National Health Regulatory Agency

HEMOVIGILANCE REPORT

Consolidated data 2007-2014

Brazil 2015

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1st Edition.

Management of Risk Monitoring

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1. LIST OF ABBREVIATIONS and ACRONYMS

ABBS	Brazilian Association of Blood Banks
Anvisa	National Health Regulatory Agency
BE	Blood establishment
CBE	Coordinator Blood Establishment
BCU	Blood Collection Unit
BN	Blood Nucleus
CGSH	General Coordination of Blood and Blood Derivatives
CNES	National Register of Health Care Facilities
CLSD	Center for Laboratory Screening of Donors
CTU	Collection and Transfusion Unit
DAHU	Department of Hospital Care and Urgency
ER	Emergency Room
FU	Federation Unit
Gemor	Management of Risk Monitoring
GGMON	General Management of Monitoring of Products Subject to Health Surveillance
GGPBS	General Management of Biological Products, Blood, Tissues, Cells and Organs
GSTCO	Management of Blood, Tissues, Cells and Organs
HCF	Health Care Facility
Hemocad	National System of Register of Blood Establishments
HM	Health Ministry
MCeO	Conceptual and Operational Framework of Hemovigilance – Guide to Hemovigilance in Brazil
NI	Normative Instruction
Notivisa	System of Notifications in Health Surveillance
RDC	Resolution of the Collegiate Board of Directors
RE	Regional Blood Establishment
SAS	Secretariat of Health Care
SIA-SUS	SUS Outpatient Information System
SIH-SUS	SUS Hospital Information System
SVS	Secretariat of Health Surveillance
Sinan	System of Information of Disease Notification
Sinasan	National System of Blood, Components and Derivatives
Sineps	System of Information on Notification of Adverse Events and Technical Complaints Related to Health Products
SNVS	National Health Regulatory System
SUS	Unified Health System
TA	Transfusion agency
TR	Transfusion reaction
Vigipós	System of Notification and Investigation in Heath Surveillance
Visa	Local Regulatory Authority

2. INDEX OF GRAPHS, TABLE AND CHARTS

3. INTRODUCTION

This edition of the Hemovigilance Report, revised and updated for 2014, was developed based on the notifications of adverse events to the use of blood and its components. Two systems are sources of the transfusion reactions (TRs) analyzed: the Information System for Notification of Adverse Events and Technical Complaints Related to Health Products (Sineps) – data source between 2002 and 2006 – and the System of Notifications in Health Surveillance (Notivisa) – data source between 2007 and 2014. Information is organized by year of occurrence and notification of TRs. These data are consolidated for Brazil, for the five regions of the country and for the 27 Federation Units (FUs). Data by year of notification are shown to demonstrate the evolution of the frequency of notifications and to enable the follow-up of the notification curve, year by year, and the adherence of health facilities to notification.

To calculate TR sub-notification rate, TR rate by blood components transfused and overall TR rate, quantitative data on the transfusion of blood and blood components were used, data were compiled and published by the General Coordination of Blood and Blood Derivatives of the Department of Hospital Care and Urgency of the Secretariat of Health Care of the Ministry of Health (CGSH/DAHU/SAS/MH), from 2008 to 2013, in the Information Notebook: Blood and Blood Derivatives (*Caderno de Informação: Sangue e Hemoderivados*). Data related to 2014 were reported to Anvisa before their publication.

It is expected that this report can be used both by the health facilities that provide care in hemotherapy and by the National Health Regulatory System (SNVS) to help in the comprehension of inherent risks to the therapeutic use of blood and blood components, in order to reduce and prevent them.

4. LEGAL BASES

In Brazil, hemovigilance, conceived in accordance with the Federal Constitution and with the legislation that rules it, has its operation focused on monitoring the adverse events resulting from the therapeutic use of blood and its components, as a strategy to enhance the quality of these products and decrease the risk of new diseases.

- **Federal Constitution**

Article 196:

> "Health is a right of all and duty of the State, ensured upon social and economic policies that aim at the reduction of risk of diseases and at the universal and equal access to actions and services for its promotion, protection, and recovery".

Article 200, the foundations of health surveillance:

> "To the unified health system it is assigned, in addition to other responsibilities, in the terms of law, to:
> I – control and supervise procedures, products and substances of health interest and to participate in the production of medicines, equipment, immunobiologicals, blood derivatives, and other inputs."

- **Federal Law 8.080**, September 1990: regulates the articles of the Constitution that concern to health and assign competences to the three management levels of the Unified Health System (SUS): federal, state, and municipal.

In general, it is assigned to the federal level the formulation, implementation, and evaluation of policies, the development of standards and parameters and collaboration in health actions, among other activities. In the case of blood and blood derivatives, these responsibilities are shared between the CGSH/MH and the National Health Regulatory Agency (Anvisa). It is delegated to states and municipalities to participate in the formulation, implementation, and evaluation of policies, in the development of standards in a supplementary way, and in the execution and evaluation of health actions.

- **Federal Law 10.205**, March 2001: regulates the § 4th of the article 199 of the Federal Constitution, related to the collection, processing, storage, distribution and application of blood, of its components and derivatives.

This law promotes institutional planning and establishes principles, guidelines and action field for the National Policy of Blood, Components and Blood derivatives, creating the National System of Blood, Components and Derivatives (Sinasan).

Article 9th. The support bodies to Sinasan are:

> "I – health and surveillance bodies, that aim to control the quality of blood, components and blood derivatives and all indispensable input to hemotherapy actions;"

The respective legislations define that it is assigned to the bodies that compose SNVS the actions on the promotion and protection of the population health, by ensuring the health safety of products and services.

- **Federal Law 9.782**, January 1999: defines the National Health Regulatory System and creates the National Health Regulatory Agency.

> "Art. 6th The Agency has the institutional purpose of promoting health protection for the population, by sanitary control of the production and commercialization of products and services subject to health surveillance, including environments, processes, inputs, and technologies related to them, as well as the control of ports, airports, and borders.
> (...)
> Art. 8th The Agency is assigned, respecting the legislation in force, to regulate, control and supervise products and services that involve risk to public health.
> § 1st The goods and products subject to control and sanitary inspection by the Agency are:
> (...)
> VII - immunobiologicals and their active substances, blood and blood derivatives;"

- **Ordinance MH 1.660,** published in July 22, 2009: instituted the System of Notification and Investigation in Heath Surveillance (Vigipós), in the context of SNVS and as an integrating part of SUS.

The management of this system is duty of Anvisa and of the Secretariat of Health Surveillance of the Ministry of Health (SVS/MH). Vigipós is responsible for monitoring, analyzing, and investigating adverse events and technical complaints related to services and products under health surveillance in the phase of post-use or post-commercialization. In the context of this system, the therapeutic use of blood and its components is included. This

ordinance assigns competences to different SUS managers. It is up to Anvisa, as a federal manager, the coordination, articulation, assistance and supervision of the actions of the system countrywide. It is up to state managers and of the Federal District to coordinate the system within their territory, to arrange the execution of actions with municipal managers, to cooperate technically and supervise the municipalities in the pertinent actions of the system. It is up to municipal managers to coordinate the system within their covering area, to arrange the actions with the state manager, to join and to cooperate technically with other SUS bodies in the local context.

- **Ordinance MH 2.712**, November 12, 2013: defines the technical regulation of hemotherapy procedures.

- **Resolution of the Anvisa Collegiate Board of Directors – RDC 34**, June 11, 2014: establishes the Good Practices of the Blood Cycle.

- **Normative Instruction of Anvisa 01**, March 17, 2015: establishes the procedures, standards and guidelines of the national system of hemovigilance cited in the Resolution of the Collegiate Board of Directors 34.

- **Resolution of the Anvisa Collegiate Board of Directors – RDC 35**, June 12, 2014: establishes the plastic bags for collection, storage and transfer of human blood and its components.

- **Resolution of the Collegiate Board of Directors – RDC 20**, April 10, 2014: establishes the sanitary regulation for the transportation of human biological material.

Section XII, articles 146 to 148, of the RDC 34 describes the actions to be taken by health facilities and professionals in the occurrence of adverse events of the blood cycle and the NI 01 sets deadlines for the communication and notification of adverse events of the blood cycle, and presents the Guide to Hemovigilance in Brazil, which establishes guidelines for the hemovigilance system.

5. HEMOVIGILANCE SYSTEM

The Brazilian hemovigilance system is composed of health care facilities (HCF), by blood establishments (HS), of local regulatory authorities (Visas) of the states, of the Federal District and municipalities and of Anvisa, by the Management of Risk Monitoring (Gemor) of the General Management of Monitoring of Products Subject to Health Surveillance (GGMON). This area comprises the former Unit of Biovigilance and Hemovigilance and keeps all the activities of hemovigilance already under development.

HCFs include hospitals, clinics, outpatients and urgency and emergency facilities that perform actions included in the blood cycle and that are not characterized as blood establishments, according to the legislation in force. There are not accurate data about the number of HCFs in Brazil that carry out these procedures. It is estimated that there are about 7,000 health facilities with complexity of actions capable of performing transfusions, having as source the facilities registered in the National Register of Health Care Facilities (CNES), in the categories of general and specialized hospital, general and specialized emergency room and hemotherapy and/or hematology center.

It is assigned to HCFs, where transfusions take place, the detection, diagnosis and investigation of the TRs, the internal record of the events and the corrective and preventive measures and their notification to SNVS, by Notivisa, and the communication to the facility processing the blood component that caused the reaction.

The blood establishments are those classified and defined by the RDC/Anvisa 151/2001. In general, they are facilities that perform several steps of the blood cycle. This resolution classifies the blood establishments as: coordinator blood establishement (CBE), regional blood establishment (RE), blood nucleus (BN), unit of collection and transfusion (UCT), Blood collection unit (BCU), center for laboratory screening of donors (CLSD), and transfusion agency (TA).

According to data of the National System of Register of Blood Establishments (Hemocad), there are about 2,300 blood establishments, in their varied types. However, there is a possibility that this number is underestimated, assuming that not all FUs regularly update data in the system. It is necessary also to consider the existence of other establishments with different nomenclature established in the RDC 151, but that conduct activities similar to the facilities named herein.

The blood establishments are responsible for the quality of production, for the storage and distribution of blood components. To do so, they must keep updated information about their procedures, collect information from HCFs about occasional adverse events, keep them under their own records and notify them, when pertinent and when the notification is not done by the health facility, they must also develop adequate preventive and corrective actions upon the occurrence of adverse events.

The state, district and municipal health surveillance authorities participate in SNVS as units linked to city halls and state governments. Following the principle of SUS decentralization, state, district and municipal Visa are bodies that implement and design the local policies of SNVS. Throughout national arrangements of actions and goals to be executed, these management spheres define their operational capacity for each of themes regarding health promotion and protection. However, hemovigilance actions are taken times at a local context, by the municipal Visa, and times by the state Visa. Naturally, because of the complexity of the actions in the area of blood quality control, larger cities are the ones, in fact, that have knowledge contribution and personnel to develop such actions. In this context, Anvisa identifies, as references for the TR monitoring in the country, 26 state Visa, the Visa of the Federal District, and the 26 Visa of the capital-cities.

Anvisa has as one of its responsibilities the coordination of SNVS, and its institutional purpose is:

> "promoting health protection of the population by the sanitary control of the production and commercialization of products and services subject to health surveillance, including environments, processes, inputs and technologies related to them."

The accomplishment of this mission, in terms of production of blood components for therapeutic use or as input for the production of blood derivatives, imposes the implementation of actions to regulate, supervise and monitor the risk of these products. The competence for regulating, supervising and monitoring the blood establishments is assigned, within Anvisa, to the General Management of Biological Products, Blood, Tissues, Cells and Organs (GGPBS) and executed by the Management of Blood, Tissues, Cells and Organs (GSTCO). It is responsibility of GGMON to monitor and investigate adverse events and technical complaints related to products and services under health surveillance, and it is up to Gemor specifically, monitoring these adverse events occurred in health care facilities or in blood establishments in the country. Hence, it must work in a articulated way with the other

bodies that compose the hemovigilance system. Gemor monitors the occurrence of these events by the daily analysis of the database of adverse events and technical complaints, Notivisa.

All the notifications of transfusion reactions are analyzed with the aim of identifying the coherence and completeness of the notification, as well as identifying the events considered as "sentinels": death attributed to transfusion, bacterial contamination, acute immune hemolytic reaction, transfusion-related acute lung injury, and blood transmitted disease.

It is still up to Gemor the analysis, consolidation and disclosure of data on transfusion reactions in the country and other actions with the aim of promoting patient's safety and improve the quality of the blood and blood components transfused.

It is up to the General Coordination of Blood and Blood Derivatives of the Ministry of Health to formulate the policies of hemotherapy and hematology care, stimulate their implementation, together with the states, Federal District and municipalities, and ensure the access of the population to the therapeutic use of blood and blood components with safety and quality. Apart from this key role, it has played a fundamental role in hemovigilance by compiling and publishing data on blood collection and transfusion in the country. From these data, notification rates and other information on hemovigilance in Brazil are calculated for international comparability.

To date, the hemovigilance system is organized focused on transfusion reaction monitoring, in other words, on the adverse events that affect blood recipient.

From March this year, with the publication of the Normative Instruction 01, the Brazilian hemovogilance proposes the amplification of its scope of work, starting to work on the monitoring of adverse events of the entire blood cycle and not only on those related to transfusion. Until March 2016, health and blood establishments and the health surveillance itself must suit to notify and follow-up the adverse events that occur in the different steps of this cycle, as well as the look-back investigation.

6. NATIONAL DATA ON BLOOD TRANSFUSIONS AND TRANSFUSION REACTIONS

6.1 Data source

In this report, data are shown by year of occurrence and by year of notification of TRs. Data by year of occurrence were obtained exclusively from Notivisa, covering the period from January 1, 2007 to December 31, 2014, once the system allows the notification of reactions occurred in previous years. Data by year of notification were obtained from Sineps, for the period of 2002 to 2006, and from Notivisa, from 2007.

Quantitative data on the production and transfusion of blood and blood components, used here for the construction of same rates, were obtained from the Information Notebook: Blood and Blood Derivatives (*Caderno de Informação: Sangue e Hemoderivados*), published by CGSH, from 2008 to 2014.

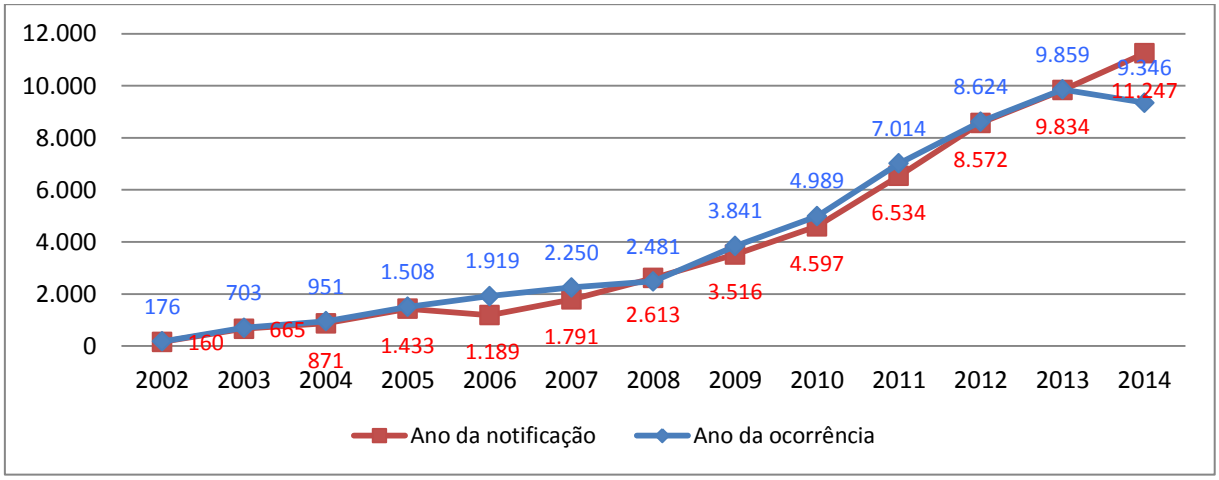
By analyzing data on blood transfusion present in the said publication, it is possible to observe important variations in the frequency of transfusions of the different regions of the country among many years compiled (see table 8). This irregularity of frequency of the transfusions reported generates variations in the rate of transfusion reactions, as well as in the estimation of sub-notification. The variation of information, basically, lies in the transfusion data from the private establishments not related to SUS, data informed by the association that congregates these establishments.

6.2 General data of notifications

Graph 1 shows the frequency of curves of transfusion reactions (TRs) by year of notification and by year of occurrence, with rising characteristics since 2002. Between 2013 and 2014, the increment in notifications was 14.5%.

The frequency of transfusion reactions that occurred in the current year is always lower than the frequency of the TRs notified in the same year, once it possible to notify transfusion reactions that occurred in previous years, fact translated in the curves represented in Graph 1.

Graph 1: Absolute frequency of notifications of transfusion reactions, according to the year of notification and the year of occurrence. Brazil, 2002 to 2014.



Source: Sineps (data from 2002 to 2006, with the addition of the frequencies in Notivisa) and Notivisa (data from 2007 to 2013).

Table 1 shows the frequency of notifications for every FU, since 2002, by year of notification, and graphs 2.1 to 2.5 show the evolution in notifications of the FUs for every region.

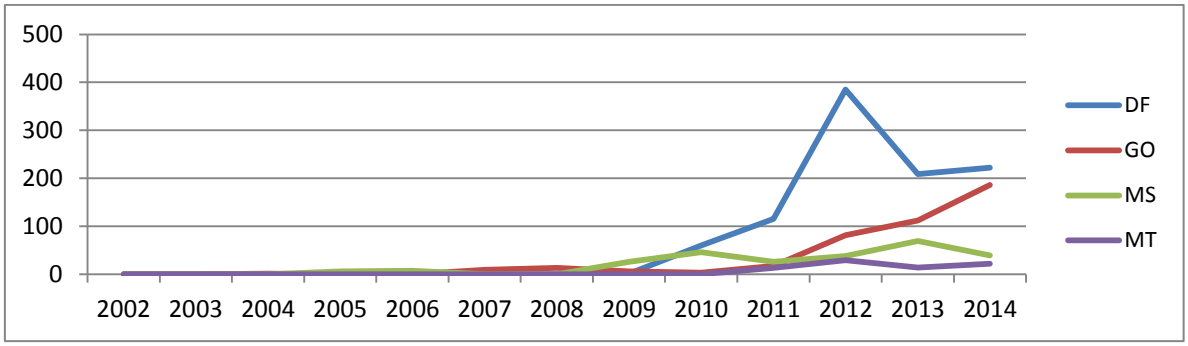
Table 1: Absolute frequency of notifications of transfusion reactions, by region and FU, according to the year of notification. Brazil, 2002 to 2014.

FU	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Federal District	0	0	0	0	0	0	0	1	60	115	385	209	222
Goiás	0	0	1	0	0	9	13	6	3	17	81	112	186
Mato Grosso do Sul	0	0	0	6	7	0	0	26	46	26	38	69	39
Mato Grosso	0	0	0	0	0	0	0	0	0	13	29	14	22
Central-West Region	**0**	**0**	**1**	**6**	**7**	**9**	**13**	**33**	**109**	**171**	**533**	**404**	**469**
Alagoas	0	16	7	8	4	9	11	44	28	30	57	77	51
Bahia	28	50	34	69	86	83	150	226	367	353	421	496	477
Ceará	1	54	24	32	76	217	113	107	359	565	413	415	574
Maranhão	0	0	0	4	3	25	31	41	67	35	185	145	139
Paraíba	0	3	0	0	0	0	17	22	108	138	124	97	105
Pernambuco	0	0	12	6	0	5	43	91	57	155	110	205	334
Piauí	0	0	0	0	0	0	0	0	0	1	59	55	45
Rio Grande do Norte	0	1	0	0	0	0	0	3	6	6	33	41	29
Sergipe	0	0	0	0	0	0	0	0	0	12	22	37	37
Northeast Region	**29**	**124**	**77**	**119**	**169**	**339**	**365**	**534**	**992**	**1.295**	**1.424**	**1.568**	**1.791**
Acre	4	10	6	9	5	1	3	6	22	22	20	27	32
Amapá	0	0	0	0	0	0	4	0	0	0	0	0	6
Amazonas	0	0	0	0	0	40	31	33	9	30	101	77	96
Pará	0	7	3	12	6	11	67	35	104	366	254	181	169
Rondônia	0	0	0	0	0	8	30	12	6	17	29	58	67
Roraima	0	0	0	0	0	0	0	0	1	0	0	0	28
Tocantins	0	0	0	0	0	0	0	2	0	13	14	2	40
North Region	**4**	**17**	**9**	**21**	**11**	**60**	**135**	**88**	**142**	**448**	**418**	**345**	**438**
Espírito Santo	0	0	0	0	0	0	32	23	21	50	159	197	289
Minas Gerais	2	4	17	0	0	26	53	93	61	173	188	315	312
Rio de Janeiro	59	54	57	140	118	157	270	247	293	512	861	1,173	1,178
São Paulo	24	98	438	777	585	806	1,212	1,603	1,845	2,536	3,306	3,831	4,424
Southeast Region	**85**	**156**	**512**	**917**	**703**	**989**	**1,567**	**1,966**	**2,220**	**3,271**	**4,514**	**5,516**	**6,203**
Paraná	41	173	186	171	204	120	246	341	326	382	558	658	734
Rio Grande do Sul	1	184	57	60	20	133	212	338	466	661	715	871	1.071
Santa Catarina	0	11	29	139	75	141	75	216	342	306	410	472	541
South Region	**42**	**368**	**272**	**370**	**299**	**394**	**533**	**895**	**1,134**	**1,349**	**1,683**	**2,001**	**2,346**
Brazil	**160**	**665**	**871**	**1,433**	**1,189**	**1,791**	**2,613**	**3,516**	**4,597**	**6,534**	**8,572**	**9,834**	**11,247**

Source: Sineps (data from 2002 to 2006) and Notivisa (data from 2007 to 2014).

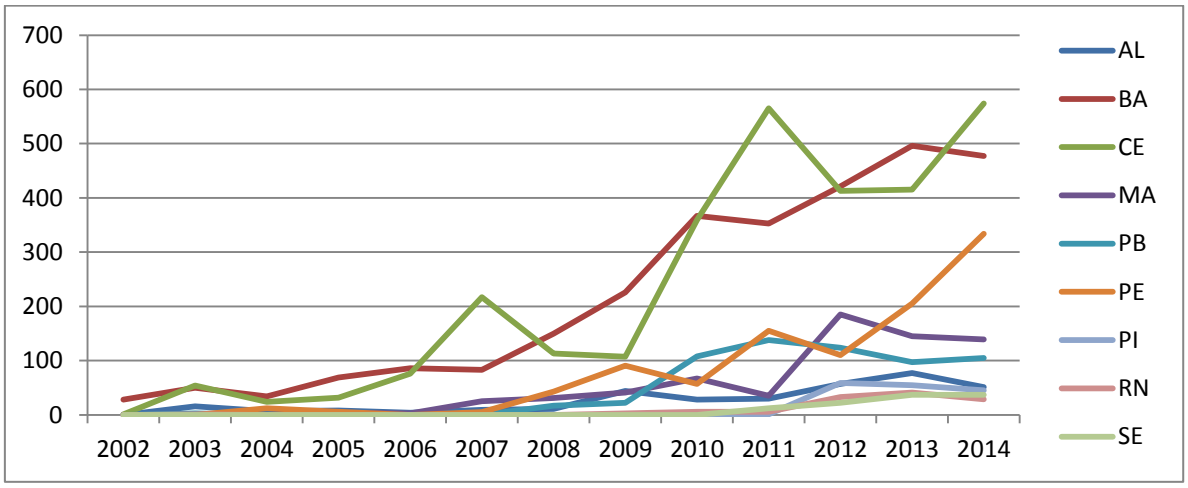
Data reveal the FUs with the lowest frequencies of notifications for every administrative regions, and if they are linked to the number of transfusion performed, they also reveal the sub-notification rates that will be presented in the item 5.1 of this report.

Graph 2.1: Evolution of the absolute frequency of notifications of transfusion reactions for the FUs of the Central-West Region. 2002 to 2014.



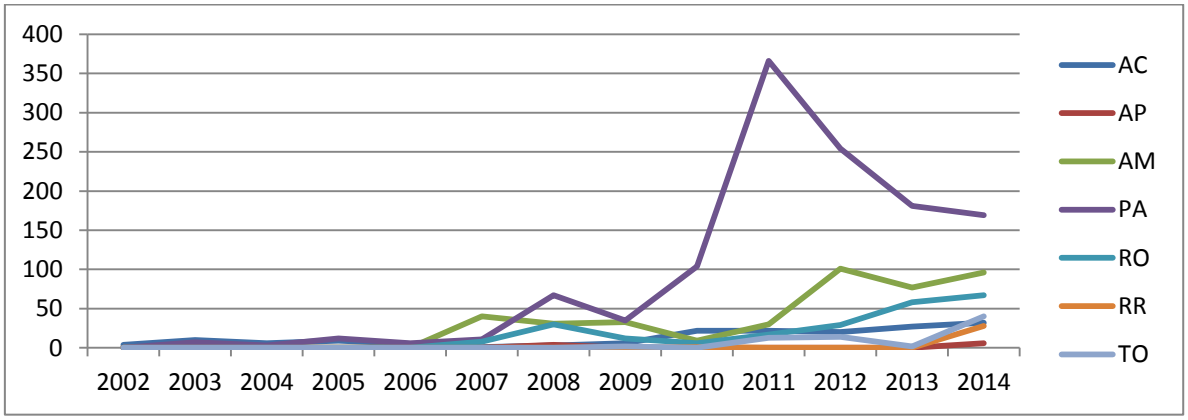
Source: Sineps (data from 2002 to 2006) and Notivisa (data from 2007 to 2014).

Graph 2.2: Evolution of the absolute frequency of notifications of transfusion reactions for the FUs of the Northeast Region. 2002 to 2014.



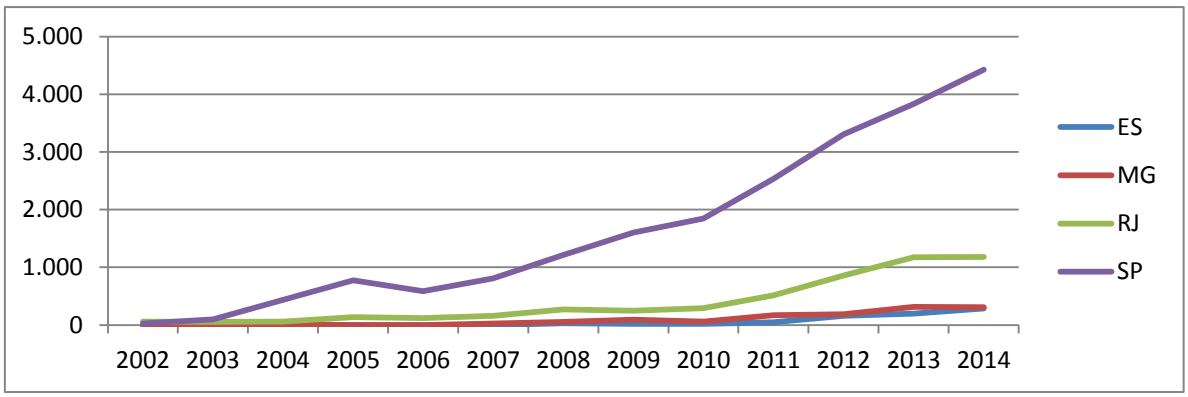
Source: Sineps (data from 2002 to 2006) and Notivisa (data from 2007 to 2014).

Graph 2.3: Evolution of the absolute frequency of notifications of transfusion reactions for the FUs of the North Region. 2002 a 2014.



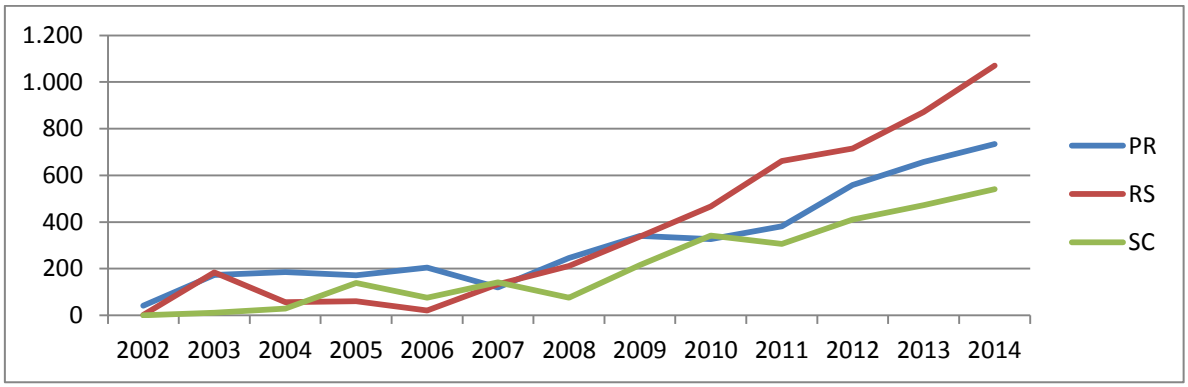
Source: Sineps (data from 2002 to 2006) and Notivisa (data from 2007 to 2014).

Graph 2.4: Evolution of the absolute frequency of notifications of transfusion reactions for the FUs of the Southeast Region. 2002 to 2014.



Source: Sineps (data from 2002 to 2006) and Notivisa (data from 2007 to 2014).

Graph 2.5: Evolution of the absolute frequency of notifications of transfusion reactions for the FUs of the South Region. 2002 to 2014.



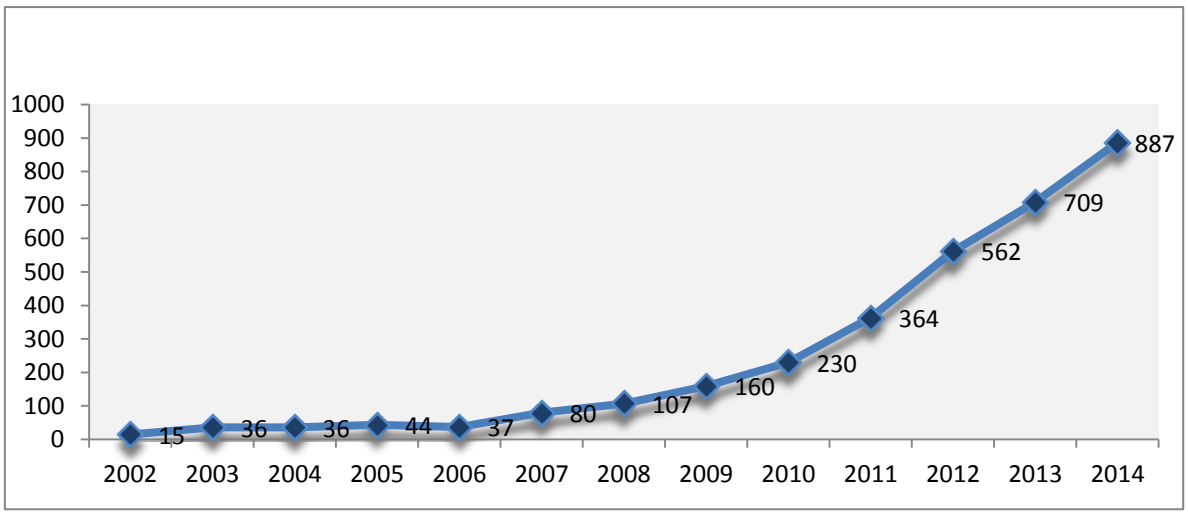
Source: Sineps (data from 2002 to 2006) and Notivisa (data from 2007 to 2014).

Graph 3 shows the evolution of the frequency of the health facilities that have notified since 2002, highlighting that, between 2002 and 2006, the notifying facilitites were only those participating in the Sentinel Network. Since 2007, with the implementation of Notivisa, all the facilities that perform transfusions are able to notify.

In this graph, it is observed that the curve becomes progressively rising from 2007, with the introduction of Notivisa, what reveals the contribution of this system to facilitate and amplify the notifications. In December 2010, with the publication of RDC 57, replaced by RDC 34/2014, the notification of TRs became mandatory, contributing to the increment observed in the respective curves.

Considering that it is estimated the existence of about seven thousand health facilities with complexity to perform transfusions in Brazil, the approximate percentage of 12% of facilities that notify is still very low, even with the considerable increment registered since 2002.

Graph 3: Absolute frequency of health facilities that notify transfusion reactions, according to the year of notification. Brazil, 2002 to 2014.



Source: Sineps (data from 2002 to 2006) and Notivisa (data from 2007 to 2014).

Since there is not information, at a national level, about the frequency of transfusion by health facility, it is not possible to evaluate if the notifying facilities are those with higher volume of transfusions. Table 2 below is an attempt to analyze the concentration of notifying facilities in each unit of the Federation and its relation with the frequency of transfusions in each one of them. The source of the estimated number of existing facilities in every state is the National Register of Health Care Facilities.

Of the ten FUs with the highest frequency of transfusions (São Paulo, Paraná, Minas Gerais, Rio Grande do Sul, Rio de Janeiro, Bahia, Goiás, Pernambuco, Ceará and Santa Catarina), only the states of Rio de Janeiro, São Paulo, Pernambuco, Santa Catarina e Rio Grande do Sul are among the ten states with higher percentage of notifying health facilities, as it can be seen in Table 2. The FU with the highest percentage of facilities that notified in 2014 is the Federal District, with 47%.

It is possible to infer from the data shown that important FUs, with high volumes of transfusion performed, possess health facilities probably with large volumes of transfusion without notifying transfusion reactions, such as Paraná, Minas Gerais, Bahia, Goiás, and Ceará. Among them, Minas Gerais draws the attention, because it is an important transfusing state, as shown in Table 2, but it has very low frequency of notifying facilities (6.3%) and with low frequency of notifications within its region, as shown in Graph 2.4. The State of Minas Gerais performs four times more transfusions than Espírito Santo, but proportionally it possesses four times less notifying facilities.

Table 2: Estimated number of health facilities with complexity to perform transfusions, number of facilities that notified transfusion reactions, number of transfusions and relative frequency of facilities that notified reactions, by FU. Brazil, 2014.

Region/FU	Estimated number of facilities	Number of notifying facilities	Transfusions performed	% notifying facilities
Distrito Federal	68	32	42,498	47.1
Goiás	744	46	157,773	6.2
Mato Grosso do Sul	136	5	29,162	3.7
Mato Grosso	183	11	67,744	6.0
Central-West	**1,131**	**94**	**297,177**	**8.3**
Alagoas	77	5	22,521	6.5
Bahia	571	42	158,651	7.4
Ceará	278	31	124,240	11.2
Maranhão	242	5	36,911	2.1
Paraíba	164	11	38,803	6.7
Pernambuco	249	37	141,509	14.9
Piauí	126	8	32,258	6.3
Rio Grande do Norte	106	9	52,713	8.5
Sergipe	54	4	15,240	7.4
Northeast	**1,867**	**152**	**622,846**	**8.1**
Acre	28	4	8,655	14.3
Amapá	13	1	16,851	7.7
Amazonas	109	13	35,559	11.9
Pará	253	34	66,600	13.4
Rondônia	83	8	12,711	9.6
Roraima	13	2	4,269	15.4
Tocantins	70	3	15,797	4.3
North	**569**	**65**	**160,442**	**11.4**
Espírito Santo	117	33	89,274	28.2
Minas Gerais	698	44	350,820	6.3
Rio de Janeiro	546	128	170,364	23.4
São Paulo	1.135	234	827,947	20.6
Southeast	**2,496**	**439**	**1,438,405**	**17.6**
Paraná	515	57	396,240	11.1
Rio Grande do Sul	377	47	257,893	12.5
Santa Catarina	234	31	121,031	13.2
South	**1,126**	**135**	**775,164**	**12.0**
Brazil	**7,189**	**885**	**3,294,034**	**12.3**

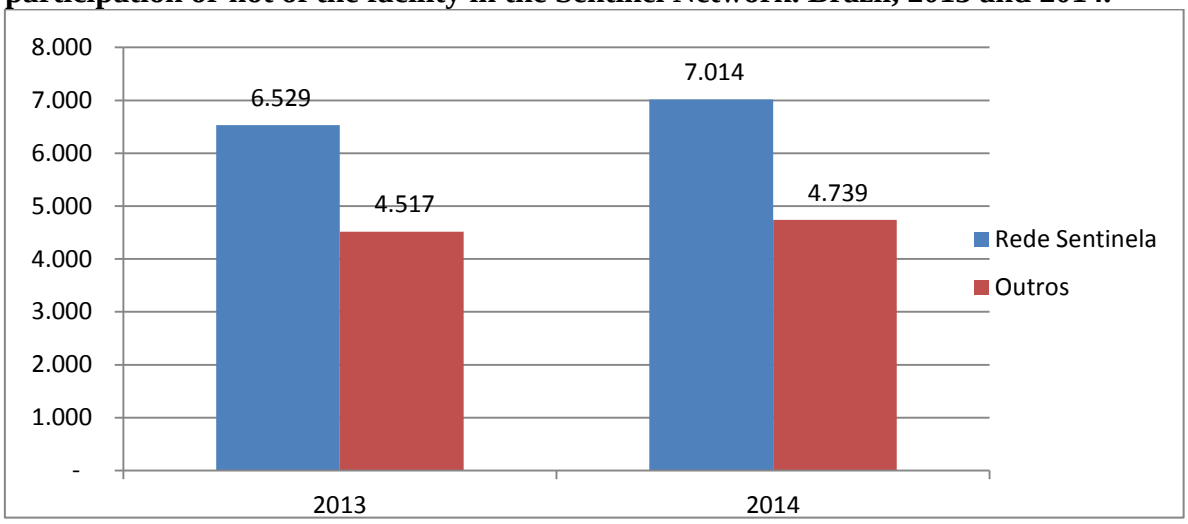
Source: Ministry of Health (National Register of Health Facilities, competence May 2015, and Information Notebook: Blood and Derivatives); Anvisa (Notivisa).

With regard to the participation of the facilities of the Sentinel Network in the notifications of transfusion reactions, in 2007 and 2008, the Network was composed of 197 hospitals, and from 2009 to 2011, of 245 hospitals. In the end of 2011, the Sentinel Network was restructured and new and different forms of connection to the Network were proposed. Since its initial formulation, there are minimum criteria to participate, one of them is the commitment with the notification of adverse events of products of health interest, including transfusion reactions. In the end of 2014, 209 facilities were registered in the Sentinel Network.

The relative participation of these facilities, from 2007, shows a decrease, if compared in numerical terms with the other notifying facilities, due to implementation of a

web based system, in case of Notivisa, and the extension of the mandatory status of notification to all facilities that perform transfusions. However, when we compare the participation in the absolute frequency of notifications among the facilities of the Sentinel Network and other establishments, we notice its importance, as shown in Graph 4. The comparative analysis reveals the extraordinary participation of these facilities in notification, especially if we consider that of the 887 facilities that notified in 2014, only 23% (209) took part in the Sentinel Network, showing its importance to the hemovigilance system. On the other hand, we verified that approximately 30% of the facilities linked to the Network did not notify transfusion reactions in 2014.

Graph 4: Absolute frequency of notifications of transfusion reactions, according to participation or not of the facility in the Sentinel Network. Brazil, 2013 and 2014.



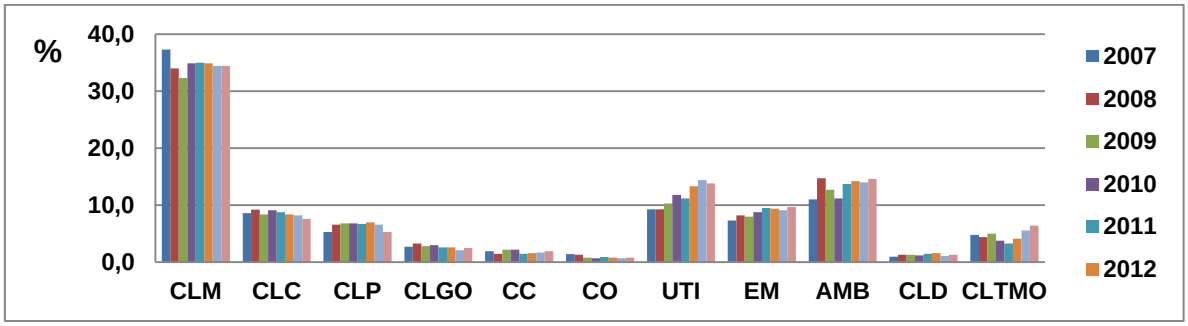
Source: Notivisa.

Once 2007 was the year of the effective implementation of Notivisa, the other analyses will be shown with the historical series, beginning by this year. Moreover, the information shown will be based on the data of notification by year of occurrence.

6.3 Reactions by sector of occurrence

Graph 5 demonstrates the relative frequency of notifications, according to the sector of occurrence of transfusion reactions for the eight years measured. In this series, the sector with the highest prevalence of TRs notified is the sector of medical clinic. However, these isolated data do not allow to estimate the risk because the denominator, it means, the frequency of transfusions performed in this sector, for the same period, is unknown.

Graph 5: Relative frequency of notifications of transfusion reactions, by sector of occurrence. Brazil, 2007 to 2014.



Source: Notivisa.
Note 1: CLM – medical clinic; CLC – surgical clinic; CLP - pediatric clinic; CLGO – gynecological and obstetric clinic; CC – surgical center; CO - obstetric center; UTI – intensive care unit and intensive therapy center; EM – emergency room; AMB – transfusion outpatient; CLD - dialysis clinic; CLTMO – bone marrow transplantation clinic.
Note 2: Home transfusion as a sector of occurrence was excluded from the presentation.

6.4 Reaction by type of blood component

Table 3 shows absolute and relative frequencies of notifications of transfusion reactions, according to the type of blood component transfused and the year of occurrence of the reaction. Red blood cell concentrate is the blood component most associated with the TRs notified, in the eight years of the series. In item 7 of this report, when the information about the rates is presented, the behavior of this blood component is analyzed, from the viewpoint of risk.

Table 3: Absolute (f) and relative (%) frequencies of the transfusion reactions notified, according to the blood components associated with reactions. Brazil, 2007 to 2014.

Type of blood component	2007		2008		2009		2010		2011		2012		2013		2014	
	F	%	F	%	F	%	F	%	F	%	F	%	F	%	F	%
Red blood cell concentrate	1,524	67.7	1,693	68.2	2,571	66.9	3,510	70.4	4,923	70.2	5,882	68.2	6,634	67.3	6,376	68.2
Platelet concentrate	481	21.4	544	21.9	850	22.1	1,017	20.4	1,372	19.6	1,885	21.9	2,281	23.1	2,157	23.1
Fresh frozen plasma	173	7.7	171	6.9	318	8.3	341	6.8	529	7.5	595	6.9	680	6.9	582	6.2
Platelets - other type	9	0.4	4	0.2	4	0.1	13	0.3	11	0.2	12	0.1	6	0.1	13	0.1
Granulocyte concentrate	0	0.0	3	0.1	3	0.1	2	0.0	0	0.0	6	0.1	7	0.1	0	0
Cryoprecipitate	3	0.1	6	0.2	11	0.3	4	0.1	16	0.2	18	0.2	16	0.2	22	0.2
Whole blood	1	0.0	0	0.0	0	0.0	4	0.1	1	0.0	2	0.0	2	0.0	2	0
Reconstituted whole blood	0	0.0	0	0.0	1	0.0	2	0.0	0	0.0	0	0.0	0	0.0	0	0
Other	19	0.8	19	0.8	27	0.7	36	0.7	65	0.9	82	1.0	44	0.4	42	0.4
Multi-component	40	1.8	41	1.7	56	1.5	60	1.2	97	1.4	142	1.6	189	1.9	152	1.6
Total	2,250		2,481		3,841		4,989		7,014		8,624		9,859		9,346	

Source: Notivisa.

6.5 Transfusion reactions by gender and age range

The distribution of the absolute frequency of notification by year of occurrence of transfusion reactions and according to recipients' gender and age range is shown in Table 4.

A slight predominance of females is noticed from the age range of 20 years, what can be explained by the increased presence of women in the health facilities, in the age range that corresponds to their reproductive period, and by longer survival after the age range of 70 years.

Table 4: Absolute frequency of notifications, by year of occurrence of transfusion reactions, according to gender and age range. Brazil, 2007 to 2014.

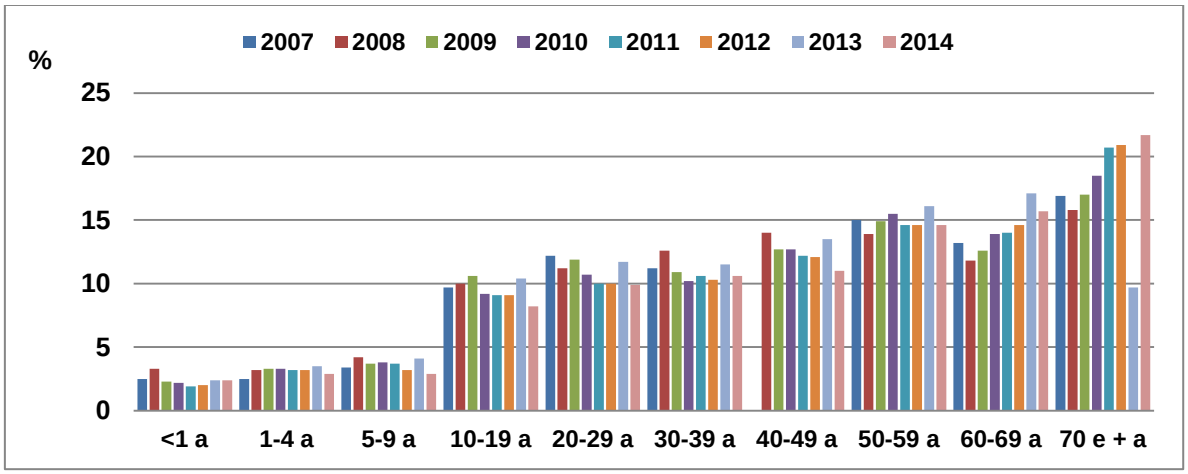
	2007		2008		2009		2010		2011		2012		2013		2014	
Age range	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	M	F
< 1 year	38	18	43	37	47	43	60	50	68	67	88	81	123	86	114	110
1 to 4 years	32	25	49	29	66	61	96	67	128	96	166	109	176	126	133	140
5 to 9 years	45	32	59	44	76	67	119	68	135	123	169	110	206	153	159	114
10 to 19 years	113	106	134	103	231	177	225	235	325	310	418	369	489	420	407	357
20 to 29 years	126	149	142	171	209	247	261	273	317	387	399	464	498	516	422	504
30 to 39 years	110	141	130	179	175	242	207	299	303	438	338	548	436	563	376	610
40 to 49 years	129	171	130	212	191	298	270	365	352	502	417	623	493	684	403	626
50 to 59 years	176	162	137	203	288	285	347	425	443	583	576	683	679	724	675	692
60 to 69 years	145	151	137	152	244	239	311	384	494	488	628	628	730	761	713	756
70 years and +	184	196	180	208	298	354	382	540	608	840	763	1,042	840	1,149	884	1,143
Total	**1,098**	**1,151**	**1,141**	**1,338**	**1,825**	**2,013**	**2,278**	**2,706**	**3,173**	**3,834**	**3,962**	**4,657**	**4,670**	**5,152**	**4,286**	**5,052**

Source: Notivisa.

Note: In the respective years of the series, were not considered the frequencies of notifications with the gender ignored: 2007 = 1; 2008 = 2; 2009 = 3; 2010 = 5; 2011 = 7; 2012 = 5; 2013 = 7; 2014 = 8 .

Graph 6 shows the relative frequency of TR notifications, by age range, for every year of the series, evidencing greater participation of more elevated age ranges in the occurrence of transfusion reactions, as shown in Table 4.

Graph 6: Relative frequency of notifications of transfusion reactions, according to the age range and the year of occurrence. Brazil, 2007 to 2014.



Source: Notivisa.

6.6 Reactions by autologous and allogeneic transfusions

- Autologous transfusion is that one where donor and recipient are the same person.
- Allogeneic transfusion is that one where donor and recipient are different people (BRASIL, 2015).

Table 5 shows the frequencies of notifications, according to the type of transfusion and the year of occurrence of the transfusion reaction, in the period from 2007 to 2014. Prevalence of notifications related to allogeneic transfusions tends to 100% in all years of the series.

Table 5: Absolute (f) and relative (%) frequencies of notifications, according to the type of transfusion and the year of occurrence of the transfusion reaction. Brazil, 2007 to 2014.

Type of transfusion	2007		2008		2009		2010		2011		2012		2013		2014	
	f	%	f	%	f	%	f	%	f	%	f	%	f	%	f	%
Allogeneic	2,241	99.6	2,477	99.8	3,834	99.8	4,979	99.8	6,997	99.8	8,615	99.9	9,813	99.5	9,286	99.4
Autologous	9	0.4	4	0.2	7	0.2	10	0.2	17	0.2	9	0.1	46	0.5	60	0.6
Total	**2,250**		**2,481**		**3,841**		**4,989**		**7,014**		**8,624**		**9,859**		**9,346**	

Source: Notivisa.

The occurrence of autologous donation in Brazil is so infrequent that the notification of this type of transfusion constitutes a sentinel-event of the quality of the notification and gives rise to questions to the notifying party, by the health surveillance, when the coherence of the information given does not match with this kind of transfusion.

6.7 Immediate and delayed transfusion reactions

- Immediate reaction is the one that occurs during or until 24 hours after transfusion.
- Delayed reaction is the one that occurs 24 hours after transfusion (BRASIL, 2015).

Table 6 shows the distribution, in absolute and relative frequencies, of TRs notifications, according to the classification of the type (immediate or delayed), the diagnosis of the reaction and the year of occurrence. In all the years of the series, immediate reactions predominate in percentages higher than 96%, with the average estimated in 98% for the period.

International literature also shows predominance of immediate reactions, although the proportion is quite different from our reality. The adoption of routine measures in the treatment of blood components, such as the universal use of filters for leukocytes and the use of satellite bags for the collection of the initial blood volume before deposition in the bag to be stored, can explain why some countries obtained a substantial decrease of some immediate transfusion reactions.

In addition to these operational factors that enhance the quality of the blood transfused and reduce the probability of an immediate reaction, we cannot rule out the sub-notification of delayed reactions, such as transfusion transmitted infectious diseases, and the sub-notification of alloimmunization (development of irregular antibodies).

6.8 Reactions by diagnosis

Table 6 and Graph 7 show, by year of occurrence, the reactions notified, according to diagnosis. Febrile non-hemolytic reactions (FNHTR) and allergic reactions (ALG) are the most prevalent, with median rates of 49% and 37%, respectively, for the period.

This pattern does not differ from the international scenario, that shows FNHTR and ALG as the most frequent, however with trend towards a gradual fall of these rates in the French hemovigilance system and towards its stability in Brazil. Data from the French system for 2013 showed respective percentages of 30.6% and 14.6% (FRANÇA, 2013).

Until the year of 2013, the reaction notified as "other immediate" was characterized as the third most notified in our hemovigilance system. In 2014, it dropped to the fourth event with the highest frequency of notification, surpassed by TACO. Although this relative number is still elevated, considering all types of reactions notified, it is believed that the difficulty in classifying the signs and symptoms of a given transfusion reaction may be lessened with the guidance contained in the chapter of Recipient Hemovigilance that integrates the Conceptual and Operational Framework of Hemovigilance (MCeO), in which the criteria were established for the case definition of every type of transfusion reaction.

MCeO, besides better characterizing the case definition for each transfusion reaction diagnosis, also proposes five categories of imputability to transfusion, what, we hope, will enable a better criterion for the diagnosis of the type of transfusion reaction by the professionals that diagnosed and reported these adverse events.

The analysis of occurrence of transfusion-associated circulatory overload (TACO), in previous years, showed this type of elevated diagnosis from the age groups older than 40 years. According to Graph 8, from 2012 on, it seems that there is a trend towards elevation in the age range from 30 to 39 years.

The Hemovigilance Report from 2007 to 2011 had already stressed this fact, what led the Anvisa personnel to conduct an analysis of all the notifications in the database whose diagnosis was TACO. The analysis resulted in a diagnosis of the quality of notifications and transfusion indication. It was verified the need to invest in health professional training in relation to the criteria internationally defined for the diagnosis of circulatory overload, once 90% of notifications did not contain the description of sufficient criteria for diagnosing it. By the end of 2013, the area of Hemovigilance at Anvisa produced and divulged the Technical Note 2/2013 (BRASIL, 2013), with guidance to diagnosis, clinical handling and notification of TACO cases.

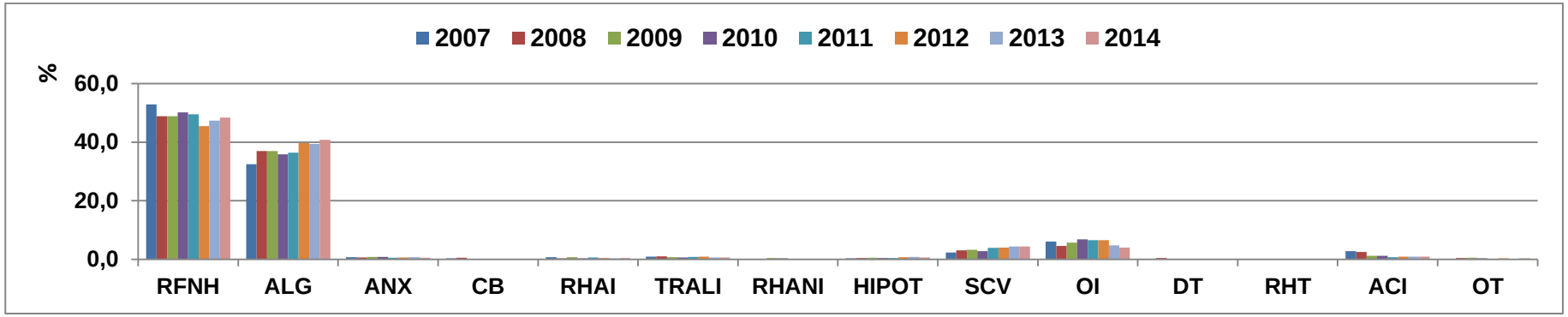
With MCeO, the case definition of TACO may better justify the diagnosis of this type of reaction and differential diagnoses.

Table 6: Absolute (f) and relative (%) frequencies of transfusion reactions notified, according to the type of reaction, diagnosis and year of occurrence. Brazil, 2007 to 2014.

	Reaction diagnosis	2007		2008		2009		2010		2011		2012		2013		2014	
		f	%	f	%	f	%	f	%	f	%	f	%	f	%	f	%
IMMEDIATE	Febrile non-hemolytic - FNHTR	1,191	52.9	1,214	48.9	1,879	48.9	2,503	50.2	3,475	49.5	3,978	46.1	4,676	47.4	4,468	47.8
	Allergic	731	32.5	919	37.0	1,422	37.0	1,784	35.8	2,552	36.4	3,388	39.3	3,885	39.4	3,761	40.2
	Anaphylactic	15	0.7	16	0.6	32	0.8	40	0.8	38	0.5	49	0.6	73	0.7	46	0.5
	Bacterial infection - TTBI	7	0.3	12	0.5	6	0.2	10	0.2	10	0.1	16	0.2	18	0.2	18	0.2
	Acute immune hemolytic reaction – AHTR	15	0.7	8	0.3	27	0.7	16	0.3	39	0.6	31	0.4	34	0.3	36	0.4
	Transfusion-associated acute lung injury – TRALI	20	0.9	25	1.0	26	0.7	30	0.6	54	0.8	78	0.9	62	0.6	51	0.6
	Nonimmune hemolysis reaction– ANIHR	4	0.2	4	0.2	14	0.4	13	0.3	9	0.1	7	0.1	21	0.2	14	0.2
	Hypotensive reaction	7	0.3	9	0.4	18	0.5	21	0.4	31	0.4	63	0.7	79	0.8	59	0.6
	TACO	51	2.3	76	3.1	124	3.2	138	2.8	272	3.9	338	3.9	437	4.4	404	4.3
	Other immediate reactions	138	6.1	115	4.6	219	5.7	338	6.8	456	6.5	555	6.4	459	4.7	371	4.0
	Subtotal	**2,179**	**9.8**	**2,398**	**96.6**	**3,767**	**9.1**	**4,893**	**98.1**	**6,936**	**98.9**	**8,503**	**98.6**	**9,744**	**98.8**	**9,228**	**98.7**
DELAYED	Transmitted infectious disease - TTID	3	0.1	10	0.4	4	0.1	11	0.2	10	0.1	18	0.2	4	0.0	0	0
	Graft versus host disease – TA-GVHD	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Delayed hemolytic reaction - DHR	3	0.1	1	0.0	4	0.1	7	0.1	1	0.0	5	0.1	11	0.1	13	0.1
	Delayed serologic reaction - DSRT /Alloimmunization	62	2.8	61	2.5	46	1.2	62	1.2	50	0.7	76	0.9	85	0.9	87	0.9
	Other delayed reactions	3	0.1	11	0.4	20	0.5	16	0.3	17	0.2	22	0.3	15	0.2	18	0.2
	Subtotal	**71**	**3.2**	**83**	**3.3**	**74**	**1.9**	**96**	**1.9**	**78**	**1.1**	**121**	**1.4**	**115**	**1.2**	**118**	**1.3**
	Total	**2,250**	**100**	**2,481**	**100**	**3,841**	**100**	**4,989**	**100**	**7,014**	**100**	**8,624**	**100**	**9,859**	**100**	**9,346**	**100.0**

Source: Notivisa.

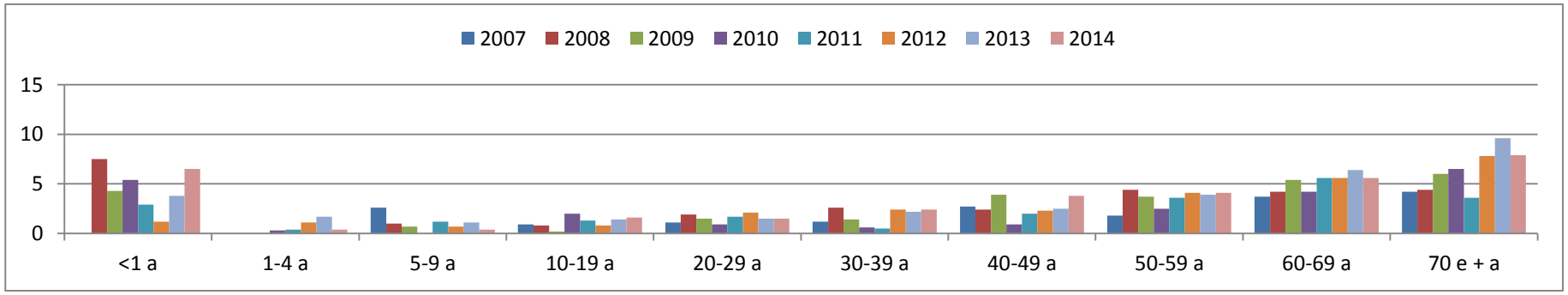
Graph 7: Relative frequency (%) of notifications of transfusion reactions, according to diagnosis. Brazil, 2007 to 2014.



Source: Notivisa.

Note 1: RFNH – febrile non-hemolytic reaction (FNHTR); ALG – allergic; ANX – anaphylactic; CB – bacterial infection (TTIB); Rhai – acute immune hemolytic reaction (AHTR); TRALI – transfusion-related acute lung injury; Rhani - nonimmune hemolysis reaction (ANIHR); Hipot – hypotensive reaction; SCV – volemic overload (TACO); OI –other immediate reactions; DT– infectious disease (TTID); RHT – delayed hemolytic reaction (DHR); ACI – Dalayed serologic reaction/Aloimmunization (DSRT); OT – other delayed reactions.
Note 2: Transfusion-associated graft versus host disease (TA-GVHD) was not notified in any years of the series.

Graph 8: Relative frequency (%) of transfusion reactions by TACO, according to age group and year of occurrence. Brazil, 2007 to 2014.



Source: Notivisa.

6.9 Transfusion reactions according to severity

In the national hemovigilance system, the following definitions are adopted to characterize TR severity:

- Grade I or mild: not life-threating; low severity.
- Grade II or moderate: when there is long-term morbidity; moderate severity, life-threating or not.
- Grade III or severe: when it is immediate life-threating, but no death.
- Grade IV or death: death attributed to transfusion reaction.

It is observed, in Table 7, the predominance of notification of Grade I reactions, with median frequency of approximately 83% in the eight years of the series.

Table 7: Absolute (f) and relative (%) frequencies of transfusion reactions notified, according to severity and year of occurrence. Brazil, 2007 to 2014.

	2007		2008		2009		2010		2011		2012		2013		2014	
Severity	f	%	f	%	f	%	f	%	f	%	f	%	f	%	f	%
Grade I	1,956	86.9	2,134	86.0	3,246	84.5	4,185	83.9	5,718	81.5	7,012	81.3	8,031	81.5	7,722	82.6
Grade II	226	10.0	257	10.4	501	13.0	661	13.2	1,109	15.8	1,332	15.4	1,482	15.0	1,335	14.3
Grade III	64	2.8	83	3.3	87	2.3	133	2.7	178	2.5	267	3.1	324	3.3	263	2.8
Grade IV	4	0.2	7	0.3	7	0.2	10	0.2	9	0.1	13	0.2	22	0.2	26	0.3
Total	2,250		2,481		3,841		4,989		7,014		8,624		9,859		9,346	

Source: Notivisa.

Considering only the notifications of immediate TRs, which represent on average 98% of the total of notifications, graphs 9.1 and 9.2 were constructed to analyze the trends of the relative frequencies of TR diagnoses, according to their severity (mild, moderate, and severe). Deaths are analyzed separately. Febrile non-hemolytic reaction is proportionally the one that stands out in the set of mild reactions, with a trend towards the reduction of this reaction in the set of moderate and severe reactions, however it still keeps an important proportional frequency. Allergic reaction is important in all the three severity categories, ranging between 17% and 45%. These two types of reaction appear even in an important way as a death cause, as it can be seen in Table 8, what may point to the poor quality of the differential diagnosis of the transfusion reaction, once these two types are commonly mild and moderate reactions.

For severity III (severe) reactions, Graph 9.2 shows the highlights for allergic reactions, by TRALI and by volemic overload. It is also noteworthy that this last type of reaction appears in the three severity grades, but it reaches more relevant proportions in the set of severe TRs.

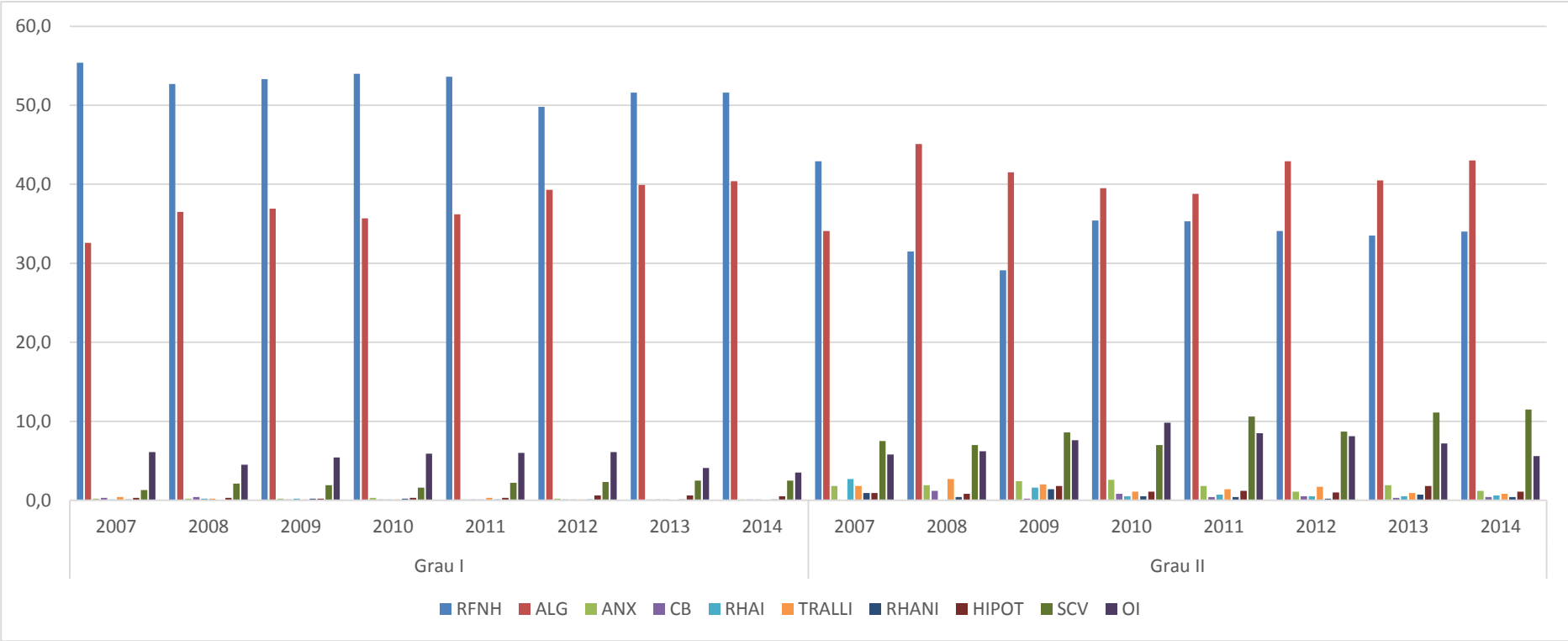
Deaths correspond to about 0.2%, on average, in the period analyzed, and were attributed to the TRs described in Table 8. However, it is verified that even the reactions that commonly have mild severity, such as febrile non-hemolytic reactions and allergic reactions, were also related to deaths. These data indicate that the imputability between reaction and death deserves to be more clarified, investigating if death should not be attributed to the underlying disease or to other clinical complications. The proportion of deaths attributed to "other immediate reactions" also call our attention. It can be an evidence of the precariousness of diagnosis or understanding of the criterion to classify the TR as severity IV – death attributed to transfusion.

Table 8: Absolute frequency of deaths attributed to blood transfusion, according to the diagnosis of the transfusion reaction and year of occurrence. Brazil, 2007 to 2014.

Reaction diagnosis	2007	2008	2009	2010	2011	2012	2013	2014	Total
Febrile non-hemolytic reaction - FNHTR	0	1	1	0	0	0	3	6	**11**
Allergic	0	1	0	0	0	0	2	2	**5**
Anaphylactic	0	0	0	0	0	0	3	1	**4**
Bacterial infection -TTBI	0	1	0	0	0	1	0	1	**3**
Acute immune hemolytic reaction – AHTR	1	0	2	2	3	1	3	1	**13**
Transfusion-associated acute lung injury – TRALI	0	1	1	1	2	5	4	4	**18**
Nonimmune hemolysis reaction– ANIHR	0	0	0	0	0	0	2	0	**2**
Hypotensive reaction	0	0	1	0	0	0	0	1	**2**
TACO	0	0	1	3	1	2	0	4	**11**
Other immediate reactions	2	0	1	4	3	4	5	6	**25**
Transmited Infeccion - TTID	1	2	0	0	0	0	0	0	**3**
Other delayed reactions	0	1	0	0	0	0	0	0	**1**
Total	**4**	**7**	**7**	**10**	**9**	**13**	**22**	**26**	**98**

Source: Notivisa.

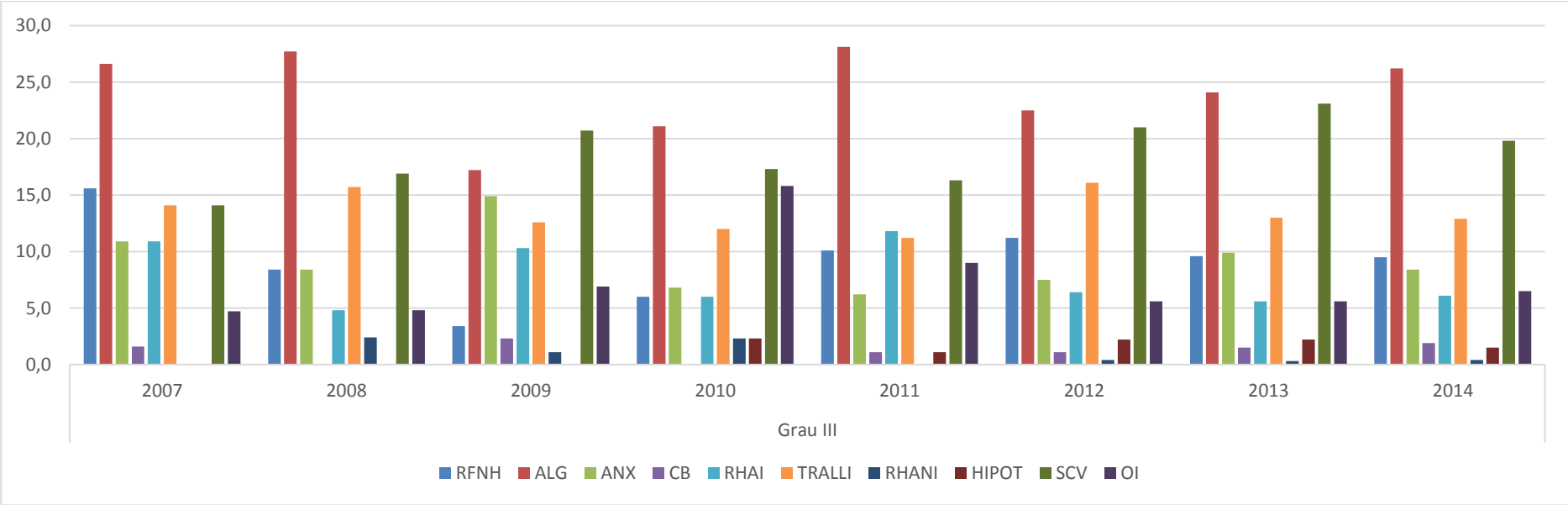
Graph 9.1: Relative frequency of notifications of immediate transfusion reactions, according to mild and moderate severity. Brazil, 2007 to 2014.



Source: Notivisa.

Note: RFNH – febrile non-hemolytic reaction; ALG – allergic; ANX – anaphylactic; CB – bacterial infection; Rhai – acute immune hemolytic reaction; TRALI – transfusion-related acute lung injury; Rhani - Nonimmune hemolysis reaction; Hipot – hypotensive reaction; SCV – volemic overload (TACO); OI –other immediate reactions.

Graph 9.2: Relative frequency of notifications of immediate transfusion reactions, according to severity III (severe). Brazil, 2007 to 2014.



Source: Notivisa.

Note: RFNH – febrile non-hemolytic reaction; ALG – allergic; ANX – anaphylactic; CB – bacterial infection; Rhai – acute immune hemolytic reaction; TRALI – transfusion-related acute lung injury; Rhani - Nonimmune hemolysis reaction; Hipot – hypotensive reaction; SCV – volemic overload (TACO); OI –other immediate reactions.

7. TRANSFUSION REACTION RATES

The denominators for the construction of transfusion reaction rates have as data source on blood transfusions, in the country, the SUS Hospital Information System (SIH-SUS) and the SUS Outpatient Information System (SIA-SUS), created to control the payment for hospital and outpatient procedures in the health facilities of SUS and in those that signed a service agreement with SUS. Therefore, these are systems that show some bias when used for another purposes.

Data from private establishments, that do not have an agreement with SUS, are provided by the Brazilian Association of Blood Banks (ABBS). ABBS did not provide information about these establishments in the North region, justifying the absence of associated establishments located there. However, data from other FUs, in other regions, show to be cyclic in the years of the series, what puts question marks over their consistency.

Nevertheless, data from the Information Notebook: Blood and Blood Derivatives of the Ministry of Health, despite the bias mentioned, still constitute the most reliable source on the transfusions performed in the country for the construction of the transfusion reaction rates presented in this report.

Some exercises for 2013, with other sources, were done from the data on transfusions provided by health facilities, forwarded by the local health surveillance teams. Such exercises are shown in the conclusion of this report as a foundation for the hypothesis formulated for the current Brazilian rates.

7.1 Transfusion reaction sub-notification rate

Table 9 shows the transfusions performed in the FUs and regions, according to data from Ministry of Health available in the Information Notebook: Blood and Blood Derivatives for the years of 2007 to 2012 (BRASIL, 2008 to 2012). For the year of 2013, the projection made based on the three previous years was kept, once the data presented in the source of the Ministry of Health are distant from the curve of the previous years. These last data, and also the data of 2014, were provided by the General Coordination of Blood and Blood Derivatives, in advance of its publication in the Information Notebook.

Table 9: Transfusions performed, according to the FU and region. Brazil, 2007 to 2014.

FU	2007	2008	2009	2010	2011	2012	2013*	2014**
Federal District	80,105	70,476	69,143	33,662	23,935	24,483	27,360	42,498
Goiás	127,873	92,230	147,612	151,062	143,919	146,962	147,314	157,773
Mato Grosso do Sul	38,702	39,528	39,112	43,509	42,204	44,706	43,473	29,162
Mato Grosso	267,983	56,282	68,862	64,507	48,155	59,573	57,412	67,744
Central-West region	**514,663**	**258,516**	**324,729**	**292,740**	**258,213**	**275,724**	**275,559**	**297,177**
Alagoas	22,954	138,615	19,480	18,647	21,430	22,857	20,978	22,521
Bahia	189,540	134,170	179,470	160,045	128,976	138,384	142,468	158,651
Ceará	164,276	128,610	128,621	128,267	87,469	127,409	114,382	124,240
Maranhão	30,042	18,165	30,757	32,448	29,256	33,736	31,813	36,911
Paraíba	39,590	38,556	48,028	48,507	46,847	46,671	47,342	38,803
Pernambuco	161,729	84,666	257,293	84,034	90,062	93,575	89,224	141,509
Piauí	110,605	101,540	107,444	96,239	26,203	30,416	50,953	32,258
Rio Grande do Norte	47,946	38,785	49,324	51,814	39,727	36,301	42,614	52,713
Sergipe	82,118	68,298	70,936	15,534	11,405	18,161	15,033	15,240
Northeast region	**848,800**	**751,405**	**891,353**	**635,535**	**481,375**	**547,510**	**554,807**	**622,846**
Acre	11,725	9,755	11,652	12,247	11,385	9,543	11,058	8,655
Amapá	43,342	25,591	27.038	39,211	20,646	7,067	22,308	16,851
Amazonas	29,369	27,741	19,632	19,321	8,626	25,473	17,807	35,559
Pará	63,670	58,948	68,183	65,555	61,120	67,010	64,562	66,500
Rondônia	2,945	4,578	4,448	8,494	9,781	7,106	8,460	12,711
Roraima	4,129	5,096	6,759	9,668	4,980	3,599	6,082	4,269
Tocantins	10,388	14,621	17,799	18,184	15,166	15,404	16,251	15,797
North region	**165,568**	**146,330**	**155,511**	**172,680**	**131,704**	**135,202**	**146,529**	**160,342**
Espírito Santo	98,354	53,348	65,664	75,503	69,173	75,009	73,228	89,274
Minas Gerais	324,917	301,871	353,634	352,332	346,607	320,524	339,821	350,820
Rio de Janeiro	291,127	216,145	247,412	202,524	160,986	168,382	177,297	170,364
São Paulo	908,096	843,332	871,825	884,328	819,194	832,110	845,211	827,947
Southeast region	**1,622,494**	**1,414,696**	**1,538,535**	**1,514,687**	**1,395,960**	**1,396,025**	**1,435,557**	**1,438,405**
Paraná	462,701	362,118	377,607	367,732	362,594	423,009	384,445	396,240
Rio Grande do Sul	265,642	238,251	218,073	248,937	235,916	233,925	239,593	257,893
Santa Catarina	122,549	142,743	110,477	105,807	114,051	116,562	112,140	121,031
South region	**850,892**	**743,112**	**706,157**	**722,476**	**712,561**	**773,496**	**736,178**	**775,164**
Brazil	**4,002,417**	**3,314,059**	**3,616,285**	**3,338,118**	**2,979,813**	**3,127,957**	**3,148,629**	**3,293,934**

Source: Information Notebook: Blood and Blood Derivatives.
Note: *Average of the three previous years, projected to 2013. ** Data provided by the Health Ministry.

Table 10 shows, by FU and by year of occurrence of TR, information about the estimation of reactions expected and the numbers of reactions notified, which enabled the calculation of sub-notification rates and the trends observed in the seven years analyzed.

The calculation of transfusion reaction sub-notification rates relies on the estimation of three transfusion reactions per every thousand transfusions. This estimation is based on the setting of the French hemovigilance system, in the beginning of the decade of 1990, when molecular biology tests for donor screening were not used and there was not the compulsory use of universal filter for blood components.

For the last year of the series, there are not units of the Federation without notifications. There are also several examples of FUs that were able to reset the sub-notification and keep themselves consistently with gradual increase of notifications. From 2011, the transfusion reaction rate for every FU started to be monitored, as shown in the following section.

7.2 Transfusion reaction rates

Table 11 shows the sub-notification rates and transfusion reaction rates, by FU, from 2011. The choice of this year to start the series of transfusion reaction rates is due to the fact that this was the year in which a good part of the FUs started to present the expected notification rates, according to the parameter used, turning sub-notification into negative.

The follow-up of the transfusion reaction rates from 2011 has the objective of trying to construct progressively a national average to be used as parameter. Although it is premature to use it as a criterion for health risk, once the denominator still represents an uncertainty in the national context, it is important that the states with rates higher than the national rates stay alert and try to gather more accurate information about the frequency of the transfusion performed by health facilities. Graph 10 shows the transfusion reaction rates by FU and by region.

Table 10: Absolute frequency of expected transfusion reactions and notified occurrences of transfusion reactions and estimated sub-notification rates, according to FU and region. Brazil, 2007 to 2014.

	Expected reactions*								Reaction occurred**								Estimated sub-notification rates							
UF	2007	2008	2009	2010	2011*	2012	2013	2014	2007	2008	2009	2010	2011	2012	2013	2014	2007	2008	2009	2010	2011	2012	2013	2014
DF	240	211	207	109	72	73	82	127	7	6	25	109	206	236	188	197	97.1	97.2	87.9	-7.9	-186.9	-221.3	-129.0	-54.5
GO	384	277	443	9	432	441	442	473	9	13	6	9	17	105	126	135	97.7	95.3	98.6	98.0	96.1	76.2	71.5	71.5
MS	116	119	117	38	127	134	130	87	0	0	35	38	34	33	65	38	100.0	100.0	70.2	70.9	73.1	75.4	50.2	56.6
MT	804	169	207	1	144	179	172	203	0	0	0	1	17	25	16	19	100.0	100.0	100.0	99.5	88.2	86.0	90.7	90.7
C. West	**1,544**	**776**	**974**	**157**	**775**	**827**	**827**	**892**	**16**	**19**	**66**	**157**	**274**	**399**	**395**	**389**	**99.0**	**97.6**	**93.2**	**82.1**	**64.6**	**51.8**	**52.2**	**56.4**
AL	69	416	58	23	64	69	63	68	12	25	28	23	40	59	77	45	82.6	94.0	52.1	58.9	37.8	14.0	-22.4	33.4
BA	569	403	538	338	387	415	427	476	100	189	285	338	347	447	488	370	82.4	53.0	47.1	29.6	10.3	-7.7	-14.2	22.3
CE	493	386	386	344	262	382	343	373	193	116	126	344	570	452	428	472	60.8	69.9	67.3	10.6	-117.2	-18.3	-24.7	-26.6
MA	90	54	92	55	88	101	95	111	20	24	64	55	74	166	161	86	77.8	56.0	30.6	43.5	15.7	-64.0	-68.7	22.3
PB	119	116	144	109	141	140	142	116	0	17	27	109	135	125	106	90	100.0	85.3	81.3	25.1	3.9	10.7	25.4	22.7
PE	485	254	772	86	270	281	268	425	15	36	95	86	117	125	188	288	96.9	85.8	87.7	65.9	56.7	55.5	29.8	32.2
PI	332	305	322	0	79	91	153	97	0	0	1	0	12	50	54	42	100.0	100.0	99.7	100.0	84.7	45.2	64.7	56.6
RN	144	116	148	6	119	109	128	158	0	2	1	6	8	39	45	17	100.0	98.3	99.3	96.1	93.3	64.2	64.8	89.2
SE	246	205	213	0	34	54	45	46	0	0	0	0	12	28	30	37	100.0	100.0	100.0	100.0	64.9	48.6	33.5	19.1
Northeast	**2,547**	**2,254**	**2,674**	**961**	**1,444**	**1,643**	**1,664**	**1,869**	**340**	**409**	**627**	**961**	**1,315**	**1,491**	**1,577**	**1,447**	**86.6**	**81.9**	**76.6**	**49.6**	**8.9**	**9.2**	**5.3**	**22.6**
AC	35	29	35	17	34	29	33	26	1	3	9	17	25	26	32	19	97.2	89.7	74.3	53.7	26.8	9.2	3.5	26.8
AP	130	77	81	0	62	21	67	51	0	4	0	0	0	1	1	4	100.0	94.8	100.0	100.0	100.0	95.3	98.5	92.1
AM	88	83	59	13	26	76	53	107	29	32	32	13	60	93	66	94	67.1	61.5	45.7	77.6	-131.9	-21.7	-23.5	11.9
PA	191	177	205	214	183	201	194	200	18	60	53	214	266	258	188	124	90.6	66.1	74.1	-8.8	-45.1	-28.3	2.9	37.8
RO	9	14	13	11	29	21	25	38	14	21	11	11	27	35	50	51	-58.5	-52.9	17.6	56.8	8.0	-64.2	-97.0	-33.7
RR	12	15	20	0	15	11	18	13	0	0	0	0	0	1	10	17	100.0	100.0	100.0	100.0	0.0	90.7	45.2	-32.7
TO	31	44	53	0	45	46	49	47	0	0	2	0	13	15	1	40	100.0	100.0	96.3	100.0	71.4	67.5	97.9	15.6
North	**496**	**439**	**467**	**255**	**395**	**406**	**440**	**481**	**62**	**120**	**107**	**255**	**391**	**429**	**348**	**349**	**87.5**	**72.7**	**77.1**	**50.8**	**1.0**	**-5.8**	**20.8**	**27.4**
ES	295	160	197	17	208	225	220	268	21	14	19	17	70	132	191	266	92.9	91.3	90.4	92.5	66.3	41.3	13.1	0.7
MG	975	906	1.061	125	1.040	962	1.019	1.052	37	73	79	125	148	220	311	248	96.2	91.9	92.6	88.2	85.8	77.1	69.5	76.4
RJ	873	648	742	404	483	505	532	511	183	238	197	404	662	1.063	1.182	928	79.0	63.3	73.5	33.5	-37.1	-110.4	-122.2	-81.6
SP	2,724	2,530	2,615	1,955	2,458	2,496	2,536	2,484	1,153	1,043	1,790	1,955	2,697	3,237	3,766	3,725	57.7	58.8	31.6	26.3	-9.7	-29.7	-48.5	-50.0
Southeast	**4,867**	**4,244**	**4,616**	**2,501**	**4,188**	**4,188**	**4,307**	**4,315**	**1,394**	**1,368**	**2,085**	**2,501**	**3,577**	**4,652**	**5,450**	**5,167**	**71.4**	**67.8**	**54.8**	**45.0**	**14.6**	**-11.1**	**-26.5**	**-19.7**
PR	1.388	1.086	1.133	369	1.088	1.269	1.153	1.189	137	256	317	369	418	517	690	647	90.1	76.4	72.0	66.6	61.6	59.3	40.2	45.6
RS	797	715	654	455	708	702	719	774	166	225	346	455	720	723	851	949	79.2	68.5	47.1	39.1	-1.7	-3.0	-18.4	-22.7
SC	368	428	331	291	342	350	336	363	135	84	293	291	319	413	548	398	63.3	80.4	11.6	8.3	6.8	-18.1	-62.9	-9.6
South	**2,553**	**2,229**	**2,118**	**1,115**	**2,138**	**2,320**	**2,209**	**2,325**	**438**	**565**	**956**	**1,115**	**1,457**	**1,653**	**2,089**	**1,994**	**82.8**	**74.7**	**54.9**	**48.6**	**31.8**	**28.8**	**5.4**	**14.3**
Brazil	**12,007**	**9,942**	**10,849**	**4,989**	**8,939**	**9,384**	**9,446**	**9,882**	**2,250**	**2,481**	**3,841**	**4,989**	**7,014**	**8,624**	**9,859**	**9,346**	**81.3**	**75.0**	**64.6**	**50.2**	**21.5**	**8.1**	**-4.4**	**5.4**

Source: Information Notebook: Blood and Blood Derivatives and Notivisa.

Note: *Parameter: 3 TRs/1,000 transfusions (median occurrence declared in the French hemovigilance system, in the beginning of the decade of 1990).

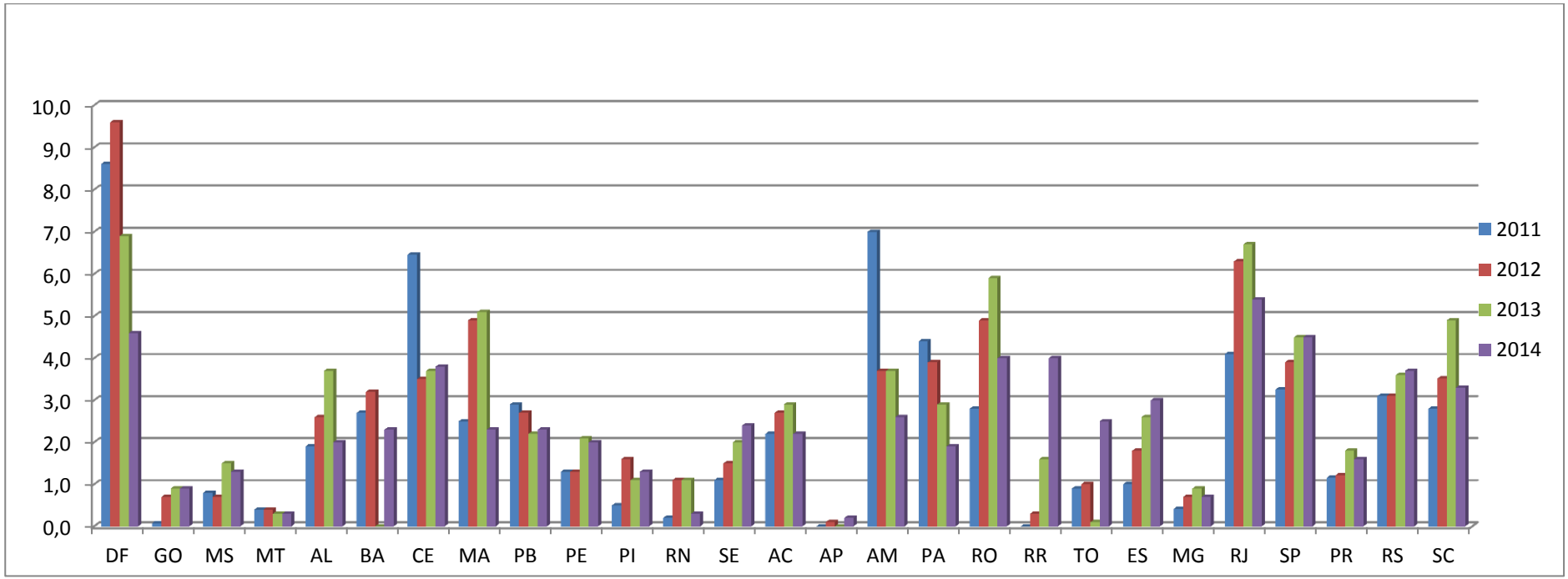
** Year of occurrence.

Table 11: Estimated sub-notification and transfusion reaction rates, according to FU and region. Brazil, 2011 to 2014.

FU	Estimated sub-notification*				Transfusion reaction rate**			
	2011	**2012**	**2013**	**2014**	**2011**	**2012**	**2013**	**2014**
DF	-186.9	-221.3	-129.0	-54.5	8.6	9.6	6.9	4.6
GO	96.1	76.2	71.5	71.5	0.1	0.7	0.9	0.9
MS	73.1	75.4	50.2	56.6	0.8	0.7	1.5	1.3
MT	88.2	86.0	90.7	90.7	0.4	0.4	0.3	0.3
C. West	**64.6**	**51.8**	**52.2**	56.4	**1.1**	**1.4**	**1.4**	**1.3**
AL	37.8	14.0	-22.4	33.4	1.9	2.6	3.7	2.0
BA	10.3	-7.7	-14.2	22.3	2.7	3.2	3.4	2.3
CE	-117.2	-18.3	-24.7	-26.6	6.5	3.5	3.7	3.8
MA	15.7	-64.0	-68.7	22.3	2.5	4.9	5.1	2.3
PB	3.9	10.7	25.4	22.7	2.9	2.7	2.2	2.3
PE	56.7	55.5	29.8	32.2	1.3	1.3	2.1	2.0
PI	84.7	45.2	64.7	56.6	0.5	1.6	1.1	1.3
RN	93.3	64.2	64.8	89.2	0.2	1.1	1.1	0.3
SE	64.9	48.6	33.5	19.1	1.1	1.5	2.0	2.4
Northeast	**8.9**	**9.2**	**5.3**	22.6	**2.7**	**2.7**	**2.8**	**2.3**
AC	26.8	9.2	3.5	26.8	2.2	2.7	2.9	2.2
AP	100.0	95.3	98.5	92.1	0.0	0.1	0.0	0.2
AM	-131.9	-21.7	-23.5	11.9	7.0	3.7	3.7	2.6
PA	-45.1	-28.3	2.9	37.8	4.4	3.9	2.9	1.9
RO	8.0	-64.2	-97.0	-33.7	2.8	4.9	5.9	4.0
RR	0.0	90.7	45.2	-32.7	0.0	0.3	1.6	4.0
TO	71. 4	67.5	97.9	15.6	0.9	1.0	0.1	2.5
North	**1.0**	**-5.8**	**20.8**	27.4	**3.0**	**3.2**	**2.4**	**2.2**
ES	66.3	41.3	13.1	0.7	1.0	1.8	2.6	3.0
MG	85.8	77.1	69.5	76.4	0.4	0.7	0.9	0.7
RJ	-37.1	-110.4	-122.2	-81.6	4.1	6.3	6.7	5.4
SP	-9.7	-29.7	-48.5	-50.0	3.3	3.9	4.5	4.5
Southeast	**14.6**	**-11.1**	**-26.5**	-19.7	**2.6**	**3.3**	**3.8**	**3.6**
PR	61.6	59.3	40.2	45.6	1.2	1.2	1.8	1.6
RS	-1.7	-3.0	-18.4	-22.7	3.1	3.1	3.6	3.7
SC	6.8	-18.1	-62.9	-9.6	2.8	3.5	4.9	3.3
South	**31.8**	**28.8**	**5.4**	14.3	**2.0**	**2.1**	**2.8**	**2.6**
Brazil	**21.5**	**8.1**	**-4.4**	5.4	**2.4**	**2.8**	**3.1**	**2.8**

Source: Information Notebook: Blood and Blood Derivatives and Notivisa.
Notes: * Parameter: 3 TRs/1,000 transfusions (median occurrence declared in the French hemovigilance system, in the beginning of the decade of 1990).
** TR/1,000 transfusions.

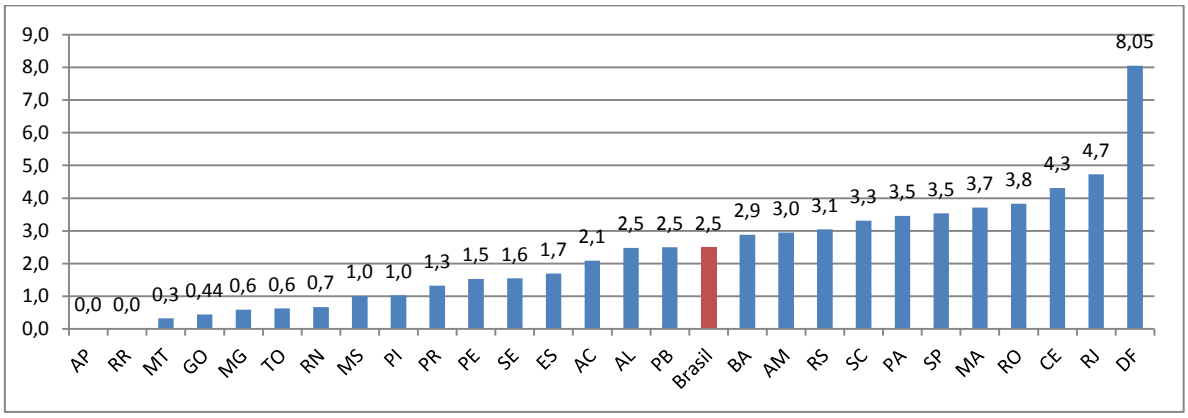
Graph 10: Transfusion reaction rate, per 1,000 transfusions, according to FU and year of occurrence. Brazil, 2011 to 2014.



Source: Information Notebook: Blood and Blood Derivatives and Notivisa.

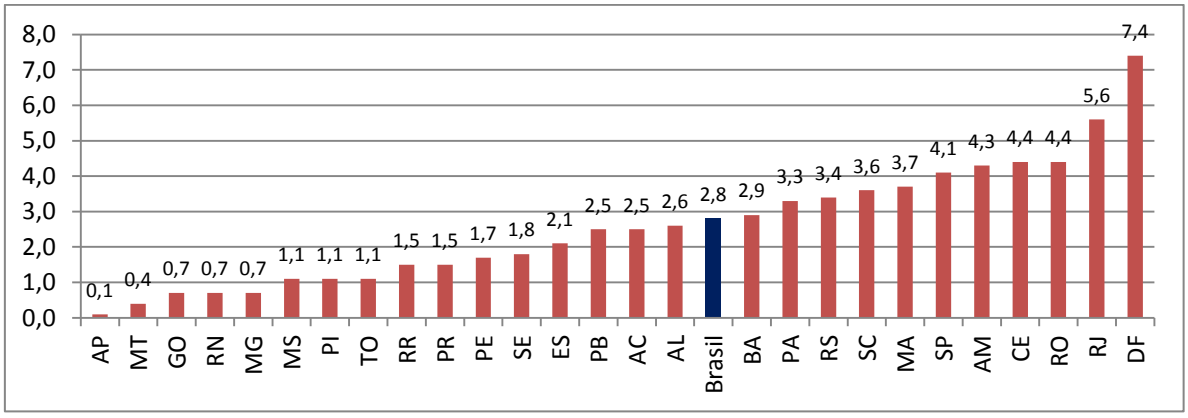
Graph 11.1 and 11.2 show the distribution of median transfusion reaction rates in the last year of the series, comparatively, in the FUs and in Brazil. Graph 11.1 is the same presented in the previous Annual Report, with data from 2011 to 2013, and Graph 11.2 contains data from 2011 to 2014, so one can visualize the median growth of this rate for the respective FUs. Safeguarding the influence of the extremes of values on the average, it is possible to verify that, except for the Federal District, which shows a decrease of the TR rate, the other units show median elevation of the rate, increasing then the Brazilian average.

Graph 11.1: Median rates of transfusion reaction notified, by year of occurrence, according to the Federation Unit. Brazil, 2011 to 2013.



Source: Information Notebook: Blood and Blood Derivatives and Notivisa.
Note: Transfusion reactions/1,000 transfusions performed.

Graph 11.2: Median rates of transfusion reaction notified, by year of occurrence, according to Federation Unit. Brazil, 2011 to 2014.



Source: Information Notebook: Blood and Blood Derivatives and Notivisa.
Note: Transfusion reactions/1,000 transfusions performed.

As highlighted in section 6.2 – "General data of notifications" –, of the ten Federation units with the highest frequency of transfusions (São Paulo, Paraná, Minas Gerais, Rio Grande do Sul, Rio de Janeiro, Bahia, Goiás, Pernambuco, Ceará, and Santa Catarina), only the states of Rio de Janeiro, São Paulo, Pernambuco, Santa Catarina, and Rio Grande do Sul are among the ten FUs with the highest percentage of notifying health facilities. The FU with the highest percentage of notifying facilities in 2014 was Distrito Federal, with 47% of notifying facilities (Table 2). **Thus, it is possible that the actual rate of median TR for Brazil is closer to the rate showed by Distrito Federal than to the one of the actual rate.**

7.3 Transfusion reaction rate by blood component

As described in item 6.4, it was identified the red blood cell concentrate as the blood component most involved in transfusion reactions (Table 3). Based on the data published on the frequency of transfusion by blood component, referring to the period from 2008 to 2014, transfusion reaction rates per 1,000 blood components transfused were calculated, by blood component type, as demonstrated in Table 12. Graph 12 shows the evolution of the respective rates in the historical series considered.

Red blood cell and platelet concentrates are the blood components with the highest TR rates per 1,000 blood components transfused, what apparently makes that they pose more risk of transfusion reactions.

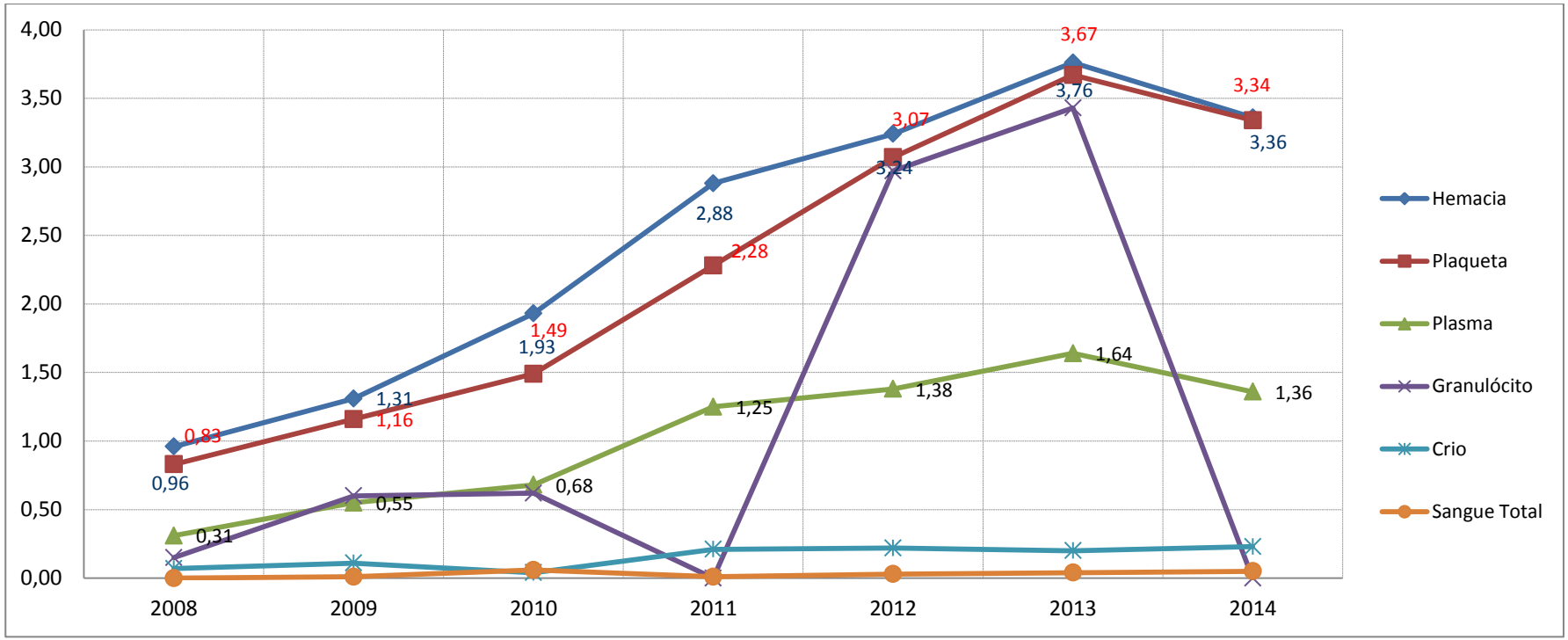
In Graph 12, the wide variation in the rate for granulocyte concentrate can be explained by inconsistency in transfusion data or in the probable variation of the rate from one year to another, when the denominator has low value, as in the case of transfusions by granulocyte concentrate.

Table 12: Transfusions performed (Transf.), absolute frequency (f) of the transfusion reactions notified and transfusion reaction rate, according to year of occurrence and blood component involved. Brazil, 2008 to 2014.

	2008			2009			2010			2011			2012			2013			2014		
TYPE	Transf.	f	Rate	Transf.	f	Rate	Transf.	f	Rate	Transf.	f	Rate	Transf.	f	Rate	Transf.	f	Rate	Transf.	f	Rate
Red blood cell concentrate	1,761,352	1,693	0.96	1,966,876	2,571	1.31	1,821,717	3,510	1.93	1,709,977	4,923	2.88	1,813,441	5,882	3.24	1,765,371	6,634	3.76	1,900,273	6,376	3.36
Platelets (all types)	654,288	544	0.83	734,348	850	1.16	683,528	1,017	1.49	600,502	1,372	2.28	614,898	1,885	3.07	621,690	2,281	3.67	651,906	2,175	3.34
Plasma (all types)	561,994	175	0.31	584,524	322	0.55	523,123	354	0.68	431,223	540	1.25	438,990	607	1.38	418,273	686	1.64	438,139	595	1.36
Granulocyte concentrate	19,489	3	0.15	5,014	3	0.60	3,248	2	0.62	2,883	0	0.00	2,,017	6	2.97	2,042	7	3.43	2,223	0	0.00
Cryoprecipitate	92,236	6	0.07	99,390	11	0.11	95,838	4	0.04	77,042	16	0.21	81,289	18	0.22	81,879	16	0.20	96,289	22	0.23
Whole blood	189,508	0	0.00	139,812	1	0.01	98,758	6	0.06	73,308	1	0.01	62,986	2	0.03	52,533	2	0.04	41,629	2	0.05

Source: Information Notebook: Blood and Blood Derivatives and Notivisa.
Note: Rate = transfusion reaction rate per 1,000 blood components transfused.

Graph 12: Rates of transfusion reactions notified, according to the blood component involved, per 1,000 transfusions performed. Brazil, 2008 to 2014.



Source: Notivisa and Information Notebook: Blood and Blood Derivatives.
Note: platelet (all types); plasma (all types); whole blood and reconstituted whole blood.

8. ANALYSIS OF NOTIFICATIONS OF SENTINEL EVENTS

In the Brazilian hemovigilance system, are considered sentinel events:

- Deaths attributed to blood transfusion.
- Acute immune hemolytic reaction.
- Transfusion transmitted bacterial infection.
- Transfusion transmitted infectious diseases.
- Transfusion-related acute lung injury.

In the occurrence of one of these events, the investigation by the health facilities, where the reaction occurred, and by the facility processing the blood component must be followed or supported by the local and national health authority, with the aim of confirming or discarding transfusion as the cause of the event and for taking actions of product quality control and patient's safety.

Table 13 shows the absolute frequency of notifications of these events, occurred since 2007.

Table 13: Absolute frequency of notifications of transfusion reactions, according to sentinel-event and year of occurrence. Brazil, 2007 to 2014.

Reaction diagnosis	2007	2008	2009	2010	2011	2012	2013	2014	Total
Death	4	7	7	10	9	13	22	26	98
Bacterial infection - TTBI	7	12	6	10	10	16	18	18	97
Acute immune hemolytic reaction - AHTR	15	8	27	16	39	31	34	36	206
Infectious disease - TTID	3	10	4	11	10	18	4	0	60
Transfusion-related acute lung injury - TRALI	20	25	26	30	54	78	62	51	346
Total	49	62	70	77	122	156	140	131	807

Source: Notivisa.

Between 2013 and 2014, the growth of notifications of sentinel-events was 37%, raising from 589 to 807. Among them, deaths increased 78% (from 55 to 98), bacterial infections 42% (from 68 to 97), AHTRs 37% (from 150 to 206), infectious diseases 22% (from 49 to 60) and TRALIs increased 29% (from 267 to 346). However, the analysis of every type of reaction, done below, shows their behavior comparatively with international data.

The Brazilian hemovigilance system nowadays classifies the notification of transfusion reaction according to the imputability of signs and symptoms to transfusion only for notifications of reactions by bacterial infection and infectious disease. This choice limits the analysis of notifications, as it is done in other countries, according to their imputability in relation to transfusion, it means, according to the grade of imputability of signs and symptoms to blood transfusion. Therefore, in the specific case of the other sentinel-events, the non-attribution to imputability can be a factor of bias of the results analyzed in comparison with other systems.

8.1 Death

According to the discussion already presented in previous reports, we can notice many doubts, by the notifying entities in Brazil, about the interpretation and attribution of death to blood transfusion when the underlying disease may have triggered or even contributed to the event. This fact is attributed to the poor clarifications on the definition of "death attributed to transfusion", but also to the notification model itself that up to now has not discriminated the imputability grades, as done in other hemovigilance systems. The Conceptual and Operational Framework of Hemovigilance proposes the classification of all reactions in relation to the imputability to transfusion. However, only from the annual report with data of 2016, comparative analyses can be done closely to international data.

The report of the French system for 2013 shows the frequency of occurrence of severity IV – death attributed to transfusion, for grades 1 to 3 of (possible, likely, and confirmed) imputability to transfusion, from 0.2/10,000 patients transfused or 0.3/100,000 bags released (FRANÇA, 2013). For the same year, in the Brazilian system, the notification of death resulting from transfusion represented 0.7 death per 100 thousand transfusions, and for 2014 the index was 0.79/100,000, with an increasing trend in the period measured. It is important to pay attention again to the effort that the system has made in order to decrease sub-notification rates, what may be depicted in data, not necessarily meaning an actual increase of deaths.

Table 14: Absolute and relative frequencies of notifications of transfusion reactions and deaths and annual and accumulated incidence rate of the deaths notified per 100 thousand transfusions. Brazil, 2007 to 2014.

	2007	2008	2009	2010	2011	2012	2013	2014	Accumulated
Deaths notified	4	7	7	10	9	13	22	26	98
All notifications	2,250	2,481	3,841	4,989	7,014	8,624	9,859	9,228	48,286
% of notifications	**0.18**	**0.28**	**0.18**	**0.20**	**0.13**	**0.15**	**0.22**	**0.28**	**0.20**
Transfusions performed	4,002,4	3,180,8	3,615,9	3,338,1	2,979,8	3,127,9	3,148.6	3,293,9	26,687,6
Rate	**0.10**	**0.22**	**0.19**	**0.30**	**0.30**	**0.42**	**0.70**	**0.79**	**0.37**

Source: Notivisa and Information Notebook: Blood and Blood Derivatives.
Note: Comma in the numbers of transfusions performed was used as a resource to make the table more concise, but the corresponding absolute hundred number must be considered after comma.

8.2 Acute immune hemolytic reaction – AHTR

The same report of the French agency for 2013 describes the occurrence of 4.4% of immune incompatibility among the notifications reported in the same year and all the imputabilities. The median incidence of ABO incompatibility in that system, between 2000 and 2013, was 0.6/100,000 bags released.

In Brazil, for the same year, Table 15 shows the percentage of AHTR occurrence of 0.34% among all reactions notified. Although different incompatibilities have not been accounted yet, the near totality of AHTR notifications are because of ABO incompatibility. The annual and accumulated incidence for the period from 2007 to 2014 can be verified in the same table. The accumulated rate calculated for the year of 2013, published in the respective annual report, was 0.64/100,000 transfusions. In 2014, as it can be seen, there was a slight increment (0.7/100,000).

Table 15: Absolute and relative frequencies of notifications of transfusion reactions and of AHTR and annual and accumulated incidence rate per 100 thousand transfusions. Brazil, 2007 to 2014.

	2007	2008	2009	2010	2011	2012	2013	2014	Accumulated
AHTR notified	15	8	27	16	39	31	34	36	206
All notifications	2,250	2,481	3,841	4,989	7,014	8,624	9,859	9,228	48,286
% of notifications	**0.67**	**0.32**	**0.70**	**0.32**	**0.56**	**0.36**	**0.34**	**0.39**	**0.43**
Transfusions performed	4,002,4	3,180,8	3,615,9	3,338,1	2,979,8	3,127,9	3,148,6	3,293,9	26,687,6
Rate	**0.37**	**0.25**	**0.75**	**0.48**	**1.31**	**0.99**	**1.08**	**1.09**	**0.77**

Source: Notivisa and Information Notebook: Blood and Blood Derivatives.
Note: Comma in the numbers of transfusions performed was used as a resource to make the table more concise, but the corresponding absolute hundred number must be considered after comma.

As shown in Table 8, of the 98 deaths occurred in the period evaluated, 13 were associated with AHTR, what represents an average of 13% of deaths in the period evaluated. Although this percentage has diminished in relation to the previous year (from 22% to 13%), it still reveals the severity of the reaction. To date, deaths by transfusion reaction have as major causes transfusion-related acute lung injury and acute immune hemolytic reaction, in this order.

It is known that AHTR is generally associated with process error in the blood cycle, mostly for human error. It happens because of exchange of samples for pre-transfusion proofs or of blood component bags. The frequent occurrence of this type of event, in the same health facility, reinforces the importance of an effective action of transfusion committees, which must work in an articulated way with other areas, such as risk and quality management, and with patient's safety nucleus, for the identification and analysis of factors that interfere in the process, indicating actions to prevent other occurrences.

Anvisa highlights that the prevention of occurrence of transfusion reactions, especially the ones related to process errors, can become effective by the fulfilment of the Ministry Ordinance 2.712, of November 12, 2013, and the RDC/Anvisa 34, of June 11, 2014, that establish the technical regulations of hemotherapy procedures and the Good Practices of the Blood Cycle – in addition, naturally, to the effective action of the transfusion committees.

8.3 Transfusion transmitted bacterial infection - TTBI

In the French hemovigilance system, the bacterial infection rate by transfusion, in 2013, corresponded to 0.19 for every 100 thousand bags released. Table 16 shows these data in Brazil, in the period from 2007 to 2014. The Brazilian rates showed to be lower in 2014, comparatively to the year of 2013, due to the change of the denominator from transfused platelets to whole transfusions. The change had as objective the comparability with the French system, that has also changed its denominator.

The comparison with the French system shows that the Brazilian rate, in the year of 2013, was three times higher. However, the comparability still shows that it is not entirely reliable due to the different case definitions in both systems.

Using the same comparative calculation shown in the report of the past year, considering the occurrence in other countries of one case of bacterial infection for every 2,000 to 3,000 transfusions of platelet concentrates (HILLYER et al., 2003), the projection of occurrence would be from 217 to 326 notifications of reactions by bacterial infection for 2014, showing that an important sub-notification is still projected.

Table 16: Absolute and relative frequencies of notifications of transfusion reactions and of bacterial infection and annual and accumulated incidence rate per 100 thousand transfusions. Brazil, 2007 to 2014.

	2007	2008	2009	2010	2011	2012	2013	2014	Accumulated
TTBI notified	7	12	6	10	10	16	18	18	97
All notifications	2,250	2,481	3,841	4,989	7,014	8,624	9,859	9,228	48,286
% of notifications	**0.31**	**0.48**	**0.16**	**0.20**	**0.14**	**0.19**	**0.18**	**0.20**	**0.20**
Transfusions performed	4,002,4	3,180,8	3,615,9	3,338,1	2,979,8	3,127,9	3,148,6	3,293,9	26,687,6
Rate	**0.17**	**0.38**	**0.17**	**0.30**	**0.34**	**0.51**	**0.57**	**0.55**	**0.36**

Source: Notivisa and Information Notebook: Blood and Blood Derivatives.
Note: Comma in the numbers of transfusions performed was used as a resource to make the table more concise, but the corresponding absolute hundred number must be considered after comma.

Tables 17.1 to 17.4 show information on the agent involved in the reaction by bacterial infection, *locus* of identification of the agent, the blood component involved and the imputability to transfusion defined by the notifying entity.

Table 17.1: Agents involved in transfusion transmitted bacterial infection and its frequency of occurrence. Brazil, 2007 to 2014.

Agent involved	2007	2008	2009	2010	2011	2012	2013	2014
Bacillus spp	-	1	-	-	-	-	2	-
Bacillus gram +/Spore	-	-	-	-	-	-	-	1
Candida albicans	-	-	-	-	-	1	-	-
Citrobacter koseri	-	1	-	-	-	-	-	-
Escherichia coli	-	-	-	-	1	3	1	-
Enterobacter aerogenes	-	1	-	1	-	3	-	-
Enterobacter cloacae	-	-	-	-	-	-	1	-
Enterococcus faecalis	-	-	-	-	-	-	1	1
Fungus	-	-	-	-	-	-	-	1
Lactobacillus spp	-	-	-	-	1	-	-	-
Klebsiella pneumoniae	1	-	-	1	-	-	-	2
Pseudomonas aeruginosa	-	-	-	-	-	-	-	1
Pseudomonas spp	-	-	-	-	-	-	-	1
Propionibacterium spp	-	-	-	-	-	-	-	1
Staphylococcus aureus	1	1	-	2	-	3	-	1
Staphylococcus capitis	-	-	1	-	-	-	-	-
Staphylococcus coagulase-negative	-	1	1	-	-	-	2	3
Staphylococcus epidermidis	-	-	-	-	-	1	1	-
Staphylococcus hominis	-	-	-	-	-	-	-	1
Staphylococcus spp	-	-	-	-	-	1	1	1
Staphylococcus warneri	-	-	-	-	-	-	1	-
Streptococcus mitis	-	-	-	-	1	-	1	-
Streptococcus pyogenes	-	-	-	-	-	1	-	-
Streptococcus viridans	-	1	-	-	-	-	1	-
Serratia marcescens	-	1	-	-	-	-	-	-
Yersinia enterocolitica	1	-	-	-	1	-	-	-
Total	**3**	**7**	**2**	**4**	**4**	**13**	**12**	**14**

Source: Notivisa.

Table 17.2: *Locus* of identification of the agent involved in the transfusion transmitted bacterial infection and its frequency of occurrence. Brazil, 2007 to 2014.

***Locus* of identification of the agent**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**
Agent identified in the blood component and in recipient.	0	6	0	2	1	6	0	1
Agent identified only in the blood component.	2	1	2	2	2	4	9	9
Agent identified only in recipient.	1	0	0	0	1	3	3	4
Agent not identified.	4	5	4	6	6	3	6	4
Total	**7**	**12**	**6**	**10**	**10**	**16**	**18**	**18**

Source: Notivisa.

It is necessary to emphasize that the choice of imputability by the notifying entity does not always follow the criteria pre-defined for confirmation and exclusion – presence or absence of the same agent in the blood component and in recipient. Therefore, comparing tables 17.2 and 17.3 year by year, it is observed the non-correspondence of the *locus* of identification in the blood component and recipient with the "confirmed" imputability to transfusion. There are much more confirmed reactions than the identification in both investigation poles.

For this type of reaction, MCeO proposes the exploration of the clinical picture at the time of the evaluation of the imputability to transfusion; thus, based on the analysis of data occurred in 2016, criteria will become broader.

Table 17.3: Imputability of transfusion transmitted bacterial infection, according to the data recorded by the notifying entity. Brazil, 2007 to 2014.

Imputability to reaction	2007	2008	2009	2010	2011	2012	2013	2014
Confirmed	1	7	1	2	2	5	6	6
Suspected	3	0	1	5	5	3	3	5
Inconclusive	1	0	2	3	1	6	6	1
Excluded	2	5	2	0	2	2	3	6
Total	7	12	6	10	10	16	18	18

Source: Notivisa.

Table 17.4 shows the frequency of occurrence of transfusion reaction by type of blood component involved. It is noticed the involvement of red blood cell concentrate in higher absolute frequency, not representing necessarily higher risk of this type of blood component.

Table 17.4: Type of blood component involved in transfusion transmitted bacterial infection and its frequency of occurrence. Brazil, 2007 to 2014.

Blood component involved	2007	2008	2009	2010	2011	2012	2013	2014
Red blood cell concentrate	4	8	5	5	6	11	14	14
Platelet concentrate	3	4	1	4	3	5	3	3
RBCC + PC	0	0	0	0	0	0	1	1
Fresh frozen plasma	0	0	0	1	1	0	0	0
Total	**7**	**12**	**6**	**10**	**10**	**16**	**18**	**18**

Source: Notivisa.

8.4 Transfusion-associated acute lung injury - TRALI

Table 18 shows the frequency of TRALI notifications, the percentage in relation to the total of notifications, incidence rate year by year and the accumulated rate for the period. According to the report of the French system for the year of 2013, the incidence rate of TRALI, within likely and confirmed imputability, is 0.62/100,000 blood components released. Since the Brazilian system still does not work with the classification according to imputability, it is not possible the current comparability of data. Accumulated rate calculated, shown in Table 18, elevated in comparison to the accumulated rate from last year (1.14 to 1.55/100,000 transfusions).

Table 18: Absolute and relative frequencies of notifications of transfusion reactions and of TRALI and annual and accumulated incidence rate per 100 thousand transfusions. Brazil, 2007 to 2014.

	2007	2008	2009	2010	2011	2012	2013	2014	Accumulated
TRALIs notified	20	25	26	30	54	78	62	51	346
All notifications	2,250	2,481	3,841	4,989	7,014	8,624	9,859	9,228	48,286
% of notifications	0.89	1.01	0.68	0.60	0.77	0.90	0.63	0.55	0.72
Transfusions performed	4,002,4	3,180,8	3,615,9	3,338,1	2,979,8	3,127,9	3,148,6	3,293,9	26,687,6
Rate	0.50	0.79	0.72	0.90	1.81	2.49	1.97	1.55	1.30

Source: Notivisa and Information Notebook: Blood and Blood Derivatives.
Note: Comma in the numbers of transfusions performed was used as a resource to make the table more concise, but the corresponding absolute hundred number must be considered after comma.

8.5 Transfusion transmitted infectious diseases – TTID

The report of the French hemovigilance system considers the transmission of viral diseases one of the events called “very rare”, with a maximum of five notifications by year and by type of diagnosis, with an incidence lower than two notifications per one million blood components released. In the year of 2013, that system computed five cases of viral transmission, four cases of hepatitis E and one case of hepatitis C, with the investigation concluded. More three cases of viral transmission by cytomegalovirus (CMV), hepatitis E and hepatitis C did not have the investigation concluded. In the period of 2006 to 2013, 15 cases of transmission of hepatitis E virus were computed (FRANÇA, 2013).

In relation to Brazil, Table 19.1 shows information on transfusion-transmitted diseases between 2007 and 2014, according to the year of occurrence described in the

notification. It has been used up to date the case definition of year of occurrence for infectious diseases as being the one in which the positivity for the respective marker was detected. However, some notifying entities choose to write the date when the transfusion occurred, what is not incorrect, but if the day chosen by the notifying entity is the same as transfusion, the reactions cannot be considered as delayed anymore, where the disease transmission is classified.

Thus, the quantitative data for every year of occurrence in the following tables are not identical; for this reason, we chose to name the frequencies in tables 19.2 and 19.3 as 'year of transfusion'.

In Table 19.1, it can be verified that, in the period from 2007 to 2014, it was notified the annual average of 7.1 cases suspected of transmission of viral diseases by year.

In the year of 2013, this average was 5.8 cases. The median or accumulated comparative rate for the period between 2013 and 2014 did not alter, remaining at 0.21 per every 100 thousand transfusions.

In this period, the country used in the routine serological tests for donor screening. Molecular tests for the detection of HIV and HCV were introduced on a mandatory and universal way in 2013, with publication of the Ordinance 2.712 of the Ministry of Health, on November 12.

Table 19.1: Absolute and relative frequencies of notifications of transfusion reactions and of TTID and annual and accumulated incidence rate per 100 thousand transfusions. Brazil, 2007 to 2014.

	2007	2008	2009	2010	2011	2012	2013	2014	Accumulated
TTIDs notified	3	10	4	11	10	18	4	**0**	**57**
All notifications	2,250	2,481	3,841	4,989	7,014	8,624	9,859	9,228	48,286
% of notifications	0.13	0.40	0.10	0.22	0.14	0.21	0.04	0.00	0.12
Transfusions performed	4,002,4	3,180,8	3,615,9	3,338,1	2,979,8	3,127,9	3,148,6	3,293,9	26,687,6
Rate	**0.07**	**0.31**	**0.11**	**0.33**	**0.34**	**0.58**	**0.13**	**0.00**	**0.21**

Source: Notivisa and Information Notebook: Blood and Blood Derivatives.
Note: Comma in the numbers of transfusions performed was used as a resource to make the table more concise, but the corresponding absolute hundred number must be considered after comma.

Table 19.2 shows the frequency of notifications of transfusion transmitted infectious diseases, received in Notivisa since its implementation, in December 2006, according to the year of notification and transfusion occurred, a total of 68 notifications in the period.

Table 19.2: Absolute frequency of notifications of TTID, according to the year of notification and year of transfusion. Brazil, 2007 to 2014.

Notification/ transfusion	2007	2008	2009	2010	2011	2012	2013	2014	Total
1995	0	0	0	1	0	0	0	0	**1**
1997	0	0	0	1	0	0	0	0	**1**
1999	0	0	0	0	0	1	0	0	**1**
2002	0	0	0	0	0	1	0	0	**1**
2003	0	0	0	2	0	0	0	0	**2**
2004	0	0	0	0	1	0	0	0	**1**
2005	0	1	1	0	0	0	0	0	**2**
2006	0	3	0	1	0	0	0	0	**4**
2007	2	0	0	0	0	0	2	0	**4**
2008	0	3	0	0	4	0	1	0	**8**
2009	0	0	1	0	5	1	3	0	**10**
2010	0	0	0	0	5	4	0	0	**9**
2011	0	0	0	0	1	4	2	1	**8**
2012	0	0	0	0	0	1	9	2	**12**
2013	0	0	0	0	0	0	4	0	**4**
Total	**2**	**7**	**2**	**5**	**16**	**12**	**21**	**3**	**68**

Source: Notivisa.

Tables 19.3 and 19.4 show the agents involved and imputability to transfusion, according to the definition of the notifying party.

Table 19.3: Absolute frequency of notifications of TTID, according to the agent involved and the year of transfusion. Brazil, 2007 to 2013.

Agent involved	1995	1997	1999	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Total
CMV	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	**1**
HBV	0	0	0	0	1	0	0	0	1	2	3	3	1	5	2	**18**
HCV	0	0	0	0	0	0	0	0	1	2	1	3	2	2	0	**11**
HIV	1	1	1	1	1	0	2	1	1	3	6	1	4	3	2	**28**
HTLV	0	0	0	0	0	0	0	0	0	0	0	0	1	2	0	**3**
Plasmodium vivax	0	0	0	0	0	0	0	3	1	0	0	0	0	0	0	**4**
Treponema	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	**2**
Not Informed	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	**1**
Total	**1**	**1**	**1**	**1**	**2**	**1**	**2**	**4**	**4**	**8**	**10**	**9**	**8**	**12**	**4**	**68**

Source: Notivisa.

The investigation of a suspected case of transfusion-transmitted infectious disease is, in general, a complex and long-lasting process, especially when its detection takes long time, even year or decades, after transfusion. In this process, the investigation only progresses

towards a conclusion with the collaboration of the several institutions involved in the hemovigilance system, mainly of the facility where the transfusion occurred, of the processing blood establishment, of the public health surveillance and health surveillance. In many cases, the investigation is not concluded because of the fragility of tracking the blood component, absence of records of transfusion or the difficulty in finding or calling the donor whose product is associated with infection transmission.

Table 19.4: Absolute frequency of notifications of TTID, according to the year of notification and imputability to transfusion, chosen by the notifying entity. Brazil, 2007 to 2014.

Imputability	2007	2008	2009	2010	2011	2012	2013	2014	Total
Confirmed	1	6	0	0	1	4	10	0	22
Suspected	1	0	2	1	9	3	4	0	20
Inconclusive	0	1	0	1	3	2	4	3	14
Excluded	0	0	0	3	3	3	3	0	12
Total	**2**	**7**	**2**	**5**	**16**	**12**	**21**	**3**	**68**

Source: Notivisa.

9. CONCLUSION: GUIDELINES AND PERSPECTIVES

The transfusion act is not free from risks, despite accumulated scientific knowledge and health regulations currently applied. Thus, hemovigilance has fundamental importance in the process of reduction and prevention of these risks. Information obtained from the analysis of notifications of adverse events attributed to the therapeutic use of blood components must be used as an essential instrument for continual improvement of the quality and safety of these products.

For the year of 2014, with the purpose of trying to approximate the national transfusion reaction rates to parameters, it was requested to local health surveillance teams that they compiled information on the frequency of transfusions in those facilitites that had notified in the previous year. With the same objective, data have been compiled on the blood transfusions performed by the health facilities that compose the Sentinel Network and the transfusion reaction rates in these facilities for the year of 2014.

Table 20 shows a comparison between the median rates calculated for some notifying facilities of the states that responded to the request, the median rates of the FUs where are located the facilities of the Sentinel Network that reported and the median rates calculated from the data supplied by the information systems, already presented in section 7.2 of this report.

It is possible to observe that there is a great variation among the different rates in each Federation unit. Although the Brazilian average is different only among the facilitites of the Sentinel Network that reported in the year of 2014, paying attention to the fact that the Federal District is the FU with the highest percentage (47%) of notifying facilities, as shown in Table 2, and observing the TR rates among the facilities of the Sentinel Network – considered the most reliable –, **it is possible to formulate the hypothesis that transfusion reaction rate in the country must be closer to 5 RTs/1,000 transfusions than the one currently measured, borrowed from the French system.**

Table 20: Median rates of comparative transfusion reaction for the FUs, according to the information source for the frequency of transfusion. Brazil, 2014.

FU	Health facilities in general	Facilities of the Sentinel Network	Information Notebook
Distrito Federal	2.3	0.7	4.6
Goiás	1.5	-	0.9
Mato Grosso do Sul	-	-	1.3
Mato Grosso	-	-	0.3
C. West	**1.9**	**0.7**	**1.3**
Alagoas	-	7.5	2.0
Bahia	-	8.0	2.3
Ceará	3.8	4.0	3.8
Maranhão	6.7	10.8	2.3
Paraíba	-	3.8	2.3
Pernambuco	1.8	2.5	2.0
Piauí	-	-	1.3
Rio Grande do Norte	4.5	-	0.3
Sergipe	-	-	2.4
Northeast	**4.2**	**6.1**	**2.3**
Acre	2.7	3.9	2.2
Amapá	-	-	0.2
Amazonas	1.5	-	2.6
Pará	1.3	-	1.9
Rondônia	-	-	4.0
Roraima	-	-	4.0
Tocantins	-	-	2.5
North	**1.8**	**2.3**	**2.2**
Espírito Santo	-	-	3.0
Mimas Gerais	-	1.8	0.7
Rio de Janeiro	-	5.0	5.4
São Paulo	-	5.3	4.5
Southeast	-	**4.0**	**3.6**
Paraná	-	8.3	1.6
Rio Grande do Sul	2.9	15.6	3.7
Santa Catarina	4.3	6.9	3.3
South	**3.6**	**10.3**	**2.6**
Brazil	**2.7**	**4.7**	**2.8**

Source: Notivisa; Information Notebook: Blood and Blood Derivatives;
Monitoring forms of the Sentinel Network and local survey in other health facilities.

Again we reinforce the need that the local teams themselves start to evaluate their transfusion reaction rates and, the most important, that they promote improvement actions so these rates are reduced to levels closer to the national level, although the national level is dragged down by the units that have higher sub-

notification. These actions are justified, because the French parameter must be the goal established now, as a parameter of quality and not only of quantity.

For the next years, the hemovigilance effort will be harder in the sense of monitoring other risks, once the Conceptual and Operational Framework of Hemovigilance – Guide to Hemovigilance in Brazil must be effective by March 2016, amplifying the hemovigilance actions for the entire blood cycle. The disclosure of these new guidelines is ongoing, with the implementation of macro-regional workshops with the participation of the parties interested (blood establishments, health facilites, public health and health surveillance, association of carriers of hematological diseases, Ministry of Health, Brazilian Association of Hematology, Hemotherapy and Cell Therapy, and industry of blood derivatives).

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