TRIP annual report 2014

Hemovigilance

Extended version

TRIP
Hemo-en biovigilantie

TRIP Report 2014

Hemovigilance

Extended version

The TRIP annual report 2014, extended version,
concerning hemovigilance reports in The Netherlands
in 2014 is published under responsibility of the TRIP Foundation
(Transfusion and Transplantation Reactions In Patients).

TRIP
Hemo- en biovigilantie

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Content

Foreword

This is the 12th TRIP hemovigilance report. The annual reports with tables and comment give an overview of adverse reactions and events related to blood transfusion in The Netherlands. TRIP would like to thank all contacts in the Dutch hospitals and members of the TRIP advisory board and hemovigilance advisory board for their contribution to this report.

Hemovigilance reporting aims to contribute to improving safety of the blood transfusion chain. Increased awareness of a certain type of transfusion reaction or event may lead to an increase in the number of reports. This effect can be seen in the category transfusion-associated circulatory overload. Once a transfusion reaction is properly recognised, correctly diagnosed and reported a drop in the number of reports after implementation of effective measures may signify an improvement of transfusion safety.

There is an overall increase in the total number of reports of incorrect blood component transfused which has largely arisen from failure to follow the new CBO blood transfusion guidelines (2011) for prevention of allo-immunisation. There is an encouraging downward trend in reports of incorrect blood component transfused where the patient was at risk from transfusion of a potentially ABO incompatible blood component.

TRIP deems active attention to the transfusion chain essential for patient safety. TRIP aims to continually convey this important message together with all stakeholders: hemovigilance staff, hospital transfusion committees, Sanquin Blood Supply, medical professional bodies and hospital boards. To all of you I warmly recommend this report.

Dr. Martin R. Schipperus
President TRIP foundation

1. Main 2014 findings

1.1 2014 hemovigilance trends

In general there is a slight decrease in the number of reports in line with the decrease in blood use (Figure 1, page 6). The number of serious reactions that were assessed as certainly, probably or possibly caused by transfusion was 89 which is comparable to previous years. Among the serious reports the largest categories were transfusion-associated circulatory overload (TACO), anaphylactic reaction and other reaction. The number of reports of incorrect blood component transfused (IBCT) and TACO was higher than in 2013. These categories particularly are amenable to preventive measures.

Errors in the transfusion chain

There was an increase in the number of reports of incorrect blood component transfused (IBCT) compared to previous years, mainly due to not following the revised guidelines for prevention of allo-immunisation. This extended prevention advice, published in the 2011 CBO guideline for blood transfusion, recommends selection of blood components compatible both for rhesus D and rhesus phenotype for women of childbearing age, patients with allo-antibodies and multiply transfused patients. There is a decreasing trend in the number of IBCT where the patient was exposed to a potentially ABO incompatible unit following an identification error (Figure 5, page 13).

The annual number of reported near miss events is small and declining, even though numbers are expected to be larger than the number of IBCTs. In general, risk analyses stress the importance of reporting, analysing and learning from near miss events. A national analysis of near miss events in the transfusion chain can contribute to a decrease in the number of errors and an increase in transfusion safety.

Infectious transfusion complications

There were no reports of confirmed transfusion-transmitted viral infection. With regard to bacterial problems, in 2014 two patients developed sepsis where the same bacterial species was demonstrated in the patient's blood culture and in the culture of the administered platelet concentrate. In one case the patient died. Based on additional investigations to establish whether the bacterial strains in the transfused unit and patient were identical, experts assessed these cases as transfusion-transmitted bacterial infections with (almost) certain and possible imputability, respectively. These reports once again show that routine screening of platelet concentrates by Sanquin does not always prevent transmission of a bacterial infection.

Transfusion-associated circulatory overload (TACO)

The number of TACO reports shows an increase and there were 23 reports of severity grade 2 or higher. This complication may be avoided by preventive measures when prescribing and administering a blood component. In cooperation with the Hemovigilance Advisory Board TRIP is developing a tool to support TACO prevention.

General

The number of reported transfusion reactions per 1000 administered blood components shows remarkable variation between hospitals. It ranges from 0 to more than 3 per 1000 units, also among the largest hospitals (Figure 4), where there seems to be an increase in variation year on year. This variation in the annual numbers of hemovigilance reports, especially in hospitals with high blood use, may give a distorted picture in analyses and calculations.

1.2 Recommendations

1. TACO In cooperation with hospitals, to validate the TACO prevention tool by additional data collection and analysis of patient characteristics and clinical circumstances in the 2014 and 2015 TACO reports.	TRIP in cooperation with hemovigilance professionals
2. Near miss reports To stimulate reporting of near miss events by hospitals and actively promote the options for near miss reporting that are available in the new TRIP haemovigilance reporting system.	Hemovigilance professionals and TRIP
3. Reports per hospital Hospital transfusion committees should annually discuss the hospital's reports to TRIP; TRIP will actively provide bench-marking graphs to the hospital transfusion committees through the hemovigilance professionals.	Hospital transfusion committees; TRIP

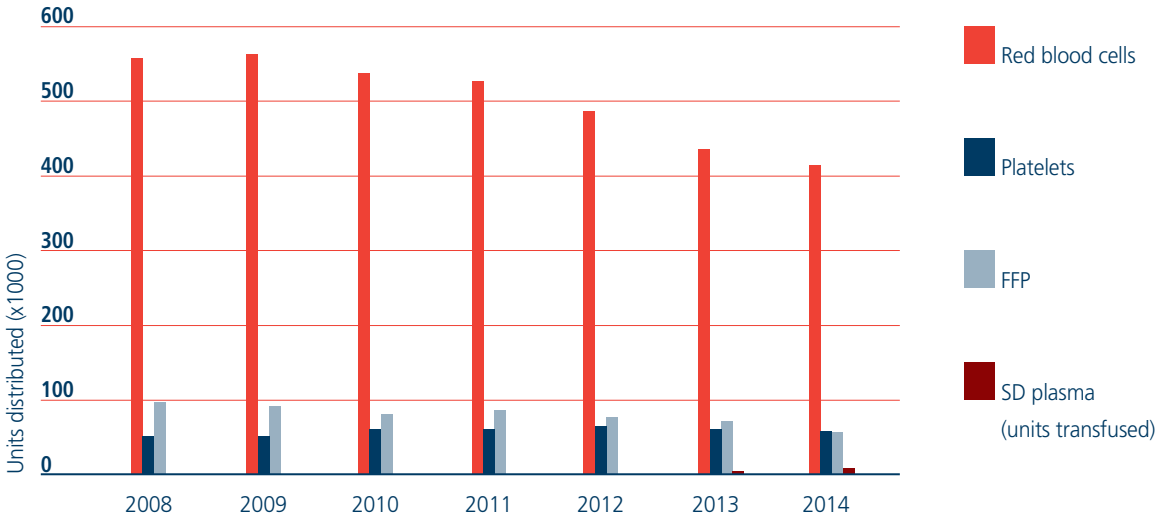


Figure 1. Distributed units of blood components per year

2. Overview of hemovigilance results in 2014

2.1 Overview of 2014 reports

All definitions can be found on: www.tripnet.nl.

Reports received

The total number of reports of transfusion reactions and events in the transfusion chain in 2014 is 2260, which is comparable to previous years taking account of the decrease in blood use. The reports were submitted by 89 hospitals. Virtually all reports were submitted via the online reporting system (>99%, 89 hospitals).

After assessment of all reports by the TRIP physicians a number of striking or complex reports (around 35) were discussed in a meeting of hospital contact people (transfusion safety officers and hemovigilance officers), members of the Expert Committee and TRIP staff. All reports in serious reporting categories as well as those of severity grade 2 or higher were reviewed by the experts.

The numbers of reports per category in reporting years 2008-2014 are shown in Tables 1 and 2. Because the incidents are potentially avoidable they are presented in the first table of this report. Transfusion reactions following incidents (total 25) are discussed separately in the paragraph about incidents in Section 3.1 and are not included in Table 2.

Table 1. Incidents per reporting category, 2008-2014

Incident category	2008	2009	2010	2011	2012	2013	2014	Number of hosp. with reports in 2014
Incorrect blood component transfused*	59	61	59	47	55	44	62	36
Near miss	55	72	70	45	50	38	28	15
Other incident	83	111	118	138	138	108	111	29
Hemolysis of product	-	-	-	2	-	-	1	1
Incidents, total	**197**	**244**	**247**	**232**	**243**	**190**	**202**	**48**

* *Including reports of calculated risk situations*

Abbreviation: *hosp.=hospital*

Table 2. Transfusion reactions, 2008-2014

Reaction	2008	2009	2010	2011	2012	2013	2014	Reports of grade 2 or higher[#]	Number of hosp. with reports in 2014
AHTR	18	18	21	17	7	11	17	2	12
DHTR	18	8	7	9	8	4	5	3	5
New allo-antibody formation	610	757	814	831	851	848	761	0	67
TACO	39	42	47	39	56	67	74	23	39
TA-GVHD	1	0	0	0	0	0	0	0	0
Hemosiderosis	5	2	4	2	0	4	3	0	2
NHTR	453	488	506	504	456	441	415	11	75
Mild febrile reaction	275	360	363	366	383	340	310	1	64
TRALI	21	13	17	12	9	9	5	4	4
Anaphylactic reaction	65	71	73	67	59	69	51	19	20
Other allergic reaction	171	181	184	191	180	194	151	1	43
Post-transfusion purpura	1	0	0	2	1	0	1	1	1
Other reaction	101	136	164	217	225	220	190	16	58
Post-tf bacteremia/sepsis	37	55	41	61	50	47	55	6	27
Post-tf viral infection	7	3	1	5	2	3	0	0	0
Post-tf malaria	0	0	0	1	0	0	0	0	0
Total transfusion reactions	**1821**	**2134**	**2242**	**2324**	**2287**	**2261**	**2037**	**87**	**89**
Total grade 2 or higher[#]*	131	102	96	102	101	98	89		
Total reports	**2055**	**2412**	**2591**	**2629**	**2570**	**2501**	**2260**		

[#] *Imputability certain, probable or possible*

* *Total including transfusion reactions following incidents*

Abbreviations: *hosp.=hospital; AHTR=acute hemolytic transfusion reaction; DHTR=delayed hemolytic transfusion reaction; TACO=transfusion-associated circulatory overload; TA-GVHD=transfusion-associated graft versus host disease; NHTR=non-hemolytic transfusion reaction; TRALI=transfusion-associated acute lung injury; tf=transfusion*

Severity and imputability of transfusion reactions

Severity grade	Definition
0	No morbidity
1	Minor morbidity, not life-threatening
2	Moderate to serious morbidity, may or may not be life-threatening; or leading to hospitalisation or prolongation of illness; or associated with chronic disability or incapacity
3	Serious morbidity, directly life-threatening
4	Mortality following a transfusion reaction

According to international practice, the transfusion reactions were rated for their severity. The definition of severity refers to the clinical features observed in the patient and is only relevant for transfusion reactions. These totalled 2062 i.e. 2037 reports in the categories of reactions and 25 following incidents. The grade 4 reports are reviewed in section 3.6. Figure 2 presents the distribution of reported severity grade for transfusion reactions in the period 2008-2014.

Figure 3 shows the imputability of the transfusion reactions, i.e. the likelihood with which the reaction can be attributed to the transfusion. The imputability rating, as that of the severity, is only relevant for reports where the patient showed a reaction.

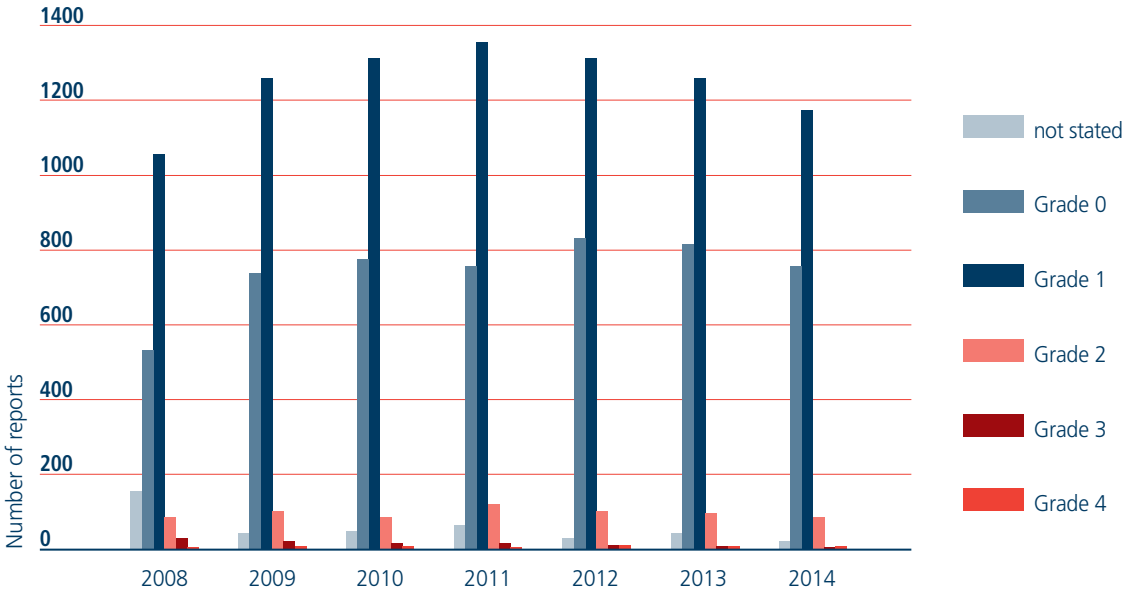


Figure 2. Severity grade of transfusion reactions, 2008-2014

The total number of serious reports in 2014 (grade 2 or higher) was 102, out of which 89 were of imputability definite, probable or possible.

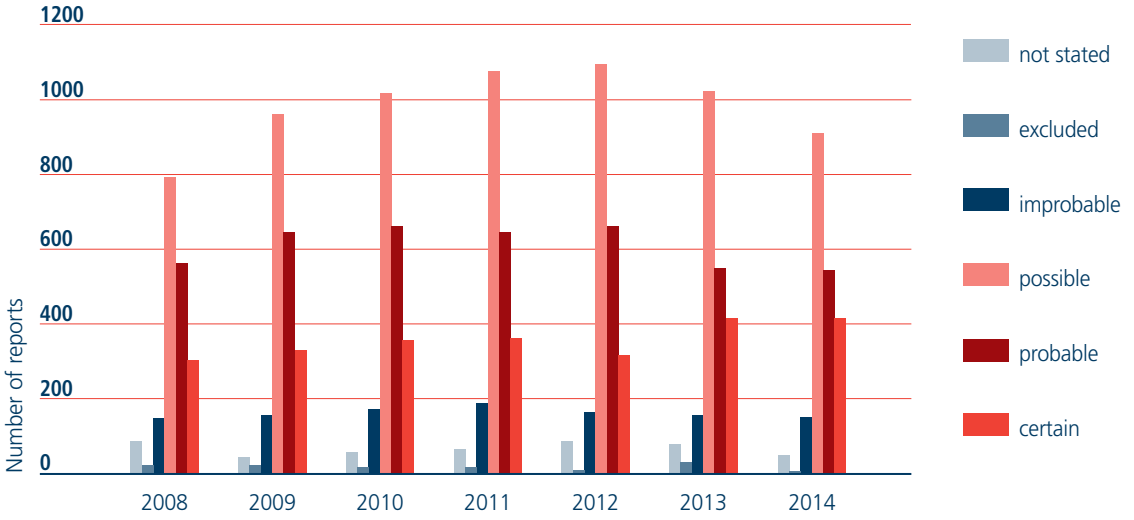


Figure 3 Imputability of the transfusion reactions, 2008-2014

Reports in relation to the number and type of distributed blood component

In 2014 Sanquin distributed a total of 540854 blood components to the Dutch hospitals; this number does not include special components like lymphocytes or granulocytes.

The total number of reports for 2014 was 2260. Using the total number of distributed blood components as a denominator, that makes 4.18 reports per 1000 blood components distributed nationally, or 4.12 excluding reports concerning SD-plasma and reports involving blood management techniques (see Section 3.4). The declining trend in blood use continued in 2014 (Figure 1, page 6). The numbers of reports in relation to the numbers of distributed blood components are shown in Table 3. Table 4 presents the distribution of the types of blood components for each of the reporting categories of incidents and transfusion reactions.

Table 3. Numbers of reports per type of blood component in 2014 and compared to 2013

Type of blood component (bc)	2014					2013			
	No.of bc supplied	No. of reports		Reports per 1000 bc		No. of reports		Reports per 1000 bc	
		All	Serious#	All	Serious#	All	Serious#	All	Serious#
Red blood cell concentrate	428245	1817	48	4.24	0.11	1989	72	4.53	0.16
Platelet concentrate	56883	266	20	4.68	0.35	298	21	5.18	0.37
Fresh frozen plasma	55726	53	6	0.95	0.11	62	5	0.92	0.07
Blood management techniques[2]	-	25	2			24	0		
SD-plasma	-	8[$]	4			8[$]	1		
Other blood product	-	0	0			0	0		
Combinations	-	53	9			64	9		
Not stated	-	38	0			55	0		
Total	**540854**	**2260**	**89**	**4.18**	**0.16**	**2500**	**108**	**4.43**	**0.19**

[#] *Imputability certain, probable, possible*

[$] *In one case labile blood components were administered as well*

[2] *See section 3.4*

TRIP analysed the numbers of reports per hospital in relation to blood use. When looking at transfusion reactions this should be roughly comparable between hospitals. Statistically there should be less variation in hospitals with high blood use. The calculated number of transfusion reactions per 1000 blood components showed considerable variation ranging from 0 to more than 3 per 1000 units, even among high blood use hospitals (Figure 4), and there seems to be increasing variation from year to year.

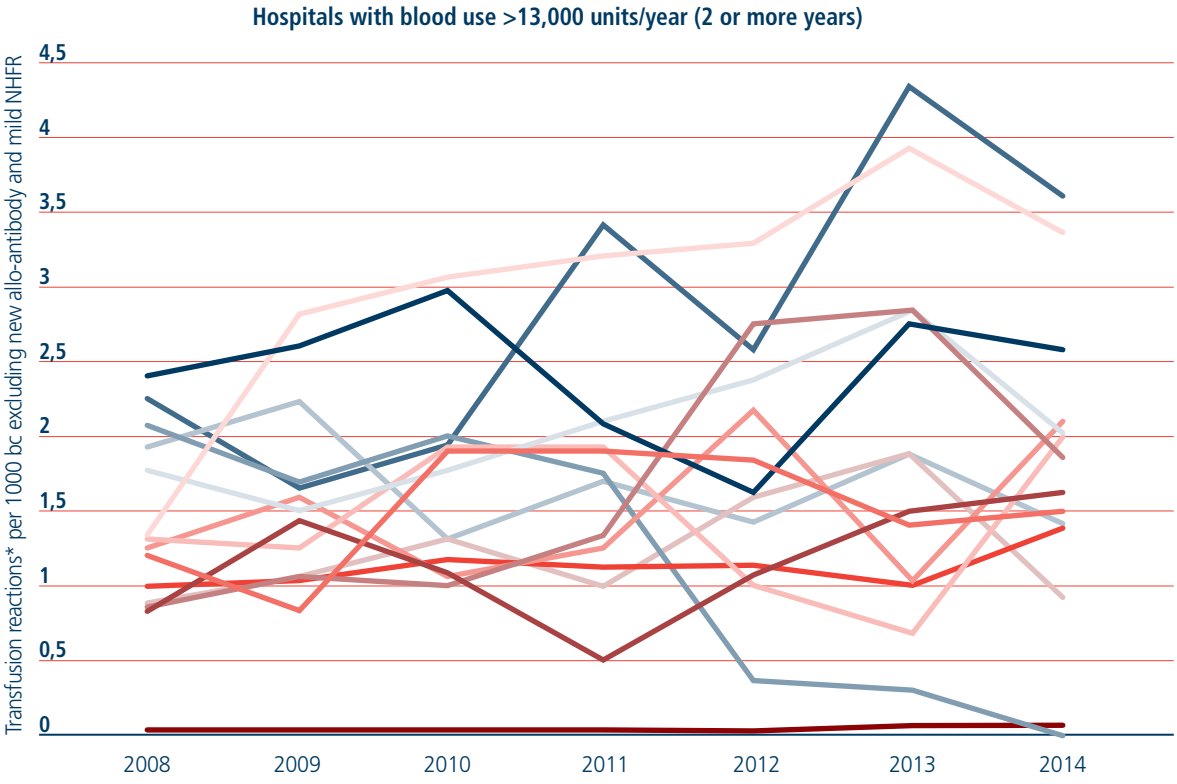


Figure 4. Annual rate of transfusion reaction reports in relation to blood use in hospitals with high blood use

* *Reports of imputability certain, probable and possible, excluding new allo-antibody formation and mild non-hemolytic febrile reaction, as these are not systematically reported by all hospitals.*

The submission of reports after the closing date by one or more hospitals makes a difference of nearly 10% in the total number of reports. This hinders evaluation of trends and potentially has an adverse impact on conclusions and recommendations.

TRIP has always made annual benchmarking graphs available to hospitals, showing the numbers of reports per 1000 units per reporting category (submitted before the deadline) compared to other hospitals. The TRIP Advisory Council and Hemovigilance Advisory Board recommend that TRIP should actively provide these benchmarking graphs to hospital transfusion committees and possibly also to hospital boards in future.

Table 4. Distribution of types of blood component per reporting category* in 2014

A. Incidents	RBCs	Platelets	Plasma	Combi-nations	Other#	SD-plasma	Not stated
Incorrect blood component transfused	58	3	1	0	0	0	0
	94%	5%	2%	0%	0%	0%	0%
Other incident	81	4	3	2	3	1	17
	73%	4%	3%	2%	3%	1%	15%
Near miss	12	1	0	0	0	0	15
	43%	4%	0%	0%	0%	0%	54%
Bacterial contamination of blood component	2	7	0	0	0	0	0
	22%	78%	0%	0%	0%	0%	0%
Lookback	3	6	0	0	0	0	0
	33%	67%	0%	0%	0%	0%	0%
B. Reactions							
Non-hemolytic transfusion reaction	325	63	1	12	12	0	3
	78%	15%	0%	3%	3%	0%	1%
Mild non-hemolytic febrile reaction	298	7	0	3	2	0	0
	96%	2%	0%	1%	1%	0%	0%
Acute hemolytic transfusion reaction	15	2	0	0	0	0	0
	88%	12%	0%	0%	0%	0%	0%
Delayed hemolytic transfusion reaction	5	0	0	0	0	0	0
	100%	0%	0%	0%	0%	0%	0%
TRALI	0	0	1	4	0	0	0
	0%	0%	20%	80%	0%	0%	0%
Anaphylactic reaction	7	31	8	1	0	4	0
	14%	61%	16%	2%	0%	8%	0%
Other allergic reaction	38	83	25	4	1	2	0
	25%	54%	16%	3%	1%	1%	0%
New allo-antibody formation	721	17	0	14	0	0	16
	94%	2%	0%	2%	0%	0%	2%
Other reaction	132	33	13	4	7	0	0
	70%	17%	7%	2%	4%	0%	0%
Post-transfusion bacteremia/sepsis	47	4	0	1	0	0	0
	90%	8%	0%	2%	0%	0%	0%
Transfusion-associated circulatory overload	62	5	1	6	0	0	0
	84%	7%	1%	8%	0%	0%	0%

* *Smallest categories not shown*

\# *Concerned blood management techniques, see section 3.4*

% Percentage of all reported incidents/reactions in that category

2.2 Late reports from previous years

Regarding reporting year 2013, 48 additional reports were received after the closing date for the 2013 report. Furthermore nine 2012 reports were finalised in 2014. These late reports have all been formally assessed and included in the figures and tables in this report.

The late reports are summarised in Table 5. Out of the 48 late 2013 reports, 15 were of severity grade 2 or higher; 12 of these had certain, probable or possible imputability. This means that 9% of the total number of serious 2013 reports were submitted or finalised after the closing date for the 2013 report. There were 10 reports of incorrect blood component transfused and 10 near miss reports. The late reports came from 11 hospitals (including two university medical centres) and from Sanquin Blood Supply; five hospitals submitted several or all their reports after the closing date. Only for a small number of reports was there an adequate explanation, usually that further investigations or analysis were ongoing. TRIP does not have insight into temporary hospital related factors that caused delayed reporting. Late reporting does however influence results of analyses.

Table 5. Late reports from 2012 and 2013

	Severity grade					
Reporting category	**0**	**1**	**2**	**3**	**4**	**No clinical reaction, severity grade N/A**
Incorrect blood component transfused						10
Near miss						10
Other incident						3
Bacterial contamination of blood component						2
Acute hemolytic transfusion reaction			1			
Anaphylactic reaction			3	1		
Other allergic reaction		2	1			
Mild non-hemolytic febrile reaction		9				
Non-hemolytic transfusion reaction		2	1			
New allo-antibody formation	1					
Other reaction		4				
Post-transfusion viral infection			2			
TRALI				2	1	
Transfusion-associated circulatory overload			1	1		

3 Discussion of reports per category

3.1 Incidents in the transfusion chain

Incorrect blood component transfused (IBCT)

All cases in which a patient was transfused with a component that did not fulfil all the requirements of a suitable component for that patient, or that was intended for a different patient.

- 58 IBCT reports from 36 reporting hospitals, 1-6 reports per hospital
- 6 further reports from 6 hospitals recorded IBCT as an additional category (Table 7)
- 4 reports of a calculated risk situation from 3 reporting hospitals
- 2 reports had an additional category noting calculated risk situation (Table 7)
- After the closing date for this report another 4 IBCT reports were submitted. These will be included in the 2015 report.

The description of the risk groups for incidents in the transfusion chain can be found on www.tripnet.nl (English translation on page hemovigilance news). The number of IBCTs has risen again to the level of 2008-2010. Analysis of the risk to which the patient was exposed shows that the increase is mainly due to cases (n=22) where the guidelines with regard to prevention of allo-immunisation for specific recipient groups were not followed (see Figure 5). It is likely that the introduction of revised guidelines for prevention of allo-immunisation in 2011 led to the observed increase in reported IBCTs. The type of error and step in the transfusion chain in the 2014 IBCT reports in each risk group is shown in Figure 6.

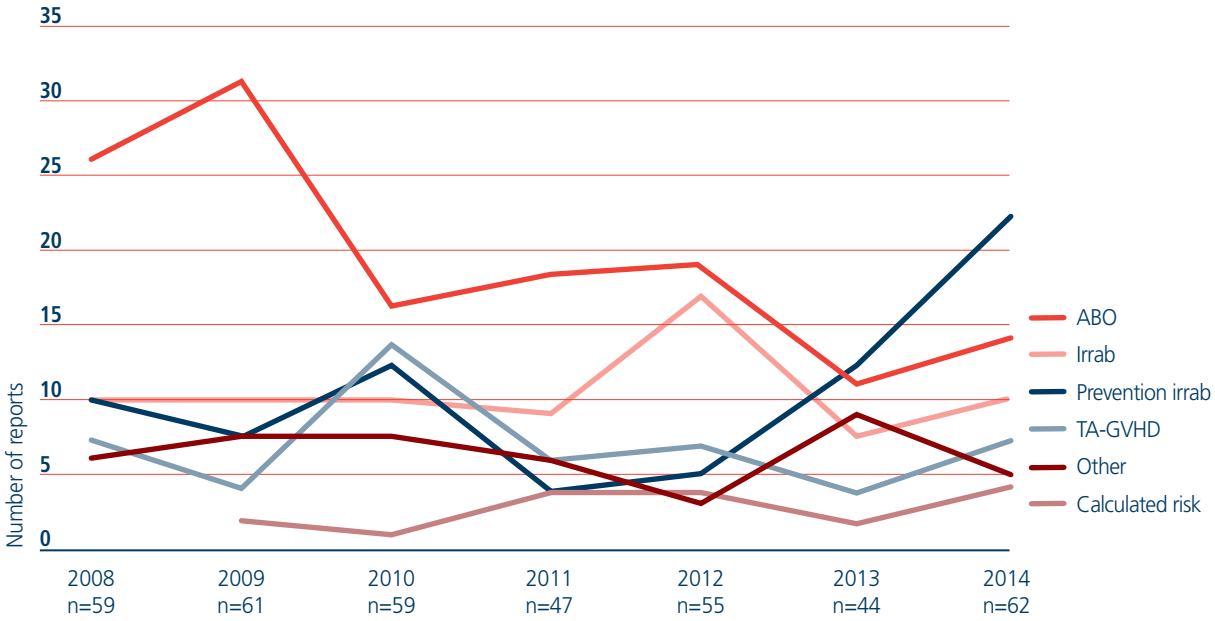


Figure 5. Incorrect blood component transfused broken down according to risk group, 2008-2014

Abbreviations:

ABO = risk of an ABO incompatible transfusion

Irrab = risk of an irregular antibody incompatible transfusion

Prevention irrab = guidelines not followed with regard to prevention of irregular antibody formation

TA-GVHD = risk of transfusion-associated graft versus host disease (after transfusion of a non-irradiated blood component)

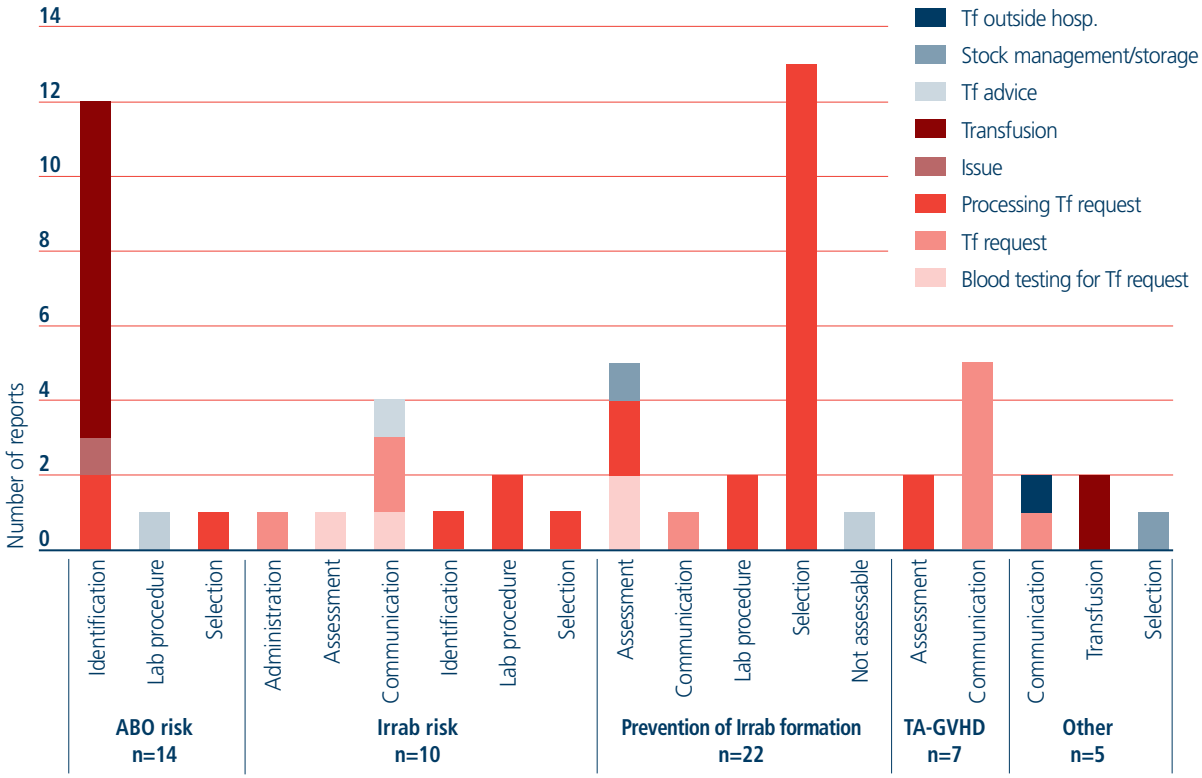


Figure 6. IBCT 2014 per risk group: step in the transfusion chain where the first error was made

Abbreviations: *Tf=transfusion; hosp.= hospital; Irrab =irregular antibody; TA-GVHD= transfusion-associated graft versus host disease*

- Out of the 14 ABO risk cases, one concerned transfusion of incompatible (O neg) plasma and two concerned transfusion of ABO incompatible RBCs. In all cases the unit was compatible for rhesus D by chance.
- Out of 10 reports concerning irregular antibody risk in 7 cases the transfused unit happened to be compatible for the known antibody.
- 14 reports were associated with a reaction (registered as an additional category): 1x acute hemolytic transfusion reaction; 3x other reaction; 10x new allo-antibody formation (Table 6).

Table 6. Clinical symptoms after transfusion of IBCT in 2014

IBCT risk group	Component	Reaction (additional category)	Imputability*	Severity grade*
ABO	RBCs	AHTR	certain	2
Irrab	RBCs	Other reaction[$]	certain	1
	RBCs	Other reaction[“]	probable	1
	RBCs	Other reaction[#]	probable	1
	RBCs	New allo-antibody formation	probable	
Prevention of Irrab		New allo-antibody formation:		
	RBCs	Anti-E[&]	not stated	
	RBCs	Anti-E	certain	
	RBCs	Anti-K[&]	certain	
	RBCs	Anti-C	certain	
	RBCs	Anti-c	certain	
	RBCs	Anti-E	certain	
	RBCs	Anti-K	probable	
	RBCs	Anti-K	certain	
	RBCs	Anti-E[&]	not stated	

* *Imputability and severity grade apply to clinical symptoms of a transfusion reaction; new allo-antibody formation is severity grade 0 by definition*

[&] *Concerns female patient < 45 yrs of age*

[$] *Boostering of historically known anti-E, small LDH increase and haptoglobin decrease.*

[“] *Chills/rigors and mild fever, hemolysis parameters normal after partial administration of an E positive RBC to a patient with anti-E*

[#] *Chills/rigors, fever, increased blood pressure, hemolysis parameters normal after administration of Fya positive RBC to patient with anti-Fya*

Table 7. 2014 Reports with additional category IBCT/IBCT in the past/calculated risk

Reporting category	Risk group of IBCT (additional category)	Description	No. of cases
Other reaction	Damage and/or quality risk	Administration error => reinfusion of drain blood > 6 hrs after start of drain blood procedure	1
	Irrab	Communication error => platelets not matched for HLA antibodies	1
IBCT	Prevention of Irrab	Selection error => in present Tf and twice in the past RBCs transfused that were not matched for rhesus phenotype in female patient < 45 yrs of age	2
Anaphylactic reaction	Irrab	Calculated risk situation => platelets not compatible with patient's HLA antibodies	1
New allo-antibody formation	Prevention of Irrab	Selection error => in the past RBCs not matched for rhesus phenotype in MDS patient with known irregular antibodies	1
		Error unknown => historically determined rhesus phenotype found to be incorrect	1
		Calculated risk situation => in emergency situation for a patient needing 2 units there was only one c and K neg unit available for patient with known anti-c	1
		Error unknown => in the past, stem cell transplant not taken into account	1
		Calculated risk situation => no D neg plus HLA compatible platelets available, followed by other incident: no anti-D administered*	1

Abbreviations: *Irrab=irregular allo-antibody; Tf=transfusion; RBC=red blood cell concentrate*

* *In this case other incident was recorded as an additional category because of failure to administer anti-D after the calculated risk situation*

Near miss

Any error that, if undetected, could have led to a wrong blood group result or issue or administration of an incorrect blood component, and which was detected before transfusion.

- 28 near miss reports from 15 reporting hospitals, 1-5 reports per hospital
- In 20 cases (71%) there was a mix-up of patients, labels, blood samples, blood units, or lab reagents
- Out of the late 2014 reports 4 reports concerned a near miss that will be included in the 2015 report

It is to be expected that the number of near misses will be larger than the number of IBCT. However, in all TRIP reporting years this has not been reflected in the reported cases. TRIP would like to encourage hospitals to report near misses in order to gain more national-level insight into the risks and error prone steps in the transfusion chain.

Other incident (OI)

Error or incident in the transfusion chain that does not fit into any of the above categories, for instance patient transfused whereas the intention was to keep the blood component in reserve, or transfusing unnecessarily on the basis of an incorrect Hb result or avoidable wastage of a blood component.

- 111 reports of OI by 29 reporting hospitals, 1-16 reports per hospital
- 9x OI with an additional category recording a reaction in the affected patient: other reaction (6x); mild non-hemolytic febrile reaction (2x) and non-hemolytic transfusion reaction (1x)
- 5 reports concerned mix-up of patient details/blood samples or labels/forms with details concerning the blood component
- 25 reports with additional category OI

The largest subgroups of OI in 2014 were (nearly) unnecessary transfusions (n=16), where in 4 cases the error was discovered before transfusion (Figure 7), and wastage of (most of) a blood component (n=68). In 35 cases the wastage of a blood component was assessed to be avoidable. Out of the remaining cases wastage was unavoidable in 33 cases or not assessable (Figure 8); 12 blood components were lost due to puncturing of the unit at administration and in 11 cases the patient's IV access was inadequate and only a small amount of the unit could be transfused. In addition there were small clusters of reports regarding traceability (n=3) and delayed transfusion (n=4), with the blood component needlessly lost in one case, incorrect transfusion rate (n=4), inappropriate use of the same IV line for administration of medication or IV fluid (n=3) and incomplete, incorrectly filled in or forgotten transfusion forms (n=7).

Additional category other incident was added in the majority of cases (n=16) due to failure to report the transfusion reaction to the transfusion laboratory.

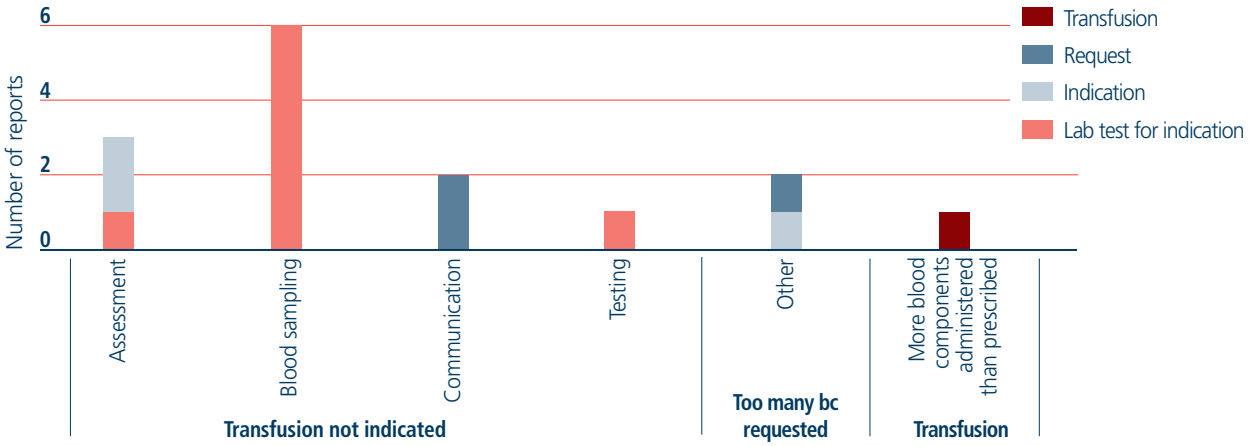


Figure 7. Other incidents in 2014 involving unnecessary transfusion*: type of error and step in the transfusion chain

* Unnecessary transfusion concerns patients for whom it should have been clear before transfusion that transfusion was not (or no longer) needed, e.g. due to incorrect blood sampling from arm with IV drip or failure to measure Hb

Abbreviations: *bc=blood component*

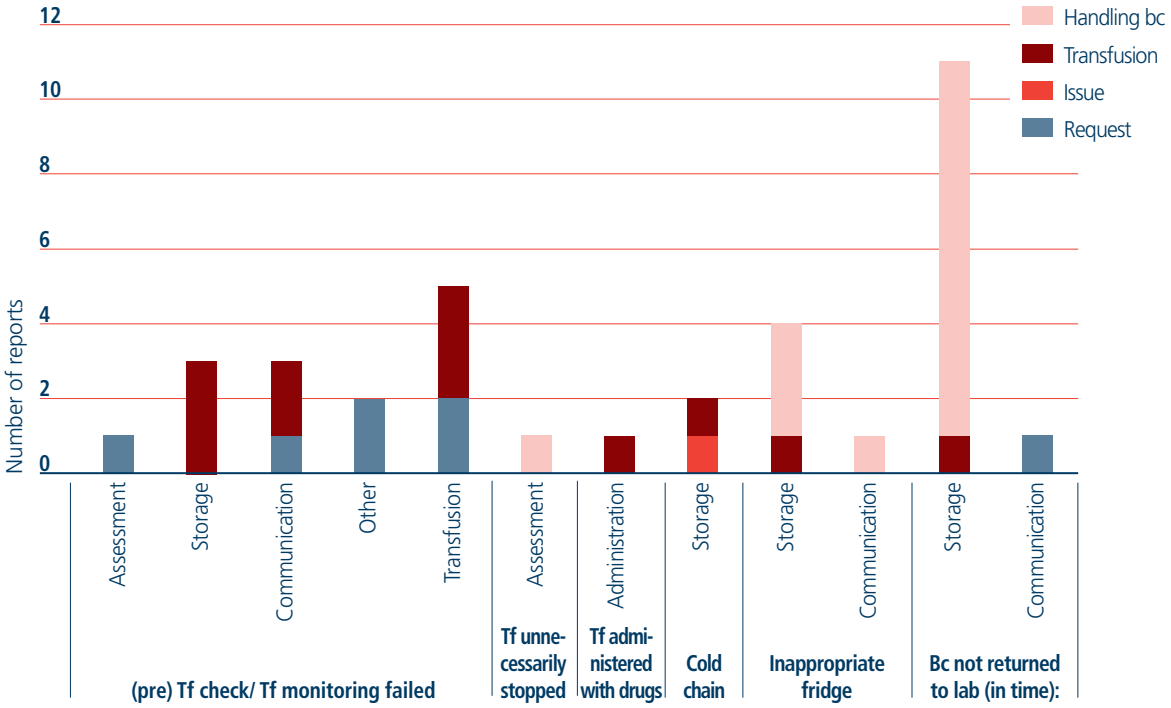


Figure 8. Other incidents leading to avoidable wastage of blood component in 2014 (n=35): cause of wastage, type of first error and step in the transfusion chain

Abbreviations: *Tf=transfusion; bc=blood component*

3.2 Infectious transfusion complications

Post-transfusion viral infection and viral contamination of blood component

Post-transfusion viral infection

A viral infection that can be attributed to a transfused blood component as demonstrated by identical viral strains in donor and recipient and where infection by another route is deemed unlikely.

Viral contamination of blood component

Retrospective analysis by Sanquin demonstrates viral contamination of an already administered blood component previously screened and found negative.

Look-back by the supplier

Retrospective notification of a possibly infectious donation, leading to investigation of the recipient for that infection, but where no infection is demonstrated in the recipient.

Information from hospitals

There were no reports in 2014 regarding post-transfusion viral contamination of a blood component. Nine hospitals sent reports to TRIP regarding a look-back procedure by Sanquin: five cases involved a donor who was found to have seroconverted at the subsequent donation (syphilis: 2 reports, hepatitis B: 3 reports), one report involved inappropriate donation by a donor during the deferral period for travel to a malaria-endemic region and in three reports the donor reported an illness (influenza, shingles) shortly after donation. None of the recipients had possible clinical symptoms or other sequelae.

Information from Sanquin

In 2014 eight seroconversions, hepatitis B (5), HIV (2) and syphilis, were found at standard testing in regular donors who made one or more donation(s) for transfusion purposes. In all cases a look-back procedure was started in accordance with the national guidelines. None of the recipients showed evidence of transfusion-transmitted viral infection. The late 2013 reports of post-transfusion viral infection (hepatitis E) have now been concluded: investigations did not reveal any evidence of viral transmission by blood transfusion.

Bacterial problems associated with blood transfusion

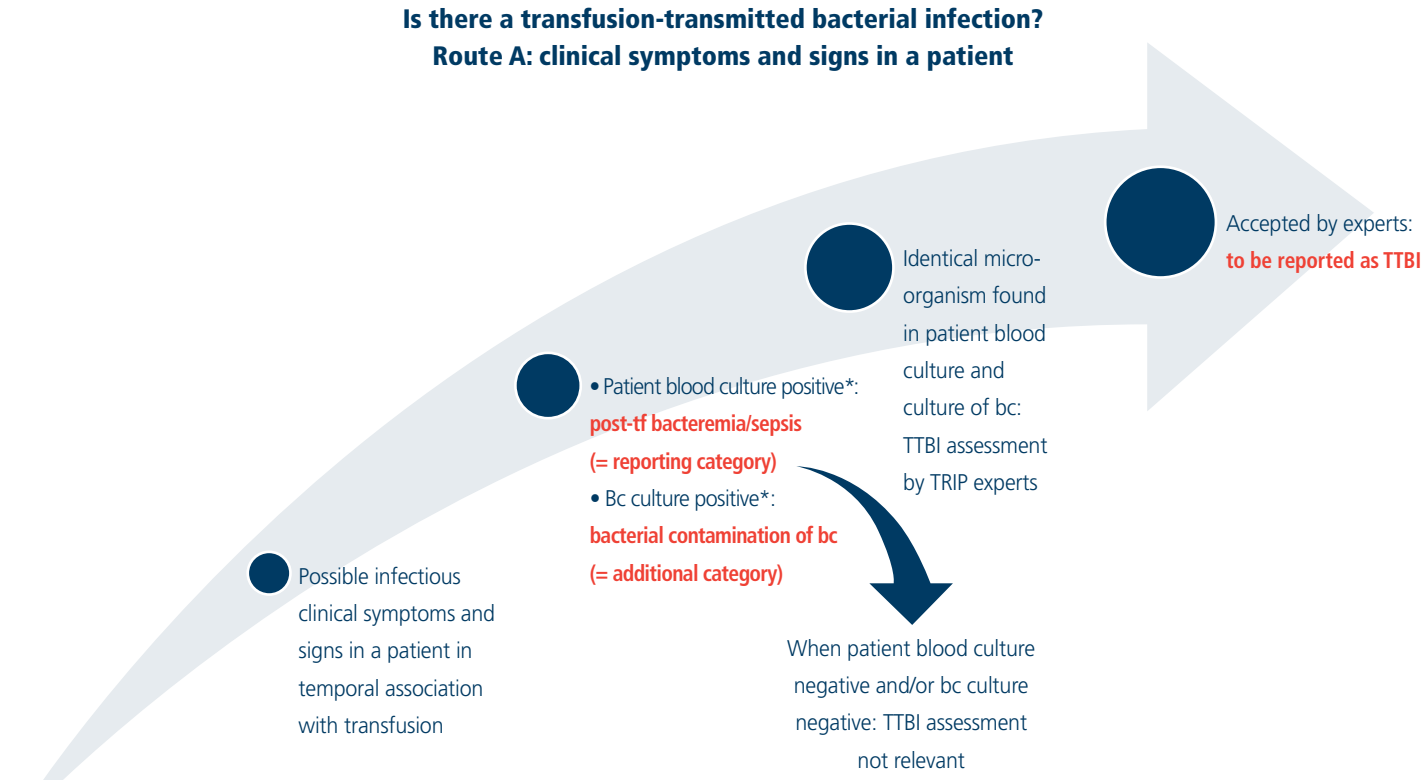
Post-transfusion bacteremia/sepsis

Clinical symptoms of bacteremia/sepsis arising during, directly after or some time subsequent to a blood transfusion, for which there is a relevant, positive blood culture of the patient with or without a causal elation to the administered blood component.

Bacterial contamination of a blood component

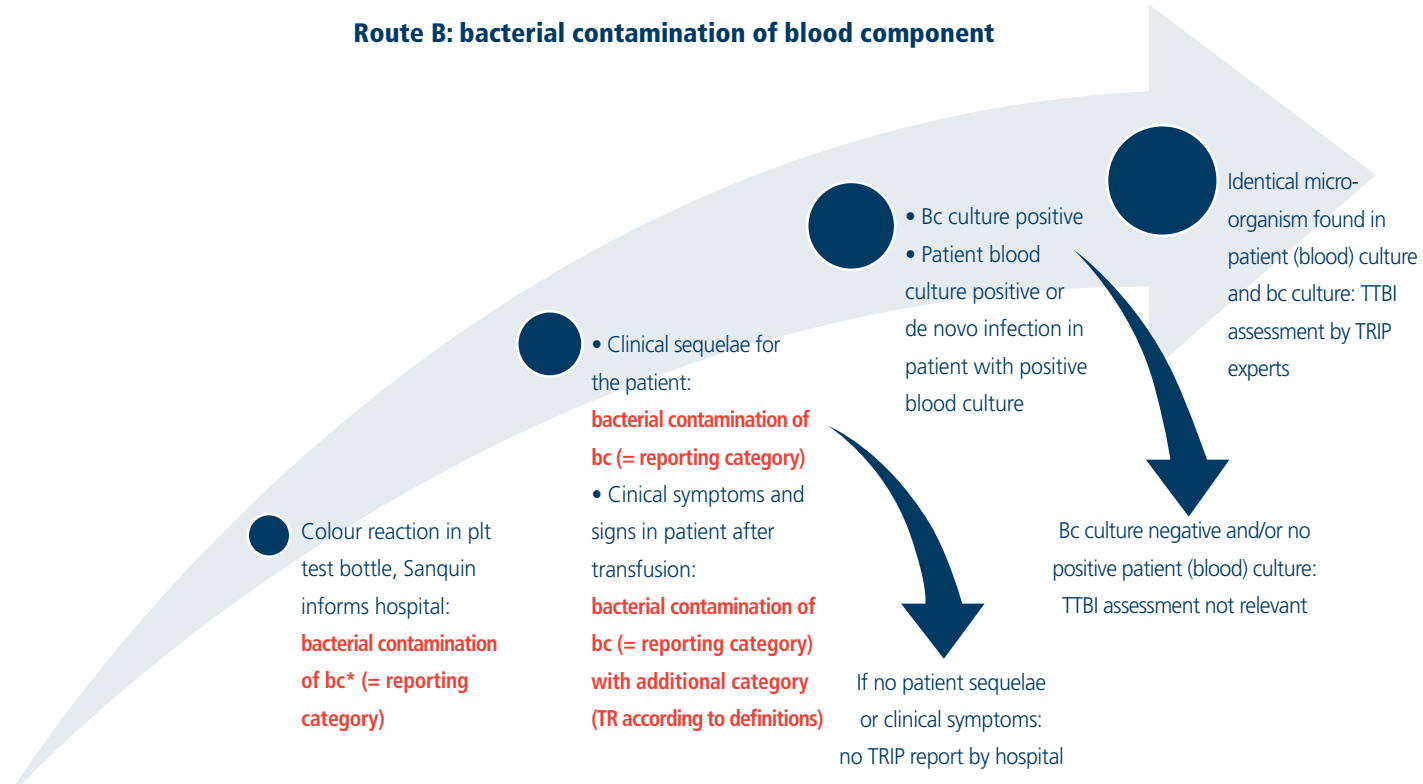
Relevant numbers of bacteria in a (remnant of) blood component or in the bacterial screen bottle of a platelet component, or in material from the same donation, demonstrated by approved laboratory techniques, preferably including typing of the bacterial strain or strains.

Table 8 presents the numbers of reports concerning bacterial problems associated with blood transfusion in the period 2008-2014. The reporting categories and additional categories relating to bacterial problems and transfusion are explained in Figures 9 A and B. These figures also clarify the classification and how results of lab investigations lead to a conclusion regarding possible transfusion-transmitted bacterial infection (TTBI). In the discussions of the different categories, further on in this section, the numbers of the 2014 reports are shown in circles in Figures 10 and 11.



** Culture result should be deemed relevant*

Figure 9A. Bacterial problems associated with blood transfusion: reporting categories and assessment of TTBI (Route A, clinical symptoms and signs in a patient)



** Total figure provided annually by Sanquin*

Figure 9B. Bacterial problems associated with blood transfusion: reporting categories and assessment of TTBI (Route B, bacterial contamination of blood component detected by hospital or blood supplier)

Abbreviations: *bc=blood component; plt=platelets TR=transfusion reaction Tf=tranfusion; TTBI=transfusion-transmitted bacterial infection*

Table 8. Overview of bacterial problems, 2008-2014

	2008	2009	2010	2011	2012	2013	2014
Bacterial contamination of blood component (including reports of positive bacterial screening)	25	26	44	43	42	25	12
Bacterial contamination of blood component (including reports of positive bacterial screening) as additional category	7	22	17	19	16	10	14
Post-transfusion bacteremia/sepsis (cases assessed by experts as TTBI)	37	55 (1)	41 (3)	61 (2)	50 (1)	47 (2)	55 (2)
Post-transfusion bacteremia/sepsis as additional category (not TTBI)	1	8	17	13	14	6	10

Post-transfusion bacteremia/sepsis

- 55 reports of post-transfusion bacteremia/sepsis from 29 reporting hospitals, 1-5 reports per hospital
- Two reports with bacterial contamination of blood component as an additional category, in one case severity grade 4 (see Cases 1 and 2, Figure 10 and Tables 8 and 10)
- 10 reports with post-transfusion bacteremia/sepsis as an additional category

Transfusion-transmitted bacterial infection (TTBI): assessment and case histories

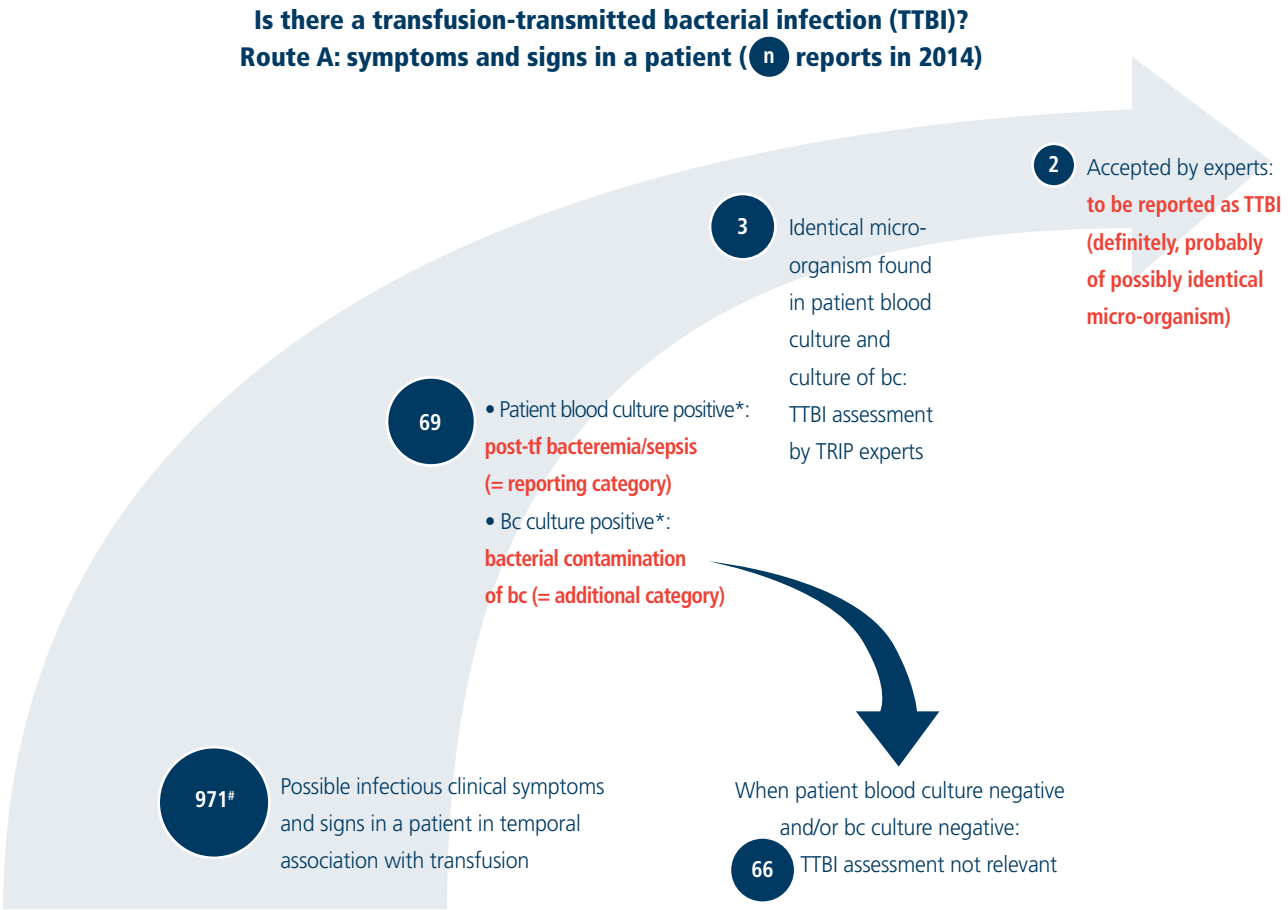


Figure 10. Assessment TTBI, route A*

Total number of reports with change in temperature and/or rigors

* *Culture result should be deemed relevant*

Abbreviations: *pt=patient; bc=blood component; Tf=transfusion; TTBI=transfusion-transmitted bacterial infection*

Case 1

Shortly after administration of a platelet transfusion a 60 year-old hematology patient, who was receiving palliative treatment, developed chills/rigors and chest pain. Before transfusion there was no (suspected) infection in the patient and culture of a pre-transfusion sample was negative. The patient developed sepsis the next day, declined ICU admission and died within 48 hours of transfusion. The patient's blood culture and platelet culture by the hospital after transfusion showed Staphylococcus aureus strains that were found to be identical on further investigation. Bacterial screening of the component on a sample taken at the time of pooling remained negative.

Post-transfusion bacteremia/sepsis was reported with certain imputability and grade 4 severity with bacterial contamination of blood component (additional category). The additional results make it (almost) certain that the infection was transmitted by the platelet concentrate and that this was a case of TTBI.

Case 2

Shortly after transfusion of a platelet unit in the day-care unit a 61 year-old patient developed chills and rigors. The patient was admitted to hospital for observation. Before transfusion there was no suspected infection. Patient blood culture and platelet culture by the hospital both revealed Staphylococcus epidermidis, the antibiograms being identical. The hospital was not notified of a positive bacterial screening result by the blood supplier.

Post-transfusion bacteremia/sepsis of grade 2 severity and possible imputability was reported. Further typing of the bacterial strains was not performed so it has not been confirmed that the Staphylococcus epidermidis strains in the patient's blood culture and platelet concentrate were. Imputability of TTBI was therefore rated as possible.

Case 3

After transfusion of a platelet unit and RBCs a 53 year-old hematology (AML) patient developed fever >2 °C with rigors. The patient's blood culture taken in the context of transfusion reaction investigations showed coagulase-negative staphylococcus (CNS). Cultures of the platelet concentrate and RBCs both revealed Staphylococcus epidermidis and Staphylococcus aureus. The antibiograms showed different resistance patterns, therefore the bacterial strains in the patient's blood culture and blood component culture were not identical. Further analysis revealed that patient's blood cultures taken four days earlier were positive for the same CNS. This transfusion reaction was classified as other reaction with bacterial contamination of blood component (additional category). Assessment of possible TTBI does not apply.

Bacterial contamination of blood component

In the reporting years 2008 up to and including 2013 the categories positive bacterial screening and bacterial contamination of blood component were used in TRIP reporting. However, the blood supplier, Sanquin, follows the same procedure in all cases of where there is an initially positive bacterial screening result for safety's sake. In cases where the initially positive bacterial screening result is not substantiated by a positive culture result and specification of the microorganism, it is still possible that the blood component contained a microorganism. In 2013 the Hemovigilance Advisory Board decided that there is no benefit in maintaining two separate categories. Hospitals particularly report cases where (sometimes on hindsight) patients showed symptoms and signs during/after transfusion or cases where the finding of a (probably) bacterially contaminated component had

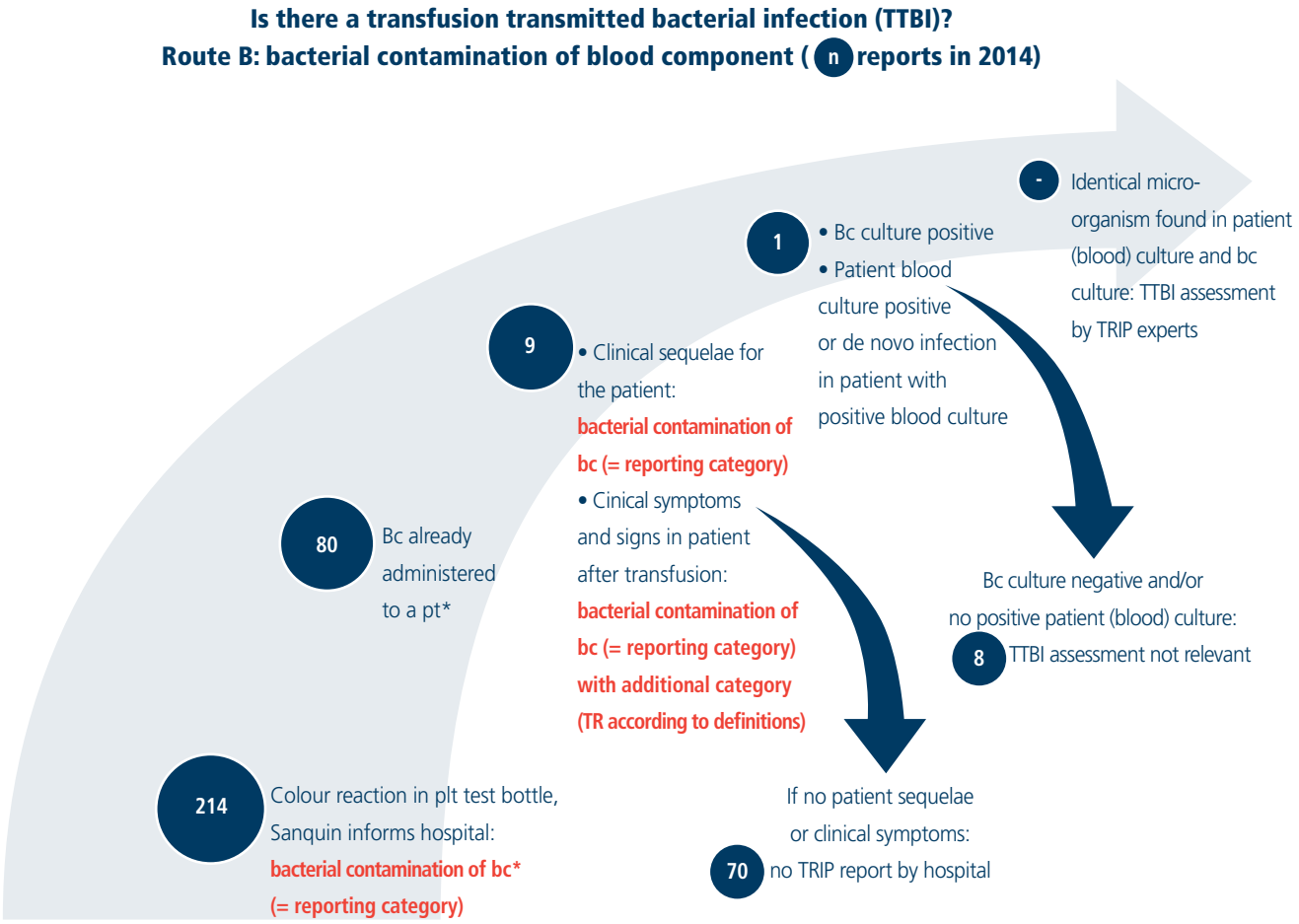
consequences for the patient to whom the component was administered. Patient sequelae include preventive administration of antibiotics or additional investigations. Annual numbers of components with positive bacterial screening results and of platelet units or associated red blood cell units which had already been transfused at the time of the positive bacterial screening result were provided by Sanquin (Table 9).

Table 9. Overview of positive bacterial screen of platelet concentrates provided by Sanquin, 2008-2014

Total Sanquin provision	2008	2009	2010	2011	2012	2013	2014
Platelets initially screened positive	Not asked	325	332	321	238	165	214
Number of already administered components (platelets and associated RBCs)	102	108	106	125	90	83	80*

* *In one case Sanquin received notification that the patient suffered a reaction*

Abbreviation: *RBC=red blood cells*



* *Total figures provided annually by Sanquin*

1x reported as additional category by the hospital

Figure 11 Assessment TTBI, route B*

**The methodology and assessment is explained in Figure 9B*

Abbreviations: *bc=blood component; plt=platelets TR=transfusion reaction Tf=tranfusion; TTBI=transfusion-transmitted bacterial infection*

Reports to TRIP

- 9 reports of bacterial contamination of blood component notification by Sanquin, sent by 5 reporting hospitals, 1-3 reports per hospital (Figure 11).
  (6x Propioni bact. sp.; 2x Staphylococcus saccharolyticus, 1x Kocuria varians.)
- 1 report recorded post-transfusion bacteremia/sepsis as an additional category. The platelet component was administered to a patient who was already on antibiotics for a serious infection. The patient's blood culture and platelet culture were positive for different microorganisms. Assessment for TTBI not applicable (Figure 11).
- 1 report recorded bacterial contamination of blood component, notification by Sanquin, as an additional category. Shortly after administration of a platelet concentrate the patient developed an allergic reaction. Platelet cultures in the hospital were negative but Sanquin's culture was positive for Propioni bacterium sp. (Table 10).
- 13 reports with bacterial contamination of blood component as an additional category where cultures were performed by the reporting hospitals following a transfusion reaction (see Case 3, Figure 10 and Table 10).
- In 2 cases (described above) of post-transfusion bacteremia/sepsis with additional category bacterial contamination of blood component the hospital's cultures revealed the same microorganism in the patient's blood culture and the component culture. These reports were judged to be TTBI (see Tables 8 and 10, Figure 10 and Case 1 & 2).

Conclusion (bacterial problems)

In 2014 there were two cases of TTBI of certain and possible imputability respectively.

Table. 10 Overview of reported reactions with bacterial contamination of blood component as additional category

Details TR* and patient	Reporting category	Bc culture result bc (culture performed by hospital)	Total	Patient blood culture result				Patient blood culture not performed or not stated
				CNS	Staph. aureus	Staph. epidermidis	Neg	
TR: symptoms/signs of bacteremia in patient without pre-existent infection	2x Post-tf bacteremia/ sepsis	Staphylococcus sp.	6		1	1		
	NHTR							1
	2x mild NHFR						2	
	Other reaction						1	
	NHTR	Brevundimonas sp.	1				1	
	Mild NHFR	Bacillus sp.	1				1	
TR in patient with pre-existent infection/sepsis	Anaphylactic reaction	Rhizobium sp.	1					1
	Other reaction	Staphylococcus sp.	1	1				
TR with symptoms/signs of bacteremia, patient already being treated with antibiotics	NHTR	Staphylococcus sp.	1				1	
	Other reaction	Brevundimonas sp.	1				1	
Generalised erythema, itching, facial swelling, chills, drop in temperature	Other allergic reaction	Negative (Propionibacterium acnes#)	1					1
Dyspnea and tachycardia	TACO	Gram negative rods	1				1	
Total			**14**	**1**	**1**	**1**	**8**	**3**

* *Symptoms/signs pointing to bacteremia: rise in temperature, rise in temperature and chills/rigors or isolated chills/rigors, may or may not present with other symptoms and signs*

\# *Sanquin's culture result*

Abbreviations: *TR=transfusion reaction; NHTR=non-hemolytic transfusion reaction; mild NHFR=mild non-hemolytic febrile reaction; TACO=transfusion-associated circulatory overload*

3.3 Non-infectious transfusion reactions

Acute hemolytic transfusion reaction (AHTR)

Symptoms of hemolysis occurring within a few minutes of commencement of until 24 hours subsequent to a transfusion: one or more of the following: fever/chills, nausea/vomiting, back pain, dark or red urine, decreasing blood pressure or laboratory results indicating hemolysis within the same period. Biochemical hemolysis testing positive; blood group serological testing possibly positive; bacteriology negative.

Table. 11 Acute hemolytic transfusion reaction, 2006-2014

	AHTR	F	M	Number of AHTR reports of possible, probable or certain imputability	Severity				
					0	1	2	3	4
2006	19	10	9	18	1	11	5	1	
2007	11	7	4	10		8	2		
2008	18	14	4	17		10	7		
2009	18	13*	4*	17		11	4	1	1
2010	21	8	13	20		14	5	1	
2011	16	10	6	14		6	7		1
2012	7	5	2	7		4	2		1
2013	11	8	3	11		5	5		1
2014	17	7	10	12		10	2		
Total	**138**	**82***	**55***	**127**	**1**	**80**	**39**	**3**	**4**

* *1x gender not stated*

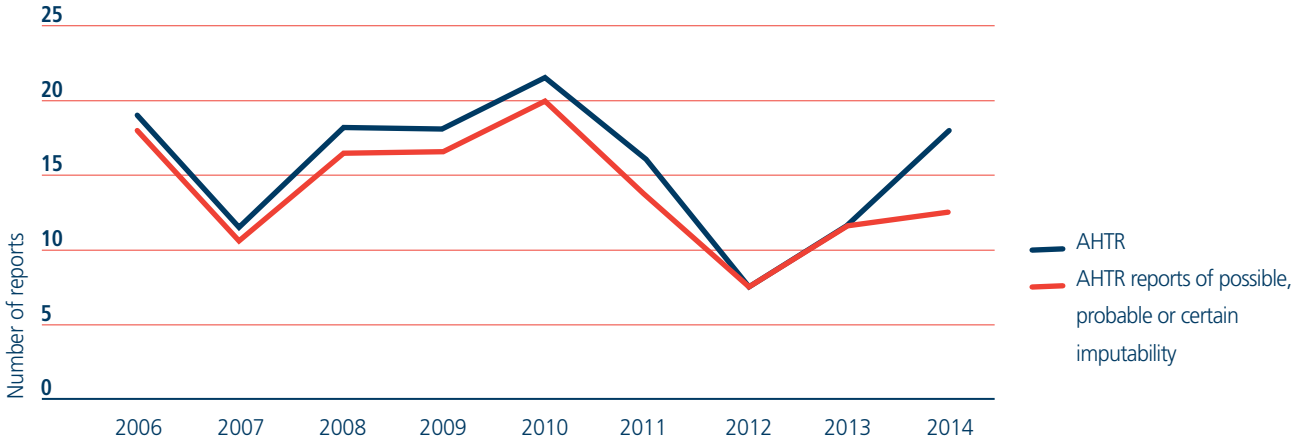


Figure 12. Acute hemolytic transfusion reactions, 2006-2014

- In 2014 there were 17 reports of an acute haemolytic transfusion reaction, out of which two reports were of severity grade 2 (Table 11).
- The declining trend that was signalled in 2013 did not continue.
- One acute hemolytic transfusion reaction of unlikely imputability was of severity grade 4 (see Section 3.6 Deceased patients).
- In addition there was one report of an incorrect blood component transfused which led to a grade 2 acute hemolytic transfusion reaction due to ABO incompatibility.
- Two reports concerned reactions with hemolysis following transfusion of platelets. In both cases O positive platelets were administered to an A positive patient. In one case the anti-A titre was determined (≥128).

- In all reports of AHTR there was biochemically confirmed hemolysis in combination with a drop in Hb level. In only one report could the causative antibody be demonstrated (anti-Wra). In all other cases blood group serology was negative. In a newborn baby an AHTR due to an activated T-antigen in necrotising enterocolitis was suspected. In seven cases the patient had pre-existing auto-immune or mechanical hemolysis that evidently increased after transfusion.

Delayed hemolytic transfusion reaction (DHTR)

Symptoms of hemolysis occurring longer than 24 hours after transfusion to a maximum of 28 days: unexplained drop in hemoglobin, dark urine, fever or chills etc.; or biochemical hemolysis within the same period. Biochemical testing and blood group serology confirm this.

If new antibodies are found without biochemical confirmation of hemolysis, report as new allo-antibody.

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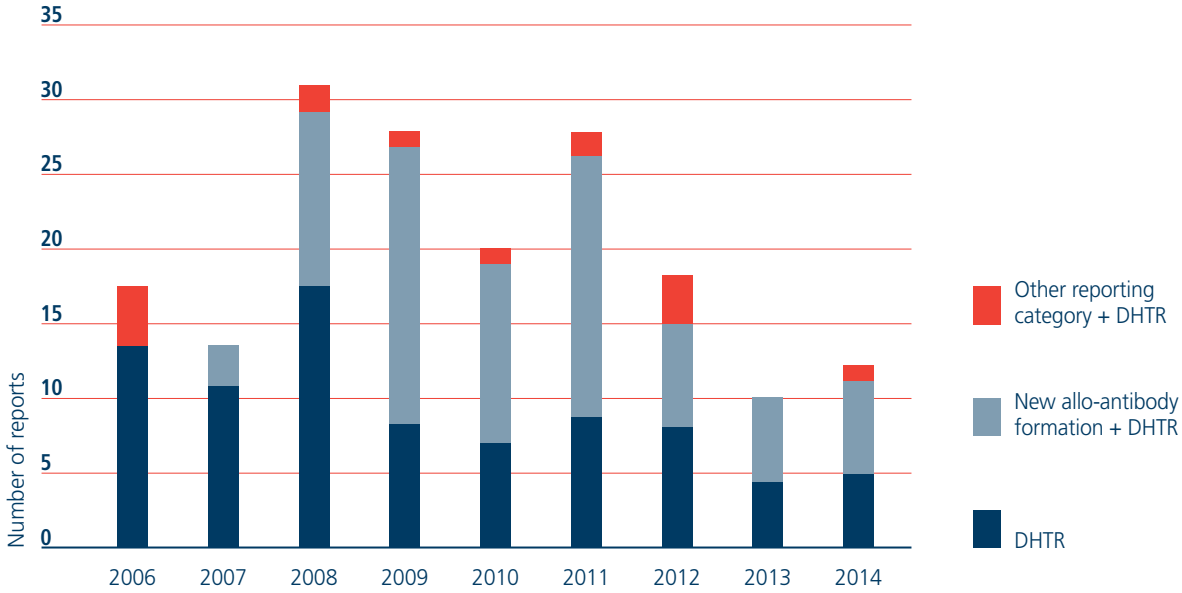

Figure 13. Delayed hemolytic transfusion reactions (reporting category or additional category), 2006-2014

Table 12. Severity of delayed hemolytic transfusion reactions, 2008-2014

	DHTR	DHTR of certain, probable or possible imputability	Severity grade 2	1	0
2006	14	13	8	5	-
2007	11	9	4	4	1
2008	18	15	4	6	5
2009	8	8	3	5	-
2010	7	7	5	2	-
2011	9	9	1	8	-
2012	8	7	1	5	1
2013	4	3	2	-	1
2014	5	5	3	2	-
Total	**84**	**76**	**31**	**37**	**8**

Table 13. New allo-antibody formation with DHTR by severity, 2006-2014

	New allo-antibody with additional category DHTR	Severity grade 2	1	0
2006	-	-	-	-
2007	3	-	1	2
2008	11	1	8	2
2009	19	1	7	11
2010	12	1	6	5
2011	17	-	5	12
2012	7	1	1	5
2013	6	-	4	2
2014	7	-	2	5
Total	**82**	**4**	**34**	**44**

In 2014 there were five reports of a delayed hemolytic transfusion reaction (DHTR) and a further seven reports of new allo-antibody formation with DHTR as an additional category. In one case reported as an other reaction, a DHTR was diagnosed and registered as additional category based on laboratory hemolysis parameters. As in 2013 there were no reports of DHTR following the administration of an incorrect blood component, but these reactions have been registered in previous reporting years. The antibody specificities that were determined with the reported transfusion reactions were: 6x anti-E (including three cases in combination with anti-c, anti-M and anti-c plus -S respectively), anti-K, anti-Lea, anti-Jka, anti-Fya, anti-c. Twice an antibody to a low frequency antigen was suspected but could not be demonstrated.

Since 2008 there has been a declining trend in the number of reports of DHTR even after taking account of the reduced blood use. The declining trend could in part be explained by the progressive implementation of the TRIX (Transfusion Registry of Irregular allo-antibodies and cross(X)match problems), the national database of irregular antibodies. Four 2014 reports came from hospitals without an operational TRIX connection at the time of component selection and transfusion. However not all cases of DHTR can be prevented. Patients are not systematically tested for new allo-antibody formation after a blood transfusion, so there will always be a small risk of missing a newly formed allo-antibody at later pre-transfusion screening if its concentration has gone below the detection threshold.

In 2008 TRIP started systematically reporting reactions according to the sequence of events, with the main reporting category corresponding to the reaction which was noted first. Since then roughly half of the DHTR have been reported as an additional category in cases where detection of a new allo-antibody and subsequent checking of biochemical hemolysis parameters or an unexpected drop in hemoglobin led to the diagnosis of a DHTR (Figure 13).

In 2009 and 2010, TRIP consistently asked reporters of clinically significant allo-antibodies whether there had been signs or test results suggestive of hemolysis. This only elicited a small number of extra cases of DHTR which was then reported as an additional category. The tactic failed to increase detection of DHTR to the published 5-10x higher incidence than that of AHTR.

New allo-antibody formation

After receiving a transfusion, demonstration of clinically relevant antibodies against blood cells (irregular antibodies, HLA or HPA antibodies) that were not present previously (as far as is known in that hospital).

- 761 reports by 67 reporting hospitals, varying from 1-48 reports per hospital
- 289 male and 472 female patients, out of whom 28 women were < 45 years of age at the time of transfusion

As in the 2013 annual report the reports of new allo-antibody formation were analysed to determine if there has been a reduction in reported anti-c, anti-C, anti-e, anti-E and anti-K in women younger than 45 years at the time of transfusion. This reduction is to be expected as the national CBO blood transfusion guideline, that was revised in 2004 and again in 2011, includes recommendations that women of childbearing potential should receive components compatible for these antigens. A number of aspects should be borne in mind when examining the results:

1. Some hospitals implemented recommendations before the formal recommendation; conversely in a few hospitals there may have been a delay.
2. An overall increase in reports of new allo-antibody formation until about 2008 was observed, in line with an increase in the number of hospitals reporting this category to TRIP.
3. There has been a decline in distributed and transfused red blood cells each year since 2002.
4. In The Netherlands there is no routine post-transfusion screening of transfused patients for possible development of irregular antibodies.
5. Development of irregular antibodies such as anti-K, -c, -C, -e, -E, and -D can also occur following transfusion of platelets or from pregnancy/delivery.
6. Besides the recommendation of preventive matching for Kell and Rhesus phenotype for females of child-bearing potential, similar recommendations have been made for preventive component matching for other at-risk patient groups. The guideline is available in English (link on www.tripnet.nl).

In Figure 14 the upper trend line indicates an increase in the total number of reports of new allo-antibody formation per year of transfusion while the lower trend line for women younger than 45 years shows a decrease. The figure fits with an initial growth of the TRIP reporting system combined with a decline of cases in the target group of females of child-bearing potential. Figure 15 shows the subgroup of women under 45 years of age with a subdivision according to type of allo-antibody and number of patients.

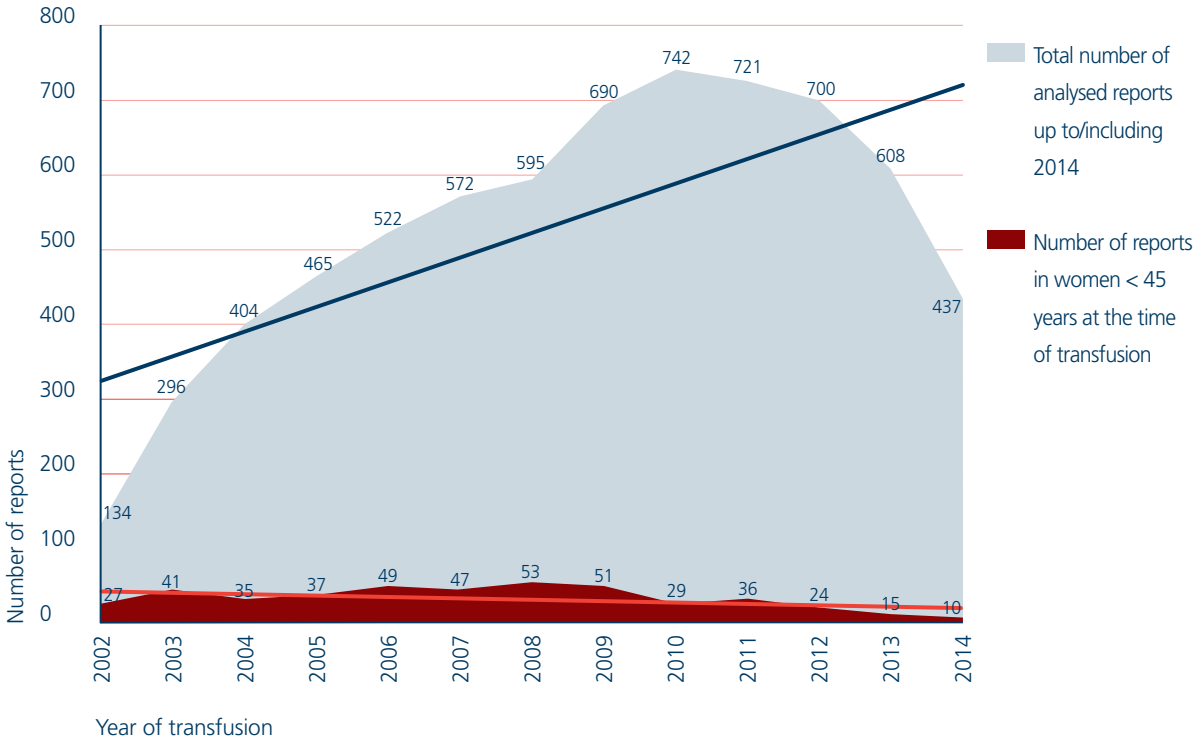

Figure 14. Total number of analysed reports and number of reports in women < 45 years of age according to year of transfusion

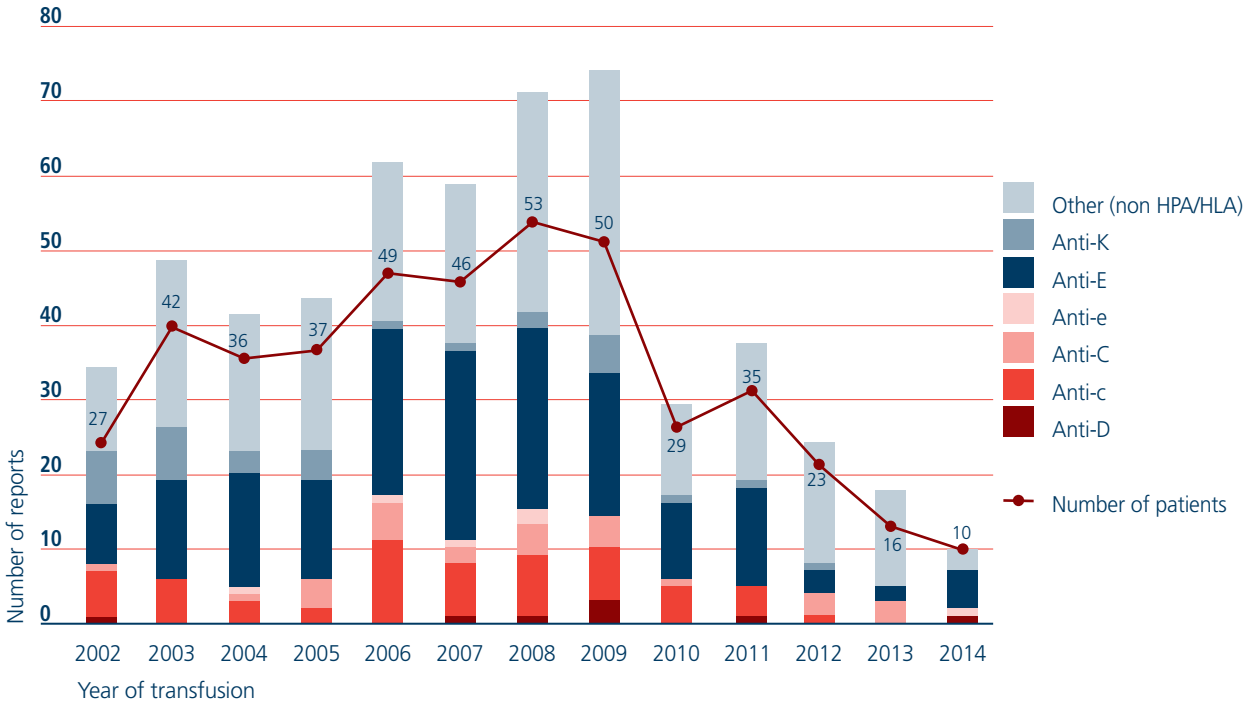

Figure 15. Allo-antibodies* in women < 45 years of age at the time of transfusion

** New allo-antibody after platelet transfusion:* *4x anti-D (2x 2009, 2011, 2014) 1x anti-c (2005) 11x anti-E (2002, 2005, 2007, 2x 2008, 2x 2009, 2010, 2011, 2x 2012)*

New allo-antibody after IBCT: *1x anti-D (2007) 2x anti-c (2009, 2012) 1x anti-C (2005) 4x anti-E (2010, 2013, 2x 2014) 13x anti-K (2x 2003, 4x 2005, 2008, 3x 2009, 2010, 2011, 2012)*

Transfusion-associated circulatory overload (TACO)

Dyspnea, orthopnea, cyanosis, tachycardia >100/min. or raised central venous pressure (one or more of these signs) within six hours of transfusion, usually in a patient with compromised cardiac function. Chest X-ray consistent.

- 74 reports from 40 reporting hospitals, 1-6 reports per hospital
- 7 reports had other incident as an additional category (4x failure to report transfusion reaction to transfusion lab; 2x unnecessary transfusion; 1x administration time >6 hours)
- 5 reports in other reporting categories had TACO as an additional category (3x NHTR, 1x other reaction and 1x AHTR)

The number of reports of TACO still shows a rising trend from year to year. Bearing in mind the clearly declining blood use it seems that TACO is recognised more frequently in the clinical setting. The cases where TACO was added as an additional category regarded patients in whom only few symptoms and signs of TACO were found, e.g. a woman of 74 years who had a pro-BNP increase from 125 to 315 or a patient for whom it is not clear whether the pre-existing symptoms and signs of TACO did actually increase after transfusion.

TACO is the reporting category that had the highest number of serious reports (Table 2 n=23) in 2014.

It is important to determine which patient groups have an evidently increased risk of developing TACO as it is assumed that a large number of TACO cases could be avoided, e.g. by adjusting the rate of transfusion, reducing the volume transfused or prescribing diuretics. Numerous factors can play a role in increasing a patient's risk of TACO. Several hospitals have committed to participating in a study of risk factors in patients who had TACO in 2014.

Table 14. Severity and imputability of TACO reports

		Severity grade			
Imputability	**Total**	**1**	**2**	**3**	**4**
Certain	**11**	4	6	1	-
Probable	**23**	17	5	1	-
Possible	**39**	29	6	1	3
Unlikely	**1**	1	-	-	-
Total	**74**	**51**	**17**	**3**	**3**

Hemosiderosis

Iron overload induced by frequent transfusion with a minimum ferritin level of 1000 micrograms/l, with or without organ damage.

Besides 3 reports received during the 2014 reporting year, several more hemosiderosis reports were received after the closing date for this report (provisional number: 13). TRIP and the professionals groups should consider developing projects to collect information about, and in future contribute to preventing health damage from hemosiderosis in multiply transfused patients..

Non-hemolytic transfusion reactions and mild febrile reactions

Non-hemolytic transfusion reaction (NHTR)

Rise in temperature of ≥2°C (with or without rigors/chills) during or in the first two hours after a transfusion, with no other relevant symptoms or signs; OR rigors/chills with or without a rise in temperature within the same time limits. No evidence (biochemical or blood group serological) for hemolysis, and no alternative explanation.

Mild (non-hemolytic) febrile reaction (mild NHFR)

Rise in temp. >1°C (<2°C) during or in the first two hours after a transfusion with no other relevant symptoms or signs; optional reporting to TRIP. Hemolysis testing and bacteriology negative if performed.

The number of NHTR and mild NHFR stayed roughly at the same level compared to 2013 when taking account of total blood use. Analysis of febrile reactions is important as fever may be the first sign of a more serious transfusion reaction. Reports to TRIP often do not state information about results of lab investigations, this is the hospital's responsibility. As the investigations can only aid in excluding other causes of fever, it is also important to assess the clinical course, including the temperature curve which should show normalisation within 24 hours.

The reporting of non-hemolytic transfusion reactions remains relevant, also because of the extra costs due to extra investigations, staff time, the unit that had to be stopped and prolongation of hospital stay. Twelve 2014 reports were reported as grade 2 severity because the patient was admitted to hospital from the day-care ward; in other cases it is difficult for hospitals and TRIP to establish whether there was prolongation of hospital stay. For patients a NHTR means morbidity and discomfort. Moreover, the reported NHTR and mild NHFR provide a signal that the hemovigilance system is functioning, both in the hospitals and at national level.

Transfusion-related acute lung injury (TRALI)

Dyspnea and hypoxia within six hours of the transfusion; chest X-ray shows bilateral pulmonary infiltrates. There are negative investigations (biochemical or blood-group serological) for hemolysis, bacteriology is negative and no other explanation exists. Depending on the findings of tests of leukocyte serology, report is classified as immune-mediated or unknown cause.

In 2014 five cases were reported and accepted by experts; in addition after the closing date for the 2013 report another three TRALI reports were received, bringing the total for 2013 to nine TRALI reports.

- 4 TRALI reports in 2014 were judged as imputability certain, probable or possible (this was the case for 7 out of the final 9 reports in 2013)
- These 4 TRALI reports were: 1x grade 3 and 3x grade 2
- The types of blood components are shown in Figure 16

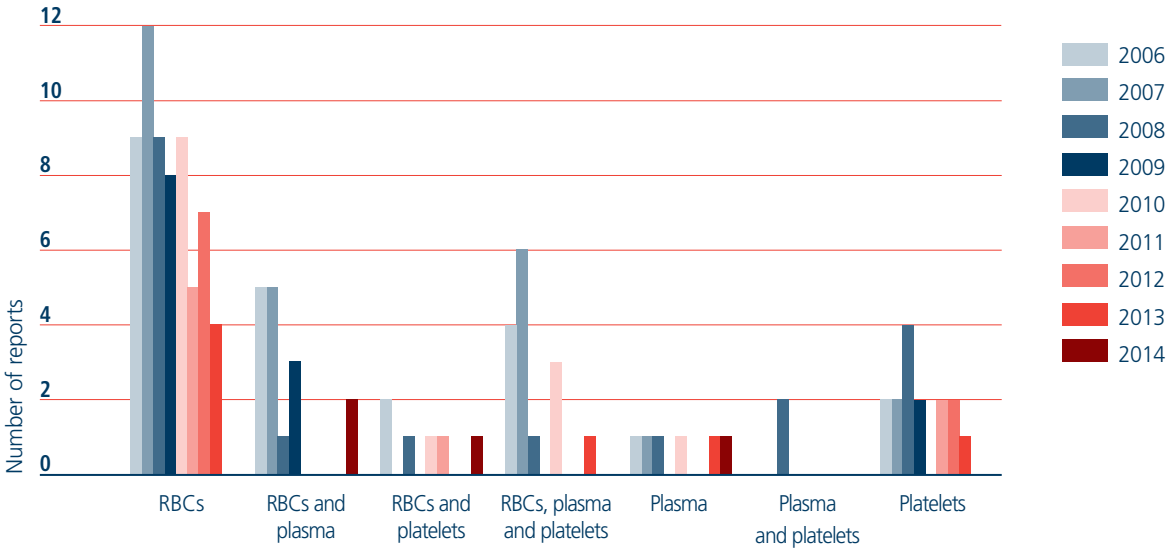

Figure 16. Type of blood component in TRALI reports of imputability certain, probable or possible, 2006-2014

In cooperation with investigators from Sanquin and the Clinical Epidemiology Department of Leiden University Medical Centre, TRIP investigated whether there was a reduced TRALI risk associated with platelet concentrates with platelet additive solution (PAS) as added conservation solution as opposed to plasma from the same donation as one of the five constituent buffy coats. No statistically significant difference could be demonstrated (poster NVB-TRIP symposium, 2015), nor was there a detectable effect from the platelet measure implemented in November 2009 that involved using plasma only from non-transfused male donors.

As to the move to SD plasma (Solvent Detergent plasma; the component issued by Sanquin is known as Omniplasma®) it can be theoretically assumed that this could lead to a further reduction of the TRALI risk from plasma, which has already been reduced by the male-only plasma measure in 2007.

Anaphylactic transfusion reaction and other allergic reaction

Anaphylactic transfusion reaction

Rapidly developing reaction occurring within a few seconds to minutes after the start of transfusion, with features such as airway obstruction, in and expiratory stridor, fall in blood pressure ≥20 mmHg systolic and/ or diastolic, nausea or vomiting or diarrhoea, possibly with skin rash. Hemolysis testing and bacteriology negative, test for IgA and anti-IgA.

Other allergic reaction

Allergic phenomena such as itching, redness or urticaria but without respiratory, cardiovascular or gastro-intestinal features, arising from a few minutes of starting transfusion until a few hours after its completion. Hemolysis testing and bacteriology negative if performed.

In 2014 the numbers of reported anaphylactic and other allergic reactions was slightly lower (51 and 151 respectively in comparison to the means of 65 and 188 in the three preceding years) but they were actually comparable when taking account of the reduced blood use. As in previous years the numbers of reported reactions are relatively high for plasma and platelet transfusions compared to red cell transfusions (Table 4).

During discussions about reporting categories the hemovigilance advisory board noted that many treating physicians understand reporting category anaphylactic reaction to be anaphylactic shock with severe hypotension. By stopping transfusion and timely administration of medication the reaction can be prevented from developing into anaphylactic shock. The TRIP definition conforms to (inter)national guidelines for an allergic type of reaction

with systemic signs like bronchospasm, vomiting or diarrhoea. Hypotension is not an obligatory sign. Fairly frequently a reaction that was initially reported in another category (the majority: other allergic reaction) is reclassified as anaphylactic reaction at TRIP's request as the TRIP category other allergic reaction is characterised by exclusively skin manifestations. Table 15 shows the distribution of reported symptoms and signs in anaphylactic and other allergic reactions.

The CBO blood transfusion guideline recommends testing for the presence of anti-IgA in an IgA deficient patient that could be the cause of the reaction. From 2003 up to and including 2014 this was demonstrated to be the cause of four anaphylactic reactions reported to TRIP (0.7%); if this mechanism has led to serious reactions, blood components from IgA deficient donors may be prescribed for future transfusions. In 2014 seven reports stated that IgA levels had been determined and were normal.

Table 15. Reported symptoms and signs in reported anaphylactic reactions and other allergic reactions in 2014

Symptom	Anaphylactic reaction (n=52) all	Anaphylactic reaction of grade 2 or higher (n=19)	Other allergic reaction (n=153)
Urticaria, local	12	7	76
Urticaria, generalised	9	3	27
Itching, local	8	2	44
Itching, generalised	9	3	26
Rise in temperature >1 °C	7	2	11
Chills/rigors	10	3	5
Skin redness/erythema	20	5	58
Drop in blood pressure	23	10	-
Dyspnea/bronchospasm or stridor	27	11	-
Gastro-intestinal	6	3	-

With regard to the reported symptoms and signs Table 15 shows:

- Rise in temperature and chills/rigors may be observed in anaphylactic and other allergic reactions

Among the serious reports of anaphylactic reactions:

- Severe drop in blood pressure was reported in 7 out of 19 serious cases
- Three reports stated that the patient needed treatment including adrenalin
- Several reports mention quick resolution of symptoms after antihistamine treatment, in some cases in combination with an H1 receptor agonist.

Post-transfusion purpura (PTP)

Serious self-limiting thrombocytopenia possibly with bleeding manifestations 1-24 days after a transfusion of a red cell and/or platelet concentrate.

In 2014 there was one report of post-transfusion purpura in a hematology patient with a history of pregnancy. She died of bleeding complications during the thrombocytopenic period. Anti-HPA 1a antibodies were demonstrated.

Other reaction

Transfusion reactions that do not fit into the categories above.

- The numbers of reports in 2014 seemed to be stable in comparison with 2011-2013 in relation to issued blood components
- Other reaction takes 4th position among reporting categories

- Since 2010 other reaction has been among the three largest categories of serious reactions (grade 2 or higher) of certain, probable or possible imputability

Table 16. Types of transfusion reactions that were registered in category other reaction in 2014 compared to 2012 and 2013

Type of reaction	Total no. 2014	No. certain, probable	No. possible	No. ≥ gr 2*	No. in 2012	No. in 2013
Reactions with hypotension	30	4	22	3	42	47
Reactions with dyspnea	21	3	15	2	30	34
Rise in blood pressure	6	1	5	1	14	6
(Possible) cardiac symptoms	6	2	3	1	10	9
Did not completely fit the TRIP definition of standard category	73	27	46	2	63	73
Unproven sepsis	3	0	1	1	Not assessed	2
Other signs	52	11	30	6	57	45
Total	**190**	**48**	**122**	**16**	**216**	**216**

* *Imputability certain, probable, possible*

In a number of cases symptoms and signs during transfusion were appropriately reported by the nursing staff to the doctor and/or hemovigilance staff. If there is no evidence of a transfusion reaction and the symptoms and signs can be explained by the patient's condition, usually reporting to TRIP is not indicated. This was the case in five reports in 2014 (4x counted as 'other symptoms', 1x as 'do not fit the standard definitions').

Cases do need to be reported where there is:

- serious morbidity, including reactions that led to prolongation of hospital stay or admission for observation
- an incident e.g. positive bacterial screening result after administration of the blood component

After reviewing the reports classified as other reaction, the expert panel remarked that demonstration of HLA antibodies is associated with e.g. fever, chills/rigors, dyspnea or anaphylactic symptoms and signs. If there is a febrile reaction, the finding of HLA antibodies does not preclude reporting as NHTR or mild NHFR.

Reactions associated with plasmapheresis

Three patients had symptoms and signs consistent with hypocalcemia during plasmapheresis (in one patient who suffered a total of six transfusion reactions only two appeared to be caused by hypocalcemia).

In 2014 a decision was taken to introduce a new reporting category of Transfusion-Associated Dyspnea (TAD). Among 21 reports mentioning dyspnea as a prominent feature or as an extra sign in a report that would otherwise have fitted another category, a chest X-ray was performed in four cases and did not show any indication of TRALI or TACO; those complications were judged to be unlikely on clinical grounds in another two reports. In several reports there were other possible causes for dyspnea. In all, three reports would have qualified for classification as TAD: two reports of grade 1 and one report of grade 2 concerning reinfusion of drain blood, all three of possible imputability.

A rise in blood pressure was noted in the 2008 TRIP report as a sign which occurred in a cluster of reports in the category of other reaction. Possibly some cases may have been TACO cases that were not substantiated by other investigations. However this did not appear to be the case in the six reports of increased blood pressure in 2014.

3.4 Blood management techniques (BMT)

Reports associated with blood management techniques

- The number of reports seems to have stabilised (Table 17)
- The majority of reports (24) as in previous years concerned reinfusion of drain blood, out of which two reports were of severity grade 2
- An other incident was reported regarding cell saver autotransfusion, where transfusion was administered without using a filter. The patient did not suffer a reaction, but was admitted to ICU as a precautionary measure.
- Five out of the six reporting hospitals in 2014 are located in the south-east region of The Netherlands
- Approximately a quarter of the Dutch hospitals have reported a reaction associated with BMT; it is remarkable that two hospitals have submitted 60% of the reports associated with BMT in the period 2008-2014.
- The two hospitals which reported 60% of cases in the period 2008-2014 have reduced their use of drain blood - one actually stopped using drain blood procedures in 2013 - with a corresponding drop/ cessation of BMT reports.
- Almost 50% of the reports involving BMT were of non-hemolytic transfusion reactions (Table 18). In 71% of these reports the patient had undergone a knee replacement surgery and in 21% of reports the patient had hip replacement surgery (in 8% of reports of NHTR the type of surgery was not stated).

Table 17. Reports regarding blood management techniques (BMT), 2008-2014

BMT	M	F	Reports drain blood	Reports cell saver	Reports PAD	Total	Reports grade ≥ 2	No. of reporting hospitals
2008	14	12	20#	5	1	26	1	9
2009	9*	23*	28	4	1	33	3	6
2010	15	22	34	3	-	37	1	5
2011	26	38	64	-	-	64	2	8
2012	25	25	50	-	-	50	3	8
2013	13	13	26	-	-	26	0	6
2014	15	10	24	1	-	25	2	6
Total	**117***	**143***	**246#**	**13**	**2**	**261**	**11**	**23**

* *1x gender not stated*

\# *1 report concerned preoperative administration of erythropoietin as pre-treatment for a drain blood procedure*

Abbreviation: *PAD=preoperative autologous blood donation*

Table 18. Reported reactions associated with drain blood procedures, 2008-2014

TRIP category	2008	2009	2010	2011	2012	2013	2014	Total	No. of reporting hospitals
Anaphylactic reaction		2	1	1			1	4	3
Other allergic reaction			1			2		4	4
Hemolysis of product				2				2	2
Mild NHFR				2	4	2	2	10	6
NHTR	6	9	18	37	24	14	12	120	12
Other incident	9	12	6	8	4	3	2	44	5
Other reaction	5	4	8	14	17	5	7	60	14
Post-transfusion bacteremia/sepsis					1			1	1
TACO		1						1	1
Total	**20**	**28**	**34**	**64**	**50**	**26**	**24**	**246**	**21**

Table 19. Application data of blood management techniques 2009-2014

BMT technique Total applied	2009*	2010*	2011*	2012*	2013*	2014*
Drain blood	7514	8821	11464	7209	5536	4811
Cell saver	3033	5001	4282	2501	5097	5521
PAD#						
- patients referred	109	153	59	26	17	7
- units donated	208	289	113	50	6	9
- units administered	187	224	38	29	4	5
Normovolemic hemodilution	122	1412	1250	?*	?*	915
Hypervolemic hemodilution	2	0	1172	?*	?*	?*
Extracorporeal circulation	2177	4430	5606	3981	3577	4570
Fibrin glue	798	1056	1437	350	1123	1331
Platelet gel	846	1225	510	30	24*	112

* *Some hospitals submit approximations for application data or state that they use BMT but do not provide numbers*

\# *PAD=preoperative autologous blood donation*

Table. 20 Numbers of hospitals that apply blood management techniques, 2010-2014

BMT type	2010			2011			2012			2013			2014		
No. of hospitals	yes	no	?	yes	no	?	yes	no	?	yes	no	?	yes	no	?
Drain blood	21	24	58	23	20	57	23	20	55	24	21	53	19	28	51
Cell saver	21	23	59	22	21	57	24	21	53	24	18	56	23	26	49
PAD#	9	47	47	10	52	38	11	62	25	5	60	33	5	62	31
Normovolemic hemodilution	3	32	68	3	33	64	2	28	68	2	37	59	4	42	55
Hypervolemic hemodilution	1	31	71	4	32	64	2	26	69	3	36	59	3	35	58
Extracorporeal circulation	4	47	52	4	46	50	4	40	54	4	45	49	5	53	40
Fibrin glue	15	24	64	20	25	55	12	22	64	8	33	55	7	37	54
Platelet gel	4	37	62	1	45	54	1	38	59	2	42	53	2	49	47

\# *PAD=preoperative autologous blood donation*

Regarding hospitals that use BMT and application data (Tables 19 and 20):

- There remains a lack of clarity concerning application of BMT in the hospitals. There is a small decrease in the number of hospitals that indicate they do not know if BMT are applied in their institution. Still, more than 50% of hospitals reply they don't know. Logically someone must know if the techniques are in use, but it is more difficult to be certain that no-one is using them and the information is not available to the hemovigilance staff.
- There has been a further drop of 13% in application of drain blood. The number of applying institutions dropped from 24 to 19. Possibly there is decreased use of this technique. This drop could be explained on the one hand by the fact that a large study (TOMaat study[1]) proved this technique not to be cost-effective, on the other hand changes in surgical techniques have led to diminished blood loss and the operations are commonly performed without a wound drain.

- Preoperative autologous donation is becoming a very rare procedure compared to 2009 and the number of units actually administered is even smaller.

[1] *Patient blood management in elective total hip- and knee-replacement surgery (Part 1): a randomized controlled trial on erythropoietin and blood salvage as transfusion alternatives using a restrictive transfusion policy in erythropoietin-eligible patients. So-Osman C, Nelissen RG, Koopman-van Gemert AW, Kluyver E, Pöll RG, Onstenk R, Van Hilten JA, Jansen-Werkhoven TM, van den Hout WB, Brand R, Brand A. Anesthesiology. 2014 Apr;120(4):839-51*

3.5 Reports associated with SD plasma in 2014

Under co-authorship of Lareb (Netherlands Pharmacovigilance centre)

In Table 4 the types of reports associated with SD plasma in 2014 are shown. Two patients undergoing therapeutic plasmapheresis had one and three serious anaphylactic reactions respectively (see Case histories).

Case history 1 anaphylactic reaction
A patient with acute renal insufficiency and anti-GBM antibodies (age group 60-80 years) had a reaction 1 hour after the start of plasmapheresis: rise in temperature 36.5 -> 37.9 °C and a drop in blood pressure 158/76 -> 50/54; she was pale and clammy. Quick recovery after administration of saline solution and Tavegil. Biochemical tests and blood group serology were normal. She was on ACE inhibitors. The next plasmapheresis procedure with SD plasma was uneventful.
Report: anaphylactic reaction grade 2, imputability possible

Case history 2 several anaphylactic reactions
A patient (age group 20-60 years) was being treated by therapeutic plasmapheresis with administration of SD-plasma for relapsing thrombotic thrombocytopenic purpura (TTP). For the first few days plasmapheresis was uneventful. Then the patient had reactions on three consecutive days.
Reaction 1, (3 hrs after start) shortness of breath, laboured blowing breathing followed by (local) urticaria, vomiting, reduced consciousness, BP barely measurable, suspected CVA.
Reaction 2, next day, premedication had been administered. 1.5 hours after the start of plasmapheresis: collapse, drop in saturation, wheezing, reduced consciousness. Systolic BP 140 -> 108 mmHg, urticaria on legs and chest, red eyelids.
Reaction 3, next day, again after premedication. 9 min after the start of plasmapheresis: urticaria and a reaction similar to the previous two days; BP stable.

After these three reactions the therapeutic plasmapheresis procedures were continued with transfusion of FFP. No further reactions observed.
Investigations: Elevated transaminase levels and LDH increase (857 on day of reaction 1 to 1382 the next day), rise in CRP. No explanation could be found. One day before levels had been normal and they normalised within a few weeks. IgA levels were normal; ASAT and ALAT that were determined in one unit of Omniplasma® were within normal limits.
Reports: three anaphylactic reactions grade 2, imputability probable

Increasing use of SD-plasma

The reported reactions associated with SD-plasma should be seen against the background of increased use. Since the beginning of 2014 Omniplasma®, a type of SD-plasma produced from Dutch plasma donations, has been progressively implemented by Sanquin as the standard plasma component for transfusion. SD stands for solvent-detergent, a pharmaceutical viral reduction method for pooled plasma donations.

SD-plasma was transfused in 20 hospitals in 2014 (blood use figures were available for 95 out of the 97 participating hospitals). Seventeen of these hospitals provided the number of recipients that were transfused with SD-plasma: the median number of units SD-plasma per patient amounted to 3.7. The reports associated with SD-plasma are presented in Table 21 and compared to reports with quarantine fresh frozen plasma (FFP).

Table 21. Reports associated with SD-plasma and FFP in 2013 and 2014

Type of bc	No. of units in 2014	No. of reported reactions[#]	No. of reporting hospitals (total n=97)	Reactions per 1000 bc, 2014*	Reactions per 1000 bc, 2013*
SD-plasma	7585	7[$]	4	0,8	1,5
FFP	52549	51	35	1,0	0,9
FFP in combinations		19			

* *Reports associated with SD and/or FFP only, without administration of other types of blood components; SD-plasma used in 20 hospitals in 2014 and 4 in 2013.*

[$] *In 1 case labile blood components were also administered*

Abbreviations: *FFP=quarantine fresh frozen plasma, bc=blood component*

Conclusion

Reports associated with SD-plasma in 2013 and 2014 show roughly the same pattern as with FFP. However, according to international literature and hemovigilance reporting fewer reports are expected. Two patients had one or more serious anaphylactic reactions in 2014 after administration of SD-plasma.

3.6 Deceased patients and transfusion reactions (grade 4)

In 2014 there were 10 reports of transfusion reactions of grade 4 severity. These are summarised in Table 22.

Table 22. Reports where a patient died after a transfusion reaction

Reporting category	Age, gender	Blood component	Imputability	Clinical situation
Post-transfusion bacteremia/sepsis	60, M	Plts	Certain	Discussed in section 3.2
Post-transfusion bacteremia/sepsis	77, F	RBC	Possible	Seriously ill patient suffering from multiple myeloma had dyspnea/septic signs and positive blood culture (E. coli) after Tf, unit culture negative.
Bact. contamination bc and post-transfusion bacteremia/sepsis	68, M	Plts	Unlikely	Septic patient (before Tf); blood culture after Tf positive for a different m.o. than that found in platelet concentrate.
Post-transfusion purpura	53, F	RBC+Plts	Probable	Patient with leukemia, discussed in section 3.3.
TACO	78, M	RBC+FFP (12 units total)	Possible	Hemorrhagic shock due to arterial bleeding after abdominal surgery, successfully coiled; hypotensive and difficult mechanical ventilation, chest X-ray consistent with TACO or ARDS.
TACO	84, M	RBC	Possible	Patient with infection and cardiac problems, terminally ill with AML.
TACO	62, F	RBC	Possible	MDS, worsening of dyspnea on Tf but little response to furosemide; chest X-ray showed bilateral pleural effusion and opacities; BNP greatly increased.
Acute hemolytic transfusion reaction	42, M	RBC	Unlikely	Patient with comorbidities, admitted for malaise, dyspnea and anemia due to AIHA. Increased hemolysis after Tf of unit incompatible for auto-antibody that was not detected in standard screening.
Other reaction	43, M	Plts	Unlikely	Non-Hodgkin lymphoma, TTP and SIRS signs before Tf; shortly after Tf drop in BP, rising lactate levels; autopsy showed i.a. intravascular tumour cells.
Other reaction	62, F	RBC	Unlikely	Transfusion-dependent MDS patient, auto-anti-i

Abbreviations: *Plts=platelets; RBC= red blood cell concentrate; FFP=fresh frozen plasma; TACO=transfusion-associated circulatory overload; ARDS=acute respiratory distress syndrome; AML=acute myeloid leukemia; MDS= myelodysplastic syndrome, TTP=thrombotic thrombocytopenic purpura; SIRS=systemic inflammatory response syndrome, Tf=transfusion, BP=blood pressure, AIHA= auto immune haemolytic anemia, BNP=brain natriuretic peptide.*

Table 23 presents an overview of grade 4 reports to TRIP with certain, probable or possible imputability from 2008. The most important categories are other reaction (8) and TACO (7) followed by TRALI (4) and post-transfusion bacteremia/sepsis (4). Table 24 shows international data for comparison.

Table 23. Reports of grade 4 (imputability certain, probable or possible,2008 - 2014

Category	2008	2009	2010	2011	2012	2013	2014	Total
AHTR		1		1	1			3
Other reaction	1		3	1	1	2		8
Post-transfusion bacteremia/ sepsis*		1*			1		2*	4
Post-transfusion purpura							1	1
TRALI		1	2		1			4
Incorrect blood component transfused (IBCT)	1							
TACO			2	1	1		3	7
Total	**2**	**3**	**7**	**3**	**5**	**2**	**5**	**27**

Abbreviations: *AHTR=acute hemolytic transfusion reaction; TRALI=transfusion-related acute lung injury; TACO=transfusion-associated circulatory overload*

* *The report in 2009 and one in 2014 were confirmed cases of transfusion-transmitted bacterial infection.*

Table 24. International data on top 3 causes of transfusion related mortality

Source Rank:	1st (no.)	2nd (no.)	3rd (no.)
FDA[1] 2012 and 2013	TRALI (31)	TACO (21)	Hemolysis (10 non-ABO, 4 ABO)
SHOT[2] 2012 and 2013	TACO (18)	Delayed transfusion (5)	Hemolytic TR (2)
France[3] 2012 and 2013	TACO (5)	TRALI (3) Bacterial contamination (3)	
ISTARE[4] 2011 and 2012 (21/22 countries)	TACO (37)	TAD (19)	Allergic (13)
EU (2013)	TACO (6)	TRALI (5) Immunological hemolysis (5)	

Abbreviations: *TRALI= transfusion-associated acute lung injury; TACO=transfusion-associated circulatory overload; TAD=Transfusion-associated dyspnea; TR=transfusion reaction*

[1] *FDA=United States Food and Drug Administration (www. http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/TransfusionDonationFatalities/default.htm)*

[2] *SHOT=Serious Hazards of Transfusion, www.shotuk.org*

[3] *ANSM=Agence nationale de sécurité du Medicament et des produits de santé. http://ansm.sante.fr/Mediatheque/Publications/Bilans-Rapports-d-activite-Bilans-et-rapports-d-activite#folder_26762*

[4] *ISTARE=International Surveillance database for Transfusion-Associated Adverse Reactions and Events, http://www.ihn-org.com/haemovigilance-databases/istare-2/*

4. General information

4.1 TRIP working method and participation

By means of a central registry of transfusion reactions (TR) and incidents the transfusion chain can be monitored and weak links can be detected. The incidence of recognised transfusion reactions is tracked and hitherto undescribed reactions to existing or new blood component types can be detected in timely fashion.

TRIP Foundation (originally: Transfusion Reactions In Patients) was created in 2001 by representatives of the professional societies involved with blood transfusion. Since 2003 the TRIP Hemovigilance Office has managed a national reporting system for transfusion reactions in collaboration with contact persons in the hospitals and in Sanquin, the national blood service. Since August 2006 TRIP has also managed a national reporting system for serious adverse reactions and events associated with the clinical use of human tissues and cells (biovigilance). When this role for TRIP became permanent in 2012, the Foundation's statutes were changed so now TRIP formally stands for Transfusion and Transplantation Reactions in Patients. TRIP produces a separate annual biovigilance report, which can also be found on www.tripnet.nl under Publications, TRIP reports.

Reporting to TRIP is anonymous and is voluntary in principle; each hospital reports using a code known to the regular contact persons, the hemovigilance officer and hemovigilance employee (transfusion safety officer). The Healthcare Inspectorate however regards participation as a professional standard, as does the national CBO blood transfusion guideline (2004 and 2011 revisions). TRIP reporting is separate from a hospital's responsibility to provide care.

Nearly all reports are sent in using the online reporting system. When a reaction or incident is reported, results of relevant investigations are also requested together with an assessment of severity and imputability, i.e. the likelihood with which a reaction can be ascribed to a blood transfusion. If necessary TRIP asks the reporter for additional information or comment. By this means the TRIP physicians check all reports for coherence and verify the type of reaction for all reported serious reactions. Each year TRIP checks for duplicate reports and merges them in consultation with the reporters.

The European directive 2002/98/EC requires reporting of all serious adverse reactions and serious adverse events which could have a link with safety and/or quality of blood components. TRIP provides the analysis of these serious (grade 2 or higher) reports and prepares the annual overview for the competent authority, the Ministry of Health and the Healthcare Inspectorate (Inspectie voor de Gezondheidszorg, IGZ). Hospitals can use the TRIP reporting system to forward serious reports to the IGZ and - if necessary - to Sanquin.

The TRIP board has instated an Expert Committee which assesses all serious reports; a random selection of non-serious reports is also checked. Only after the expert assessment are the reports included in the reported data. The Expert Committee is composed of representatives of professional societies as well as a number of professionals approached because of their specific expertise; they are also members of TRIP's hemovigilance advisory board.

The effectiveness of national reporting of transfusion reactions and incidents depends on the participation of all the relevant organisations. In 2014 the number of hemovigilance contact addresses in principle was unchanged: there were 98 hospitals and four "designated" independent treatment centres which have been licensed by the Ministry to receive and administer blood components to patients.

In 2014, 89 of the 98 hospitals reported transfusion reactions and/or events and five indicated that they had no reports in the TRIP categories. Two hospitals submitted their reports after the closing date for this report. Among the four designated clinics one informed TRIP that they had not transfused any components in 2014. The three other designated clinics either did not transfuse labile blood components or received their blood components from a regular hospital that also was responsible for the reporting of transfusion reactions.

This was also the case for one small hospital. This brings the total participation in 2014 to 94/97=97%. The closing date for inclusion of submitted reports was 1 February 2015. Hospitals which had not submitted their information before the closing date have the status of non-participant in this annual report.

Additionally, the Sanquin central quality department provided information to TRIP: overviews of serious reports and figures concerning blood components which had been transfused but later were found to be positive on bacteriological screening (see section 3.2).

A total of 93 hospitals supplied figures about blood use. For the second time TRIP also asked about numbers of patients transfused because this information is also requested in the annual data submission to the European Commission. Alongside the transfused units, the number of transfused patients can also be used as a denominator for the reported transfusion reactions and events. In total, 81 facilities provided this information for each type of blood component (2013: 74).

4.2 Overview of mandatory reports of serious adverse reactions

Annually TRIP provides an overview of mandatory reports of serious adverse reactions and events. In accordance with the Common Approach drawn up by the European Commission, only reports with certain, probable or possible imputability have been included. Reactions that occurred after administration of an incorrect blood component or other incident have been included here in the relevant category. Table 25 shows the data for 2014. Figure 17 presents the number of serious reactions (grade 2 or higher) in 2008-2014. In this graph transfusion reactions that followed administration of an incorrect blood component or another incident are included in the figures for the relevant category. Reports associated with SD-plasma are also included in the table and figure to provide an overall picture, although in accordance with the legal status of SD-plasma they are reported to the pharmacovigilance system.

Table 25. Number and imputability of reports of grade 2 and higher in 2014

	Grade 2			Grade 3			Grade 4		
	Possible	Probable	Certain	Possible	Probable	Certain	Possible	Probable	Certain
Hemolytic TR	3	-	3	-	-	-	-	-	-
TACO	6	5	6	1	1	1	3	-	-
NHTR / mild NHFR	7	5	-	-	-	-	-	-	-
TRALI	2	1	-	-	1	-	-	-	-
Anafylactic TR	5	11	2	-	1	-	-	-	-
Other allergic TR	1	-	-	-	-	-	-	-	-
Post-transfusion purpura	-	-	-	-	-	-	-	1	-
Other reaction	13	3	1	-	-	-	-	-	-
Post-transfusion bacteremia / sepsis	3	-	1	-	-	-	1	-	1
Total	**40**	**25**	**13**	**1**	**3**	**1**	**4**	**1**	**1**

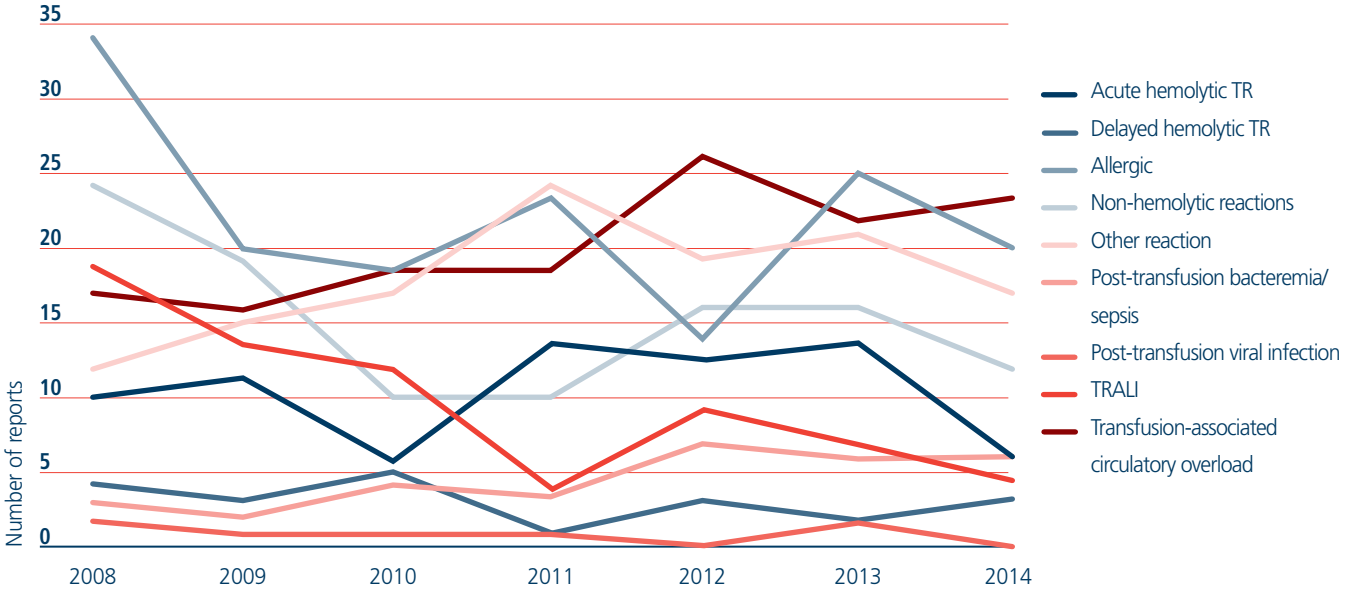

Figure 17. Serious reactions[#] of imputability certain, probable or possible, 2008-2014

[#] *PTP, new allo-antibody formation, hemosiderosis and post-transfusion other infection (total n=19) not shown. Reactions following incidents are included in the relevant category.*

* *Anaphylactic reactions + other allergic reactions*

List of terms and abbreviations

AHTR	acute hemolytic transfusion reacton
BMT	blood management techniques
Bc	blood component
CBO	CBO quality organisation in healthcare
DHTR	Delayed hemolytic transfusion reaction
EU	European Union
FFP	fresh frozen plasma
Hosp.	Hospital
IBCT	Incorrect blood component transfused
ICU	intensive care unit
IGZ	Inspectie voor de Gezondheidszorg (Dutch Healthcare Inspectorate)
Irrab	irregular antibody (formation)
Mild NHFR	mild non-hemolytic febrile reaction
NHTR	non-hemolytic transfusion reaction
OI	other incident
PAD	preoperative autologous donation
PAS	platelet additive solution
Plt	platelets
Pt	patient
Post-Tf bact/sepsis	post-transfusion bacteremia/sepsis
PTP	post-transfusion purpura
RBC	Red blood cell concentrate
Sanquin	Sanquin Blood Supply
SD	solvent detergent (a viral reduction method)
TA-GvHD	Transfusion-associated graft versus host disease
TACO	Transfusion-associated circulatory overload
TAD	Transfusion-associated dyspnea
Tf	transfusion
TR	transfusion reaction
TRALI	Transfusion-related acute lung injury
TRIP	TRIP Foundation (Transfusion and Transplantation Reactions In Patients)
TTBI	transfusion-transmitted bacterial infection
Tx	transplantation

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Hemo-en biovigilantie