REVIEW
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Regulation of medical devices: post market surveillance as risk management strategy

Regulação de dispositivos médicos: vigilância pós-mercado como estratégia de gerenciamento de riscos

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ABSTRACT

Introduction: Managing medical device risks is an activity that spans all phases of the life cycle of the product and is essential for the products available for use to behave effectively and safely. **Objective:** To discuss on the post-marketing surveillance model of medical device (technovigilance) in Brazil, present international experiences and reflect on their insertion in risk management. **Method:** Narrative review, based on regulations published on institutional sites and on texts published from 2000 on the Portal Capes, Virtual Health Library, SciELO and on the bases Bireme, ScienceDirect and Pubmed, in which technovigilance is presented as the action of State and as part of risk management in health services. **Results:** Different countries adopt the registration and inspection of good manufacturing practices as a way to regulate devices, which does not exhaust the risk assessment. Notification of medical devices related problems is one of the post-market surveillance strategies, in addition to cross-country information exchange, technology assessment studies, active surveillance in health services, and aggregating actual behavioral data during use. **Conclusions:** The technological advancement and incremental changes of DM challenge the State to review risk assessment criteria based on pre-market data, aggregating post-market related data, enabling risk identification and event chain intervention.

KEYWORDS: Technovigilance; Risk Management; Medical Devices; Health Surveillance

RESUMO

Introdução: Gerenciar riscos de dispositivos médicos é uma atividade que perpassa todas as fases do ciclo de vida, sendo essencial para que os produtos disponíveis para uso se comportem de maneira efetiva e segura. **Objetivo:** Discutir o modelo de vigilância pós-comercialização de dispositivos médicos (tecnovigilância) no Brasil, apresentar experiências internacionais e refletir sobre sua inserção na gestão do risco. **Método:** Revisão narrativa, com base em regulamentos publicados em sítios institucionais e em textos publicados a partir do ano 2000 no Portal Capes, Biblioteca Virtual em Saúde, SciELO e nas bases Bireme, ScienceDirect e Pubmed, em que a tecnovigilância é apresentada como ação do Estado e como parte do gerenciamento de risco em serviços de saúde. **Resultados:** Diferentes países adotam o registro e a inspeção de boas práticas de fabricação como formas de regularização de produtos, o que não esgota a avaliação do risco. A notificação de problemas relacionados aos dispositivos médicos é uma das estratégias de vigilância pós-mercado, que se soma ao intercâmbio de informações entre países, a estudos de avaliação de tecnologias e à vigilância ativa nos serviços de saúde, agregando dados reais do comportamento durante o uso. **Conclusões:** O avanço tecnológico e as mudanças incrementais destes produtos desafiam o Estado a rever critérios de avaliação de riscos baseado em dados pré-mercado, agregando dados relacionados ao pós-mercado, possibilitando a identificação de riscos e intervenção na cadeia de acontecimentos.

PALAVRAS-CHAVE: Tecnovigilância; Gerenciamento de Risco; Dispositivos Médicos; Vigilância Sanitária

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INTRODUCTION

Innovation in health-related technologies has guided discussions about access policies and regulation of various medical devices and processes. While on the one hand innovation brings countless possibilities for new treatments, with possible improvement in quality of life, on the other hand, it may also present risks (anticipated or not) that need to be managed and controlled[1].

Several health-related technologies that are part of the healthcare universe involve various levels of sophistication and are subject to health surveillance, including medical devices (MDs)[2].

MDs, also known as healthcare products, include medical products (medical supplies and equipment) and products for *in vitro* diagnosis. These products are part of the routine of the most distinguished healthcare services in their effort to diagnose and treat people with medical needs and to relieve the problems faced by those with functional disabilities[3]. They may be involved in simple procedures and have smaller technological complexity, like tongue depressors, procedure gloves and syringes, or have greater complexity, like hip and spine orthopedic implants, cardiac stents, products for diagnosis of diseases like hepatitis, HIV/AIDS, tuberculosis, life monitoring and support equipment, among other items that are essential in healthcare[3,4].

Managing risk in the use of MDs is a challenge, not only because there are many products and distinct levels of technological complexity and density, but also because of the very notion of risk, which is built according to each social context and therefore has multiple meanings[5]. In general, countries seek to act in risk control through Regulatory Authorities (RAs), represented by various institutions, both in the pre-marketing and in the post-marketing phases (technovigilance). At any rate, it should be noted that there are several regulatory models around the world, including countries where there is no regulation at all[1,4].

Although different health technologies pose risks in their context of use, MDs have some particularities that pose challenges in their monitoring process, such as implantation in the human body (permanently or not), need for a learning curve, influence of human factors in the use process, dependence on structural factors related to installation, interdependence between MDs, the complexity of these products, among others[6].

Recognized therapeutic propositions go hand in hand with new technologies, thus turning healthcare services into privileged spaces for observing product behavior, both for comparing technologies and for identifying adverse events (AEs) and technical complaints (TCs). New technologies that enable countless benefits in healthcare require close surveillance in risk control. Additionally, some of these risks can only be recognized when available to the public. In this sense, surveillance strategies that enable the monitoring of products on a daily basis have been recognized as particularly important in MD monitoring and as drivers of more thorough risk management plans. Healthcare services, with their different profiles, are able to provide more robust information on MD performance and, with that, support risk control and mitigation measures. On another management front are manufacturing companies that, in order to make a product available on the market, must have information that ensures that the risks are "acceptable in relation to the benefit provided to the patient", as well as demonstrate that they have been "reduced to a level that is compatible with the protection of human health and safety"[7]. They must also sustain this surveillance throughout the life cycle of the product. The State has functions related to social and economic development and plays an important role in questions related to access to health technologies. It also plays a leading role in health protection questions. In its role as health regulator, the State is responsible for conducting health control activities as a mediator between users and producers, thus providing "a minimum level of safety as regards the quality of the products marketed and the quality of what is purchased"[8].

The State is supposed to safeguard the society and, acting in the regulation of MDs, to determine minimum criteria for a product to be authorized for use, as well as to monitor its performance. Using post-marketing information, the risk management process can be fully understood, not only with information obtained from bench studies or controlled processes, but from routine use.

In Brazil, MD surveillance is the responsibility of the National Health Surveillance System (SNVS), which, according to the Unified Health System precepts, has its activities decentralized in coordinated actions between the three entities of the federation, with different levels of organization, as well as structural limitations and different perceptions of the role of health surveillance. Federation entities have different responsibilities in managing MD risk, both in the authorization (pre-marketing) phase and in post-marketing questions.

Risk management pervades the entire life cycle of MDs. It is therefore necessary to associate and balance the use of activities from both the authorization phase and those that enable post-marketing monitoring. The purpose of this paper is to discuss the post-marketing surveillance model in MD risk management within the SNVS. This paper also intends to present international regulatory experiences and contribute to the reflection on the need for the adoption of technovigilance as an important element of risk management, against the background of sentinel services as instruments for monitoring the behavior of MDs.

The topic of MDs, from the perspective of technovigilance, does not stand out in the field of research, neither in Brazil nor internationally. This represents an opportunity for a more careful look into the topic, especially in terms of management.

METHOD

This is a narrative review related to the topic of MD risk management, focused on technovigilance activities. Searches were carried out from 2000 onwards (date of creation of technovigilance in Brazil), on Portal Capes, Virtual Health Library (BVS), in the Scientific Electronic Library Online (SciELO) and in the Bireme, ScienceDirect and Pubmed databases, from February 2016 to May 2019. Some cross references were accessed occasionally. We used keywords indexed as "*vigilância de produtos para a saúde*" (medical device surveillance) (which includes medicines), "*dispositivos médicos*" (medical devices), "*vigilância sanitária*" (health surveillance), "*gerenciamento de risco*" (risk management), as well as their correspondents in English. We also included non-indexed but commonly used terms in health surveillance in Brazil, like "*produtos para a saúde*" (medical devices), "*vigilância pós-comercialização de produtos para a saúde*" (medical device post-marketing surveillance) and "*tecnovigilância*" (technovigilance). The keywords were identified in the title and abstract/subject. The texts included in this analysis bring post-marketing surveillance as a public policy and a State practice. Experiences in health technovigilance have also been included. Texts that addressed the follow-up of specific MDs and protocols and professional practices were excluded. Some references could be found via free search on Google. Institutional websites were used to search for regulations, texts and documents that support MD surveillance at national and international levels.

RESULTS AND DISCUSSION

Experiences in the medical device regulation and surveillance process in the United States, the European Union, Japan, and Brazil

MD marketing authorization follows risk classifications, which have different nomenclatures and rules, depending on the country, as well as post-marketing actions.

Manufacturers' compliance with the requirements related to Good Manufacturing Practices (GMP) has been evaluated to support the decision on whether or not to authorize the marketing of a product. Clinical research data are also part of the requirements for MD assessment, especially for higher risk class products[1].

Established regulatory models do not prevent the occurrence of failures, and this can be confirmed by countless recall actions done worldwide. Frequent reports of AEs related to MDs, as well as the large number of corrective and recall actions, reinforce the idea that pre-marketing controls are insufficient to prevent products from failing or causing harm[9]. They also reinforce the importance of establishing post-marketing control mechanisms to anticipate risks. The recall of the French PIP breast implant, due to increased reports and the identification of GMP failures, triggered many surveillance actions around the world, leading to changes in regulatory frameworks[1,9]. Recall actions have affected several products over the years, such as pacemakers, cardiac defibrillators, cochlear and orthopedic implants, surgical instruments, infusion pumps, pulmonary ventilators, among others, manufactured in several countries[6,11].

The Chart outlines the MD pre-marketing approval model of the United States, the European Union (EU) and Japan, which together account for about 85% of the world's production[12], making them relevant in discussions about regulatory models and surveillance strategies. The model adopted in Brazil is also presented. The data provided are not exhaustive but intended to provide elements for the presentation of post-marketing surveillance models.

The legal mechanisms established by the United States and Japan, which enable the request of a post-marketing study, can be seen as a possibility of revitalizing the regulatory process, in a perspective of technology follow-up[4,6]. From this standpoint, Japan has a more cohesive system, since it has set a deadline for certain technologies to be reassessed. This demands stronger surveillance from manufacturers and, based on post-marketing experiences, enables the verification of whether or not the safety and efficacy data presented in the pre-registration phase actually match what was found in the use phase[6].

In Brazil, there is no legal provision requiring the authorization holder to submit post-marketing studies to the SNVS based on product behavior reports.

Post-marketing surveillance and its challenges

Even if there are control mechanisms for the regulation of MDs, it is impossible to predict all the problems that will occur, given the impossibility of anticipating all risks or situations of use of a product. Therefore, RAs seek to establish post-marketing control mechanisms in order to manage risks.

As a rule, GMP regulations and guidelines state that manufacturers should evaluate all complaints related to the behavior of their products, decide which ones should be investigated or not and, whenever appropriate, take corrective and preventive action. Activities that derive from compliance with GMP may vary in each country, which reflects the level of risk control of each society in a given time and space.

Legal representatives should continually monitor the safety and performance of their products that are already approved and in use[17] in order to eliminate or mitigate risks. To learn more about the behavior of products in the market, RAs work with severe AE reports related to product use. TC reports are evaluated if the identified failure has contributed to or, if recurrent, has the potential to contribute to severe AEs.

The Food and Drug Administration (FDA) uses different platforms and strategies for MD follow-up after the regularization of a product and its availability on the market. Reporting AEs to MD manufacturers is mandatory and should be done in accordance with the regulation, which determines what reports must be made, as well as deadlines and necessary information[26]. The

Chart. Key points in the process of regulating medical devices in Brazil, the United States, the European Union and Japan.

	Brazil	United States	European Union	Japan
Regulatory model	Decentralized - The federal entity has specific (and exclusive) attributions, such as product marketing authorization, Business Operation Authorization and the granting of the GMP certificate. Inspection, overseeing and technovigilance actions are the responsibility of the SNVS.	FDA-centralized regulatory activities. States have limited competence with respect to regulatory requirements[4].	Mixed model of regulation, divided between RA and NBs, private entities supervised by the AR[20,21]. Post-marketing actions are the responsibility of the local RA.	Regulatory activities are divided between the MHLW and the PMDA[24,25].
Pre-marketing approval	Medical materials and equipment are classified as I - Low risk; II - Medium low risk; III - Medium high risk and IV - High risk[13], whereas diagnostic products for *in vitro* use follow the classification according to individual and collective risk[14]. Risk class I and II products undergo reporting or registration process and do not require revalidation. Those belonging to classes III and IV must receive marketing authorization, and it is mandatory to present a GMP certificate, as well as clinical research data. Specific products go through the certification process, which is the responsibility of Inmetro, in joint work with Anvisa[15,16].	Products are classified as I - Low risk, II - Medium risk and III - High risk. For release, they follow the Marketing Clearance (release system known as 510k), used for medium risk products, where substantial equivalence to another approved product is evaluated. Risk I products are usually exempt from the 510k process. PMA, a pre-marketing authorization system, is applied to high-risk products where safety and efficacy must be proven by clinical research[9,10,17,18,19]. Post-approval studies may be requested, either for PMA-approved MDs (whose approval has been conditional on the study), for specific products approved through the 510k process or for those exempt from approval.	Adopts the NBs to evaluate products in their pre-authorization phase. Classifies products as I - Low risk, IIa - Moderate risk; IIb - Moderate to high risk; III - High risk. There is no pre-marketing approval for risk class I products, and manufacturers are required to submit to the RA the declaration of compliance with regulatory requirements. For class IIa and IIb products, manufacturers submit a dossier to the NB, with safety and performance data as required. Risk class III products usually must present clinical trials for approval by the NB, as well as implantable devices. The approval of the NB gives the manufacturer the right to affix the CE marking to its product and allows it to be marketed throughout the EU[22,23].	The PMDA establishes the policies related to testing, approval, marketing/distribution and monitoring of MDs and the MHLW is responsible for approving new products. Products classified as risk I are considered to be extremely low risk. To make these products available on the market, manufacturers must submit a marketing notification to the PMDA. Class II (low risk) needs to be certified by the NB. Risk III and IV, medium and high risk products, respectively, are MHLW approved, based on PMDA review[24,25]. High-risk products undergo a reassessment within three to seven years of their entry into the market, where companies must provide data on safety and efficacy in their actual use[6].

GMP: Good Manufacturing Practices; SNVS: National Health Surveillance System; Inmetro: National Institute of Metrology; Anvisa: National Health Surveillance Agency; FDA: Food and Drug Administration; PMA: Pre-Market Approval; MD: Medical Device; RA: Regulatory agencies; NB: Notified Body; CE: Conformité Européenne; EU: European Union; MHLW: Ministry of Health, Labor, and Welfare; PMDA: Pharmaceuticals and Medical Devices Agency.
Source: Own elaboration.

Manufacturer and User Facility Device Experience Database (Maude Reports) is a system created in the 1990s to collect voluntary reports from healthcare services, physicians, patients, manufacturers and dealers[18]. The MedWatch system was launched at about the same time; it is user-friendly and enables anyone to file a report[19,27]. The system receives voluntary (users and healthcare professionals) and compulsory (healthcare services, manufacturers, importers, dealers) reports[28]. The Medical Product Safety Network (MedSun), launched in 2002, is a collaborative network of nearly 300 hospitals of various levels of complexity that report AEs and seek to understand medical device issues[29] to anticipate events.

In 2008, the FDA launched the Sentinel Initiative, a product tracking strategy in response to a demand from the US Congress to establish an active product risk identification and analysis program. It was designed in collaboration with various public and private bodies and the academia. The system should be able to have access and gather information from different electronic databases and records, enabling proactive evaluation of safety data. Initially, a pilot was launched. It was replaced in 2014 by the full version of the system[30]. Despite its importance, this system still has limitations for MD-related data, given the use of various nomenclatures and lack of product identification data[31,32].

The EU uses guidance documents regarding the treatment of reported AEs. Manufacturers are required to report severe AEs to the RA of the Member State where the event occurred. Reports should be entered into the European Database on Medical Devices (Eudamed). TCs identified by product users are not reportable to the RA, but must be reported to the manufacturer. Member States should ensure that the products made available meet the essential requirements for their free movement[22,23].

In Japan, competence for post-marketing actions is divided between the Ministry of Health, Labor, and Welfare (MHLW) and the Pharmaceuticals and Medical Devices Agency (PMDA). The PMDS surveys manufacturers' and hospitals' data on AEs for analysis and investigation and reports the results of the investigations to the MHLW, which adopts the relevant administrative

measures. AE reports, both from Brazil and from other countries, should be entered into a database, which is also used to identify safety-related indicators. The law requires healthcare providers to cooperate with manufacturers during any investigation process. They have a sentinel service network as a surveillance strategy that aims to improve problem identification and response capability[4,33].

In Brazil, technovigilance is the responsibility of all SNVS entities. Specific regulations on technovigilance, such as the reporting and organization of this activity in companies[34] and on field actions[35], associated with other resolutions and legislations, which support the topic of MDs, subsidize post-marketing actions. These regulations determine the types of reports and deadlines for submission to the SNVS. Overall, healthcare services must report AEs[36] and, in any case, the Sentinel Network is recognized as a reference in capturing data on the behavior of products for technovigilance[15]. Reports are entered into the Health Surveillance Notification System (Notivisa), which hosts both voluntary and compulsory reports, giving access to all SNVS entities in real time. AE- and TC-related data (regardless of risk potential) make up the reporting basis and companies are urged to comment on the investigation.

As a strategy for strengthening post-marketing surveillance, countries have the responsibility (and challenge) to encourage healthcare product users (primarily healthcare services and healthcare professionals) to report incidents involving the use of these products[15,32,33]. Initiatives like the Sentinel Network in Brazil, the MedSun and the Sentinel Initiative in the United States, and the Japanese Sentinel Network have all pointed toward this direction.

The Network as a strategy for surveillance and risk management

Considering the patterns of production, technological evolution and intervention, risk management can be understood as a practice that supports actions for health promotion, protection and prevention and actions that enable the identification, mitigation and reduction of risks as part of public health actions[37].

In order to be able to effectively intervene in the risks, they must be known and recognized. ABNT ISO 31000:2018[38] provides that different sources of information can be used as a basis for the risk management process (like experiences, observations, expert opinions, among others), and it is up to those who evaluate the screening process and data conformation. In this sense, Gondim pointed out that identifying the problems that affect a place or population and performing the risk assessment are baseline elements for risk management to come about. "The assessment should support decision making, choice of strategies and actions, guidance and monitoring of the entire process"[37]. He also states that the assessment process involves a number of factors and that context needs to be provided. ABNT ISO 31000:2018 supports this statement by saying that the provision of context is essential and should take into account the particularities of each organization, environment, population and the perception of risk itself[38].

The need for surveillance outside the boundaries of the SNVS led to the establishment of the Sentinel Hospital Network, back in 2001, with formalization through contracts in 2002[15]. Several meetings, workshops, and joint activities provided for its institutionalization through Resolution of the Collegiate Board (RDC) n. 51 of September 29, 2014[39].

Since it is formed by different types of hospitals, public and private, scattered about Brazil, the Sentinel Network occupies a privileged space as an observatory of the use of MDs. This surveillance strategy has been successful over the years in Brazil. In data released in 2014, of 69,395 reports made from December 2006 to December 2013, the Sentinel Network accounted for 42,428 reports, about 60% of the total[40]. Notivisa enables reports to be accessed in real time by all SNVS entities and allows surveillance strategies to be structured based on product behavior.

Internal surveillance in healthcare services enables the identification of problems that could have led to the event, thus providing subsidies for the SNVS investigation process, as well as data to improve the service's internal processes and prevent future events. Usually, there is a confluence of factors that should be investigated and addressed in cases of harm, since these rarely occur in isolation. In this landscape, research should consider all the elements surrounding the use of an MD and address all the factors related to the use, the patient and the characteristics of the product and service structure.

Over the years, the partnership established between the Sentinel Network and the technovigilance area of the National Health Surveillance Agency (Anvisa) has been instrumental in identifying problems involving MDs. It has, therefore, subsidized investigative procedures and regulatory measures, such as product recall and the certification of gloves[41] and other products.

Still focusing on surveillance, but from a broader perspective related to product performance (in addition to TCs and AEs), Sentinel Network hospitals act as Technology Assessment Centers (NATs) and make up the Brazilian Health Technology Assessment Network (Rebrats), coordinated by the Ministry of Health. The network aims to promote and raise awareness about the area of technology assessment (ATS) in Brazil. NATs aim to embed the culture of technology assessment in health services, making use of the best possible evidence that a technology can be incorporated into the healthcare system or should be withdrawn due to obsolescence. The work done by the NATs exceeds the internal demands of the hospitals themselves; it is also a reference for the health departments of the Brazilian states and Federal District, the municipalities where they are located, and the Ministry of Health itself[42]. According to this rationale, the production and sharing of information can be considered strategic for the surveillance process, both for increasing knowledge about risks and for providing safe access to MDs.

On another front, the Sentinel Network contributes to the dissemination and active search of products that are under the action of the companies holding the marketing authorization, allowing the management cycle to pervade the entire hospital. On the Anvisa Portal and via e-mails of the Network, the technovigilance area shares risk-related communications about ongoing field actions. Most of these communications originate from investigations done by companies because of market data or the revision of their internal processes, and these are also reported to Anvisa, in compliance with current regulations[35]. The active search for products, the target of field actions in the work environment, requires commitment to patient safety. It is also a means of identifying, for the SNVS, the proper compliance with GMP by companies, considering their primary responsibility for product quality and traceability.

Regulation and post-marketing surveillance: a necessary balance

The need to regulate locally, but bearing in mind that products have global reach, has encouraged the debate about processes related to MD regulation.

RAs, through different strategies and forums, have sought to converge regulations to make the regulatory environment less heterogeneous. Various topics are debated in these spaces, but those related to marketing authorization and GMP inspection stand out. It is understood that globalization does not recognize some borders and, therefore, there is the need to converge regulations and expand the possibility of access to multiple technologies. According to this rationale, the risks arising from the use of technologies do not recognize some borders either, and it is necessary that control mechanisms be redesigned and strengthened.

In current regulatory models there are weaknesses that eventually enable the marketing of products that do not have full compliance with the safety and efficacy criteria set out in the regulation. For example: Campillo-Artero[43] reported the possibility of using the medium-risk product approval mechanism (510k system) for high-risk products in the FDA. The author also points out that the mixed regulatory mechanism adopted by the EU has some weaknesses, once it enables some notified bodies (NBs) to adopt practices that are different from those provided for in the regulations. Heneghan and Thompson[44] highlighted that both the United States and the EU use the logic of substantial equivalence between products as a marketing authorization criterion, but there are situations where there is no longer any guarantee about the safety and efficacy of the originally authorized product. Hand et al.[45] reported that in Japan, some products undergo incremental processes to meet market demands, but the process is not reevaluated by the RA. In Brazil, changes in the requirements related to the marketing authorization model and its expiration date[34] gave the post-marketing phase greater responsibility for monitoring the behavior of technologies, but without an articulated process of agreement and structuring of the SNVS itself to perform this post-marketing surveillance.

These countries have different structural, economic and social realities, and different regulatory evolution paths, but they all need to work to monitor the risks found in technologies, promoting actions that lead to safe use.

In addition to the aspect of regulating the products, in their different production and marketing processes, it is necessary that they be monitored in their context of use, relating the proposed use of the MDs with their actual application. It must be understood that at the end of the authorization process of an MD there will be patients and healthcare professionals and that they will be fundamental for the full understanding of the product's behavior. The combination of the processes related to document assessment and use assessment enables better understanding of the risks, as well as the enhancement of their management.

On that note and in the pursuit of a balance between the State's competence to regulate and its responsibility to oversee the products that are made available for use, the strategy of exchanging MD-related events among several RAs proves to be valuable. This topic has been discussed since the 1990s in the framework of the Global Harmonization Task Force (GHTF), which resulted in a document proposing the exchange of reports between RAs, focusing on field actions done by companies[46,47]. Currently, the International Medical Device Regulation Forum (IMDRF), which replaced the GHTF, is focused on exchanging reports involving severe AEs that jeopardize public health, as well as unusual events[48]. The exchange of information enables the prevention of harm or, at least, interventions to prevent its recurrence.

The partnership between professional councils and health surveillance bodies, both for professional training and information exchange, as well as in the process of identifying TCs and AEs in the professional routine, can help improve health surveillance actions[49,50].

The same rationale of event and harm prevention is attributed to the work done in service networks. Healthcare services identified as Teaching Hospitals are supposed to conduct activities related to different types of surveillance, including technovigilance, improving and bridging the gap between education and actual practice[51]. Healthcare settings, with their several processes and technologies, combined with complex health cases and different specialties, are environments that require ongoing surveillance with focus on the safety of patients and other stakeholders. Studies like those by the Institute for Studies on Supplementary Health[52] and Mendes et al.[53] pointed to a high number of AEs in Brazilian hospitals, related to different products and processes, many of which could have been prevented. Information stands out as one of the key elements for the improvement of activities. Reports are also important tools. In Brazil, several authors have indicated AE and TC reports as important elements in the process of improving the internal work of healthcares services, both in relation to the improvement of patient care and greater care with the products in use. There are studies that also point to

problems in the culture and quality of reports, with lack of fundamental data for the analysis and investigation process, which impacts both the internal activities of the healthcare services and the SNVS[54,55,56].

CONCLUSIONS

There are several regulatory mechanisms and surveillance strategies related to MD use around the world. Regulation based on authorization models has been showing some signs of exhaustion. This is both because of the dynamism of the market and because of strong and continuous competitiveness, which leads to constant innovation and product improvement by the industry. This context demands more and more from the RAs' processes of assessment and authorization. Gaps in regulatory models around the world drive discussions about which way to go, converging pre- and post-marketing steps. There is economic and social pressure (and friction) driven by new and old demands on health, which, while calling for more access and technologies, also demand quality, safety and efficacy. In this sense, and in order to have better risk management, we need strategies that improve the training of different healthcare professionals in issues related to post-marketing surveillance, as well as training and encouragement for MD professionals and users to engage in the process of technovigilance reporting.

MD post-marketing surveillance has been considered to be an alternative to fill information gaps from the marketing authorization phase. The exhaustion of the authorization model could be compensated with data coming from actual product usage, and any signs of failure would provide for the review of the product's authorization. But the fact is that post-marketing surveillance is still remarkably passive (receiving reports), dependent on the look and commitment of healthcare services and product users, as well as on data generated by the marketing authorization holders themselves, as a result of the compliance with current regulations. In Brazil, it is also marked by the ability of the SNVS to conduct surveillance, and the very concept of risk does not have the same impact across the country.

Post-marketing follow-up strategies, based on information surveyed from healthcare services, are of paramount importance for proper MD risk management. In addition, it is necessary to make better use of this complex structure where there are MDs, patients, healthcare professionals and other stakeholders. This should be achieved in a structured manner that can be less dependent on personal awareness. Sentinel services, which today play a significant role in the search for data, can, because of their expertise, work in the production of information by systematically identifying risks not available in the phase of introduction of an MD in the market. Sentinel services can, therefore, help strike a balance between pre- and post-marketing data.

Managing MD-related risks is a challenge that several stakeholders and institutions have to face every day. There is no way to guarantee that a given technology will not pose any risk. It is necessary, however, to think about how the State, in its role as a regulator and fulfilling its surveillance function, and the other players involved in the various stages of the MD life cycle, are prepared to recognize these risks and address them.

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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.