https://doi.org/10.31925/farmacia.2023.3.25 **ORIGINAL ARTICLE**

INVOLVING PHARMACIES IN PHARMACOVIGILANCE – A COMPARISON BETWEEN FRANCE AND ROMANIA

ALEXANDRA TOMA *, OFELIA CRIŞAN

Department of Pharmaceutical Legislation and Management, Faculty of Pharmacy, "Iuliu Haţieganu" University of Medicine and Pharmacy, 12 Ion Creangă Street, 400010, Cluj-Napoca, Romania

**corresponding author: toma.alexandra@umfcluj.ro*

Manuscript received: February 2023

Abstract

The considerable interest in monitoring the safety of medicines prompted for a change of the European pharmacovigilance legislation, setting specific attributions for the marketing authorization holders and the competent authorities for human medicines. However, each Member State has remained responsible for organising its own pharmacovigilance system. Consequently, the degree of involvement of other entities of the health care system, such as pharmacies, in the national pharmacovigilance system, will differ among countries. The aim of this study was to compare the pharmacovigilance legislation of France and Romania, in order to identify the best practices for involving pharmacies in pharmacovigilance. The normative texts found by legal documentary research were analysed using the comparative method and methods of legal interpretation. In France, the pharmacovigilance system is decentralised, being organised both at national and regional levels, and coordinated by the national competent authority, which established a set of specific good practices for all the entities involved in pharmacovigilance, including pharmacists working in pharmacies. In Romania, the pharmacovigilance system is centralised, organised only at the national level, and coordinated by the national competent authority, which has made considerable efforts to develop it in our country. To make progress in that way, it is necessary to set up local pharmacovigilance centres, in collaboration with universities and hospitals. To better involve pharmacies in pharmacovigilance, the development and implementation of specific rules of good pharmacy practice are needed.

Rezumat

Interesul considerabil pentru monitorizarea siguranței medicamentelor a dus la modificarea legislației europene privind farmacovigilența, cu stabilirea de atribuții specifice pentru deținătorii de autorizații de punere pe piață și pentru autoritățile competente în domeniul medicamentului. Fiecare stat membru a rămas însă responsabil de organizarea propriului sistem de farmacovigilență. De aceea, măsura în care în fiecare sistem național de farmacovigilență sunt implicate și alte entități din sistemul sanitar, precum farmaciile, poate fi diferită. Scopul lucrării a fost cercetarea comparativă a legislației privind farmacovigilența din Franța și România, pentru identificarea celor mai bune practici de implicare a farmaciilor în farmacovigilență. Textele normative identificate prin cercetarea legală documentară s-au analizat folosind metoda comparativă și metodele interpretării juridice. În Franța, sistemul de farmacovigilență este descentralizat, organizat la nivel național și regional, sub tutela autorității naționale competente, care a elaborat reguli de bună practică specifice pentru toate entitățile cu atribuții în farmacovigilență, inclusiv pentru farmaciștii din farmacii. În România, sistemul de farmacovigilență este centralizat, organizat doar la nivel național și gestionat de autoritatea națională competentă, care a depus eforturi importante pentru dezvoltarea acestei activități în țara noastră. Pentru a avansa în acest demers, este necesară organizarea unor centre locale de farmacovigilență, în colaborare cu universități și spitale. Dezvoltarea implicării farmaciilor în farmacovigilență necesită elaborarea și implementarea unor reguli specifice de bună practică farmaceutică.

Keywords: pharmacovigilance, national pharmacovigilance systems, pharmacies

Introduction

The development of pharmacovigilance activities is very useful for the community, as it increases knowledge and awareness regarding the prevention and management of risks associated with the use of medicines. The constant preoccupations at the international level regarding pharmacovigilance activities led, among others, to specific regulations aiming at protecting the patients' health and life. Thus, at the level of the European Union (EU), the existing legislation on medicines for human use has been modified, namely the Directive 2001/83/EC and Regulation (EC) no. 726/2004, by the Directive 2010/84/EU, Regulation (EU) no. 1235/2010, Directive 2012/26/EU and Regulation (EU) no. 1027/2012, all meant to optimize the legal frame in the field of pharmacovigilance [11-13, 42-44]. Based on these, the European Commission adopted the Commission Implementing Regulation (EU) no. 520/2012 on the performance of pharmacovigilance activities, while the European Medicines Agency (EMA) drawn up the guideline on good pharmaco-vigilance practices (GVP) [8, 14]. These regulations include provisions that establish the responsibility of each Member State to organise its own national pharmacovigilance system.

The most important duties of monitoring the safety of human medicines belong to the competent authorities (EMA, national authorities) and the marketing authorisation holders [8, 11-14, 42-44]. However, some pharmacovigilance activities are also performed by other important entities, such as pharmacies, hospitals, universities, professional associations, patients and their organisations. For those entities, the European legislation does not have mandatory provisions; therefore, the way they are involved in pharmacovigilance falls into the responsibility of each Member State [8, 9, 11, 14, 20, 42, 52].

The pharmacy is the most accessible health institution, providing medicines, health products and quality pharmaceutical services, including information and counselling on the rational, efficient, and safe use of medicines [7, 40, 41]. In our country, the national pharmacovigilance system is coordinated by the National Agency for Medicines and Medical Devices of Romania (NAMMDR) [48]. Together with the Romanian College of Pharmacists, the Agency tried to stimulate the participation of pharmacists to this activity, by crediting it as continuous education [31, 34]. Despite those favourable circumstances, it is well known that the involvement of Romanian pharmacies in pharmacovigilance is extremely low. Consequently, to identify the best practices for developing the national pharmacovigilance system in Romania and for involving pharmacies in pharmacovigilance, we investigated the Romanian legislation related to pharmacovigilance in comparison with those of a more advanced EU Member State.

Materials and Methods

We chose France as a term of comparison for several reasons. First, France has a health system in which the state plays an important role in regulating, providing and financing of health services to the population, mainly through the mandatory contributions to social security and the Romanian health system is similar from this point of view [9, 16, 20, 48, 52]. Second, France is among the European countries preoccupied with the development of high-quality regulations at the national level [39]. Third, in the field of pharmacovigilance, France is recognised for its excellent communication and education, as well as its decentralised national pharmacovigilance system involving pharmacists working in pharmacies [15, 17, 20]. For the study purpose, in a first stage we performed a legal documentary research to identify the legal documents related to pharmacovigilance in France and Romania [10, 18]. In the second stage, we investigated the legal documents of the two countries, using the comparative method and methods of legal interpretation [9, 10, 18, 21]. We chose as comparative criteria the fields in which the national legislation of the Member States is variable within the context of the European legislation, more precisely: the organisation of national pharmacovigilance systems, the involvement of hospital pharmacies in pharmacovigilance and the involvement of community pharmacies in pharmaco-vigilance [52]. Using these criteria, we have structured below the results and discussion of the comparative analysis. On their basis, in the third stage of our study, we made proposals to improve the pharmacovigilance regulations and practices in Romania, for enhancing the performance of the national pharmacovigilance system and for better involving pharmacies in pharmacovigilance.

Results and Discussion

Organisation of national pharmacovigilance systems

In France, the legal frame for the activities related to human medicines, including pharmacovigilance, is provided by the Code of Public Health. The National Agency for Medicines and Health Products Safety (Agence Nationale de Sécurité du Médicament et des Produits de Santé, ANSM) is the French competent authority responsible for the organisation and coordination of the national pharmacovigilance system [23]. By the Decision of the General Director of ANSM, this authority has adopted national rules of GVP. These rules clearly define the responsibilities of each entity involved in pharmacovigilance: ANSM, regional centres, marketing authorisation holders, health professionals and patients. Regarding the responsibilities of marketing authorisation holders and ANSM, the Decision mention attributions already established by the European legislation. For the other entities involved in monitoring the safety of human medicines, the text includes rules that are specific to the organisation of the French pharmacovigilance system. Thus, according to these rules, the regional pharmacovigilance centres have the following responsibilities: monitoring and investigating risks associated with the use of medicines, through gathering reports on suspected adverse reactions, their assessment and validation; identifying safety signals; providing information of the risks associated with the use of medicines; training of personnel and participating in pharmacovigilance research; stimulating and encouraging anyone to report suspected adverse reactions of human medicines. Moreover, these centres may provide information and counselling for health professionals directly involved in patient care, by performing individual evaluations of the benefits and risks of the respective medication therapy [1]. At present, there is a well-structured network of 31 such centres, which serve all the regions of France, responsible for the pharmacovigilance activity at a local level [2, 23, 45]. The French legislation indicates a decentralised pharmacovigilance system, in which local actions take place through the regional centres, under the ANSM coordination, which is responsible for the management of the pharmacovigilance process at the national level.

In Romania, the legal frame for the activities related to human medicines is provided by Law no. 95/2006 on healthcare reform, Title XVIII Medicine, which transposed the European provisions into Romanian law, including those on pharmacovigilance. According to this law, NAMMDR is the national competent authority for human medicines. NAMMDR has been responsible for the regulation and organisation of the national pharmacovigilance system in our country, including the translation in Romanian of the guideline on GVP drawn up by EMA [36, 48]. In addition, Law no. 134/2019, on the reorganisation of NAMMDR, has established that its general pharmaco-vigilance responsibility is to monitor the safety of human medicines, through coordinating and inspecting the pharmacovigilance activities performed by marketing authorisation holders in Romania [50]. Thus, NAMMDR includes the Directorate of Pharmacovigilance and Risk Management, whose main attributions are represented by the management of the national pharmacovigilance system. NAMMDR also includes 12 territorial units of inspection and/or control and surveillance of the market, subordinated to the Directorate of Medicine Quality Surveillance, Alerts and Territorial Units, but these 12 units are not involved in pharmacovigilance. Nor do they have attributions of pharmacovigilance inspection, the latter belonging to the Directorate of Inspection of Good Practices in Manufacturing, Laboratory, Analytical Laboratory, Clinical Trials and Pharmacovigilance [29]. The Romanian legislation indicates that the national pharmacovigilance system is centralised, all the activities being performed by NAMMDR.

By comparison, though ANSM and NAMMDR have similar responsibilities regarding the management of pharmacovigilance activities at a national level, established by the European legislation, there are important differences between the two countries. The creation of regional centres is very useful and fruitful for the pharmaco-vigilance activity, as proven by the large number of reports of adverse reactions received by the regional pharmacovigilance centres in France in 2021, more exactly 169.336 such reports [3]. Unlike ANSM, NAMMDR recorded a number 21.941 reports of adverse reactions in 2021 [31]. Though NAMMDR has led public campaigns to raise the awareness on the importance of reporting suspected adverse reactions, the number of reports remains very low, considering the Romanian population and consumption of medicines [32, 38]. In our opinion, following the French model, the Romanian pharmaco-vigilance system may be organised also at a local level, using the territorial units of NAMMDR. By staff training and attributing them pharmacovigilance responsibilities, the territorial units could become real pharmacovigilance centres at regional level in Romania. They could collaborate with universities and research centres, benefitting from the knowledge and expertise of academics and researchers, as well as from the easy access to high-quality scientific information [19, 52]. Also, these centres could collaborate in special training programs for health professionals, in partnership with professional associations and patient organisations. Such actions are paramount in educating the population regarding the safe use of medicines and the importance of reporting suspected adverse reactions, for advancing knowledge, promoting health, and improving the quality of life [52].

Involving hospital pharmacies in pharmacovigilance

The regional pharmacovigilance centres in France were initially set up within public hospitals. At present, they support the pharmacovigilance activity of ANSM at the local level, as previously mentioned [23]. For example, the Regional Centre of Pharmacovigilance in Rouen has functioned within the Department of Clinical Biology of the Rouen University Hospital since 1978. Its activity consists in collecting and analysing suspected adverse reactions reported by health professionals and patients, analysing reported medication errors and quality defects, providing answers to any questions regarding medicines and publishing an information newsletter [4]. According to the Code of Public Health, all hospitals must organise their activity to ensure the safety of inpatients, namely report all information on health monitoring, including those on pharmacovigilance [23]. For example, in the Regional Hospital of Orléans a specialized group was created to manage all risks of health vigilance, including pharmacovigilance. It monitors the patients' treatments to protect their right to safety in a context of hospital care [5, 6]. According to the Code of Public Health, the hospital pharmacy must observe the specific good practices, its mission being to contribute to the hospital pharmacovigilance activities, including informing patients and health professionals about medicines, promoting their appropriate use and evaluating practices related to medicines [23]. The rules of GVP, established by the Decision of the ANSM Director, include the obligation of all pharmacists to report the suspected adverse reactions to the regional centres and failure to acknowledge it is punished, being considered a contravention [1]. The French Society of Clinical Pharmacy elaborated in 2022 the Guidelines of good clinical pharmacy practice, including rules of risk management related to the use of medicines, such as knowing and identifying adverse reactions, identifying and preventing drug interactions [51]. We emphasise the preoccupation of French authorities for involving hospitals and their pharmacies in pharmacovigilance. In practice, it was raised the issue of the lack of interconnectivity between the hospital and regional centres IT systems and the necessity of additional training [20], which in fact point to the interest in improving cooperation regarding pharmacovigilance processes and facilitating fulfilment of professional responsibilities in this field.

In Romania, the legal frame for the establishment, organisation and functioning of hospitals is provided by Law no. 95/2006 on healthcare reform, Title VII

Hospitals [48]. The law does not include provisions for pharmacovigilance activities in hospitals. Moreover, though the hospital pharmacy is one of the hospital units, its organisation and functioning are established by Law no. 266/2008 of pharmacy and its application norms approved by Order of the Minister of Health no. 444/2019 [27, 49]. However, neither this law, nor its application norms include pharmacovigilance responsibilities for the hospital pharmacy. The Order of the Minister of Health no. 446/2017 establishes the standards, procedure and methodology for the evaluation and accreditation of hospitals in Romania, with the aim to ensure quality health services and patient safety [25]. The institution responsible with hospital accreditation is the National Authority of Quality Management in Health (NAQMH), which elaborated a Handbook of quality standards [37]. One of the standards states that the medication management should assure treatment continuity and patient safety, including through pharmacovigilance activities performed by the hospital pharmacy and/or the clinical pharmacist [25, 37]. The handbook establishes principles and recommends practices for monitoring the safety of medicines, managing adverse reactions, preventing medication errors, and minimising risks entailed by inappropriate medicines associations [37]. It also states that one of the functional structures of the hospital should be the Commission of Pharmacovigilance, without establishing specific responsibilities or rules regarding its members [25, 37]. The Order of the Minister of Health no. 444/2019 only provides for the possibility for the head pharmacist of the hospital pharmacy or another pharmacist to be part of the Commission of Pharmacovigilance [27]. The responsibility for monitoring the safety of medicines belongs to this Commission, as stated by the regulations of organisation and functioning of certain hospitals, such as "Ana Aslan" National Institute of Gerontology and Geriatrics in Bucharest and "Ion Chiricuță" Institute of Oncology in Cluj-Napoca [26, 30]. However, for this Commission to exist and properly function in all the Romanian hospitals, consistent rules should be established for the pharmacovigilance activities in hospitals. At the present time, the good pharmacy practices (GPP), approved by the Order of the Minister of Health no. 75/2010, do not include quality standards for the pharmacovigilance activities performed by hospital pharmacies [24]. In 2011, the Romanian College of Pharmacists elaborated a set of models of standard operating procedures for hospital pharmacies. The procedure of dispensing medicines includes the pharmacists' obligation to monitor patients and report on adverse reactions, but there is no model for a pharmacovigilance procedure [47, 52]. We consider that putting into practice the NAQMH documents would be extremely important for developing the pharmacovigilance activities in Romanian hospitals, including the involvement of hospital pharmacies in monitoring the safety of medicines administered to the inpatients. Unfortunately, the pharmacovigilance activities in hospitals suffer because of the lack of involvement of the hospital pharmacies, mainly because they don't have contact with the inpatients. A possible solution to this deficiency might be the appointment of clinical pharmacists in hospitals, even setting up clinical pharmacy services, which would improve the pharmacovigilance activities. Regardless of the solution, to achieve quality in this area we need specific practice regulations, possibly following the French model [52].

By comparison, in Romania, the implication of hospitals and their pharmacies in pharmacovigilance it is found in a smaller way than in France. One of the main causes, we believe, is the hospital managers' less concern for implementing the existing rules of pharmacovigilance, the absence of local partners such as regional centres of pharmacovigilance and of pharmacovigilance software tools integrated with the hospital management ones. Given the complexity of the activities of pharmacovigilance in hospitals, a cooperation between the Ministry of Health, NAQMH, NAMMDR and the Romanian College of Pharmacists would be beneficial to create a specific good practice framework, with responsibilities for all the entities involved in pharmacovigilance, which would constitute a basis for developing and implementing institutional procedures adapted to each hospital needs.

Involving community pharmacies in pharmacovigilance

In France, the rules of GVP, established by the Decision of the ANSM Director, are applied in the community pharmacy as well, pharmacists having to report to the regional centres on adverse reactions brought to their knowledge; failure to acknowledge this obligation is punished, being considered a contravention [1]. Moreover, according to the GPP, pharmacies must have all the information to be able to report the suspected adverse reactions of medicines. These refer to the contact data of the regional centre of pharmacovigilance, the reporting form, and a working protocol that helps the pharmacist detect possible adverse reactions. In addition, specific alerts may be included in the pharmaceutical management software used by pharmacies, to help identify medicines with a specific risk management plan [22]. Also, the pharmacy is the ideal place in which patients receive information on how to report adverse reactions themselves, the rules of GVP providing specific provisions in this respect. There are two methods of reporting, the electronic one, on the specially created website, or by filling in a form that is sent by post, fax, phone, or email [1]. Indeed, French community pharmacies are actively involved in pharmacovigilance activities, especially in reporting suspected adverse reactions. Of the total number of reports in 2021, 12.2% were reported by pharmacists [3].

In Romania, the Law no. 266/2008 of pharmacy and its application norms, approved by the Order of the Minister of Health no. 444/2019, establish the

responsibilities of the community pharmacy professionals referring to the pharmacovigilance activities [27, 49]. For example, identification and prevention of adverse reactions of medicines represents a pharmaceutical service provided by the pharmacists [49]. Also, the Order of the Minister of Health no. 2382/2021, which sets the frame of pharmaceutical services provision, refers to the proper identification and management of risks associated with the use of medicines, as important elements of the pharmaceutical services of medicine dispensing and patient treatment monitoring. According to this Order, specific good practices will be developed for the provision of pharmaceutical services [28]. The existing GPP, approved by the Order of the Minister of Health no. 75/2010, do not include quality standards for the pharmacovigilance activities in the community pharmacies. However, they stipulate that the monitorization of medication therapy includes the reporting to NAMMDR of adverse reactions that may occur during treatment [24]. Adverse reactions may be reported to NAMMDR in two ways: online or in writing by post or fax [33, 35], like in France. The Romanian College of Pharmacists elaborated in 2011 a set of models of standard operating procedures for implementing GPP in community pharmacies [46]. The procedure of medicine dispensing includes the pharmacists' obligation to monitor patients and report adverse reactions, though there is no model for a pharmacovigilance procedure [47, 52]. We consider that the Romanian GPP need to be optimised and updated to include pharmacovigilance activities specific for community pharmacies (management of adverse reactions, medication errors, medication abuse and so on), possible taking the French rules as a model. As Pharmaceutical Group of the European Union (PGEU) and other authors have maintained, the evolution of pharmacovigilance regulations and their implementation in pharmacies could be extremely beneficial for both patients and pharmacies, which would demonstrate in this way too their will to improve their performance as providers of quality health services [7, 15, 20, 40, 41, 52]. Thus, community pharmacies need standard operating procedures to manage safety issues, including for reporting suspected adverse reactions, as well as working protocols for special situations, for example dispensing medicines with severe safety problems. In addition, information dissemination methods could be devised to raise the awareness on the importance of adverse reactions reporting and patient counselling regarding pharmacovigilance, including self-reporting of adverse reactions [52].

By comparison, in Romania the involvement of community pharmacies in pharmacovigilance is inferior than in France. Among the main causes is the less concern of authorities for the implementation of good practices in this area, absence of local partners such as regional centres of pharmacovigilance and lack of pharmacovigilance computer applications integrated with the pharmaceutical management software used in pharmacies. Considering the tradition of the cooperation in the pharmaceutical field, a collaboration between the Ministry of Health, NAMMDR and the Romanian College of Pharmacists could be considered to develop a specific framework of good practices, with responsibilities for all those involved in pharmacovigilance, which could serve as a basis for developing and implementing appropriate pharmacovigilance procedures and protocols in community pharmacies.

Conclusions

At the EU level, the pharmacovigilance legislation is principally focused on the obligations of marketing authorisation holders and the competent authorities, while no obligations are specified for the other entities involved in pharmacovigilance.

The French pharmacovigilance system is well established, with a decentralised structure that involves regional centres of pharmacovigilance, hospitals, pharmacies, health professionals and patients. The national rules of GVP include responsibilities for all these entities regarding the safe use of medicines.

To abide by the European legislation, NAMMDR has made considerable effort to organise and regulate the national pharmacovigilance system in Romania. However, there are important aspects that could be improved to increase the performance of this activity in our country. Competent authorities in the public health and pharmaceutical fields should cooperate to develop a body of regulations by which a network of local pharmacovigilance centres and a consistent framework of responsibilities for all entities involved in this activity should be created. For better involving community and hospital pharmacies in pharmacovigilance, an update of the GPP is needed, including specific standards of quality assurance in pharmacovigilance activities, with procedures, protocols, and software applications to facilitate their implementation.

The most important remains the willpower to fulfil this task, implying the sustained work of competent authorities, professionals and their employers, as only a joint effort could lead to a successful project of improving the safety of medicines for all the Romanian patients.

Conflict of interest

The authors declare no conflict of interest.

References

1. Agence Nationale de Sécurité du Médicament et des Produits de Santé, Décision du 01 juin 2022 relative aux bonnes pratiques de pharmacovigilance, 02.06.2022, https://ansm.sante.fr/documents/reference/bonnes-pratiques-de-pharmacovigilance.
2. Agence Nationale de Sécurité du Médicament et des Produits de Santé, Liste des Centres Régionaux de

Pharmacovigilance, https://ansm.sante.fr/page/liste-des-centres-regionaux-de-pharmacovigilance.
3. Agence Nationale de Sécurité du Médicament et des Produits de Santé – ANSM, Rapport d'activité 2021, 05.10.2022, https://ansm-rapport-annuel.fr/.2021/#page=1.
4. Centre Hospitalier Universitaire de Rouen Normandie, Pharmacovigilance, www.chu-rouen.fr/service/pharmacovigilance/.
5. Centre Hospitalier Regional d'Orléans, Les vigilances sanitaires, www.chr-orleans.fr/chr-orleans/letablissement/prevention-des-risques/les-vigilances-sanitaires.
6. Centre Hospitalier Regional d'Orléans, Politique de gestion des risques. www.chr-orleans.fr/chr-orleans/letablissement/prevention-des-risques/politique-de-gestion-des-risques.
7. Chertes A, Crișan O, Standards for good pharmacy practice – a comparative analysis. *Farmacia*, 2019; 67(3): 545-550.
8. Commission Implementing Regulation no. 520/2012 of 19 June 2012 on the performance of pharmacovigilance activities provided for in Regulation (EC) no. 726/2004 of the European Parliament and of the Council and Directive 2001/83/EC of the European Parliament and of the Council. *Official Journal of the European Union*, L 159/2012.
9. Crișan O, Pharmacist profession – legal issues, online edition. "Iuliu Haţieganu" Publishing House: Cluj-Napoca, Romania, 2022; 15, 40-43, 184-194. (available in Romanian).
10. Delnoy P, Éléments de méthodologie juridique: 1. Méthodologie de l'interprétation juridique; 2. Méthodologie de l'application du droit, 3e édition. Larcier: Bruxelles, Belgium, 2008; 23-31, 155-180, (available in French).
11. Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the community code relating to medicinal products for human use. *Official Journal of the European Union*, L 311/2001.
12. Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use. *Official Journal of the European Union*, L 348/2010.
13. Directive 2012/26/EU of the European Parliament and of the Council of 25 October 2012 amending Directive 2001/83/EC as regards pharmacovigilance. *Official Journal of the European Union*, L 299/2012.
14. European Medicines Agency, Human regulatory, Good pharmacovigilance practices, www.ema.europa.eu/en/human-regulatory/post-authorisation/pharmacovigilance/good-pharmacovigilance-practices.
15. Furon J, Guerriaud M, Chambin O, Michiels Y, La pharmacovigilance à l'officine, de la définition à la mise en œuvre. *Actual Pharm.*, 2017; 56(571): 24-27, (available in French).
16. Gaeta M, Campanella F, Capasso L, Schifino GM, Gentile L, Banfi G, Pelissero G, Ricci C, An overview of different health indicators used in the European Health Systems. *J Prev Med Hyg.*, 2017; 58(2): E114-E120.
17. Géniaux H, Laroche ML, La pharmacovigilance, fonctionnement et missions. *Actual Pharm.*, 2017; 56(571): 20-23, (available in French).
18. Hutchison T, Duncan N, Defining and Describing What We Do: Doctrinal Legal Research. *Deakin Law Rev.*, 2012; 17(1): 83-119.
19. "Iuliu Haţieganu" University of Medicine and Pharmacy Cluj-Napoca, Center for Preclinical Pharmacological and Post-marketing Pharmacological Studies, https://eeris.eu/ERIF-2000-000G-1136.
20. Kaeding M, Schmälter J, Klika C, Pharmacovigilance in the European Union. Practical Implementation across Member States. Springer: Wiesbaden, Germany, 2017; 1-10, 73-81.
21. Kischel U, La méthode en droit comparé. L'approche contextuelle. *Rev Intl Dr Comp.*, 2016; 68(4): 907-926, (available in French).
22. Légifrance, Arrêté du ministre des affaires sociales et de la santé du 28 novembre 2016 relatif aux bonnes pratiques de dispensation des médicaments dans les pharmacies d'officine, les pharmacies mutualistes et les pharmacies de secours minières, mentionnées à l'article L. 5121-5 du code de la santé publique, www.legifrance.gouv.fr/loda/id/JORFTEXT000033507633.
23. Légifrance, Code de la santé publique, 08.02.2023, www.legifrance.gouv.fr/codes/texte_lc/LEGITEXT000006072665/?isSuggest=true.
24. Ministry of Health, Order no. 75/2010 on approval of the rules of good pharmacy practice. *Official Journal of Romania*, part I, no. 91/2010, (available in Romanian).
25. Ministry of Health, Order no. 446/2017 on the approval of the Standards, procedure and methodology for the assessment and accreditation of hospitals. *Official Journal of Romania*, part I, no. 300/2017, (available in Romanian).
26. Ministry of Health, Order no. 351/2018 on approval of Organisational and functioning regulation of "Ion Chiricuță" Institute of Oncology in Cluj-Napoca. *Official Journal of Romania*, part I, no. 272/2018, (available in Romanian).
27. Ministry of Health, Order no. 444/2019 on the approval of the Rules on the establishment, organisation and operation of pharmaceutical units. *Official Journal of Romania*, part I, no. 270/2019, latest consolidated version, (available in Romanian).
28. Ministry of Health, Order no. 2382/2021 on the approval of the Methodology for the implementation of pharmaceutical services and the Nomenclature of pharmaceutical services. *Official Journal of Romania*, part I, no. 1061/2021, (available in Romanian).
29. Ministry of Health, Order no. 857/2022 for the approval of Organisational and operational rules and regulations of National Agency for Medicines and Medical Devices of Romania. *Official Journal of Romania*, part I, no. 283/2022, (available in Romanian).
30. Ministry of Health, Order no. 3695/2022 on approval of Organisational and functioning regulation of "Ana Aslan" National Institute of Gerontology and Geriatrics in Bucharest. *Official Journal of Romania*, part I, no. 1201/2022, (available in Romanian).
31. National Agency for Medicines and Medical Devices of Romania, Activity report for 2021. *Official Journal*

of Romania, part III, no. 1074/2022, (available in Romanian).
32. National Agency for Medicines and Medical Devices of Romania, #MedSafetyWeek2022, www.anm.ro/medsafetyweek2022/.
33. National Agency for Medicines and Medical Devices of Romania, Other ways to report adverse reactions, www.anm.ro/medicamente-de-uz-uman/farmaco-vigilenta/alte-modalitati-de-raportare-a-reactiilor-adverse/ (available in Romanian)..
34. National Agency for Medicines and Medical Devices of Romania, Report an adverse reaction, www.anm.ro/en/medicamente-de-uz-uman/farmacovigilenta/raporteaza-o-reactie-adversa/ (available in Romanian).
35. National Agency for Medicines and Medical Devices of Romania, Report an adverse reaction online, https://adr.anm.ro/ (available in Romanian).
36. National Agency for Medicines and Medical Devices of Romania, Scientific council decisions – Medicines for human use, 2013-2018, www.anm.ro/en/medicamente-de-uz-uman/legislatie/hotarari-ale-consiliului-stiintific/ (available in Romanian).
37. National Authority of Quality Management in Health, Handbook regarding accreditation standards for hospitals. Second cycle of accreditation, 2020, https://anmcs.gov.ro/web/wp-content/uploads/2022/01/Manualul-standardelor-de-acreditare-2020-1.pdf, (available in Romanian).
38. OECD/European Union, Health at a Glance: Europe 2022: State of Health in the EU Cycle. OECD Publishing, Paris, France, 2022; 140-142.
39. OECD, France. In: Better Regulation Practices across the European Union 2022, OECD Publishing: Paris, France, 2022; 164-165.
40. Oltean AM, Crișan O, Risk management in preventing medication errors in a community pharmacy. *Farmacia*, 2018; 66(4): 725-732.
41. Pharmaceutical Group of the European Union (PGEU), PGEU Best Practice Paper: Pharmacovigilance and Risk Minimisation, 06.05.2019, www.pgeu.eu/wp-content/uploads/2019/03/170926-PGEU-Best-Practice-Paper-on-Pharmacovigilance-and-Risk-Minimisation.pdf.
42. Regulation (EC) no. 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency. *Official Journal of the European Union*, L 136/2004.
43. Regulation (EU) no. 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) no. 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products. *Official Journal of the European Union*, L 348/2010.
44. Regulation (EU) no. 1027/2012 of the European Parliament and of the Council of 25 October 2012 amending Regulation (EC) no. 726/2004 as regards pharmacovigilance. *Official Journal of the European Union*, L316/2012.
45. Réseau Français des Centres Régionaux de Pharmacovigilance – RFCRPV, Découvrez le Réseau des CRPV. www.rfcrpv.fr/, (available in French).
46. Romanian College of Pharmacists, Iacob S. (coordinator), Legislation and Models of Standard Operating Procedures for Applying the Rules of Good Pharmacy Practice, February 2011, http://colegfarmbv.ro/legislatie/, (available in Romanian).
47. Romanian College of Pharmacists, Iacob S. (coordinator), Legislation and Models of Standard Operating Procedures for Hospital, May 2011, http://colegfarmbv.ro/legislatie/, (available in Romanian).
48. Romanian Parliament, Law no. 95/2006 on healthcare reform, republished. *Official Journal of Romania*, part I, no. 652/2015, latest consolidated version, (available in Romanian).
49. Romanian Parliament, Law no. 266/2008 of pharmacy, republished. *Official Journal of Romania*, part I, no. 85/2015, latest consolidated version, (available in Romanian).
50. Romanian Parliament, Law no. 134/2019 on reorganisation of the National Agency for Medicines and Medical Devices and amendment of further ruling provisions. *Official Journal of Romania*, part I, no. 587/2019, latest consolidated version, (available in Romanian).
51. Société Française de Pharmacie Clinique, Recommandations de Bonnes Pratiques. Bonnes Pratiques de Pharmacie Clinique, Mars 2022, https://sfpc.eu/wp-content/uploads/2022/03/Bonnes-Pratiques-de-pharmacie-Clinique-2022.pdf, (available in French).
52. Toma A, Regulations on pharmacovigilance in France and Romania (master's dissertation). "Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania, 2022; 5, 23-48, (available in Romanian).