικότητας και της ασφάλειάς τους πριν εγκριθούν είτε σε επίπεδο κράτους μέλους είτε σε επίπεδο ΕΕ. Μόλις κυκλοφορήσουν στην αγορά συνεχίζουν να παρακολουθούνται από δραστηριότητες φαρμακοεπαγρύπνησης. Το νομικό πλαίσιο της ΕΕ για τη φαρμακοεπαγρύπνηση ορίζεται στον κανονισμό αριθ. 726/20041 και στην οδηγία 2001/83/ΕΚ2. Αυτό αναθεωρήθηκε το 2010 (Οδηγία 2010/84/ΕΕ) και το 2012 (Οδηγία 2012/26/ΕΕ). Διαφορές στα ρυθμιστικά πλαίσια φαρμακοεπαγρύπνησης μεταξύ των κρατών μελών της ΕΕ εντοπίζονται στα συστήματα φαρμακοεπαγρύπνησης, στην εποπτεία, στην αναφορά ανεπιθύμητων ενεργειών φαρμάκων από επαγγελματίες υγείας και ασθενείς και στην ιχνηλασιμότητα των βιολογικών φαρμάκων. Αυτές οι διαφορές οδηγούν σε υποαναφορά ανεπιθύμητων ενεργειών, κυρίως λόγω έλλειψης ενημέρωσης και εκπαίδευσης, συνεργασίας μεταξύ των σχετικών ενδιαφερομένων και πολυπλοκότητας της αναφοράς ανεπιθύμητων ενεργειών. Επομένως, υπάρχουν προκλήσεις που πρέπει να αντιμετωπιστούν (κατάρτιση επαγγελματιών υγείας, επάρκεια οικονομικών πόρων, βελτίωση συστημάτων αναφοράς ανεπιθύμητων συμβάντων), προς όφελος των ευρωπαίων πολιτών.

Λέξεις Κλειδιά: Φαρμακοεπαγρύπνηση, κανονισμοί, Ευρωπαϊκή Ένωση, φάρμακα, ανεπιθύμητες ενέργειες.

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SPECIAL ARTICLE

Pharmacovigilance in the European Union

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ABSTRACT

The present article aims to examine pharmacovigilance in the European Union (EU) and to identify the regulatory frameworks across its Member States. In the EU, responsibility for pharmacovigilance lies with the European Commission, the European Medicines Agency, and the authorities of each Member State. Effective pharmacovigilance requires close collaboration among EU Member States, the pharmaceutical industry, health and academic institutions, individual health professionals, and patients. Medicines within the EU undergo rigorous testing and evaluation of their quality, efficacy, and safety before approval at either the Member State or EU level. After market authorization, medicines continue to be closely monitored through ongoing pharmacovigilance activities. The legal framework for pharmacovigilance in the EU is established by Regulation No 726/2004 and Directive 2001/83/EC, which were revised respectively in 2010 (Directive 2010/84/EU) and 2012 (Directive 2012/26/EU). Variations in pharmacovigilance regulatory frameworks among Member States are observed in their pharmacovigilance systems, supervisory mechanisms, reporting of adverse drug events by healthcare professionals and patients, and in the traceability of biological medicines. These differences often result in under-reporting of adverse events, primarily due to lack of awareness and training, insufficient collaboration among stakeholders, and the complexity of adverse event reporting processes. Consequently, several challenges must be addressed, including enhanced training for healthcare professionals, adequate financial resources, and improved adverse event reporting systems, ultimately benefiting European citizens.

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Keywords: Pharmacovigilance, regulations, European Union, drugs, adverse events.

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INTRODUCTION

Healthcare is a cornerstone of a modern welfare state, and the safety of pharmaceutical products is a critical aspect of safeguarding public health. Adverse drug reactions (ADRs) are an inherent risk of medicinal therapy, and identifying and managing these risks is essential for patient safety.[1] By the time a medicine is approved for use, clinical trials will have demonstrated that its benefits outweigh its risks. However, real-world use introduces variability—patients may differ from those in clinical trials in terms of age, comorbidities, or concurrent medications. Some side effects may only become apparent post-marketing, once a drug is used by a broader population. It is therefore vital that ADRs are detected early, reported accurately and promptly, and linked to the correct medicinal product using essential details such as the product name, manufacturer, and batch number.[2]

Pharmacovigilance, as defined by the World Health Organization (WHO), is "the science and activities concerned with the detection, evaluation, understanding and prevention of adverse reactions or any other problem related to medicines."[3] It encompasses both the obligations of marketing authorisation holders to monitor safety and the role of regulatory authorities in assessing and acting on safety data. These obligations include timely transmission of pharmacovigilance data, notification of emerging risks, and possible initiation of further studies.[4] The overarching goals of pharmacovigilance are to improve patient and public health outcomes by evaluating medicines' benefits and risks, supporting rational and cost-effective use, and fostering communication and education among stakeholders.[3,5]

A broad range of actors contribute to pharmacovigilance: regulatory agencies, pharmaceutical companies, healthcare institutions, professionals, academic institutions, patients, and even the media and WHO. Effective collaboration among these stakeholders is essential but often hampered by systemic barriers, including fragmented health systems, insufficient resources, political inertia, and a lack of scientific infrastructure.[6] These challenges must be addressed to ensure the continued development of pharmacovigilance systems.

Pharmacovigilance encompasses risk management planning, collection and analysis

of adverse reaction reports, signal detection, and benefit-risk monitoring through periodic reports. Other key components include managing referrals, coordinating post-marketing studies, communicating safety issues, developing systems and guidelines, addressing knowledge gaps through research, monitoring system performance, and building stakeholder capacity.[3]

Over the last two decades, pharmacovigilance has rapidly evolved, gaining prominence across research, development, and clinical domains.[7] Within the European Union (EU), this evolution has been formalized through a progressively refined legal framework. Since 2004, successive EU directives—amended in 2010 and 2012—have strengthened post-marketing surveillance requirements.[8] These reforms culminated in a more robust pharmacovigilance system designed to improve the detection and management of ADRs across Member States. Despite these efforts, there remains no comprehensive synthesis of how these legislative changes have impacted reporting practices and regulatory implementation across the EU.

Thus, the aim of this review is to investigate the concept of pharmacovigilance and its regulatory framework, with a particular focus on the implementation of pharmacovigilance procedures within the EU.

PHARMACOVIGILANCE AND REGULATORY FRAMEWORK

The regulatory framework provides the basis for a national culture of medicine safety and public confidence in medicines. To be effective, the remit of medicines regulators must go beyond the approval of new medicines to include a wider range of issues related to medicine safety, in particular clinical trials, the safety of complementary and alternative or traditional medicines, vaccines and biological medicines, the development of lines of communication between all stakeholders in medicine safety, ensuring that they are able to operate effectively and ethically, particularly in times of crisis.[9]

In order to achieve their respective objectives, pharmacovigilance programmes and medicines regulators must be mutually supportive. On the one hand, pharmacovigilance programmes need to maintain strong links with drug regulators to ensure that the latter are well informed about safety issues in everyday clinical practice, whether these issues are related to future regulatory actions or concerns raised by the public. On the other hand, regulators need to understand the specialized and central role that pharmacovigilance plays in ensuring the ongoing safety of pharmaceutical products. [9]

The provision of good quality, safe and effective medicines and their appropriate use

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is also the responsibility of national governments. The establishment of a national medicines regulatory agency to study adverse reactions is essential to achieve pharmacovigilance. Inter-disciplinary cooperation is of great importance. In particular, links should be established between the Ministry of Health and other stakeholders, such as the pharmaceutical industry. The key elements of pharmacovigilance in national medicines policy include the establishment of national pharmacovigilance systems for reporting adverse reactions, which encompasses national and regional pharmacovigilance centres. It also involves the development of legislation on pharmacovigilance and the formulation of national policy that covers costing, budgeting, and financing. Continuous education of healthcare professionals on safe and effective pharmacotherapy is essential, along with the provision of up-to-date information on adverse reactions to medicines for both professionals and consumers or patients. Additionally, monitoring the impact of pharmacovigilance through indicators and process evaluations is a critical component.[10,11]

The effectiveness and safety of medicines is one of the primary objectives of ensuring public health. WHO considers it essential to have national policies on pharmacovigilance, as part of the national health policy and health care system. The objectives of the national pharmacovigilance policy should be consistent with the overall health objectives of the state. In each state, there should be an organization that functions as the regulatory authority for medicines and implements the laws and regulations on medicines, so that safe and effective medicines are circulated for patients. [11,12]

National regulatory authorities control the development and circulation of medicines to ensure that medicines are of good quality, safe, and effective. They oversee that medicines are produced, stored, distributed, and administered according to proper procedures. Additionally, they identify and sanction illegal trade practices, provide health professionals and patients with accurate information on the rational use of medicines, prevent unjustified obstruction of access to medicines by the regulatory authority, and ensure that promotion and advertising of medicines are fair and aimed at their rational use.[6,12]

REGULATORY FRAMEWORK IN THE EUROPEAN UNION

The EU operates through a system of supranational independent institutions and intergovernmental negotiated decisions by the EU Member States. The EU is a legal entity and can negotiate international agreements on behalf of the Member States. The EU has 28

Member States: Luxembourg, Austria Belgium Bulgaria Croatia Cyprus Czech Republic Denmark Estonia Finland France Germany Greece Hungary Ireland, Italy Latvia Lithuania Malta Netherlands Poland Portugal Romania Slovakia Slovakia Slovenia Spain Sweden United Kingdom. The European Economic Area (EEA) consists of the 28 EU Member States plus Iceland Liechtenstein Norway. The European Commission is the competent authority for centrally authorized medicines and provides the legal authority underpinning the European Union's pharmacovigilance system.[8]

The regulatory system of pharmacovigilance in the European Union includes the competent authorities for regulation in the Member States, the European Commission (EC) as the competent authority for medicines centrally in the EU and the European Medicines Agency (EMA), with responsibilities for centrally authorized products and coordination of systems. [8]

The EU regulatory system undertakes the tasks of collection of data from all available sources, mainly case reports from individual patients and results from epidemiological studies and trials, analysis of data for potential new or changing risks, assessment of risk management plans, reports, study reports, periodic safety update reports and benefit-risk assessments submitted by marketing authorisation holders, inspection of marketing authorisation holders, assessment of risks, in terms of frequency, severity and risk factors and last risk management, often through further investigations as well as measures to minimize risk.[8]

The pharmacovigilance system for human medicines is laid down in Regulation No 726/2004, Directive 2001/83/EC and Commission Implementing Regulation No 520/2012. In order to comply with the obligations relating to the promotion and protection of public health by monitoring the safety of authorized medicines to identify and confirm any changes to their risk-benefit balance, EMA operates an accredited pharmacovigilance system. EMA has a central role in the EU system and has a coordinating role in the functioning of the EU pharmacovigilance system in cooperation with the Member States and the EC. It supports the competent authorities in the Member States and coordinates the pharmacovigilance system through several key components, including the EU reporting and data storage system for case reports known as EudraVigilance, the EU system for timely and adequate responses to new safety data along with the EU alert and incident management system, the Pharmacovigilance Risk Assessment Committee which provides recommendations on all aspects of pharmacovigilance and risk management, the

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European Network of Centres for Pharmacoepidemiology and Pharmacovigilance, the Good Pharmacovigilance Practices (GVP) guidelines and other standards, and the development of scientific networks aimed at improving decision-making.[13]

In addition, EMA has issued Good Pharmacovigilance Practices (GVP) to facilitate the performance of pharmacovigilance in the EU. The GVP apply to marketing authorisation holders, EMA and medicines regulatory authorities in the EU Member States. They cover medicines authorised centrally by the Agency as well as medicines authorised nationally. The GVP guideline is part of the 2010 pharmacovigilance legislation. Each chapter is developed by a group of experts from EMA and the EU Member States.[14]

The EU pharmacovigilance legislation, which entered into action in July 2012, was the biggest change to the regulation of human medicines in the EU since 1995. It had significant implications for applicants and marketing authorisation holders of medicines in the EU, as well as for patients, healthcare professionals and regulators. The development of the pharmacovigilance legislation was based on the observation that adverse drug reactions, 'harmful and unintended' reactions to a medicine, caused around 197,000 deaths per year in the EU. As a result, in 2005 the EC launched a review of the European safety monitoring system, including the commissioning of an independent study, as well as an extensive public consultation through 2006 and 2007.[15] This process resulted in the adoption of a Directive and Regulation by the European Parliament and the Council of Ministers in December 2010, bringing about significant changes to the monitoring of the safety of medicines across the EU, Directive 2010/84/EU, Regulation (EU) No 1235/2010. The legislation amended the existing pharmacovigilance laws contained in Directive 2001/83/EC and Regulation No 726/2004. This legislation was accompanied by the implementing regulation, a legally binding act published by the EC in June 2012, which provides details on the operational aspects of the legislation; "Commission Implementing Regulation 520/2012" of June 19th 2012. [15]

In October 2012, the pharmacovigilance legislation was amended again following the withdrawal of the drug Mediator (benfluorex). The new amendments aimed to further strengthen the protection of patients' health by allowing for the timely notification and assessment of drug safety issues [Regulation No 1027/2012 (applicable from 5 June 2013), Directive 2012/26/EU (applicable from 28 October 2013)]. [15]

Pharmacovigilance legislation aims to reduce the number of adverse reactions in the EU. This is achieved through collecting better data on medicines and their safety, rapid and robust evaluation of issues related to the safety of medicines, effective regulatory action for the safe and effective use of medicines, empowering patients through reporting and involvement, increased levels of transparency and better communication. In addition, the legislative framework indirectly affects the pharmaceutical industry, applicants and marketing authorization holders and aims to clarify their roles and responsibilities, minimize duplication of effort, free up resources by streamlining and simplifying safety reporting, establish a clear legal framework for post-authorization monitoring.[15]

So, to promote and exchange regulatory frameworks and scientific expertise in a timely manner to develop best practices in pharmacovigilance, the EC and the EMA work with Member States. The EMA also works with WHO. Ensuring that regulators can respond to emerging or urgent health issues in a timely and effective manner is a pillar of the new pharmacovigilance legislation. To this end, medicines regulators in 31 EEA countries, EMA and the EU work closely and as a network to address any emerging problems quickly in the interest of patients' access to safe and effective medicines. The ability to take swift and strong regulatory action is strengthened through legislation by the creation of the Pharmacovigilance Risk Assessment Committee, the strengthening of the coordination group for the mutual recognition of serious issues, the introduction of new procedures for fast-tracking decision-making when public health is at risk The individual Member States of the EEA strengthen the pharmacovigilance system. They provide much of the resources and expertise for the assessment of adverse reactions and take a leading role in the assessment and analysis of data when a safety issue is assessed at European level. In addition, they carry out inspections to ensure that medicines placed on the EU market are manufactured properly and of appropriate quality, and that pharmacovigilance and industry systems are working as they should. [16]

COMPARISONS ACROSS MEMBER STATES

A comparative report published in a book of 2017 analyzes national implementation measures in six Member States—Germany, France, Portugal, Poland, Finland, and the United Kingdom. It examines their adherence to EU pharmacovigilance guidelines, implementation procedures, and the quality of national systems (e.g., structure, reporting mechanisms, and supervision). Rather than merely examining legal transposition, it emphasizes the practical execution of the

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directive, addressing a notable gap in research on EU law compliance.[17]

Variations in national pharmacovigilance systems contribute to under-reporting of adverse drug reactions (ADRs). Key contributing factors include limited awareness among healthcare professionals, the complexity of reporting procedures, insufficient inter-institutional cooperation, and lack of technological interoperability.[19] EU pharmacovigilance operates as a multi-level system involving various actors linked through inter-institutional relationships. Member States also vary in how centralized or decentralized their systems are. For instance, Germany, the UK, Finland, and Poland operate centralized systems, while Portugal and France employ decentralized models with regional centers handling pharmacovigilance data.[17] Portugal transitioned from a centralized to a decentralized system in the early 2000s, whereas the UK supplements its centralized model with regional Yellow Card centers. In Germany, despite its centralized structure, scientific associations facilitate links between stakeholders, resulting in a complex but functionally interconnected network.[17]

Supervisory structures also differ. In most Member States, pharmacovigilance bodies operate under the ministries of health and social security and are accountable to them.[17] Additionally, the classification and treatment of biological agents vary. Germany maintains separate pharmacovigilance systems for synthetic medicines and biologics, while Finland and Poland have distinct frameworks for biological vaccines. In contrast, France, Portugal, and the UK do not distinguish biologics from other medicinal products in their systems.[18]

Traceability and batch-number reporting for biologics are inconsistent across Member States. For example, batch numbers are rarely reported in France,[19] not reported at all in Poland,[20] and reliably captured only in Finland.[8] This inconsistency hampers pharmacovigilance effectiveness, particularly for biologics, where traceability is critical.

Legal requirements for ADR reporting also vary. While France mandates the inclusion of trade names and batch numbers of biologics in reports submitted by healthcare professionals, the UK and Germany rely on professional codes of conduct rather than legal obligations.[17,21] Poland has legal reporting requirements, but lacks enforcement mechanisms or penalties for non-compliance.[22] Across all countries surveyed, patients are not legally required to report ADRs, whereas marketing authorization holders are legally obligated to do so.[23]

Directive 2010/84/EU aimed to enhance patient involvement in pharmacovigilance. All 28 EU Member States have since implemented

patient reporting systems, with most introduced between 2012 and 2013, although a few date back to 1968 and 1996.[8] As a result, patient reports in the EEA have increased by approximately 50%, contributing data not captured through healthcare professionals. However, reporting challenges persist—particularly with biologics. For instance, although UK packaging regulations require batch numbers to appear on biologics, patients often lack access to the packaging when administration occurs in clinical settings, making traceability difficult.[18,21-23]

INTEGRATION OF PHARMACOVIGILANCE IN THE EU MEMBER STATES

There is a presumption that the EU has a problem with the transposition of pharmacovigilance regulations into national law. When considering the timeliness of national pharmacovigilance transposition processes for all EU Member States, this assessment shows that many countries face a serious problem with timely transposition into their national pharmacovigilance systems.[17,24,25]

There is indeed a gap between the transposition deadline, set by the EU Pharmacovigilance Directive (July 21st 2012), and the date of publication in the national law of the EU Member States. Delays in weeks are visible for the 101 national implementing measures of Directive 2010/84/EU. While the average number of implementing measures required to transpose the EU Pharmacovigilance Directive was 3.6, twelve Member States notified only one transposition act. However, Malta, Hungary and Lithuania required nine, 13 and 14 measures, respectively. Furthermore, only 16 out of 101 (15%) national implementing measures were transposed on time. At the extreme end of the late transposition chain are Finland, Spain, Poland and Slovenia. These countries transposed the first national implementing measures more than a year after the transposition deadline. Overall, the EU appears to have shortcomings in European pharmacovigilance. Almost 85% of national transposition acts are not transposed on time and are in fact delayed by more than two years. Differences between countries in the transposition of the EU Pharmacovigilance Directive are significant. There is a significant difference between “latecomers” (Denmark and Slovenia) and “early comers” (Cyprus, Romania, Sweden, Estonia, the United Kingdom and Ireland). Overall, however, Member States pay almost no attention to the guiding principles of implementation. The EU also has a problem of incorrect transposition into national law. The procedures, number of actors, quality and content of national implementing measures vary considerably

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between Member States, leading to great diversity across Europe. [17,24,25]

Many Member States have adopted so-called guiding principles for the transposition of EU legislation. These principles are addressed to policy makers and legal teams across all government bodies and explain what is needed to properly implement EU legislation. When transposing EU legislation, the aim should be to avoid going beyond the minimum requirements of the legal instrument.[19] Adopting such an approach will ensure that EU legislation does not create unnecessary legislative burdens. Furthermore, any gold-plating by extending the scope, adding in some way to the substantive requirement, not making full use of any derogations, maintaining pre-existing national standards where they are higher than those required by EU law or are applied early before the date given in a directive, should either be avoided or ultimately approved by a reductionist regulatory committee. Another guiding principle of implementation is to always use copying for transfer, where available, unless doing so would adversely affect national interests.[26]

COMPARISON OF FACTORS CONTRIBUTING TO THE UNDERREPORTING OF ADVERSE EFFECTS

Lack of awareness

Awareness encompasses a range of factors, including not only general awareness of the reporting obligation, but also indifference about the importance of reporting adverse reactions. Member States have focused on informing healthcare professionals and patients about the importance of reporting adverse reactions, particularly with regard to biological medicines.[20] However, it appears that lack of awareness is a widespread feature in the EU (United Kingdom, Finland, Poland, France, Portugal and Germany). However, the lack of awareness affects healthcare professionals and patients to varying degrees. While in Finland, most healthcare professionals are aware of their obligation to report adverse reactions, the level of public awareness is particularly low. Similarly, in the United Kingdom around 80% of healthcare professionals are aware of the yellow card scheme, while only 10% of patients have heard of it. [27,28]

In some Member States, the lack of awareness about biologics seems to be particularly serious (Poland, Portugal). This is an interesting finding because the decentralised system in Portugal seems well equipped with a key recommendation on the role of regional pharmacovigilance centers for awareness campaigns. Poland also revealed that the problems with reporting adverse reactions to biologics stemmed mainly from its

inexperience and, therefore, ignorance in the field.[27]

Complexity in reporting

Complexity includes a number of factors related to the task of reporting adverse reactions, including not only the descriptive elements of the report, but also the constraints in the working environment of healthcare professionals. For example, in Finland only healthcare professionals (doctors and pharmacists) can report adverse reactions electronically, while patients and nurses must report by regular mail. In Germany, reports are difficult to filter because strict data protection laws make it difficult to link databases. Providing key and supplementary information within the electronic or printed version of the report form improves the quality of the reports submitted. However, in Poland, France and Portugal, a high workload is reported that hinders more effective pharmacovigilance.[27,28]

The most important challenge to the effective implementation of the European Directive 2010/84/EU is the underreporting of adverse drug reactions. In 22 countries (79%) reporting of adverse drug reactions is a legal obligation for healthcare professionals and in 26 countries (89%) there is a mandatory reporting of adverse drug reactions for vaccines. 38% of reports are made via electronic applications. A minority of French regional pharmacovigilance centers appeared to have websites where adverse drug reactions can be reported.[8,29]

There are two important aspects of underreporting: the quantity and the quality of information. Quantity refers to the number of adverse drug reactions reported. Quality refers to the value of the information. The two dimensions are sometimes mutually exclusive, as increases in quantity can lead to a decrease in quality. While the quantity of information is important, an appropriate level of quality is essential for effective pharmacovigilance. Reporting is also perceived by healthcare professionals as time-consuming and complex. The need to be available for follow-up questions further discourages healthcare professionals, as reporting is not a one-off activity but can become a time-consuming process. This also has negative consequences for the quantity and quality of safety data.[8]

Pharmacovigilance training

The lack of quality (as well as the lack of reporting and the lack of quantity) is related to the neglect of pharmacovigilance training in medical and pharmaceutical education. Finland, however, offers a very elaborate training system for healthcare professionals on pharmacovigilance and France is one of the first Member States to introduce a postgraduate programme in pharmacovigilance. A minority of national competent authorities offer e-learning tools

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and online training materials for healthcare professionals, although these tools are very effective and significantly improve professional training. However, in order to implement the EU legal provisions on pharmacovigilance in full force, training is essential to internalize practices that favor the implementation of these provisions. [8]

Since most adverse reactions are known effects of old medicines, harm can be avoided if healthcare professionals (and also patients) were better trained or at least informed.[30] In general, national pharmacovigilance systems should be seen as dependent on developments in general health policy. In the current political climate, one such development is the structural lack of funding for regulatory activity.[31]

Lack of collaboration

Collaboration is a key analytical category for integrating adverse effects reporting by healthcare professionals into complex national pharmacovigilance systems. Many national pharmacovigilance systems require collaboration between institutions involved in pharmacovigilance in order to ensure the effectiveness of the system.[32] Member States, regulatory authorities, healthcare professionals and the pharmaceutical industry need to exchange information and best practices. However, there is considerable variation across Member States due to their institutional differences. On the one hand is Portugal with successful collaboration between agencies, healthcare professionals and universities. On the other hand is Poland with no collaboration between the relevant stakeholders.[8,32]

Interconnectivity issues

To cope with the increasing data, Member States have introduced new functionalities in reporting systems and cooperation between hospital and pharmacy information and technology systems.[20] Sound and uniform information and technology systems for reporting adverse reactions at national and international level would lead to increased efficiency, better data quality and error prevention.[29,32] However, different information and technology systems and separate web portals are considered to hinder interconnection in some Member States (United Kingdom, France and Germany). [8]

Financial resources

Pharmacovigilance is no exception here, as many Member States have to fulfill their tasks with limited financial resources. While finances are an issue in general, the problem is big in Southern European Member States, which were particularly affected by the economic crisis.[8]

DISCUSSION

Essentially all EU Member States are required to comply with the EU directives on pharmacovigilance and to incorporate them

into their regulatory frameworks and to establish sound pharmacovigilance systems. However, there are differences in the timely integration of the EU directives into the regulatory frameworks of the countries and in individual features of the pharmacovigilance systems. Findings show that in some countries, medical liability is a significant obstacle to the reporting of adverse reactions by healthcare professionals. However, the fear of medical liability depends on the national health policy and the legal system on which it is based. In general, there are two compensation systems for patients who have suffered medical harm. On the one hand, so-called no-fault systems provide compensation through national healthcare services. On the other hand, private healthcare providers or even individual healthcare professionals can be held liable. Therefore, error-free systems are usually associated with healthcare systems in which the states are the main providers of healthcare services and claims made by patients are made directly to them. For example, France has an error-free system, while Portugal and Germany have error-based models. [33]

In this regard, the Council of Europe has made some recommendations to improve patient safety and prevent adverse events in healthcare. As regards the reporting of adverse reactions, the recommendations are very similar to the provisions enshrined in Article 102 of Directive 2010/84/EU. However, the recommendations are based on an error-free approach, in which patients' rights are met with the requirements of extensive adverse reaction reporting. Therefore, the recommendations include that legal protection of reporting healthcare professionals should be ensured. When reforming the EU pharmacovigilance system, the European Parliament aimed to include the same approach by amending Article 102, stating that 'the reporting of suspected adverse reactions due to medication errors should be on a 'no liability' basis and should be legally privileged'. Given the diversity of national health systems, it is not surprising that this amendment was rejected by Member States. Its inclusion would entail a comprehensive review of established legal principles that goes beyond pharmacovigilance.[17] Furthermore, in many countries reporting adverse reactions is perceived as an admission of failure. Healthcare professionals may therefore decide not to report them. Their behavior is influenced by institutional norms and values. The fact that adverse events are seen as failures is such a value, as is the perceived loss of reputation. These norms and values cannot be changed suddenly at the individual level. Instead, national policy makers, healthcare providers and hospital managements are called upon to introduce a different culture of

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patient care and safety, where reporting adverse reactions is considered a core responsibility of healthcare professionals.[2]

In any case, pharmacovigilance should play a more important role in the education of healthcare professionals, be they doctors, pharmacists or nurses. Institutional changes in healthcare units and healthcare systems need to be made and healthcare professionals, both at undergraduate and postgraduate level, should be sensitized and trained about pharmacovigilance and its benefits.[32]

Additionally, a high level of cooperation between relevant stakeholders is particularly beneficial for pharmacovigilance in the EU. Here emphasis should be placed on the diversity of national systems. Some Member States have centralized pharmacovigilance systems, while others have decentralised systems. Some Member States have separate systems for biological products, while others do not. Cooperation should therefore take into account the institutional framework of each country and the respective cultures. In general, national and regional competent authorities working under the auspices of national ministries should be provided with sufficient financial means to fulfill their functions, as should healthcare units. This allows healthcare units to rely on a strong workforce that reduces the workload of individual healthcare providers and increases the possibility of widespread reporting of drug related adverse events.[34]

CONCLUSIONS

Pharmacovigilance plays a vital role in protecting public health and ensuring patient safety, especially given that all medicines, even after approval, carry the risk of adverse events during therapeutic use.[2] While EU Member States have made progress, challenges remain in the legal transposition and practical implementation of pharmacovigilance measures across the region.

Despite its 40-year history, pharmacovigilance remains a dynamic field essential to managing the risks posed by an expanding and increasingly potent range of medicines. Effective systems for reporting, analyzing, and communicating adverse reactions—especially previously unknown ones—are critical for ensuring appropriate regulatory responses.[35]

The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance exemplifies effective EU-level collaboration, enabling knowledge sharing and harmonized action across Member States.[36] Tools introduced under the revised legislation—such as risk management plans, post-authorisation studies, signal detection, and periodic safety update

reports—reflect a more proactive and transparent approach to medicine safety.

Public and stakeholder engagement is growing, including mechanisms for patient reporting and public communication. Future directions include expanding public participation through hearings on major safety issues and undertaking new comparative studies to better understand national variations in pharmacovigilance practice.

Ultimately, national healthcare policies and systems differ widely. While cross-country comparisons can support mutual learning, this depends on deeper structural and cultural factors that shape how EU legislation is implemented across Member States.

ABBREVIATIONS

EC European Commission

EEA European Economic Area

EMA European Medicines Agency

EU European Union

WHO World Health Organization

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None.

CONFLICT OF INTEREST

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