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Medical devices post-market surveillance: analysis of notifications of Notivisa registered in the state of Paraná, Brazil

Tecnovigilância: análise das notificações do Notivisa registradas no estado do Paraná, Brasil

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ABSTRACT

Introduction: The medical devices post-market surveillance monitors adverse events and technical complaints of the medical devices through the National Notification Health Surveillance System (Notivisa). Companies holding the registration of products must investigate and adopt measures related to notifications. **Objective:** To analyze the profile of notifications of Notivisa medical devices registered in Paraná from 2006 to 2018 and the investigations of companies that own the register of medical devices notified in 2018. **Method:** A descriptive, retrospective, documental study of medical devices post-market surveillance notifications registered in Paraná from 2006 to 2018 and investigations registered by the 2018 notifications companies. **Results:** 17,122 medical devices notifications were registered in Paraná from 2007 to 2018, with only 109 notifications related to the line of equipments and 255 of products for *in vitro* diagnosis. From the 2,327 notifications of 2018, the responses of 404 notifications were analyzed, and the description of the adoption of corrective and, or preventive measures by the companies was identified in 20 confirmed, 22 inconclusive, 32 probable and 3 discarded notifications. In 126 notifications, there was a need for more information from the notifier to subsidize the investigation by the company. **Conclusions:** Notivisa contributes to the monitoring of the quality, efficacy and safety of medical devices and enables the analysis of the companies' performance in containing health risks.

KEYWORDS: Product Surveillance Post-market; Health Surveillance; Health Risk

RESUMO

Introdução: A tecnovigilância monitora os eventos adversos e as queixas técnicas dos produtos para saúde por meio do Sistema Nacional de Notificação em Vigilância Sanitária (Notivisa). Cabe às empresas detentoras de registro dos produtos investigar e adotar as medidas cabíveis frente às notificações. **Objetivo:** Analisar o perfil das notificações de tecnovigilância do Notivisa registradas no Paraná, no período de 2006 a 2018, e das investigações das empresas detentoras de registro dos produtos para saúde notificados em 2018. **Método:** Estudo descritivo, retrospectivo e documental das notificações de tecnovigilância do Notivisa registradas no Paraná, no período de 2006 a 2018, e investigações registradas pelas empresas das notificações de 2018. **Resultados:** Foram registradas no Paraná 17.122 notificações de tecnovigilância de 2007 a 2018, sendo apenas 109 notificações relacionadas à linha de equipamentos e 255 de produtos para diagnóstico *in vitro*. Das 2.327 notificações de 2018, foram analisadas as respostas de 404 notificações, sendo identificada a descrição de adoção de medidas corretivas e/ou preventivas adicionais pelas empresas em 20 notificações confirmadas, 22 inconclusivas, 32 prováveis e três descartadas. Em 126 notificações foram relatadas necessidade de mais informações do notificador para subsidiar a investigação pela empresa. **Conclusões:** O Notivisa contribui com o monitoramento da qualidade, eficácia e segurança dos produtos para saúde e possibilita a análise da atuação das empresas na contenção de riscos sanitários.

PALAVRAS-CHAVE: Vigilância de Produtos Comercializados; Vigilância Sanitária; Risco à Saúde Humana

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INTRODUCTION

Correlates (*correlatos*, in Portuguese), also called medical devices, are some of the products subject to health control by the Brazilian National Health Surveillance System (SNVS)[1,2]. This category covers a wide range of products used in medical, dental and physical therapy procedures, as well as in the diagnosis, treatment, rehabilitation or follow-up of patients. These products may be divided into groups of materials, medical equipment or diagnostic products for *in vitro* use[3].

According to data from the Brazilian National Health Surveillance Agency (Anvisa), there was a 27% increase in the number of requests for regularization of new medical devices from 2016 to 2018, and in 2018 alone a total of 5,780 items were approved[4]. Considering that the use of these products may pose risks to patients when exposed to actual conditions of large-scale use, and since in these circumstances rare events and unforeseen problems can occur, monitoring the use of medical devices is essential. Therefore, medical device post-market surveillance actions are essential to ensure safety in the use of medical devices made available to the population[5].

Medical device post-market surveillance is understood as a surveillance system for adverse events and technical complaints of medical devices in the post-marketing phase, with a view to recommending measures to ensure the protection and promotion of the population's health[6]. Adverse events can be defined as unwanted effects in humans resulting from the use of products subject to health surveillance, like death, disability or permanent harm to an organism's structure, fetal disturbance or risk, among others. Technical complaints, in turn, are suspected changes/irregularities of a product or company in their technical or legal aspects, and which may or may not cause harm to individual and collective health[7].

The registration and monitoring of adverse events and technical complaints related to products subject to health surveillance have been done by the National Health Surveillance Notification System (Notivisa) since December 2006. In this system, healthcare facilities, companies holding the registration of products, health surveillance bodies and independent professionals can file reports after making their own registration in the system[5]. Other unregistered users can make reports through electronic forms available on Anvisa's website. Medical device reports are analyzed according to the criticality of the occurrence and, based on that, the need for SNVS investigation is determined. Reports of death, permanent or severe temporary injury must always be investigated. Other reports of adverse events are investigated according to their severity, frequency and the operational capacity of the technical unit. The criterion for investigating reports of less severe temporary injuries and technical complaints is the increase in their occurrence in the system and the operational capacity of the technical unit[5].

Companies holding the registration of products are responsible for setting up and implementing a medical device post-market surveillance system in their companies and assigning at least one professional, with higher education and trade association registration, to be responsible for this activity[7]. Companies holding the registration of products have access to the system to check reports without identifying the reporting party. After company analysis, companies can attach their investigation to the report and conclude it as confirmed, probable, inconclusive, or discarded, as defined below[5].

a. Confirmed: confirmed causal relationship between product and occurrence;

b. Probable: the causal relationship between the product and the occurrence is not confirmed, but there is evidence of likelihood that the use of the product could have caused the occurrence;

c. Inconclusive: the causal relationship between the product and the occurrence is not confirmed, since the information surveyed during the investigation is insufficient or contradictory and could not be completed or verified;

d. Discarded: there is confirmation of the absence of causality between the use of the product and the occurrence or there is clear evidence of the impossibility of the use of the product being the cause of the occurrence. In this case, the information verified in the investigation is sufficient to discard the case.

Notivisa reports assume the existence of risks that may pose threats to the health of users of products suspected of quality deviation. These occurrences may be associated with poor product quality, misuse, inherent user factors, as well as factors related to the product itself, which may have been indicated in the registration process, such as Acceptable Quality Level or expected adverse events[5].

Companies holding the registration of products are responsible for investigating the cause of nonconformities related to the product, process, or quality system by taking corrective and preventive actions. The effectiveness of these actions must be verified and recorded. All complaints involving possible nonconformities of the product or that may lead to death, injury or threat to public health should be examined, assessed and investigated[8,9].

Therefore, the actions of the companies holding the registration of products in investigating the report and adopting corrective and preventive measures, if applicable, are essential to ensure the quality and safety of marketed medical devices.

The objective of this study was to analyze the profile of Notivisa's medical device post-market surveillance reports made in the Brazilian state of Paraná from 2006 to 2018 and the investigations of the companies holding the registration of medical devices reported in 2018.

METHOD

The Division of Health Surveillance of Products (DVVSP) of the Paraná State Department of Health conducted a descriptive, retrospective, documentary study of the medical device post-market surveillance reports filed with Notivisa in Paraná, from 2006 to 2018, and the responses of the companies holding the registration of medical devices reported in 2018. Monitoring Notivisa is one of the state's responsibilities, as determined by Ordinance n. 1.660, of July 22, 2009, to subsidize decision making and strengthen health promotion and protection[10].

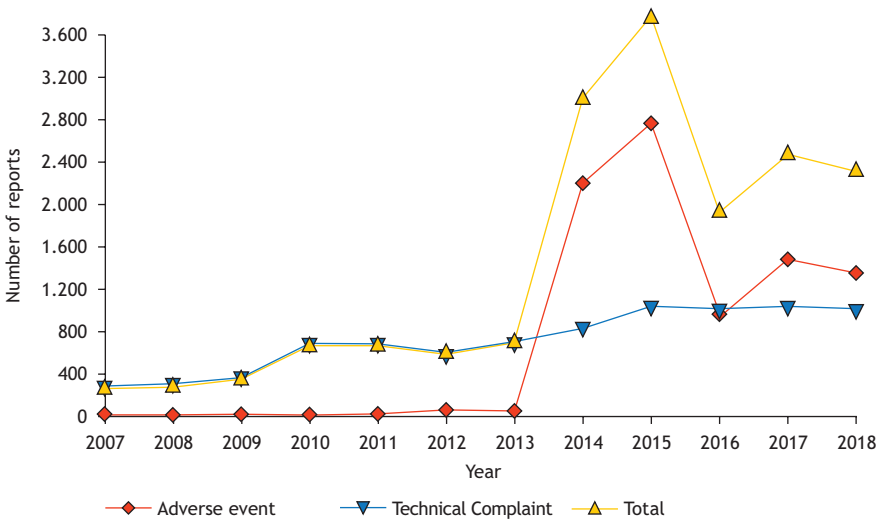
Report data were exported to a Libre Office spreadsheet via the Notivisa Report Management topic on February 14, 2019. The following filters were applied to the system to retrieve the data: start date and end date (January 1 to December 31 of each year); product that motivated the report (medical device, hospital equipment, reagent kit for *in vitro* diagnosis); type (technical complaint, adverse event) and state of the federation where the identification or occurrence took place (Paraná-PR). Reports were quantified by: year, report type, and product line.

The second stage of the study excluded reports from the company that had the highest number of reports in the period, since there had already been an investigation by SNVS in that company. For the assessment of the responses, the reports that presented conclusion by the company were selected in the spreadsheet. The description of the investigation conducted by the companies was consulted in the history of each report in Notivisa. We analyzed whether or not the companies' responses mentioned the adoption of corrective and/or preventive measures and the justifications of those companies that did not do any investigation. Responses that described the need for more information about the occurrence or need for guidance to the reporting party were also analyzed, since information about the reporting party is confidential in the access granted to the companies. The disclosure of the results of the analysis was authorized by the Health Surveillance Coordination where the DVVSP is located.

RESULTS AND DISCUSSION

Paraná has had a high number of reports of medical device post-market surveillance in Notivisa ever since its implementation, as shown in Figure 1. The system was implemented in December 2006, so we considered reports made as from 2007, totaling 17,122 by 2018. These reports represent occurrences related to medical devices used in the state, although manufacturers or importers of these products may be located in any other region of the country. Over time, there has been a significant increase in the number of reports, which highlights the importance of the system for the detection, monitoring, control and availability of data related to medical devices. These data corroborate previous studies showing the increase in the number of reports over the years in other regions of the country and types of products submitted to health surveillance[12,13,14].

There is an increase in the number of reports after 2014, because a company located in Paraná intensified its reporting process. Among the reports of said year, 2,177 originated in this company. The high number of adverse event reports as from 2014 was also a result of reports made by the same company, which recorded 2,169 cases that year. It should be noted that most of these reports were made by the company itself considering the occurrences reported to its Customer Service. As required by Resolution of the Collegiate Board (RDC) n. 67 of December 21, 2009[7], medical device manufacturers must notify SNVS of: technical complaints, adverse events, deaths, situations of serious threat to public health and any medical device counterfeits that they become aware of. Thus, reports made by companies



Source: Notivisa (2019).

Figure 1. Number of Notivisa medical device post-market surveillance reports recorded in Paraná, from 2007 to 2018.

should always be encouraged, as well as the proper handling of any deviations. Therefore, the existence of reports in the system is not the only factor for assessing product quality, because, in addition to the possibility of underreported cases, the company's dealings with the occurrence must also be considered.

It is also noteworthy that the increase in the number of reports over the years was also driven by the intensification of DVVSP initiatives to promote and encourage the use of Notivisa.

There are more reports in the line of articles (97.9%, n = 16,758) and fewer reports in the line of equipment (1.5%, n = 255) and *in vitro* diagnosis (0.6%, n = 109), as shown in Figure 2. The detection of quality deviations involving equipment and *in vitro* diagnosis products occurred mainly in the area of clinical engineering and clinical analysis laboratories, respectively. Thus, there is a need for greater involvement of these sectors in the detection and investigation of potential adverse events and technical complaints in various classes of medical devices.

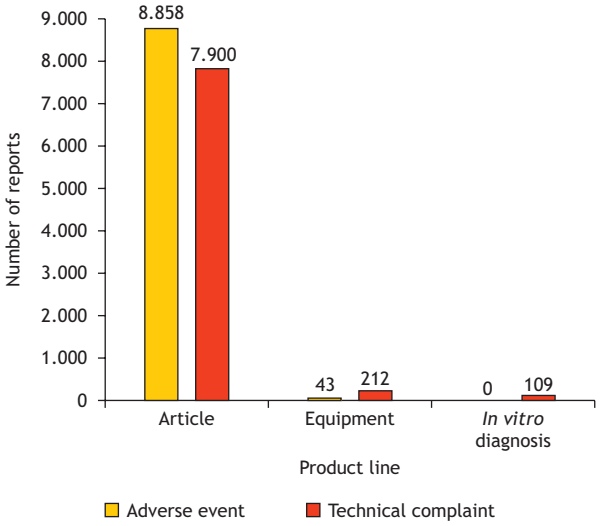
In the analysis of the results of the investigations made by the companies, we found that 1,929 (82.9%) of the reports made in 2018 were concluded as confirmed (5.6%, n = 108), probable (5.5%, n = 107), inconclusive (60.3%, n = 1,163) or discarded (28.6%, n = 551). The higher number of unconfirmed reports demonstrates the need to assess the causes that lead to these conclusions and the possible remaining risk of these episodes occurring again. Of these reports, 1,302 were excluded because they originated in the company that was already being investigated by the SNVS. Therefore, 627 reports were selected and 404 responses (64.3%) were analyzed.

The investigation of the reports by the companies holding the registration should be able to identify the correlation of adverse events or technical complaints with the product, in order to support the adoption of measures to control or minimize the risks to the population. Therefore, the assessment of the company that holds the authorization is essential for taking action regarding reports in Notivisa.

Note that the aforementioned reports may be related to medical devices manufactured or imported by companies located in other Brazilian states. Nevertheless, when the company that holds the registration is located in the state of Paraná, there is a greater scope for investigating the occurrence of adverse events and technical complaints, since these companies are periodically inspected by health surveillance. The standard operating procedures harmonized in the SNVS determine that evidence of post-marketing surveillance should be verified in inspections at these companies to identify trends, risk situations, and more.

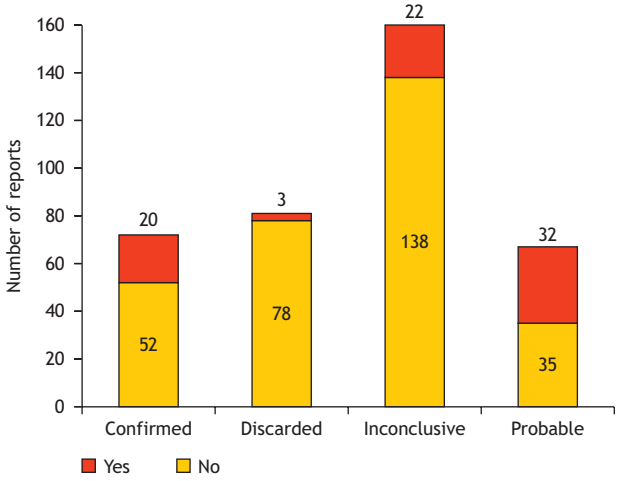
Of the 404 reports analyzed, the adoption of additional corrective and/or preventive measures was described by the companies holding the registration of products as follows: 27.4% of reports were concluded as confirmed, 12.9% inconclusive, 47.8% probable and 3.2% discarded, according to Figure 3. Therefore, it is verified that the confirmation of the report is not directly related to the adoption of measures by the companies, as well as the other conclusions may result in the adoption of complementary measures.

It was further noted that companies did not investigate 23 reports due to batch-related issues (n = 14), expired product (n = 1), discontinued product (n = 1), report access not authorized due to system inconsistency (n = 5) and rectification of the report by Anvisa (n = 2). It is noteworthy that 126 reports described the need for more information about the occurrence, sample, product photo and/or contact with the reporting party to support the investigation. These data demonstrate the need for qualification of the data provided by the reporting party, since companies do not have access to data about the reporting parties to ask for further information. Therefore, to enable



Source: Notivisa (2019).

Figure 2. Number of Notivisa medical device post-market surveillance reports recorded in Paraná, by line and type, 2007 to 2018.



Source: Notivisa, 2019.

Figure 3. Number of reports that described the adoption of corrective and/or preventive measures to respond to Notivisa medical device post-market surveillance reports recorded in Paraná, 2018.

insight into the causality, the reports must be complete and consistent. It is noteworthy that the need for qualification of the information provided by the reporting parties was also identified in other studies[12,15]. Considering that occurrence reporting by companies is compulsory, the analysis of the possibility of different outcomes in reports between those made by the company itself regarding its products and those made by other reporting parties can confirm response trends.

Monitoring the outcome of investigations enables the analysis of trends such as the recurrence of reports of the same product after the adoption of corrective and preventive measures by the company, in order to demonstrate possible failure in the investigation system and assess the effectiveness of the adopted measures. Furthermore, it can be identified whether there is any bias in the request for additional information by companies from the same reporting party or if the lack of essential information is related to the information system.

Considering that Notivisa does not provide information from companies' investigations in a grouped format, we have to analyze it case by case. Therefore, the system should be improved for better data availability and, with that, facilitate the adoption of this practice in work routines and contribute to the decision making process.

CONCLUSIONS

Health precaution and prevention actions are a priority in the health control agenda of the SNVS. Medical device post-market surveillance is one of the cornerstones for the control and safety of products available in the domestic market. However, it still needs to be strengthened and articulated with other strategies of health protection and promotion, both those done by health surveillance bodies and those by other stakeholders, like healthcare services, companies, healthcare professionals and users[16].

The occurrence of adverse events and technical complaints related to medical devices presuppose the existence of risks and threats to human health. Thus, Notivisa becomes a fundamental tool for monitoring the quality and safety of products available on the market and for adopting appropriate control measures, safety alerts, updating health legislation, among other actions to protect the population's health[17].

The qualification of the information provided by the reporting party supports the investigation of the occurrence by the companies that hold the registration of the product in question. However, the robustness of the investigation and the adoption of corrective and preventive measures are also directly related to the Quality System of the manufacturer or importer of the product.

The decentralization of medical device post-market surveillance actions toward state and municipal health surveillance bodies, with the strengthening of regionalized actions, enables greater monitoring of products supplied to the population. However, the decentralization of these activities is not yet consolidated, given the primacy of inspection initiatives and the various forms of organization and structuring of states and municipalities[16].

The setup of a continuous and effective process of monitoring, investigation and control contributes to the identification and minimization of health risks. It is noteworthy that the main resource used in this study was the human resource for systematization and data analysis. Therefore, the restructuring of health surveillance teams to increase operational and technical capacity is essential for the fulfillment of state and municipal duties defined in Ordinance n. 1.660/2009[10], as well as for improving the system. We also highlight that it is necessary to discuss and strengthen the decentralization process through strategic actions that can be more comprehensive than simply using the information system[16].

The results of this study demonstrate the possibility of local health surveillance bodies acting in the continuous monitoring of companies' responses to Notivisa reports. Considering that health surveillance has access to data on the reporting party, its role as an interlocutor in the communication demands between the company and the reporting party can contribute to the improvement of investigations and the adoption of appropriate measures. Monitoring of reports also enables the identification of trends, investigations, collection of samples for Fiscal Analysis, among other actions. As described in a study by Branco et al.[17], it is important to design monitoring programs agreed upon among SNVS entities in order to enable laboratory analyses to assess the quality of products used at the national level.

Another thing health surveillance can do is to analyze possible quality deviations underreported by companies during inspections. Therefore, the qualification of the technical teams to assess the adequacy of investigations carried out by companies is fundamental to the identification of faulty Quality Management Systems in risk containment.

Notivisa enables the filing of report information in a single channel through the SNVS, however, improving it to expedite and enhance user interface and communication is critical to the fast identification and containment of health risks.

Corroborating previous studies on the possibility of underreported cases, we should encourage the promotion of Notivisa as an official channel for reporting cases, raising awareness of healthcare professionals to use the system and strengthening the Sentinel Network, which is one of the most important reporting parties[13,14,17].

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Conflict of Interest

Authors have no potential conflict of interest to declare, related to this study's political or financial peers and institutions.