

UNDERREPORTING OF ADVERSE DRUG REACTIONS FROM A LEGAL PERSPECTIVE

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ABSTRACT: *The pharmacovigilance system was designed and developed to ensure better monitoring of adverse drug reactions, with the aim of safeguarding patients' right to health. This reporting process begins as early as the clinical trial phase and continues after the drug is marketed through ongoing monitoring.*

Research in this field has highlighted underreporting of adverse drug reactions, even though reporting can now be done not only by healthcare professionals but also by patients.

This study aims to analyze the legal nature of the reporting obligation, the factors influencing underreporting, and the impact of regulations on this phenomenon. Furthermore, a key issue that needs to be debated in this context is whether this failure to report adverse reactions could give rise to legal liability.

KEYWORDS: *pharmacovigilance; underreporting; obligation; healthcare professionals; sanctions.*

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1. THE CONCEPT OF ADVERSE REACTION AND TYPES OF INCIDENT REPORTING

Before providing a definition of the concept of “adverse reaction,” it is important to mention the scope of pharmacovigilance. Thus, it represents “the science and activities related to the detection, evaluation, understanding, and prevention of adverse reactions (ARs) to drugs or any other drug-related issues”¹.

In this context of pharmacovigilance analysis, the basic concepts—namely, the relationship between the drug, the adverse reaction, and vigilance—must serve as a reference point.

In fact, a defining feature is the system for collecting, storing, scientifically evaluating, and assessing incidents resulting from the use of medical devices, as well as reporting them to the competent authorities for the purpose of continuously monitoring the risk-benefit ratio and taking the necessary measures—a process known as “vigilance” (*vigilantia*).

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¹ See the definition provided by the World Health Organization, available online at: <https://www.who.int/teams/regulation-prequalification/regulation-and-safety/pharmacovigilance>

On the other hand, an adverse reaction is a harmful and undesirable response caused by a medication, as defined in Law No. 95/2006 on health care reform. The same law clarifies, in Article 699(1)(13) and (14), the meaning of the term “serious adverse reaction”—“an adverse reaction that causes death, is life-threatening, requires hospitalization or prolongation of hospitalization, results in a lasting or significant disability or incapacity, or causes congenital anomalies or malformations,” as well as “unexpected adverse reaction”—“an adverse reaction whose nature, severity, or course does not correspond to the information in the summary of product characteristics”².

From this perspective, a distinction must be made between an adverse reaction and an adverse event, which refers to any harmful occurrence in a patient or clinical trial participant who has been administered a drug and which is not necessarily causally related to that treatment (Pirmohamed M, 1998). Consequently, an adverse event may consist of any unfavorable and undesirable sign (e.g., an abnormal laboratory finding), symptom, or disease that is temporally associated with the use of a medicinal product, whether or not it is considered to be related to the medicinal product.

Why is such a distinction important, including from the perspective of the concept of “response,” as it appears in the definition of an adverse reaction contained in Law No. 95/2006? We consider this distinction necessary in light of the legal consequences it entails. Thus, for the reporting obligation to apply, there need not be scientifically proven certainty; rather, a “reasonable suspicion” is sufficient. This position is also confirmed by the provisions of Directive 2010/84/EU³. Furthermore, it is essential to distinguish between an “adverse reaction” and an “adverse event,” since the reporting obligation applies to suspected adverse reactions, not to any unfavorable event that has occurred in connection with a drug.

One aspect that must be taken into account relates to the types of reporting that may occur; the European regulatory framework refers to spontaneous reporting, periodic reporting, reporting conducted within the framework of clinical trials, as well as the reporting of adverse reactions that are not serious, each with its own procedural framework and deadlines. Without providing an exhaustive overview of these—as they are not the subject of this study—we will limit ourselves to making a few observations. Spontaneous reporting is carried out by patients or healthcare professionals and can be submitted directly to the National Agency for Medicines and Medical Devices (ANMDMR) through various means, such as mail, fax, email, or even online.

Another type of reporting occurs within the context of clinical trials, which covers not only adverse reactions identified in subjects but also adverse events, and follows a distinct reporting procedure from spontaneous reporting.

Furthermore, national legislation (transposed from European directives) regulates the reporting of serious and non-serious adverse reactions, and periodic safety reports ensure an assessment of the benefit-risk balance of the drug over a specified period.

² See, in this regard, Law No. 95/2006 on health care reform, published in the Official Gazette No. 652 of August 28, 2015

³ Published in the Official Journal of the European Union No. L348/74 on December 31, 2010

2. THE LEGAL NATURE OF THE REPORTING OBLIGATION

Identifying the legal nature of the reporting obligation is essential for establishing the standard of conduct required of the party responsible for it. The legal characterization of this obligation varies depending on the party to whom it applies. A review of the national legislative framework reveals that, for the marketing authorization holder, this obligation is a legal one, arising from the provisions of Law No. 95/2006⁴. Thus, the marketing authorization holder is required to record all suspected adverse reactions of which it becomes aware and to report them to the competent authority in this field.

With regard to healthcare professionals, we can observe that the reporting obligation is imposed on them under Law No. 95/2006⁵, but it can also be inferred from the ethical standards specific to the profession of pharmacist.

This legal framework for the reporting obligation means that it cannot be limited or waived by contractual provisions, as it is a public policy obligation designed specifically to ensure the protection of citizens' health.

In this context as well, an important criterion for characterizing the reporting obligation is its classification as an obligation of means or of result (L. Pop, 2015). National legislation and doctrine do not provide an express provision in this regard, but it can be inferred by interpreting the provisions of Article 1481 of the Civil Code⁶, which constitutes the general law on the matter. Applying these provisions to the reporting obligation, it becomes clear that it is a means-based obligation (duty of care) rather than a result-based one. In other words, the healthcare professional or the marketing authorization holder is not obligated to guarantee the detection and reporting of every adverse reaction that may occur with a medication, but only to exercise the necessary diligence to identify and subsequently report them to the competent authorities. This argument is also confirmed by the legal text of Directive 2010/84/EU, which refers, as we have pointed out, to a "reasonable suspicion."

Determining the legal nature of the reporting obligation is not without legal consequences. If we consider the possibility of legal liability arising from a failure to comply with the reporting obligation, then classifying it as a duty of means implies, from an evidentiary standpoint, that the professional was aware of the existence of an adverse

⁴ According to the provisions of Article 835(1) of Law No. 95/2006: "(1) Marketing authorization holders must record all suspected adverse reactions, whether in the EU or in third countries, that are brought to their attention, regardless of whether these reactions are spontaneously reported by patients or healthcare professionals or are observed during a post-authorization study. Marketing authorization holders must ensure that these reports are accessible at a single point of contact within the EU. As an exception to the provisions of the first sentence, suspected adverse reactions observed during a clinical trial shall be recorded and reported in accordance with the Rules on the Implementation of Good Clinical Practice in the Conduct of Clinical Trials on Medicinal Products for Human Use, approved by order of the Minister of Health."

⁵ Article 568(1)(j) of Law No. 95/2006 expressly provides: "The practice of the profession of pharmacist is carried out through the following activities: (j) reporting adverse reactions to pharmaceutical products to the competent authorities."

⁶ Art. 1481 of the Civil Code provides that "(1) In the case of an obligation of result, the debtor is required to provide the creditor with the promised result. (2) In the case of obligations of means, the debtor is required to use all necessary means to achieve the promised result. (3) To determine whether an obligation is one of means or of result, particular consideration shall be given to: a) the manner in which the obligation is stipulated in the contract; b) the existence and nature of the consideration and the other elements of the contract; c) the degree of risk involved in achieving the result; d) the influence that the other party has over the performance of the obligation."

reaction and failed to act with the diligence required by professional standards (Tița-Niculescu, 2018). Therefore, the mere finding that an adverse reaction was not reported is not sufficient to automatically give rise to legal liability.

In other countries, this obligation to report adverse reactions is also legally mandated, but sanctions are also imposed in cases of noncompliance. By way of example, we note the situation in France, where all healthcare professionals have a legal obligation to report adverse drug reactions, with the consequence that sanctions (criminal or civil) are imposed in the event of noncompliance (M. Kaeding, 2017). On the other hand, Germany is also a notable example, where the reporting obligation is stipulated only in codes of ethics, constituting a professional conduct requirement that does not result in sanctions (M. Kaeding, 2017). The same is true in the U.S., where the reporting obligation is not a legal requirement but rather an ethical one (E. Klein, 2013).

From the provisions as a whole, it can be seen that there is no regulatory harmonization in this regard, and it remains up to each Member State to decide how it chooses to legislate the reporting of adverse reactions. However, if we consider the provisions of Directive 2010/84/EU, we can see that Article 102 is not mandatory in nature: “Member States shall take all necessary measures to encourage patients, physicians, pharmacists, and other healthcare professionals to report suspected adverse reactions to the competent national authority or to the marketing authorization holder.”

Last but not least, we consider it essential to distinguish between a failure to comply with the reporting obligation and a failure to inform the patient about possible adverse reactions. Regarding the latter, it is unanimously recognized that a breach of such an obligation may give rise to legal liability for medical malpractice (J.S. Kass, 2019).

3. CAUSES OF UNDERREPORTING OF ADVERSE DRUG REACTIONS

The scientific literature has established that adverse drug reactions are significantly underreported internationally, with estimates of underreporting reaching as high as 94% (Hazell L, 2006). This results in a delay in detecting safety signals and, consequently, jeopardizes the entire process of understanding a drug’s safety profile (Härmark L, 2008). Furthermore, despite patients’ recognition of this right, their contribution remains limited.

This raises the question: what might be the causes or factors leading to the underreporting of adverse drug reactions? A study addressing this issue dates back to 1976, in which a framework was developed outlining the behaviors of healthcare professionals that influence the reporting process⁷. Among these factors were, for example, a certain belief among healthcare professionals that only safe drugs were approved for the market, as any adverse reactions were already known; a fear of facing potential legal liability as a result of reporting; the mistaken belief that only serious adverse reactions should be reported; a certain indifference toward the potential impact of the report; or even a lack of time to complete the form (Palleria C, 2013).

At present, it can be said that these factors still persist, and additional causes of underreporting have even emerged. Thus, specialized studies have highlighted as causes

⁷ See, in this regard, the diagram developed by the founder of pharmacovigilance, W.H.W. Inman, which highlights the seven attitudes or behaviors associated with underreporting of adverse reactions; this information is available online at: <https://philpapers.org/archive/AUSSAR.pdf>

the lack of training for professionals on how to report adverse reactions or their limited knowledge of this process (Ishaqui AA, 2026). In addition, certain causes related to the organization of the reporting process have been identified, such as a lack of time to complete the forms, limited access in certain areas to electronic reporting platforms, or even bureaucratic hurdles (Shafei, 2023).

From another perspective, the causes of underreporting among patients differ from those among healthcare professionals; in the case of patients, these include, for example, a lack of information regarding reporting systems, the absence of feedback on submitted reports, and potential costs associated with submitting the forms (Al Dweik R, 2017).

Essentially, specialized studies have shown that the main factor discouraging the reporting of adverse reactions is the possibility of legal liability. In this regard, we believe it would be useful to distinguish between this reporting obligation and the prior conduct of the physician or pharmacist that led to the adverse reaction. Consequently, one possible solution to prevent such reluctance to report is to ensure that reporting remains anonymous and confidential.

Another issue that must be addressed in this context is the impact of regulations on the reporting obligation, in which regard several clarifications are necessary. Thus, the existence of a mandatory legal provision establishing this obligation does not always guarantee an increase in the reporting of adverse reactions. Notably, a study has shown that in countries such as France, Sweden, Norway, and Italy, despite explicit regulations, the reporting rate remains low; however, this does not mean that making reporting mandatory is entirely ineffective⁸. On the other hand, the existence of appropriate regulations in this area can also contribute to improving other aspects of the reporting process, such as the quality of the data provided. In fact, this aspect has been further strengthened by the implementation of the EudraVigilance platform.

In summary, what can be observed from the body of research conducted in this field is that the impact of regulations on the reporting of adverse reactions is not uniform, but depends on how this obligation is established in each country. Furthermore, patients play a growing role in increasing reporting, as does a more efficient organization of the entire system.

4. LEGAL CONSEQUENCES OF UNDERREPORTING ADVERSE REACTIONS

Under national law, based on the provisions of Law No. 95/2006, we can conclude that marketing authorization holders are subject to administrative liability for violating pharmacovigilance obligations. Specifically, failure to comply with the obligations to record and report adverse reactions is punishable by an administrative fine⁹.

Similarly, at the European level, with the adoption of Regulation (EU) No. 1235/2010 and Directive No. 2010/84/EU, penalties were established for non-compliance with

⁸ See in this regard: <https://dash.harvard.edu/server/api/core/bitstreams/7312037c-accf-6bd4-e053-0100007fdf3b/content>

⁹ For more information, see the provisions of Article 875(1)(d) of Law No. 95/2006

pharmacovigilance obligations, although it remains up to the individual member states to determine how they choose to transpose these into their domestic legislation¹⁰.

Specifically, with regard to healthcare professionals, it should be noted that they are not subject to administrative liability as marketing authorization holders are; however, a breach of the reporting obligation may be sanctioned in accordance with the provisions of the profession's specific codes of ethics. On the other hand, any potential civil liability appears difficult to establish. We state this because, for civil liability to arise, the conditions set forth by general law in this area—namely, the Civil Code—must be met, specifically: an unlawful act, damage, fault, and a causal link. However, proving a causal relationship between the failure to report an adverse reaction in a patient and the resulting harm to another person is a complex undertaking. In any case, we believe that one cannot equate a professional's failure to report an adverse reaction with medical negligence, a requirement that must be met for civil liability to apply. The distinction between these is all the more essential given that one of the factors contributing to underreporting, as we have pointed out, is precisely this possibility of being held liable.

5. CONCLUSIONS

The analysis of the obligation to report adverse reactions, as well as the possible causes of their underreporting, highlighted not only a simple statistical shortfall but also issues with the way the entire reporting system is structured. It was found that legislators' approaches to regulating this obligation vary from one country to another, and the adoption of a mandatory legal provision does not always lead to the desired effect. Instead, what is essential to emphasize is the distinction between failure to report and the establishment of potential medical negligence that could give rise to legal liability. We believe that this misconception among professionals represents an obstacle to the pharmacovigilance system.

Regarding the factors influencing the reporting of adverse reactions, a consensus has emerged among specialized studies, with liability concerns and a lack of training in this area being the predominant factors.

Given these considerations, we believe that the effectiveness of the pharmacovigilance system can be improved, not necessarily by increasing the applicable penalties, but by reshaping the legal perception of what this obligation entails.

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¹⁰ Paragraph 29 of Directive 2010/84/EU provides that "For the purposes of applying the provisions on pharmacovigilance, Member States should ensure that effective, proportionate, and dissuasive penalties are imposed on marketing authorization holders in the event of noncompliance with pharmacovigilance obligations."

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