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Potentialities and limitations of the Sentinel Network to improve the post-marketing/post-use monitoring of products subject to health surveillance adopted by Anvisa

Potencialidades e limitações da Rede Sentinela para o aperfeiçoamento do monitoramento pós-comercialização/pós-uso de produtos sob vigilância sanitária adotado pela Anvisa

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ABSTRACT

Introduction: Hospitals are essential for the universal coverage of any health system, as well as sources of valuable information on adverse events and technical complaints of products subjects to health surveillance. **Objective:** To identify the potentialities and limitations of the Sentinel Network to improve post-marketing/post-use monitoring of products subject to health surveillance adopted by Anvisa. **Method:** A descriptive quantitative study that used data from a national administrative survey applied to the Sentinel Network, which was conducted between August 4 and September 2, 2021, by the Anvisa. Data were collected using an electronic structured questionnaire. Statistical analyzes were performed in the Gretl-2022a software, including the calculation of absolute and relative frequencies, medians, and interquartile ranges. **Results:** A response rate of 69.1% (181/262) was obtained. Among the potentialities, the following stand out: acting as a center for study, teaching, and research of health establishments (n = 145; 80.1%), presence of implanted electronic medical records (n = 142; 78.4%) and the development of initiatives focused on innovation involving risk management of health products (n = 94; 52.0%). As one of the limitations, health establishments that do not have any current excellence/quality certifications predominate (n = 104; 57.5%). **Conclusions:** The Sentinel Network has several potentialities and limitations that affect the post-marketing/post-use monitoring of products subject to health surveillance. Identifying them, as was the objective of this study, demonstrates the need to promote actions that offer the possibility of expanding the potentialities and mitigate the limiting factors to the improvement of post-marketing/post-use monitoring adopted by Anvisa.

KEYWORDS: Brazilian National Health Surveillance Agency; Drug-Related Side Effects and Adverse Reactions; Health Monitoring; Patient Safety; Marketed Products Surveillance

RESUMO

Introdução: Os hospitais são essenciais para a cobertura universal de qualquer sistema de saúde, bem como são fontes de informações valiosas sobre eventos adversos e queixas técnicas de produtos sob vigilância sanitária. **Objetivo:** Identificar as potencialidades e limitações da Rede Sentinela para o aperfeiçoamento do monitoramento pós-comercialização/pós-uso de produtos sob vigilância sanitária adotado pela Anvisa. **Método:** Estudo descritivo quantitativo que utilizou dados de levantamento administrativo nacional aplicado à Rede Sentinela realizado entre 4 de agosto e 2 de setembro de 2021 pela Anvisa. Os dados foram coletados por meio de questionário estruturado eletrônico. As análises estatísticas foram executadas

no *software* Gretl-2022a, compreendendo o cálculo das frequências absoluta e relativa, medianas e intervalos interquartis. **Resultados:** Obteve-se uma taxa de resposta de 69,1% (181/262). Dentre as potencialidades, destacam-se: a atuação como centro de estudo, ensino e pesquisa dos estabelecimentos de saúde (n = 145; 80,1%), a presença de prontuário eletrônico implantado (n = 142; 78,4%) e o desenvolvimento de iniciativas voltadas para a inovação envolvendo a gestão de risco de produtos de saúde (n = 94; 52,0%). Como uma das limitações, predominam os estabelecimentos de saúde que não possuem quaisquer certificações de excelência/qualidade vigentes (n = 104; 57,5%). **Conclusões:** A Rede Sentinela apresenta várias potencialidades e limitações que afetam o monitoramento pós-comercialização/pós-uso de produtos sob vigilância sanitária. Identificá-las, como foi o objetivo deste estudo, demonstra a necessidade de fomentar ações que ofereçam a possibilidade de ampliar as potencialidades e mitigar os fatores limitantes ao aperfeiçoamento do monitoramento pós-comercialização/pós-uso adotado pela Anvisa.

PALAVRAS-CHAVE: Agência Nacional de Vigilância Sanitária; Efeitos Colaterais e Reações Adversas Relacionados a Medicamentos; Monitoramento Sanitário; Segurança do Paciente; Vigilância de Produtos Comercializados

INTRODUCTION

Hospitals are essential for universal coverage of any health system and a source of valuable information on morbidity and mortality[1]. These institutions provide care for patients affected by adverse events (AE) related to products under health surveillance[2,3,4], defined as incidents that result in damage to health[5]. However, in the hospital environment, patient safety can be compromised, resulting in the occurrence of AEs during hospitalization[6,7]. Studies show that between 1.6% and 41.4% of hospitalized patients have experienced drug AE[8,9,10]. In another study, AEs involving medical devices were present in 2.8% of hospitalizations, 24% of which were potentially preventable[11].

The Brazilian National Health Surveillance Agency (Anvisa) and the other entities of the National Health Surveillance System (SNVS)5, for 20 years (2002 to 2022), have had a set of health establishments, called the Sentinel Network, which is mostly represented by hospitals[12]. The Network operates in the post-marketing/post-use monitoring of products under health surveillance, used in health care, with the objective of identifying, analyzing, evaluating, treating, monitoring, and communicating risks, AEs and technical complaints (TC) resulting from use or exposure to these products5. It should be noted that QT is defined as any notification of suspected alteration or irregularity of a product or company related to technical or legal aspects, and which may or may not cause damage to individual and collective health[5].

The adhesion and permanence of health establishments in the Sentinel Network is a voluntary act and does not involve any direct transfer of financial resources by Anvisa[13]. The Participant membership profile is mandatory for all health establishments accredited in the Sentinel Network, which must: institute a risk management, use the computerized system of notification and investigation in health surveillance of Anvisa, Notivisa, and Vigimed and regularly feed TC and AE within the scope of the Health Surveillance Notification and Investigation System (VIGIPÓS)[13]. Institutions can also qualify for the Collaborator, Cooperation Center, or Reference Center profiles, playing different roles within the Sentinel Network[13].

Risk management develops reactive surveillance actions, such as notifying AE and TC suspicions to Anvisa[13,14], and proactive surveillance, such as the identification and prevention of potential risks associated with care practice[15]. These actions contribute to post-marketing/post-use monitoring of drugs, vaccines, blood and blood components, therapeutic use of cells, tissues and organs, medical devices and other products in the real world and to fill in gaps arising from limitations of pre-marketing clinical studies[16].

Admittedly, the Sentinel Network is the main notifying source of AE related to products under health surveillance by Anvisa[14]. Notifications coming from hospitals are relevant because, often, new drugs and medical devices authorized for sale in Brazil are first used in these care units[14]. Furthermore, notifications tend to be more accurate, complete, and differentiated in terms of the severity of AEs recorded in Notivisa and VigiMed[14,17].

The Sentinel Network complements and expands AE and TC capture strategies related to products under sanitary surveillance adopted by Anvisa. Clarity about the potentialities and limitations of the Sentinel Network to improve post-marketing/post-use monitoring, within the scope of health services, can help in the planning, execution, monitoring, and evaluation of regulatory actions that favor the reduction and control of risks, AE and TC related to those products. Therefore, this study aimed to identify the strengths and limitations of the Sentinel Network for improving the post-marketing/post-use monitoring of products under health surveillance adopted by Anvisa, after two decades of its implementation.

METHOD

Study design and data collection

This is a quantitative descriptive study that used data from a national administrative survey applied to the Sentinel Network, which was carried out between August 4 and September 2, 2021, by Anvisa. This survey, which consisted of a cover letter and structured electronic questionnaire, involved an organizational effort to collect information, with a view to improving post-marketing/post-use monitoring of products under sanitary surveillance in Brazil. Administrative surveys are important tools for collecting

information used to support managerial decision-making as part of organizational assessment processes[18].

The introduction letter, sent by Anvisa's institutional e-mail, was directed to all directors and risk managers of the 262 health establishments, at the time, accredited in the Sentinel Network. It indicated the objective of the survey and informed about the voluntary nature of participation, as well as the electronic address that gave access to the questionnaire to be answered.

The questionnaire was prepared on the Microsoft Forms® platform and had 33 questions, of which four were related to the identification of institutions (n = 2) and respondents (n = 2). Participants answered the questionnaire sent directly to the online platform.

The questionnaire consisted of five types of questions (n = 29), namely: i) fourteen "yes" or "no" questions; ii) seven multiple choice questions; iii) four open questions; iv) two questions that displayed a scale of response options ranging from 0 (no understanding/no capacity) to 10 (very understanding/a lot of capacity); and v) two questions evaluated on a 5-point *Likert* scale, ranging from 1 (totally disagree) to 5 (totally agree).

The questions were prepared by professionals who make up the technical group responsible for planning, executing, monitoring, and evaluating actions related to the Sentinel Network, within the scope of the Agency. The group is made up of managers and civil servants who work in Anvisa's post-marketing/post-use monitoring. The elaboration of the questions was inspired, mainly, in provisions foreseen in the Resolution of the Collegiate Board (RDC) of Anvisa No. 51, of September 29, 20145.

Initially, the survey was open between August 4 and 16, 2021. Five days before the end of the period, telephone contact was made with the health establishments that had not yet answered the questionnaire. After this procedure, the deadline to respond was extended to September 2, 2021. In the telephone contact, if the risk manager informed that they had not received the introduction letter, the e-mail was sent again.

Data on the health facilities of the Sentinel Network regarding the legal nature, type and subtype of establishment, care capacity, represented by the number of beds, whether or not it serves the Unified Health System (SUS) and the municipality where the institution is located were obtained from the National Registry of Healthcare Establishments (CNES) of the Ministry of Health[19].

The classification of the size of the health establishment, according to the number of beds, referred to by De Negri Filho and Barbosa (2014), was used for the purpose of characterizing the hospitals in the Sentinel Network[20].

Data treatment and analysis

The data from the Microsoft Forms® platform were exported to a Microsoft Excel® spreadsheet, followed by the identification and exclusion of duplicate answers. The CNES number was used to identify duplications in the database, remaining, when found, the answers that were forwarded by the director of the health facility, risk manager, or professionals related to patient safety/risks and quality of care.

The list of health establishments from the Anvisa Sentinel Network, containing the names of directors and risk managers, was used to confirm the duplication in the database. This procedure was necessary due to the presence of two or more institutions with the same CNES number but representing independent risk management. For example, the National Cancer Institute of the Ministry of Health (INCA/MS), nominally described in the CNES as "MS INCA Cancer Hospital I", presented two sets of responses in the database, with the same CNES number (2273454). However, on Anvisa's list there was the accreditation of two institutions (Cancer Hospital I – INCA/MS and Bone Marrow Transplant Center of INCA/MS), representing INCA/MS, with independent risk managers. It should be noted that, in these cases, the analyzes involving the number of hospital beds accounted for each number of institutional CNES only once.

The list of health establishments in the Sentinel Network managed by Anvisa was also used to identify and characterize the institutions that did not forward the completed questionnaire, aiming at a comparative analysis with those that sent their responses.

Not all questions in the questionnaire were analyzed in this study. Were excluded two questions of the "yes" or "no" type, two that displayed a range of response options ranging from 0 to 10, two multiple choice, and four open questions. The two main reasons for the exclusion of the questions were due to the quantitative approach of the study, preferring closed questions, and the prioritization of the most relevant questions to answer the research objective.

Descriptive statistical analyzes of the data were performed using the free software Gretl-2022a, comprising the calculation of absolute and relative frequencies, medians, and interquartile ranges. When necessary, Microsoft Excel® was also used to calculate the absolute and relative frequencies of the study data.

Variables with differences in relative values equal to or less than four were considered reasonably similar in the comparative analysis of the sample groups. The Mann-Whitney test was applied to compare the medians in relation to the number of hospital beds between the groups of responding health facilities (Group 1) and non-responding ones (Group 2). The comparison was considered statistically significant with $p < 0.05$. The test was performed on the Social Science Statistics website[21].

Regulatory requirements provided for in RDC No. 51/20145 and Normative Instruction No. 8, of September 29, 201413, were also used to identify potentialities and limitations of the Sentinel Network to improve the post-marketing/post-use monitoring of products under sanitary surveillance adopted by Anvisa.

The survey response rate, in percentage terms, was calculated as the number of questionnaires returned divided by the total population of health facilities in the Sentinel Network to which the institutional e-mail was sent, multiplied by one hundred.

Ethical considerations

This study was based on data obtained from an administrative survey and from a secondary source in the public domain, therefore not requiring submission to the research ethics committee[22].

Participation was voluntary, that is, it was guaranteed that directors/risk managers/other professionals answered the questionnaire without any pressure or stress that could force them to do so.

No type of incentive was offered to participants, as well as, prior to data analysis, their personal information collected was kept confidential: name, job function, and e-mail.

It is also noteworthy that in studies based on surveys, no intervention is delivered to research participants. As a result, there are no risks of physical harm for those participating[23]. Furthermore, it is reasonable to state that the administrative survey conducted by Anvisa did not produce significant psychological or informational harm to the participants, nor did it involve vulnerable subjects who deserved approval by the research ethics committee[23].

Finally, it seems, the only foreseeable risk of the administrative survey was the "inconvenience" to respond to the electronic questionnaire. In this case, national regulations in some countries establish that low-risk research, defined as those in which the only foreseeable risks are those of "annoyance", do not need to be evaluated by a research ethics committee[23].

RESULTS

The questionnaire was sent to all health establishments that were accredited to the Sentinel Network during the data collection period (n = 262). Three cases of duplicates were recorded, resulting in 181 health facilities that responded to the electronic questionnaire, comprising the population of this study. The administrative survey response rate was 69.1%. Six responses were identified with the same CNES number.

Table 1 presents the characteristics of the Sentinel Network health facilities that responded to the questionnaire (Group 1) versus those that did not forward their responses (Group 2). In the first group, given the type of establishment (Hemotherapy and/or Hematology Care Center and Diagnosis and Therapy Support Unit), three questionnaires were not included in the analyzes related to the quantification of the number of beds. For Group 2, this number was nine health facilities (Emergency Care) (Table 1).

The health establishments that answered the questionnaire were characterized, for the most part, as public administrations (n = 89; 49.2%), general hospitals (n = 141; 78.0%), which provide care to the SUS (n = 162; 89.5%), are large hospitals (151 to 500 beds), which are located in the Southeast Region (n = 78; 43.1%) and with participant profile in the Sentinel Network (n = 128; 70.7%), followed by the Participant + Collaborating Center profile (n = 17; 9.4%) (Table 1).

Among the hospitals that reported the subtype of care (n = 30), specialists in oncology (n = 10; 33.3%), maternity (n = 8; 26.7%), and cardiology (n = 5; 16.7%) prevailed. Regarding the health establishments that did not respond to the questionnaire and that included information on the subtype of hospital care (n = 7), the following specialties were identified: i) oncology (n = 2); ii) maternity (n = 2), pediatrics (n = 2), and infectology (n = 1).

It is observed that, of the 30 variables analyzed, 17 (56.7%) have reasonable similarities in the relative values or in the medians between the health establishments that answered the questionnaire and those that did not. In these conditions, stand out the characteristics related to public administration (49.2% *vs* 49.4%), general hospital (78.0% *vs* 76.6%), median number of beds (246 *vs* 220), small hospital (up to 50 beds) (4.6% vs 4.2%) and special (≥ 501 beds) (12.8% *vs* 11.1%), geographic region: North (7.2% *vs* 5.0%), Midwest (5.0% *vs* 3.7%) and South (20.4% *vs* 16.0%) and profiles of health facilities, as Participant + Cooperation Center (6.6% *vs* 3.7%), Participant + Reference Center (4.4% *vs* 2.5%), Participant + Collaborating/cooperation center (5.0% *vs* 5.0%) and Participating + Collaborating/cooperation/reference center (3.9% *vs* 3.7%) (Table 1).

The potentialities and limitations of the Sentinel Network for improving the post-marketing/post-use monitoring of products under health surveillance adopted by Anvisa can be seen in Table 2. Most of the institutions that answered the questions act as study, teaching, and research centers (n = 145; 80.1%), have initiatives aimed at sustainability in the disposal of obsolete health products/technologies (n = 104; 57.5%) and also for innovation involving risk management of health products/technologies (n = 94; 52.0%) and have their own computerized system for risk management of products under surveillance (n = 66; 36.5%) and implanted electronic medical records (n = 142; 78.4%) (Table 2).

Of the institutions that reported having certifications of excellence/quality, one of them did not mention the type and 1.4 responses were obtained per respondent (106 responses/76 health establishments). Of the 76 health establishments that answered the question, 54 (71.0%) had an excellence/quality certification; 16 (21.0%), two; five (6.7%), three, and one (1.3%), five certifications.

Based on the total number of responses to the question (n = 106), the top five certifications of excellence/quality referred to by the health establishments, in this order, were: National Accreditation Organization (ONA) (n = 51; 48.1%), International Organization for Standardization (ISO) (n = 13; 12.3%), Joint Commission International (JCI) (n = 12; 11.3%), *Qmentum International (n = 9; 8.5%), and Clinical Laboratories Accreditation Program (PALC) (n = 4; 3.8%)*.

Five (5.3%) health establishments reported having six initiatives aimed at innovation involving the risk management of health products/technologies, compared to 31 (33.0%) who mentioned developing a type of innovation activity at the institutional

Tabela 1. Perfil comparativo dos estabelecimentos de saúde credenciados à Rede Sentinela.

Characteristic	Group 1 n (%)	Group 2 n (%)
Legal nature		
Public administration	89 (49.2)	40 (49.4)
Non-profit entities	58 (32.0)	21 (25.9)
Business entities	34 (18.8)	20 (24.7)
Type of establishment		
General hospital	141 (78.0)	62 (76.6)
Specialized hospital	34 (18.8)	9 (11.1)
Emergency service	0 (0.0)	9 (11.1)
General emergency room	0 (0.0)	1 (1.2)
Isolated day hospital	3 (1.6)	0 (0.0)
Hemotherapy and/or Hematology Care Center	2 (1.1)	0 (0.0)
Diagnosis and Therapy Support Unit	1 (0.5)	0 (0.0)
Serves the Unified Health System (SUS)		
Yes	162 (89.5)	63 (77.8)
No	19 (10.5)	18 (22.2)
Number of beds (care capacity)*, **		
Median (minimum - maximum)a	246 (4 - 1.543)	220 (6 - 907)
Interquartile range (Q1 - Q3)	231 (153 - 384)	190 (132 - 322)
Hospital size*, **		
Small (up to 50 beds)	8 (4.6)	3 (4.2)
Medium (51 to 150 beds)	32 (18.6)	20 (27.8)
Large (151 to 500 beds)	110 (64.0)	41 (56.9)
Special (≥ 501 beds)	22 (12.8)	8 (11.1)
Geographic region		
North	13 (7.2)	4 (5.0)
Northeast	44 (24.3)	11 (13.6)
Midwest	9 (5.0)	3 (3.7)
Southeast	78 (43.1)	50 (61.7)
South	37 (20.4)	13 (16.0)
Profile of the health establishment in the Sentinel Network		
Participant	128 (70.7)	65 (80.2)
Participant + Collaborating Center	17 (9.4)	3 (3.7)
Participant + Cooperation Center	12 (6.6)	3 (3.7)
Participant + Reference Center	8 (4.4)	2 (2.5)
Participant + Collaborating/cooperation center	9 (5.0)	4 (5.0)
Participant + Collaborating/cooperation/reference center	7 (3.9)	3 (3.7)
Participant + Cooperation/reference Center	0 (0.0)	1 (1.2)

Source: Elaborated by the authors, 2022.
Group1 (n = 181): set of health facilities that answered the questionnaire; Group 2 (n = 81): set of health facilities that did not respond to the questionnaire; Q1 = first quartile; Q3 = third quartile.
* values calculated for 172 valid observations; **values calculated for 72 valid observations; [a]Mann-Whitney test (p = 0.27).

level. Another 28 (29.8%) establishments develop two innovation activities; 18 (19.2%), three; five (5.3%), four; and seven (7.4%), five.

The five initiatives aimed at innovation in the risk management of health products/technologies that most prevailed, according to the total number of responses (n = 225), were: humanization and holistic care (n = 62; 27.6%), telecare and audiovisual technology for real-time patient provider interactions (n = 55; 24.4%), use of real-world data/evidence (n = 43; 19.1%), attracting companies to new partnerships (n = 37; 16.4%) and Data Science and Artificial Intelligence Hub (n = 12; 5.3%). A total of 2.4 responses per

Table 2. Potentialities and limitations of the Sentinel Network to improve the post-marketing/post-use monitoring of products under health surveillance adopted by Anvisa.

Potentialities and limitation	Yes n (%)	No n (%)
• Does the institution have, on this date, certification(s) of excellence/quality in effect?	77 (42.5)	104 (57.5)
• Does the institution act as a Study, Teaching, and Research center?	145 (80.1)	36 (19.9)
• Is there any initiative(s) aimed at sustainability in the disposal of obsolete health products/technologies?	104 (57.5)	77 (42.5)
• Is there any initiative(s) aimed at innovation involving the risk management of health products/technologies?	94 (52.0)	87 (48.0)
• Does it have its own computerized system for risk management of products under sanitary surveillance?*	66 (36.5)	28 (15.5)
• Does it have an implanted electronic medical record?	142 (78.4)	39 (21.6)
• Has already developed or is developing any evaluation about adverse events or technical product complaints using the electronic medical record resources?**	64 (35.4)	78 (43.1)
• Is there study/research involving products under sanitary surveillance in progress or completed in the last three years? (e.g., vaccine effectiveness, monitoring of drugs imported for intubation, usability of syringes, effectiveness of sanitizers, etc.)	39 (21.5)	142 (78.5)
• Participate in or coordinate clinical trials?***	23 (12.7)	16 (8.8)

Source: Elaborated by the authors, 2022.
Did not answer the question: *n = 87; **n = 39; and ***n = 142.

respondent (225 responses/94 health facilities) were achieved for this multiple-choice question in the questionnaire.

There was a prevalence of health establishments that carried out or were in progress of carrying out study/research involving products under sanitary surveillance in the last three years (n = 27; 69.2%), followed by those with two (n = 8; 20.5%) and four (n = 2; 5.1%) studies/research. One institution reported conducting or completing five studies involving products under health surveillance in the last three years.

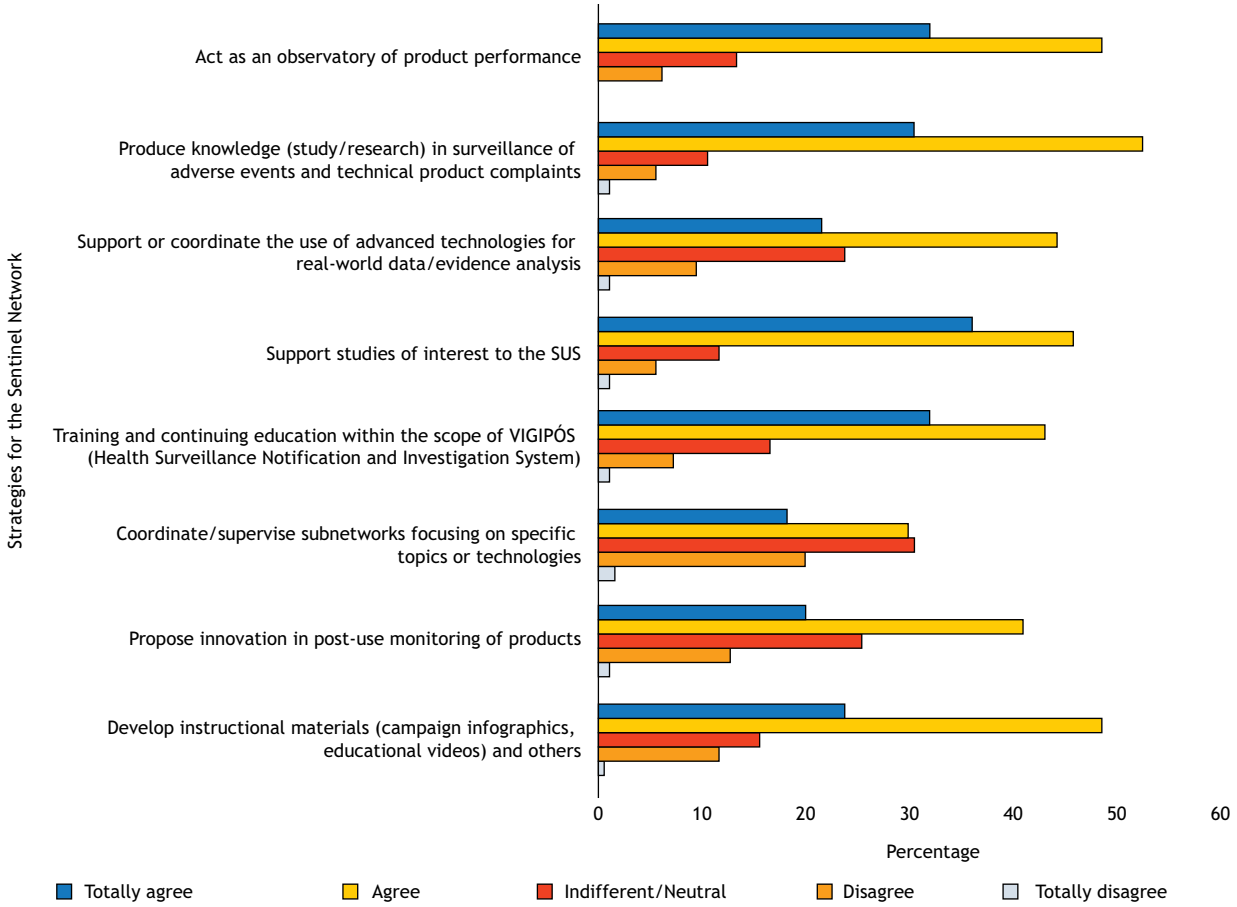
The four main products under health surveillance involved in the studies carried out (or in progress), according to the total number of responses (n = 59) were: drugs and vaccines (n = 33; 55.9%); medical devices (n = 9; 15.3%); blood and blood components (n = 8; 13.6%); and cells, tissues, and organs (n = 3; 5.1%). Other products/activities that counted with studies included: cosmetics (n = 2), food (n = 1), sanitizing products (n = 1), intoxication by products (n = 1), and rejection and infection (n = 1). Regarding this multiple-choice question, 1.5 responses were obtained per respondent (59 responses/39 health establishments).

Figure 1 presents the opinion on the overall capacity of the health facility to participate in pre-defined strategies within the scope of the Sentinel Network. The interests of collaborating in all of them prevailed when adding the opinions "totally agree" and "agree", exceeding values above 60%, with the exception of the strategy "coordinate/supervise subnets focusing on specific themes or technologies" (48,0%). Three strategies reached values greater than 80%, when added to the opinions of "totally agree" and "agree". They were: i) producing knowledge (study/research) on AE surveillance and TC of products (82.9%); ii) supporting studies of interest to the SUS (81.8%); and iii) acting as an observatory of product performance (80.6%).

It should be noted that the strategy "coordinate/supervise subnetworks focusing on specific topics or technologies" obtained the highest percentage of "completely disagree" and "disagree" responses, which together accounted for 21.6%. This same strategy was the only one that recorded the highest percentage of "indifferent/neutral" (30.4%) when compared to the other response opinions (Figure 1).

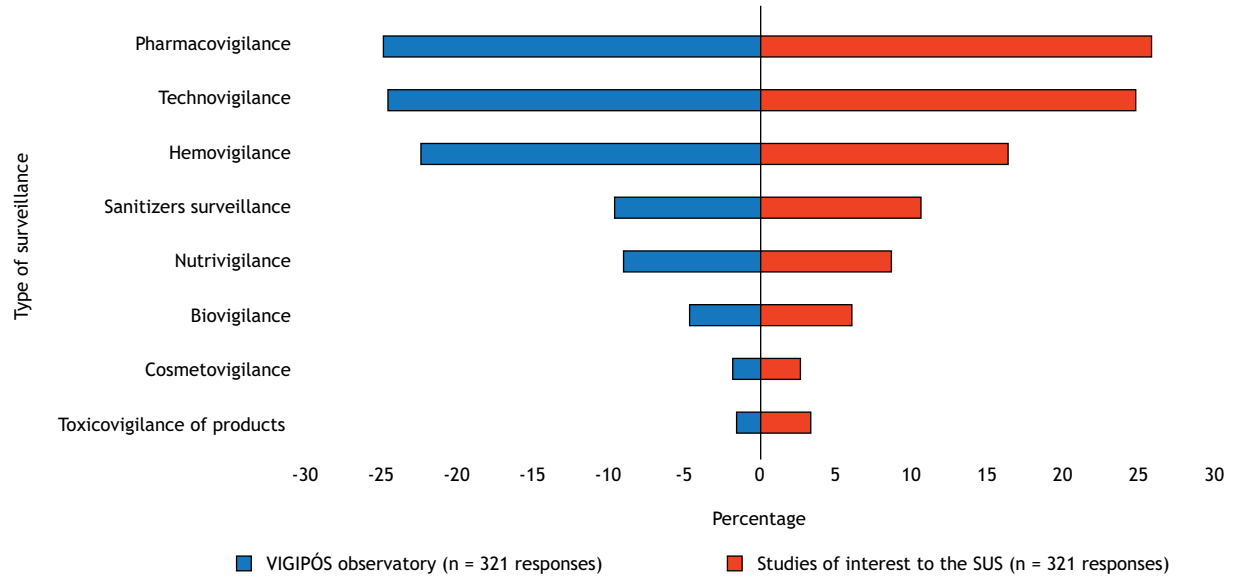
A total of 54.1% (n = 98) health establishments showed interest in acting as an observatory of the performance of products and services under health surveillance through risk management actions. Another 33.7% (n = 61) said they were not sure, while 12.2% (n = 22) said they were not interested in this type of activity. Among those who demonstrated willingness to act as an observatory, 3.3 responses were obtained per respondent (321 responses/98 health establishments). Based on the total number of responses to this multiple-choice question (n = 312), the interest in acting as an observatory in pharmacovigilance (n = 80; 24.9%), technovigilance (n = 79; 24.6%), and hemovigilance prevailed (n = 72; 22.4%) (Figure 2).

Almost half of the health establishments (n = 90; 49.7%) signaled their willingness to develop or support studies of interest to the SUS. It is noteworthy that 83 (45.7%) health establishments did not respond to the question, while eight (4.4%) reported not being interested in carrying out this type of activity. Among the health establishments that demonstrated willingness to develop or support studies of interest to the SUS, there were 3.3 responses per respondent (298 responses/90 health establishments). Considering the total number of responses (n = 298), interest in developing or supporting studies in pharmacovigilance (n = 77; 25.8%), technovigilance (n = 74; 24.8%), and hemovigilance (n = 49; 16.4%) (Figure 2). It should be noted that, of the 33 health establishments also accredited as collaborators, that is, the health service must have the capacity to develop studies



Source: Elaborated by the authors, 2022.

Figure 1. Opinion on overall capacity of health facility to participate in strategies for the Sentinel Network (n = 181).



Source: Elaborated by the authors, 2022.

Figure 2. Disposition of Sentinel Network health establishments to act as an observatory in the Health Surveillance Notification and Investigation System (VIGIPÓS) (n = 98) and to develop or support studies of interest to the Unified Health System (SUS) (n = 90), according to type of surveillance.

of interest to the SUS, 21 (63.6%) expressed an interest in carrying out or supporting such studies.

Adding up the opinions "totally agree" and "agree" of the respondents, which exceeded values above 65%, the health establishments of the Sentinel Network can be active, mainly, in the surveillance of medical-hospital materials (94.0%), blood and blood components (92.3%), medical and hospital articles (91.7%), drugs (89.5%), medical and hospital equipment (89.5%), sanitizing products (78.5%), implants (69.0%), and intoxication by products (67.4%) (Figure 3).

Surveillance of the five products with the highest percentages of "totally disagree" and "disagree" regarding the performance of health establishments in the Sentinel Network involved, in this order: cosmetics (36.5%), diagnosis of use *in vitro* (33.7%), cells (30.4%), tissues (27.1%) and organs (23.7%) (Figure 3).

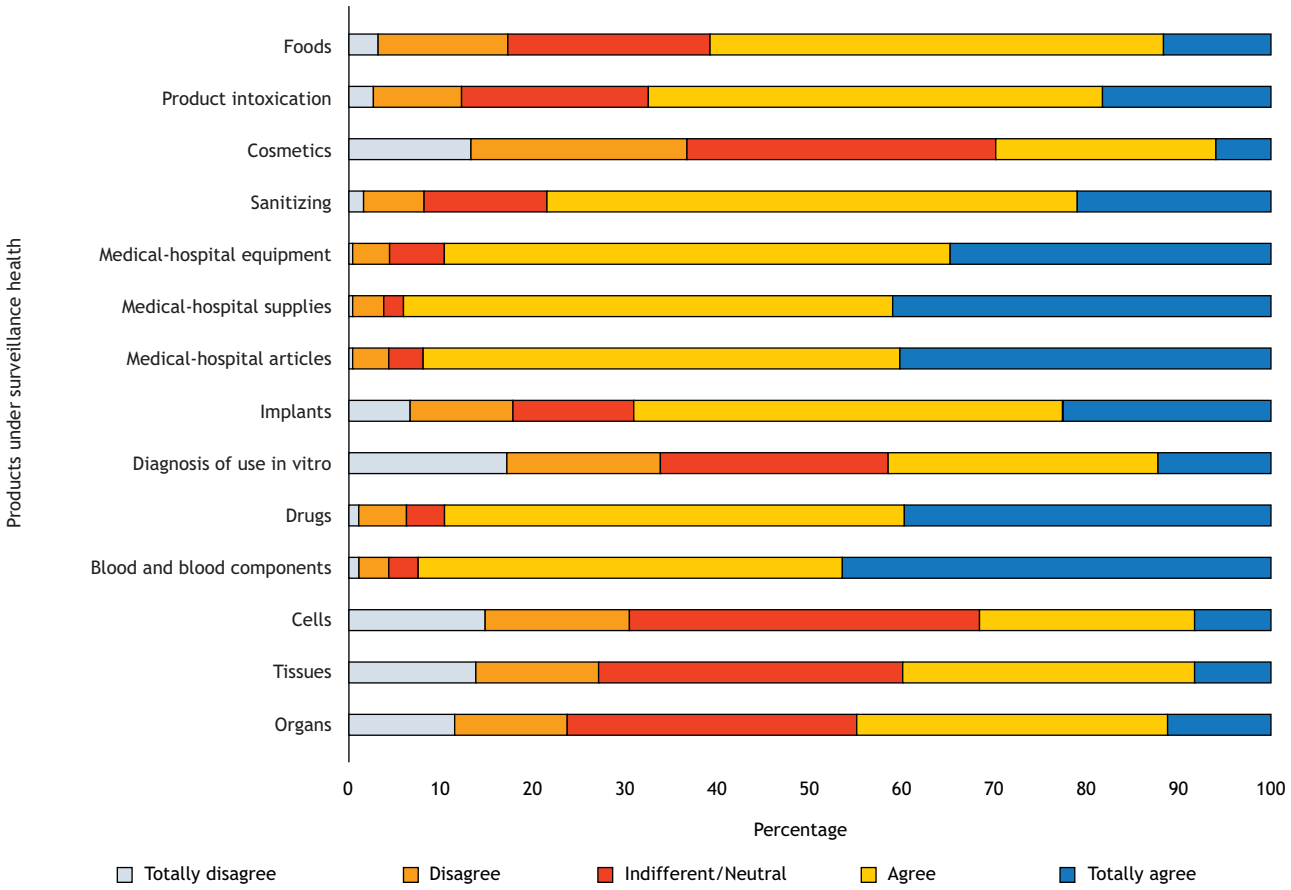
The opinion of "indifferent/neutral" for cell surveillance (38.1%) and cosmetics (33.7%) showed the highest percentages when compared to the other possible responses (Figure 3).

A total of 84 (46.4%) health establishments are willing to cooperate or coordinate staff training and continuing education activities within the scope of VIGIPÓS, against eight (4.4%) that showed no interest. About half of the Sentinel Network institutions did not answer the question (n = 89; 49.2%). It was evidenced that, of the 28 health establishments also accredited as a cooperation center, that is, the health service must have the capacity to carry out staff training and continuing education activities, 19 (67.8%) expressed willingness to carry out such activities.

Regarding VIGIPOS themes in which health establishments could immediately contribute to training and continuing education, pharmacovigilance (n = 60; 26.4%), technovigilance (n = 56; 24.7%), hemovigilance (n = 54; 23.8%), sanitizing surveillance (n = 16; 7.0%), and nutrivigilance (n = 13; 5.7%) predominated. These results were based on the total number of responses to the multiple-choice question (n = 227), recording a quantity of 2.7 responses per respondent (227 responses/84 health facilities).

DISCUSSION

This study identified the potentialities and limitations of the Sentinel Network for improving post-marketing/post-use monitoring of products under health surveillance adopted by Anvisa, about which little was known. The Sentinel Network serves a large number of patients, including those affected by AEs related to products, and produces data and information



Source: Elaborated by the authors,2022.

Figure 3. Potential actions of the Sentinel Network health establishments in the surveillance of products under sanitary surveillance (n = 181).

for post-marketing/post-use monitoring, thus supporting the SNVS in regulatory decision-making in the country. Furthermore, the creation of the Sentinel Network has contributed to increasing the sensitivity of the Notivisa and VigiMed systems in relation to AE and TC notifications related to products under sanitary surveillance.

Among the potentialities, the following stand out, in summary: acting as a study, teaching, and research center for health establishments, the development of initiatives aimed at sustainability in the disposal of obsolete health products/technologies, and also towards innovation involving the risk management of health products/technologies and the presence of its own computerized system for risk management of products under sanitary surveillance and implanted electronic medical records.

The implanted electronic medical record, as an example of the potential of the Sentinel Network, ensures a more uniform recording of AEs, as well as being important to monitor progress and ensure that all responsible parties are aware of these possible risks to patient safety. AEs that are not registered will not be communicated. Such communication is crucial when several health professionals are involved in patient care, mentioned the study by Hoon et al.[24] referencing other authors. The findings of a systematic review showed that most of the studies examined used electronic patient records as a source of data for detecting AEs related to medications on an outpatient basis[25].

Among the innovation-oriented initiatives involving the risk management of health products/technologies that most prevailed in the study, the use of data/evidence in the real world stands out as important for the improvement of post-marketing/post-use monitoring. This initiative has been used by regulatory authorities, such as those in the United States, Canada, Europe, and China, to support drug development, evaluate the performance of medical devices and make regulatory decisions[26,27]. More specifically, the use of real-world data/evidence can produce new information relating to, for example, the benefits and risks of a medical device as a result of its use in wider populations, for longer periods and under different conditions of use[27].

Most health establishments do not have any existing excellence/quality certifications, which translates into one of the limitations that may negatively influence the improvement of post-marketing/post-use monitoring of products under health surveillance adopted by Anvisa. Accreditation and certification are quality strategies that aim to encourage compliance of health facilities with published standards through external evaluation. Most existing external evaluation schemes in the health area use structure and process indicators and generally aim to improve quality in terms of effectiveness and patient safety, this includes prevention and risk detection actions and AE to products used in healthcare[28].

Other limitations involved the little use of electronic medical records resources for the development of assessments on AE or TC of products, as well as the scarce conduction of studies/research, in the last three years, involving those products. Less than a third of the health establishments answered about the participation or coordination of clinical trials, making it difficult to generate more assertive hypotheses for future studies. These limitations are opposed to the fact that most health establishments in the Sentinel Network act as study, teaching, and research centers.

Compliance with regulatory requirements for the Sentinel Network, in particular for health establishments accredited beyond the participating profile[13], was another identified limitation that should be considered when planning actions to improve the post-marketing/post-use monitoring adopted by Anvisa. These conditions include, in particular, activities related to the capacity of health establishments to develop studies of interest to the SUS (collaborating profile) and carry out staff training and continuing education activities (cooperation center profile).

Given the complex causes associated with the occurrence of AEs, it is not surprising that improved post-market/post-use monitoring (also called post-market/post-use surveillance) within the Sentinel Network is important to ensure the patient's safety. This monitoring seeks to analyze the safety and effectiveness in the real world of medical devices and drugs among other products. The United States Food and Drug Administration (FDA) defines it as "the active, systematic, and scientifically valid collection, analysis, and interpretation of data or other information about a marketed device"[29]. Acting as a performance observatory for products used in health care and producing knowledge (studies/research) on AE and TC surveillance contribute to the fulfillment of this conceptual mission. These two strategies, which showed a high profile of agreement in this study, make up the activities that the Sentinel Network must develop and that are not linked to the accreditation profile of the health establishment, according to RDC No. 51/2014[5].

Pharmacovigilance, technovigilance, and hemovigilance were the ones that stood out the most in the questions that had as answers the position on the types of post-marketing/post-use surveillance. In these conditions were the general performance of the service in the surveillance of products and as an observatory, development, or support of studies of interest to the SUS and immediate contribution to the training and continuing education of health professionals. Two reasons for the predominance of these three types of surveillance are: i) the greater expertise of the Sentinel Network, which since its creation has focused on actions aimed at pharmacovigilance, technovigilance, and hemovigilance[30]; and ii) the product of interest for each of these surveillances (drugs, medical devices, and blood and its components) are the most commonly used in health care as therapeutic responses.

The use of the questionnaire sent by e-mail with an incorporated QR code allowed more flexibility in the design, handling, completion, and transmission of data to the researchers. Furthermore, individuals, in general, are more likely to respond to surveys that are relevant or of interest to them[31]. Such factors may have contributed to the increase in the response rate of this study, as well as the format of the questions, which were mostly

composed of the "yes or "no" type and, also, the length of the questionnaire, which for the authors was not excessive.

Questionnaire responses depended on the knowledge, recall, and honesty of risk managers and other professionals, resulting in another possible source of bias. Another limitation of this study is related to potential problems with undelivered emails due to the outdated list of the Sentinel Network or incorrect email addresses, affecting the calculation of the response rate, regarding the definition of the most appropriate denominator[32]. To overcome these limitations, telephone contacts were made with risk managers at health facilities that had not responded to the questionnaire, as well as extending the response deadline.

The response rate of a study is seen as an important indicator of the quality of the research. A high response rate reduces the chances of non-response bias[32]. This bias affects the reliability and validity of the study results and stems from the fact that survey participants who did not respond to the questionnaire are somehow different from those who forwarded their responses[32,33]. If a survey achieves a response rate of just 30%, the study suffers a non-response bias of 70%[33]. Most of the time, response bias is very difficult to rule out due to lack of sufficient information about non-responders[32]. The response rate observed in our study can be considered above "acceptable" (~50%) and even "very good" (~70%), as defended by some authors[34]. It was also possible to observe in the comparative analysis of Groups 1 and 2 that, for most of the variables that characterized the profile of the Sentinel Network health establishments, there are reasonable similarities in their relative and median values. In addition, a reasonable number of respondents were obtained from each segment of the population, regarding their characteristics analyzed in this study, resulting in good coverage and representativeness of the administrative survey. The exception that deserves to be highlighted occurred for the variable "emergency care", which did not register any health establishment that responded to the questionnaire.

Despite the limitations of our study, its findings in terms of similarities, coverage and population representativeness reinforce the possibility of cautiously generalizing the results of this study to the entire Sentinel Network.

CONCLUSIONS

Although the implementation of health surveillance actions in Brazil is an old practice that emerged with the arrival of the Portuguese Court in 1808[35], the active participation of hospitals and other health establishments in the monitoring of AE and TC of products used in health care only occurred with the creation of the Sentinel Network, in 2002.

In its 20 years of existence, the Sentinel Network has several potentialities and limitations that affect the improvement of post-marketing/post-use monitoring of products under health surveillance and which continue to be a concern for health surveillance in Brazil, given the constant advancement and use of science in regulatory actions. Identifying them, as was the objective of this study, demonstrates the need to promote actions that offer the possibility of expanding the potential and mitigating the limiting factors to the improvement of post-marketing/post-use monitoring adopted by Anvisa.

It is recommended that a national administrative survey be carried out biannually in order to monitor the historical evolution of potentialities and limitations, with regard to its actions and activities related to the improvement of post-marketing/post-use monitoring of products under health surveillance within the scope of the health services that are part of the Sentinel Network.

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Author's Contributions

Mota DM – Acquisition, analysis, data interpretation, and writing of the work. Cammarota DMOT, Leitão LO, Teixeira APCP, Barreiros VVM, Gomes FR, Surita LE – Data interpretation and writing of the work. Gomes SMT – Conception, planning (study design), data interpretation, and writing of the work. All authors approved the final version of the work.

Conflict of Interests

The authors inform that there is no potential conflict of interest with peers and institutions, politicians, or financial in this study.