TRIP annual report 2012

Hemovigilance

Extended version

TRIP
Hemo-en biovigilantie

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Extended version

The TRIP annual report 2012, extended version, concerning hemovigilance reports in the Netherlands in 2012 is published under editorial responsibility of the TRIP Foundation (Transfusion and Transplantation Reactions In Patients). The TRIP board and the TRIP Office are advised by representatives of the various professional bodies and stakeholder organisations involved in blood transfusion and in the transplantation or application of human tissues and cells.

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Hemo- en biovigilantie

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Foreword

The 2012 TRIP rapport is the tenth annual hemovigilance report about reported transfusion reactions and incidents in the transfusion chain. It shows that the number of reports has remained stable in comparison to previous years in most of the reporting categories. Ideally, after 10 years a decline should be seen. Absence of a decrease could mean that many of the recommendations in past TRIP reports have not (yet) led to implementation of measures to improve safety in the hospitals.

The recommendations in this report once again stress the importance of correct identification of patients, blood samples and blood components, as well as of accurate performance of laboratory procedures. It is also important, when an error has been discovered, to establish what led to it through a careful root cause analysis and to implement appropriate measures, which should go beyond "speaking to" the involved staff.

The TRIP office, together with the TRIP board and the members of the Expert Committee - known as the Hemovigilance advisory board since the statutes were changed in 2012 - has built the reporting system, fixed definitions and developed an electronic reporting system. In the last ten years, participation has been over 95% since 2006, but has never been 100%. All serious reports have been reviewed by transfusion experts from different hospital disciplines. The data, reported by the hospitals and Sanquin and collected in the TRIP database, provides transparency about what happens in the transfusion chain. We should continue to strive to obtain and improve this transparency. TRIP's intention is to review the reporting arrangements and redesign the online reporting tool in 2013, with the involvement of the hemovigilance advisory board, with a view to ensuring optimal usefulness of the data for purposes of safety in the transfusion chain. Where necessary, improvements in efficiency and user-friendliness of the system will be implemented,

On behalf of the TRIP board and the Office I wish to express thanks to all those who have participated in producing this hemovigilance report. I commend its learning points and recommendations to you and wish you every success in all your hemovigilance activities.

Dr. Martin R. Schipperus
President, TRIP Foundation

Executive Summary

Goals and procedures of TRIP Office (hemovigilance)

The objective of TRIP (Transfusion and Transplantation Reactions In Patients) Hemovigilance and biovigilance office is to inventory, record and report publicly on the safety of clinical use of labile blood products. Reporting is anonymous as to the patient and the treating physician. The reports are assessed by the medical staff of the TRIP office and additional questions are asked if necessary. An advisory board of transfusion experts from different disciplines reviews all serious reports and broadly checks the non-serious reports. In compliance with mandatory reporting as required under the European directives 2002/98/EC and 2005/61/EC, TRIP provides the analysis and reporting of serious adverse reactions (grade 2 or higher) and adverse events associated with blood components on behalf of the competent authority, the Healthcare Inspectorate (Inspectie voor de Gezondheidszorg, IGZ). Reporters can use the TRIP electronic reporting system to send a report to the IGZ or to the blood supply organisation, Sanquin.

Participation

In total, 97 of the 98 Dutch hospitals participated in the TRIP registration in 2012. Transfusion reactions were reported by 93 hospitals and four hospitals indicated that they did not have any transfusion reactions to report in the TRIP categories. The four "designated" institutions (independent treatment clinics which have been authorised to receive blood components and transfuse them to patients, but which do not themselves perform compatibility testing) were also requested to supply information about transfused units in 2012. One supplied this data and two indicated that blood use and reports if these ever occurred would be sent to TRIP together with data from the hospital with which they had a contract, or that there had been no transfusions in 2012. This brought the total participation to 98%. The closing date for the report was 1 February 2013.

The reports in 2012

The number of reports received in 2012 was 2502 in total (2011: 2633 including late reports). Of this total, 2218 (89%) were reports of transfusion reactions and 284 (11%) were reports of incidents in the transfusion chain. A transfusion reaction occurred and was reported as a subsidiary category in 24 incidents. Of all the reports, 2397 (96%, 90 hospitals) were submitted electronically.

Categorisation according to severity and imputability

In accordance with international practices, transfusion reactions are categorised according to severity. Of all the reactions reported in 2012 the severity was listed for 2210 (98.6%). The total number of serious reports (grade 2 or higher) was 123; since 2006 this figure has varied between 116 (2010) and 145 (2008).

The transfusion reactions were also assessed for imputability: the likelihood with which the observed signs and symptoms can be ascribed to the transfusion. Out of the 2242 transfusion reactions in 2012 the imputability was rated in 2159 reports (96.3%). A total of 1994 of these were judged to be definitely, probably or possibly related to the transfusion. Among the serious reports, 100 (81%) were judged to be of definite, probable or possible imputability, which is similar to previous years.

Types of reactions and incidents

The total number of reports in the different categories was stable in comparison to 2011 and 2010.

The numbers of reported reactions were as follows (Table 2): non-hemolytic transfusion reaction 447, mild non-hemolytic febrile reaction 377, acute hemolytic transfusion reaction 7, delayed hemolytic transfusion reaction 8, transfusion related acute lung injury (TRALI) 9, anaphylactic reaction 57, other allergic reaction 177, transfusion-associated circulatory overload (TACO) 56, post-transfusion purpura 1, post-transfusion bacteremia/sepsis 49, post-transfusion viral infection 2, other reaction 216 and new alloantibody 12. There was a trend towards a lower number of reported non-hemolytic transfusion reactions in comparison to 2011 and more reports of TACO.

The reported incidents (Table 1) include 52 reports of incorrect blood component transfused (component intended for another patient or not meeting appropriate specifications for that patient), with a subsequent clinical reaction in ten cases, three of these of grade 2 and definite, probable or possible imputability. TRIP also received 137 reports concerning other incidents, of which eight were followed by transfusion reactions (three of grade 2) and 46 reports of near misses. There were 34 reports from hospitals concerning bacterial contamination of a blood component; these concerned blood components that had already been administered and for which a positive bacterial screening result was later found by Sanquin. In four of these case a non-serious transfusion reaction was observed. One report was of improbable imputability and the other was probable. The remaining incidents were: initially positive bacterial screening 8 (in these cases, reported by the hospitals, no bacterial species was confirmed by Sanquin), look back 7.

Among the grade 4 reports (six in total), in two cases the reported reaction probably contributed to the death of the patient. The first of these cases concerned an acute hemolytic transfusion reaction following emergency administration of multiple (antibody compatible) uncrossmatched units to a patient who was previously known to have an alloantibody. The second was a case of TRALI. In the other grade 4 reports, a relation between the reaction and the patient's signs and symptoms was deemed to be at most possible but more often unlikely.

Number of reports in relation to the number of distributed and transfused blood components

In 2012 the national blood supply organisation, Sanquin, distributed a total of 624,627 blood components to the hospitals. The total number of reports about 2012 was 2502. This gives an overall rate of 4.0 reports per 1000 distributed bloed components. This is similar to the final numbers for 2011. After a number of years with little change in the numbers of distributed and transfused units, there was a declining trend in the number of distributed red blood cells in 2012 (Figure 1 on page 8). The number of units of plasma also showed a decrease in 2012.

Discussion and conclusions

Incorrect blood component transfused (IBCT)

The total number of reports of IBCT (52) was similar to 2011 (47) and was lower in those two years than it had been since 2006 (59-64). The number of reported IBCT where the patient was transfused with a unit which was ABO-incompatible or could have been ("ABO risk", 19) remained stable in comparison to 2010 and 2011, and lower than the numbers in 2008 and 2009 (the first years in which TRIP applied this risk assessment).

Administration of an incorrect blood component remains a cause of preventable morbidity for patients. The reported cases in 2012 again point at the risk of errors in identification, not only at the time of administration of blood components, but also in earlier steps of the transfusion chain. In addition, there are risks attached to incorrect performance of laboratory procedures for irregular antibody screening and for selection of antibody compatible blood components.

Other reported incidents

The analysis of near misses showed that the standard checks play an important role in the detection and correction of errors. Among the other incidents, once again there were cases where unnecessary transfusions were administered on the basis of incorrect (19) or too old laboratory results. In addition there were other incidents which led to blood components avoidably becoming unsuitable for use or being wasted. Causes for this include: fetching a blood component too early, i.e. before it is sufficiently certain that the patient needs to receive the transfusion and is ready for the procedure; failure to return a unit in timely fashion if it has become clear that the transfusion will not be given.

Infectious complications

In 2012 there was no confirmed report of viral transmission. One case of transfusion transmission of a bacterial infection (TTBI; group C hemolytic streptococci) was reported with a grade 2 reaction, caused by a platelet concentrate. In none of the other reports of possible bacterial problems associated with blood transfusion was the same bacterial species cultured in the patient's blood as in the (remnant of) the transfused unit.

Serious transfusion reactions

Among the reported serious reactions with definite, probable or possible imputability, transfusion-associated circulatory overload was the largest category in 2012 (24 reports plus two following other incidents), followed by other reaction (16 plus two reported following IBCT) and anaphylactic reaction (14 reports).

Transfusion-associated circulatory overload (TACO)

The reported cases of TACO have shown a rising trend since 2006. Sometimes the diagnosis of TRALI is considered at first but subsequently revised based on investigations. TRIP recommends that a procedure should be developed in collaboration with clinicians, so that assessment of a patient's risk factors for developing TACO can take place at the time of prescribing a blood transfusion (Figure 11). This will allow these risk factors to be taken into account when a transfusion is written up and when it is administered.

TRALI

The number of TRALI reports in 2012 was nine, which were all of definite, probable or possibility and could be verified as meeting the criteria of the TRALI case definition. The number remains lower than in the years up to and including 2007, when the male-only plasma measure was introduced.

Other reaction

The reporting category of other reaction is used for reports that do not meet the definitions for the standard categories. The number of these reports was stable. For a number of years there has been a cluster of reports where dyspnea or hypoxia was the predominant feature – TRIP is developing a separate definition for these. Currently they are (still) registered as other reaction after TRALI, TACO or other causes of dyspnea have been excluded. Appropriate investigations, which will usually include chest radiography, are necessary in order to correctly diagnose and treat these cases.

New alloantibodies

The number of reports of newly developed anti-K, anti-c and anti-E in women of child-bearing potential (aged under 45 years) at the time of transfusion shows a declining trend. This fits in with increased implementation the preventive policy of selecting not only Kell negative or compatible but also Rhesus phenotype compatible red blood cells in this patient group, as recommended in the 2011 revision of the national "CBO" Blood Transfusion Guideline.

Transfusions and reported reactions and incidents in patients under 21 years of age

The Dutch data for 2012, like that in 2011, shows a higher incidence of allergic reactions and of febrile reactions in patients under 21 in comparison to older patients. However the calculations are based on a small number of reports and the data are not homogenous. TRIP is in contact with international groups with a view to collaborating on hemovigilance and definitions for specific categories for (very) young patients.

Autologous blood management techniques

The number of reports relating to the use of drain blood for reinfusion was similar to 2011. It is likely that there is still under-reporting since quite a few hemovigilance officers and blood transfusion committees are unable to obtain information on the volume of practice of these techniques in their hospitals.

Other conclusions and recommendations

In general the reporting shows a stable picture in comparison to 2011. The safety level of blood components in The Netherlands remains high. In consultation with the members of the hemovigilance advisory board, TRIP will focus on optimizing the application of the collected data in improving the safety of blood transfusion.

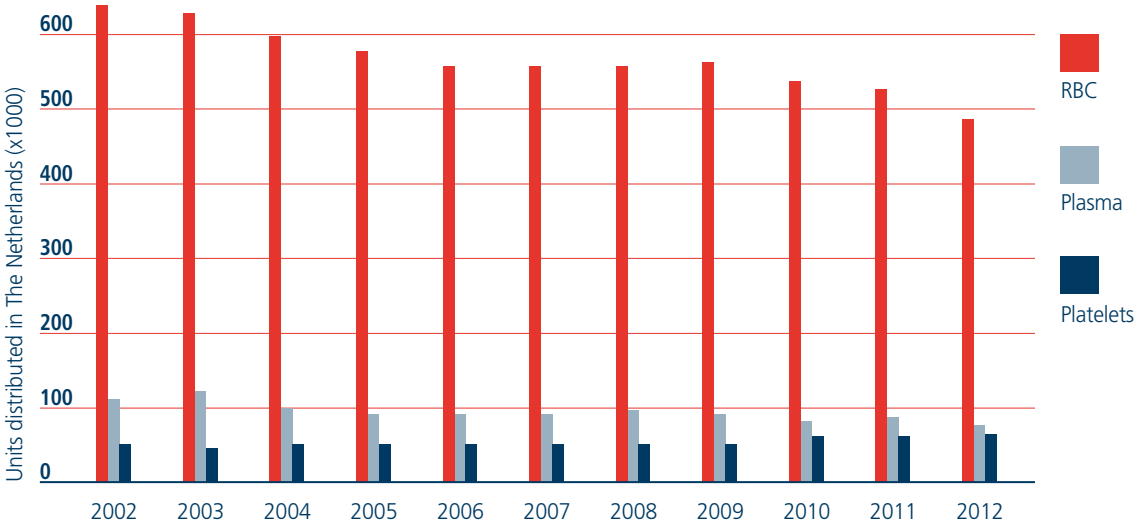


Figure 1 Distributed units of labile blood products from year to year

(Data supplied by Sanquin for TRIP annual reports)

1. Introduction

TRIP working method

Through centralised data collection about transfusion reactions (TR) and incidents it is possible to monitor the transfusion chain and discover weak areas (links) where errors or problems are prone to occur. The incidence of known types of adverse reaction can be tracked and previously unknown complications of current or new blood component types can be detected in a timely manner.

TRIP (Transfusion Reactions In Patients) Foundation was founded in 2001 by representatives of the various professional organisations involved in the field of blood transfusion. Since 2003, the TRIP National Hemovigilance Office has also operated a national reporting system for transfusion reactions in collaboration with contact persons in the hospitals and the blood establishment, Sanquin Blood Supply. Since 2006, TRIP has also operated a national reporting system for serious adverse reactions and/or serious adverse events in the "chain" of the application of human tissues and cells. In 2012, when it was acknowledged by the Ministry of Health that this should be a regular task for TRIP, the statutes were renewed and TRIP is now known as the TRIP (Transfusion and Transplantation Reactions in Patients) Foundation. Findings of tissue and cell vigilance are reported in separate reports, available on www.tripnet.nl.

Reporting to TRIP is anonymous and is voluntary in principle. However, reporting to TRIP is considered the norm by the Healthcare Inspectorate (Inspectie voor de Gezondheidszorg, IGZ) and the CBO Guidelines for Blood Transfusion (2004 and 2011 versions). Digital reporting has been available since 2006 and is now used by nearly all the hospitals. Reporting to TRIP is separate from an institution's responsibility to provide medical care for the patient.

Reported reactions or incidents should be accompanied by relevant findings of investigations and an assessment of the degree of severity of the clinical symptoms is requested. An assessment is also given of the imputability, the degree of likelihood with which a reaction can be attributed to a blood transfusion. If necessary, TRIP will ask the reporting party for further explanations or additional data. This allows the TRIP physicians to assess the coherence of the reports and to verify the reported category of (potentially) serious reports.

Under the requirements of European directive 2002/98/EC, there is an obligation to report serious adverse reactions and adverse events that may be associated with the quality and/or safety of blood components. TRIP provides the analysis and reporting of these serious (grade 2 or higher) reports on behalf of the competent authority, the Ministry of Health and IGZ. The reporting party remains responsible for submitting the report to the IGZ. Since the end of 2008 it has been possible to make serious reports directly available to the IGZ and where relevant to Sanquin Blood Supply using the TRIP online reporting system.

An Expert Committee appointed by the TRIP Governing Board assesses all submitted serious reports and a sample of non-serious reports. Definitive inclusion in the TRIP report is subsequent to approval by the Expert Committee. Since the renewal of the statutes and governance structure, the members of the (former) Expert Committee, and representatives of professional societies from the domain of blood transfusion together assume this role in the Hemovigilance Advisory Board.

2. Hemovigilance reports in 2012

2.1 Participation

The value of national registration and reporting about transfusion reactions and incidents depends on the participation of all the hospitals and other involved institutions. The number of contact addresses went from 100 to 98 in 2012 through one merger, cessation of blood transfusion activity by two specialty hospitals (these hospitals offer a limited range of services) and an agreement by two hospitals, which previously contracted out their hemovigilance work to an external laboratory organisation providing their blood transfusion laboratory services, to report separately. In 2012, 93 of the 98 hospitals reported transfusion reactions and four hospitals indicated that there were no transfusion reactions in the TRIP categories to report. Data about blood use were received from 95 institutions. The closing date for reports about 2012 to be included in this report was 1 February 2013. Hospitals which did not send in their information before the closing date, have the status of non-participant in this report.

Blood transfusions can be given in hospitals, but also in independent treatment centres (clinics) which have been "designated" for this by the Ministry of Health. The four clinics designated by the Ministry are authorised to receive blood components and to administer them to patients, but do not themselves perform compatibility testing. These institutions were approached by TRIP for the first time for information about the number of transfused units. One supplied this information, and two informed TRIP that their blood use and any reports had been included with the information submitted by the hospital which was contracted to issue blood components, or that no transfusions had been performed in 2013. This brings the overall participation level to 98%.

Additionally, Sanquin's central departments made summary data available to TRIP on serious reports and on administered blood components for which positive bacterial screen results were subsequently obtained (see section 3.2). Annually, TRIP checks on double reports and merges these in consultation with the reporters.

After the closing date for the 2011 report, 32 late submissions (1.2% of the final total) were received for 2011. The advisory board has since formally assessed these reports. One mild non-hemolytic febrile reaction and a report of incorrect blood component transfused which was associated with an acute hemolytic transfusion reaction were assessed as severity grade 2. Late information from previous years has been incorporated in the figures and tables of this report.

2.2 Summary of data regarding the reports for 2012

Readers can find all definitions used at www.tripnet.nl.

Reports received

In total, 2502 reports of transfusion reactions and of incidents in the transfusion chain were received in 2012, which represents a 5% reduction in comparison to the 2011 reports (including those received after the closing date). The reports were submitted by 93 hospitals. Out of the total, 2398 were submitted electronically (96%, 90 hospitals).

Following assessment by the TRIP staff a number of complex cases (approximately 35) were discussed in a joint meeting of members of the hemovigilance advisory board with reporters from the hospitals. All remaining serious reports were subsequently also assessed by members of the advisory board, who also reviewed summary data of non-serious reports. In consultation with the advisory board, the data in this report have been presented in tabular fashion as far as possible, presenting trends from year to year.

Table 1 Incidents per reporting category, 2006–2012

Incident	2006	2007	2008	2009	2010	2011	2012	No. of hospitals with reports in 2012	No. of hospitals with reports ever
Incorrect bc transfused	64	64	59	61	59	47	52	33	73
Near miss	77	74	55	72	70	45	46*	18	51
Other incident	86	100	83	111	118	138	137*	30	70
Look-back (info reported by hospital to TRIP)	1	4	9	7	52	30	7	7	32
Viral contamination of bc	2	0	2	1	4	0	0	-	4
Positive bacterial screen[$]	27	29	2	4	5	6	8	20	51
Bacterial contamination of bc[$]	-	5	23	22	41	37	34		
Hemolysed product	-	-	-	-	-	2	-	-	2
Total no. of incidents	**257**	**276**	**233**	**278**	**349**	**303**	**284**	**54**	**90**

* *Correction after print of short TRIP report: one report was modified from near miss to other incident after expert assessment.*

[$] *In these cases no bacterial species was confirmed. Cases where confirmatory culturing was positive are reported as bacterial contamination of blood component.*

Abbreviation: *bc = blood component*

Table 2 General overview of transfusion reactions per category, 2006–2012

Reaction	2006	2007	2008	2009	2010	2011	2012	Number of grade 2 or higher[#]	Number of hospitals with reports in 2012
NHTR	490	452	453	488	506	504	447	10	81
Mild febrile reaction	363	328	275	360	363	366	377	6	70
AHTR	19	11	18	18	21	16	7	3	6
DHTR	14	11	18	8	7	9	8	1	6
TRALI	25	31	21	13	17	12	9	9	5
Anaphylactic reaction	19	54	65	71	73	65	57	14	24
Other allergic reaction	222	202	171	181	184	191	177	1	48
TACO	34	31	39	42	47	39	56	24	32
Post-transfusion purpura	0	0	1	0	0	2	1	0	1
TA-GVHD	0	0	1	0	0	0	0	0	-
Hemosiderosis	5	3	5	2	4	2	0	0	-
New alloantibody formation	607	602	610	757	814	831	812	2	65
Other reaction	61	55	101	136	164	217	216	16	60
Post-tf bacteremia/sepsis[§]	7	19	37	55	41	61	49	7	37
Post-tf viral infection	7	7	7	3	1	5	2	0	1
Post-tf malaria	0	0	0	0	0	1	0	0	-
Total transfusion	**1873**	**1806**	**1822**	**2134**	**2242**	**2321**	**2218**	**93**	**93**
Total grade 2 or higher[#]*	108	103	131	102	93	102	100	100	
Total reports*	**2130**	**2082**	**2055**	**2412**	**2591**	**2628**	**2502**	**93**	**93**

[#] *imputability definite, probable, possible*

[§] *up to and including 2007: bacterial contamination*

* *Total number including reactions following incidents*

Abbreviations: *NHTR = non-hemolytic transfusion reaction; AHTR = acute hemolytic transfusion reaction; DHTR = delayed hemolytic transfusion reaction; TRALI = transfusion-related acute lung injury; TA-GVHD = transfusion-associated graft versus host disease; tf = transfusion*

Tables 1 and 2 show the numbers of reports per category in the years 2006 to 2012. The incidents are presented first because they can potentially be avoided. Transfusion reactions following incidents (24 in total) are discussed separately in the paragraphs about incidents in chapter 3.1 and are not included in Table 2.

Severity and imputability of the 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

International usage is to categorise transfusion reactions as to their grade of severity. The definition of severity relates to clinical symptoms observed in the patient and is only meaningful for transfusion reactions. The total number was 2242 transfusion reactions, i.e. the reports in the categories of transfusion reaction (2218) plus the 24 reactions that occurred following incidents. The grade 4 reports are discussed further in chapter 3.5.

Figure 2 shows the severity of the reported transfusion reactions from 2006 to 2012. The total number of serious reactions (grades 2, 3 and 4) was 123; the number has varied from 114 to 145 since 2006.

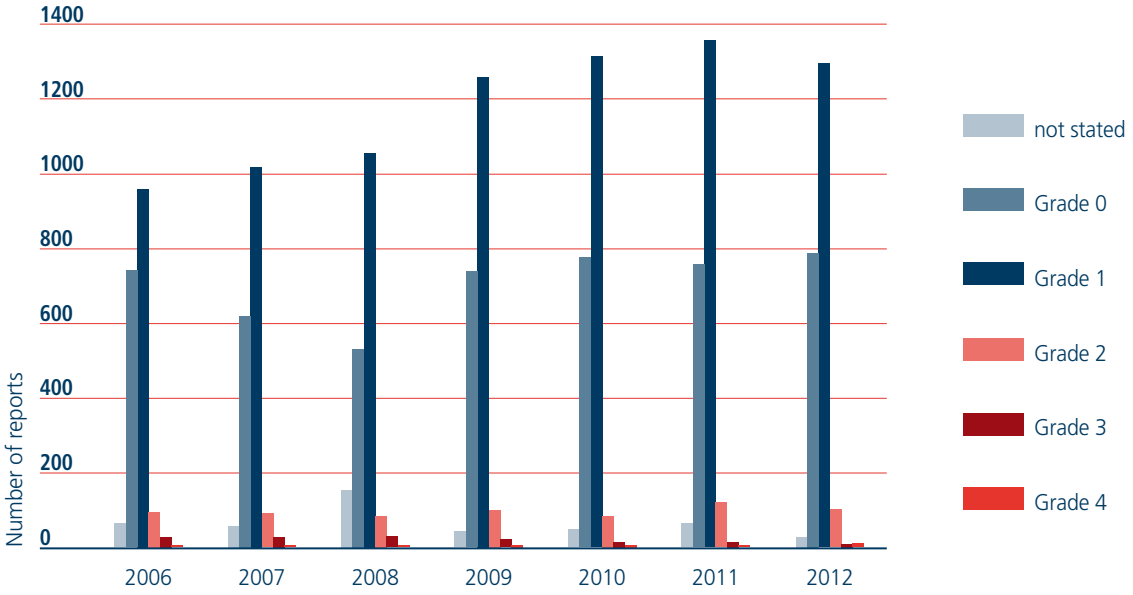


Figure 2 Severity of the transfusion reactions, 2006 – 2012

Relationship to the blood transfusion (imputability)

Imputability	*Definition (Imputability is applicable to transfusion reactions)*	
Certain	*clinical symptoms present, and*	• *clear course of events, temporally related to the transfusion, and* • *confirmed by laboratory findings, and* • *other causes excluded*
Probable	*clinical symptoms present, but*	• *no clear course of events or not temporally related to the transfusion, or* • *not confirmed by laboratory findings, or* • *other possible cause present*
Possible	*clinical symptoms present, but*	• *not temporally related to the transfusion, and* • *not confirmed by laboratory findings, and* • *other possible cause present*
Unlikely	*clinical symptoms present, but*	• *not temporally related to the transfusion, and* • *not confirmed by laboratory findings, and* • *another more probable explanation present*
Excluded	*clearly demonstrable other cause*	

The reports were also categorised according to imputability, the degree of likelihood with which the reaction can be ascribed to the transfusion. The rating of imputability, like severity, is only relevant if the patient experienced a reaction. Figure 3 shows the imputability of the 2242 transfusion reactions in 2012 in comparison to previous years. Of the 123 transfusion reactions which were of grade 2 or higher, 100 were of certain, probable or possible imputability (2011: also 100).

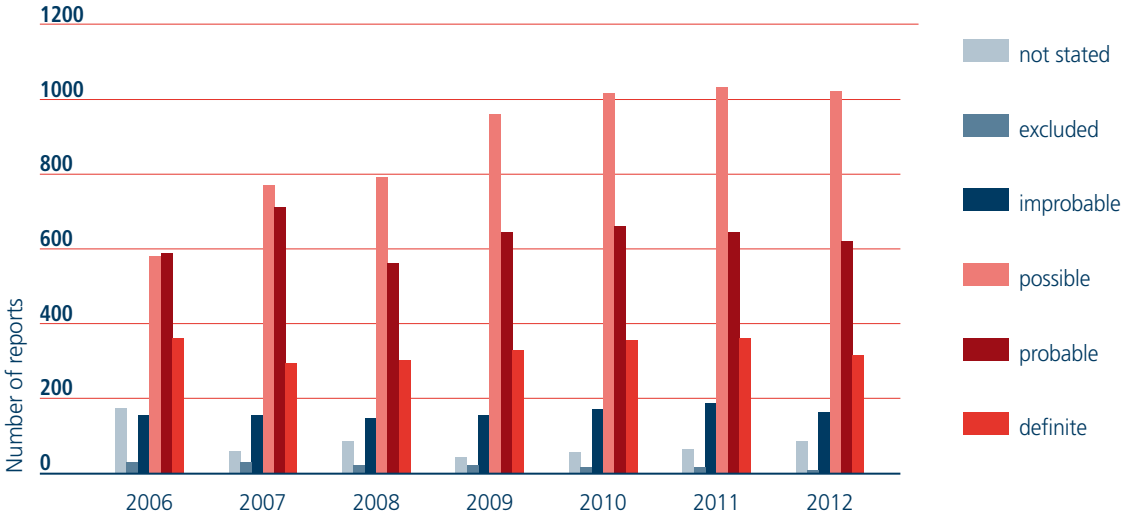


Figure 3 Imputability of the transfusion reactions, 2006 – 2012

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

In 2010, Sanquin supplied hospitals with a total of 624,647 blood components; this number does not include special components like lymphocytes and granulocytes. The total number of reports for 2012 was 2502. Using the total number of distributed blood components as a denominator, that makes 4.0 reports per 1000 blood components distributed nationally, or 3.95 after exclusion of the reports relating to autologous blood management techniques (see paragraph 3.4).

After a number of years with only slight change in the numbers of distributed red blood cell units, there was a decline in the distribution of red blood cell concentrates in 2012 (Figure 1 on page 8). Table 3 shows the relationship between distributed blood components and the number of reports.

Table 3 Number of reports per type of blood component in comparison to 2010 and 2011

Type of blood component (bc)	2012					2011		2010	
	Number of bc supplied	Number of reports		Reports per 1000 bc		Reports per 1000 bc		Reports per 1000 bc	
		All	Serious#	All	Serious#	All	Serious#	All	Serious#
Red blood cell concentrate	486,711	1986	70	4.08	0.14	3.78	0.12	3.57	0.10
Platelet concentrate	61,978	268	12	4.32	0.19	5.77	0.29	5.81	0.33
Fresh frozen plasma	75,958	95	5	1.25	0.07	0.94	0.13	1.00	0.08
Cell-saver and drain blood[1]	-	50	4						
SD plasma	-	1[2]	0						
Other products	-	1[3]	0						
Combinations	-	64	8						
Not stated	-	37	1						
Total	624,647	2502	100	3.99	0.16	3.88	0.15	3.73	0.14

Imputability certain, probable, possible

[1] *2012: drain blood only*

[2] *In one case among the combinations SD-plasma had been administered as well as FFP, RBC and platelets*

[3] *Unit for intrauterine transfusion*

Abbreviations: *SD plasma=solvent detergent plasma*

Table 4 Distribution of types of blood components per category of report* in 2012

A. Incident	RBCs	Platelets	Plasma	Combination	Other#	Not stated
Incorrect blood component transfused	41	5	3	3	-	-
	79%	10%	6%	6%		
Other incident	108	10	7	2	5	5
	79%	7%	5%	1%	4%	4%
Near miss	16	3	-	-	-	27
	35 %	7%				59%
Bacterially contaminated blood component	5	28	-	-	-	1
	15%	82%				3%
Virally infected component	5	1	1	-	-	-
	71%	14%	14%			
B. Reaction						
Non-hemolytic transfusion reaction	370	44	5	4	24	-
	83%	10%	1%	1%	5%	
Mild non-hemolytic febrile reaction	350	16	4	3	4	1
	93%	4%	1%	1 %	1%	0%
Acute hemolytic transfusion reaction	6	-	-	-	-	1
	86%					14%
Delayed hemolytic transfusion reaction	8	-	-	-	-	-
	100 %					
TRALI	7	2	-	-	-	-
	78%	22%				
Anaphylactic reaction	9	23	20	5	-	-
	16%	40%	35%	9%		
Other allergic reaction	35	81	50	10	-	1
	20%	46%	28%	6%		1%
Circulatory overload	49	2	1	4	-	-
	88%	4%	2%	7%		
New alloantibody	763	24	-	23	-	2
	94%	3%		3%		0%
Other reaction	164	21	5	8	17	1
	76%	10%	2%	4%	8%	0%
Post-transfusion bacteremia / sepsis	45	2	-	1	1	-
	92%	4%		2%	2%	

* *Smallest categories not shown*

\# *Cases involving drain blood with the exception of one report (an other incident) which concerned a unit for intra-uterine transfusion*

% Percentage of reports in that incident/reaction category

2.3 Incidents and transfusion reactions per age group and sex

Table 5 shows the number of reports per age group and sex for each type of incident or reaction report.

Table 5 Distribution of age groups of patients category of report* in 2012

A. Incidents	<1y		1-20		20-60		60-80		>80y		Not stated or N/A[1]
	M	F	M	F	M	F		FV	M	F	
Incorrect blood component transfused	3	-	-	2	6	8	17	8	3	5	-
Other incident	2	1	1	-	13	17	34	32	10	21	6
Near miss	-	1	-	1	4	6	10	3	3	3	15
Bacterially contaminated blood	-	1	1	-	9	10	7	4	1	1	-
Look-back	-	-	-	-	-	1	3	1	-	2	-
Total (incidents)*	**5**	**3**	**2**	**3**	**33**	**42**	**73**	**49**	**17**	**32**	**25**
% of incidents per age group	3%		2%		29%		47%		19%		
B. Incidents											
Non-hemolytic transfusion reaction	-	-	18	9	50	70	136	91	32	41	-
Mild non-hemolytic febrile reaction	2	-	12	6	36	50	113	75	41	42	-
Acute hemolytic transfusion reaction	-	-	-	-	-	1	1	4	1	-	-
Delayed hemolytic transfusion reaction	-	-	-	-	-	3	1	1	-	3	-
TRALI	-	-	-	1	3	2	2	1	-	-	-
Anaphylactic reaction	1	1	7	5	6	13	14	5	2	3	-
Other allergic reaction	-	1	24	13	44	43	26	13	6	7	-
Circulatory overload	-	-	2	-	5	4	17	9	5	14	-
New alloantibody	-	1	3	5	64	137	192	234	66	108	2
Other reaction	-	2	3	2	20	30	67	49	19	24	-
Post-transfusion bacteremia / sepsis	-	-	-	3	7	4	20	8	5	2	-
Total (reactions)*	**3**	**5**	**69**	**44**	**235**	**358**	**589**	**492**	**177**	**244**	**2**
% of reactions per age group	0.5%		5%		27%		49%		19%		

* *Smallest categories not shown but included in totals*

[1] *Patient age and/or gender not stated or not applicable*

3. Discussion of reports by categories

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.

- 48 IBCT reports and 4 calculated risk reports received from 33 hospitals
- range 1-5 reports per hospital
- 10x reaction observed in the recipient during / after administration, of which 7 considered avoidable
- 5 reports (10%) relate to patients less than 20 years of age, 3 of them < 1 year
- 8 reports (16%) relate to patients older than 80 years of age, 2 of these reports involving calculated risk.

Table 6 shows the classification of the reported IBCT according to risk, i.e. what might have happened. For example ABO risk means that a unit was administered which could have been ABO incompatible. If an error leads to the patient receiving a unit intended for another patient, then this may be ABO incompatible. Fortunately in such incidents, blood groups of donor and patient are often by chance compatible. The description of risks that are used in this risk classification can be found on www.tripnet.nl. In four reports a calculated risk was taken in an emergency situation. The hospitals reported these occurrences to highlight the potential consequences. They have not been included in the analyses of errors in this chapter because there was no error.

Table 6. Classification according to risk, IBCT 2008 – 2012

Risk type	2008	2009	2010	2011	2012	Total
ABO	26	31	16	18	19	110
Irregular antibody	10	10	10	9	17	56
Preventive selection policy:						
• Irregular antibody	10	7	12	4	3	36
• B19	2	3	4	2	2	13
TA-GVHD	7	4	13	6	6	36
Other	4	4	3	4	1	16
Calculated risk		2	1	4	4	11
Total IBCT	**59**	**61**	**59**	**47**	**52**	**278**

Abbreviation: *TA-GVHD= transfusion-associated graft versus host disease*

Table 7 shows a summary of all IBCT reports in which also a reaction in the patient has been observed. In addition to the errors leading to ABO risk, those with risk from irregular antibodies regularly lead to a serious transfusion reaction. Not always a relationship between the reaction and the error was made plausible. Imputability generally refers to the likelihood with which the reaction can be attributed to the product. When a febrile reaction occurs upon administration of a erroneously not irradiated component, then it is to be expected that this reaction could also have occurred if the component had been irradiated. Nine of the ten reactions were rated with imputability possible or higher. Based on the observed symptoms and results of further investigations it can be concluded that in seven cases it is plausible that the reaction would not have occurred if there had not been a mistake.

Table 7. Clinical symptoms after incorrect blood component transfused 2012

Risk type	Blood component	Reaction	Imputability*	Severity*
AB0	RBC	Acute hemolytic transfusion reaction	certain	1
	RBC	Delayed hemolytic transfusion reaction	certain	2
	RBC	Other reaction	probable	1
Irregular antibody	RBC	Delayed hemolytic transfusion reaction	probable	2
	RBC	Delayed hemolytic transfusion reaction	certain	2
	platelets	Non-hemolytic transfusion reaction	certain	1
	combination	Other reaction	unlikely	2
Preventive selection policy	RBC	New alloantibody	probable	0
TA-GVHD	RBC	Non-hemolytic transfusion reaction	possible	1
Calculated risk	RBC	Other reaction	possible	1

** imputability and severity relate to the transfusion reaction*

Abbreviation: *TA-GVHD= transfusion-associated graft versus host disease*

With IBCT reports the goal is to grasp what went wrong and how errors can be prevented. Figure 4 shows the nature of the first error in IBCT reports 2012, which step of the transfusion chain errors were made in and what hazard there was for the patient. Failure of correct identification as first error at administration of a blood product (i.e. at the step of transfusion) was an important, but certainly not the only, first error leading to IBCT with ABO risk. In IBCTs leading to exposure of the patient to possible hazards from irregular antibodies most first errors were made in laboratory procedures concerning antibody screening (n=6) and selection of antibody compatible blood components (n=3). Faulty communication was also a factor in reports with risk due to irregulair antibodies (n=2) and this was the most common error in reports with TA-GVHD risk (n=3) through administration of erroneously not irradiated blood components.

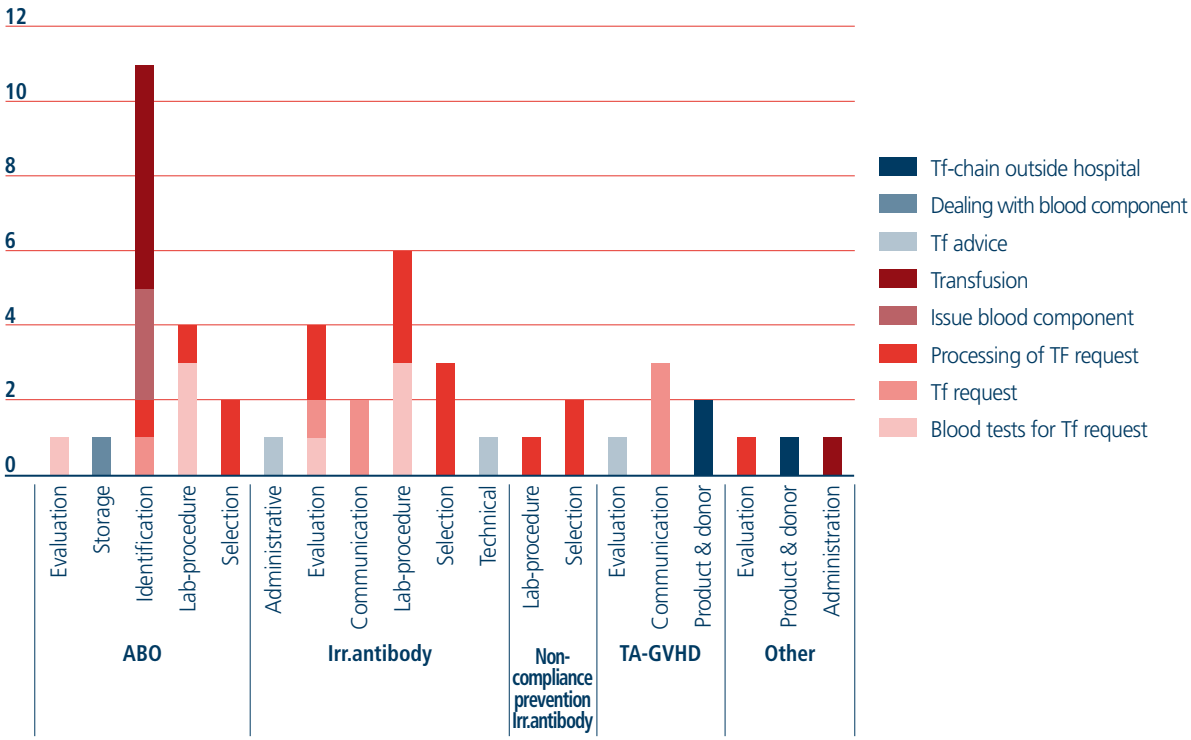


Figure 4 IBCT 2012: Step in the Tf chain where 1st error was made and type of error according to risk

Abbreviations: *Tf=transfusion; Irr=irregular; TA-GVHD= transfusion-associated graft versus host disease*

How often did errors giving rise to a situation with ABO or irregulair antibody risk actually lead to transfusion of an incompatible blood component? Figure 5 shows the answer.

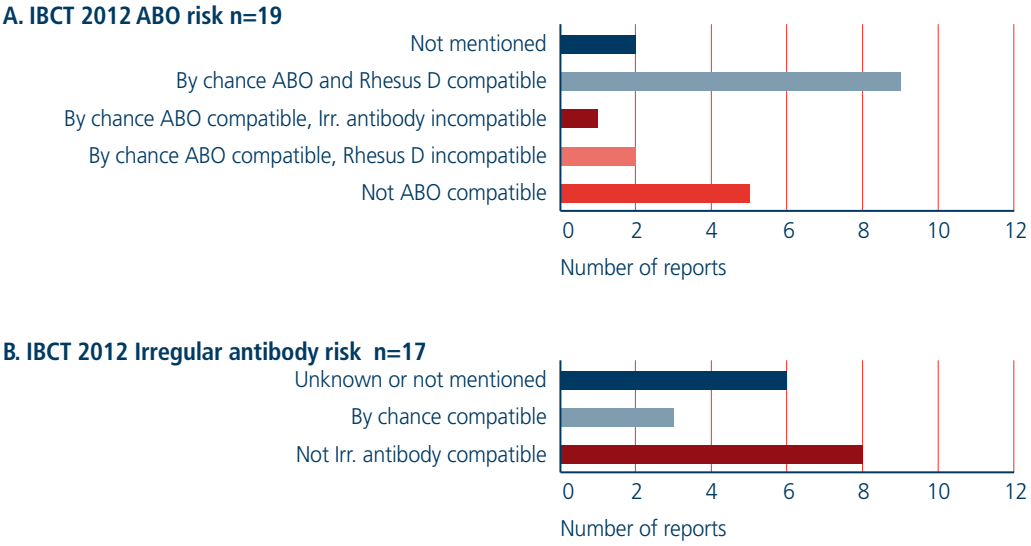


Figure 5 Compatibility of the administered blood component

Abbreviations: *IBCT=incorrect blood component transfused; Irr=irregular*

In five reports IBCT is recorded as an additional category to highlight a reaction or other incident where subsequent actions revealed that (in the past) a blood product had been transfused that did not fulfil all the requirements of a suitable component for that patient (Table 8).

Table 8. Reports 2012 with additional category IBCT

Blood component	Report category	Risk type (additional category)	Description	Number
RBC	new allo antibody	preventive policy	specific requirements not met	2
	mild non-hemolytic TR	contamination	punctured bag sealed with tape	1
	other incident	contamination	cold chain error	2

Abbreviations: *IBCT= Incorrect blood component transfused; TR=transfusion reaction*

Was there a mix-up?

Figure 6 shows an overview of reports IBCT (n=13) and near miss (n=28) in which there was a patient misidentification or a mix-up of blood tubes, laboratory results, forms or blood bags. The figure shows that the mix-ups that were not detected in time, the IBCTs (red in the figure), relate to mix-up of patients (n=9), mostly at the step transfusion, or mix-up of blood bags in the step of processing the request or of issuing the blood component (n=4). Almost all the first errors were identification errors.

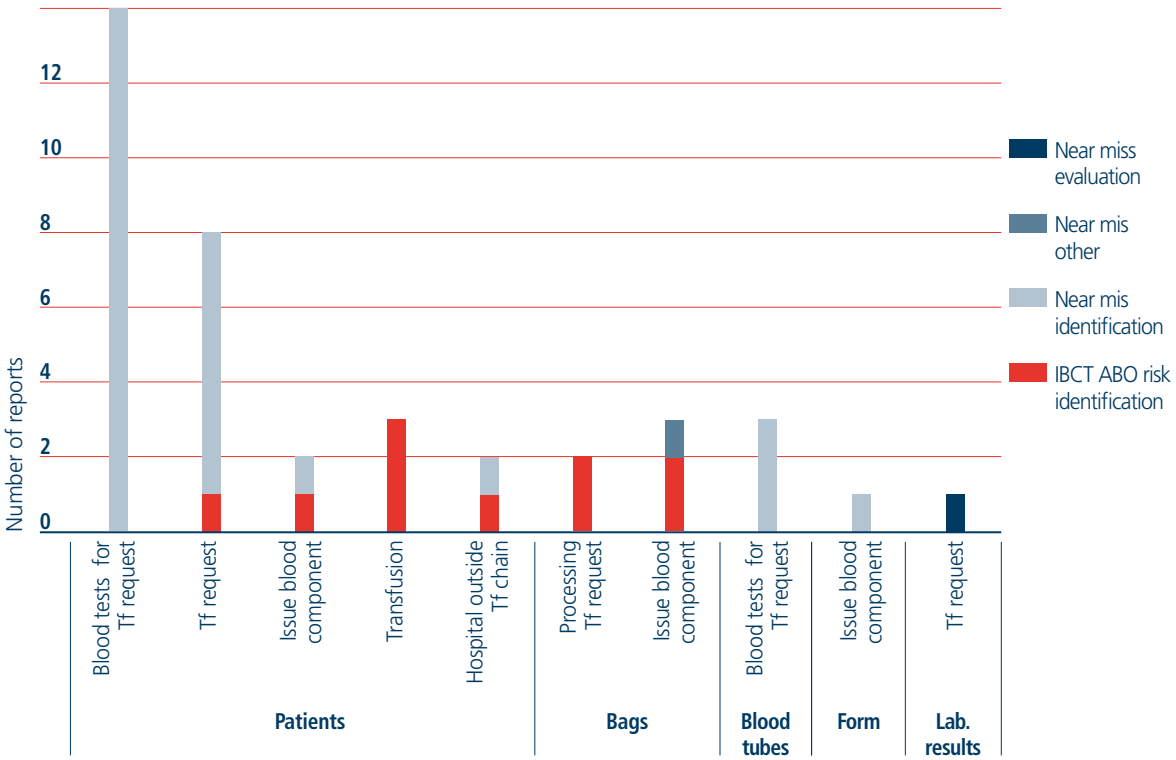


Figure 6 Step of the Tf chain and type of 1st error in IBCT and near miss where a mix-up occurred in 2012
Abbreviations: *IBCT=Incorrect blood component transfused; Tf=transfusion*

IBCT conclusions

Since 2010 the number of IBCT with ABO risk has looked lower. Is this a sign of increased safety of the transfusion chain? Additional analyses are needed to answer this question. At present the reporting of the errors and failures in order to point out the weak links in the chain have the priority.

The reports in 2012 once again point at the hazard of identification errors, not only at the time of administration of the blood component but also in earlier steps of the transfusion chain. Moreover there are risks from not correctly carrying out laboratory procedures relating to irregular antibody screening and selection of antibody compatible blood components.

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.

- 46 near miss reports received from 18 hospitals
- Range 1 - 15 reports per hospital
- In 34 out of 46 cases the incident was noticed through a planned check or investigation
- Nearly 80% of the near miss reports related to identification errors (n=36)

Figure 7 shows an overview of the way in which the reported near misses were detected. Bedside identity check detected an error in (only) two cases. Six reports did not state how the error was detected.

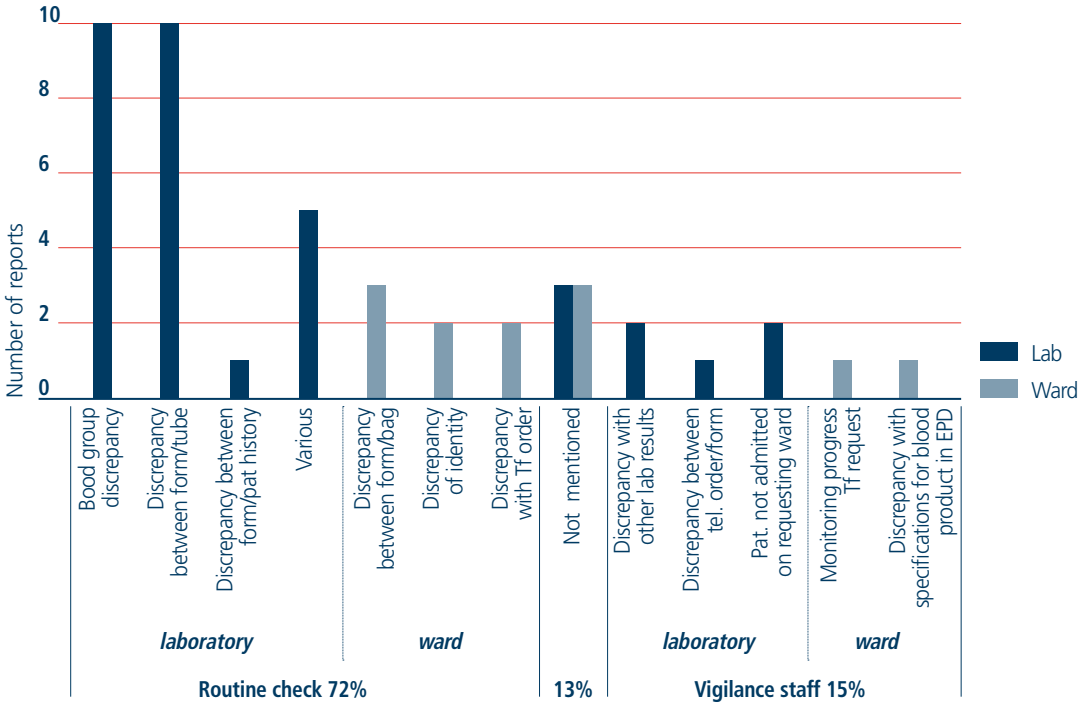


Figure 7 Mode of detection of near misses in 2012

Abbreviations: *pat=patient; tel=telephone; Tf=transfusion; EPD=electronic patient dossier*

Other incident

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.

- 137 other incident reports received from 30 hospitals
- Range 1 - 36 reports per hospital
- 9x reaction observed in the recipient during/after administration (Table 9)
- 83 of these reports relate to unnecessary transfusion (n=17) and/or wastage of blood components
- 8x near unnecessary transfusion was reported
- 19 of the remaining 46 reports relate to unnecessary delay of a transfusion
- Other incident was also recorded 26x as additional category, mostly because of failure to report a reaction, or reporting a reaction too late, or incompletely to the laboratory (Table 10)

Table 9. Clinical symptoms with or after an other incident 2012

Type of other incident#	Reaction	Total#	Imputability*	Severity grade*				
				0	1	2	3	4
Unnecessary transfusion	Circulatory overload	2	Certain			2		
	Mild NHFR	1	Probable		1			
Problem with IV line	Other reaction (large hematoma due to drip running subcutaneously)	3	Certain		2	1		
Reaction not reported to BTL	Mild NHFR	2	Possible		2			
Miscellaneous	NHTR	1	Possible		1			

All cases relate to RBC transfusion

* *Imputability and severity grade relate to the transfusion reaction*

Abbreviations: *BTL=blood transfusion laboratory; NHTR=non-hemolytic transfusion reaction; mild NHFR=mild non-hemolytic febrile reaction*

More than 50% of the hospitals that reported one or more other incidents, reported a case of (near) unnecessary transfusion. Blood sampling errors and errors of assessment/judgement were the most frequent errors in these cases. Strikingly no unnecessary transfusion was attributed to an identification error. Among the 137 reports of other incident 66 reports relate to wastage of one or more blood components, in 49 cases the wastage was regarded as avoidable.

As in 2011, reports were broken down according to whether unnecessary transfusion and wastage of blood components occurred and TRIP assessment whether the wastage of blood could have been avoided by timely detection of and response to the first error or failure. The avoidable cases of wastage of blood components were for a large part (42%) attributable to storage errors: blood units became unsuitable for transfusion because of exceeding the maximum time outside controlled storage conditions, e.g. because ward staff forgot to administer the unit or the unit was not returned to the laboratory on time in cases where there was no longer an indication for transfusion (Figure 8).

Delayed transfusion was mostly attributable to communication errors and failures like incorrect form filling or unclear arrangements about request or administration of blood components. However it should be noted that reports of delayed transfusion were received from only a small number of hospitals.

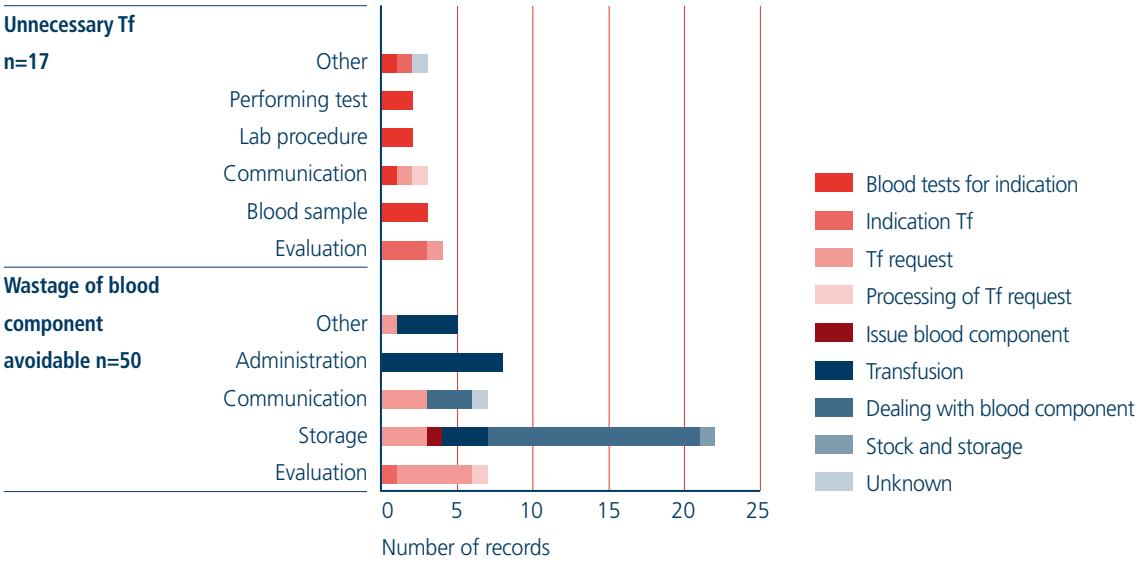


Figure 8 Other incident 2012 associated with unnecessary transfusion and/or avoidable wastage of blood products: type of 1st error and step of the transfusion chain

Two recommendations result from the other incident reports in 2012. Firstly unnecessary transfusions turn out to be based on incorrect/unreliable lab results in 50% (n=8) and outdated or untested increment results following a transfusion in 38% (n=6) of the cases: extra attention is required when determining that a transfusion is necessary. Secondly blood components are avoidably wasted. Causes for this include: prematurely collecting a blood unit, i.e. before it is definite that the patient can and may receive the transfusion, and not returning a blood unit or not returning it on time if the transfusion cannot (yet) be started after all. Compliance with the requirements in the hospital transfusion protocol can reduce this avoidable wastage. Moreover, it is important to evaluate the standard conditions (including the 30 minute criterion set in the 2011 CBO national transfusion guideline) for returning a blood component into stock.

Table 10. Other incident as additional category in 2012

Blood component	Reporting category	Type of other incident (additional category)	Description	Aantal
RBCs and plasma	Circulatory overload	Unnecessary transfusion	Tf on suspicion of major blood loss, retrospective analysis found no indication for 2 RBCs and 1 FFP.	1
RBCs	DHTR		The transfusion following which antibodies were formed was not indicated in retrospect.	1
RBCs	Circulatory overload	Incorrect administration of Tf	IV setting too fast.	1
2x RBCs	NHTR	Wastage of blood component	Next RBC started in error, discontinued following discussion with doctor.	1
	Near miss		Issue of RBC intended for another patient with the same name, unit not returned to BTL in time.	1
15x RBCs 4x drain blood	NHTR (n=5) Mild NHFR (n=8) Circulatory overload (n=3) Post-Tf bacteremia/sepsis* Other reaction (n=2)	Not reported /delay in reporting to BTL	No or only partial investigation of TR performed.	19
2x RBCs	Other allergic reaction Other reaction	Incomplete report to BTL	Missing data vital signs. Missing time TR and time discontinuation Tf.	1 1

Abbreviations: *TR=transfusion reaction; BTL=blood transfusion laboratory; Tf=transfusion; NHTR=non-hemolytic transfusion reaction; mild NHFR=mild non-hemolytic febrile reaction; DHTR=delayed hemolytic transfusion reaction; RBC=red blood cell concentrate; FFP=fresh frozen plasma*

* *Further information in section on post-transfusion bacteremia/sepsis*

3.2 Infectious transfusion complications

Post-transfusion viral infection and viral contamination of the 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.

In 2012 two reports of post-transfusion viral infection were submitted. When such cases are reported to the blood establishment, Sanquin, if they concern viruses for which each donation is tested the donors of all units transfused to the patient are traced and investigated (this is called a "traceback" investigation). In one of the reports (involving HIV) more than 50 blood components had been administered to the recipient in The Netherlands and abroad. The investigations established that the infection could not have been transmitted by a Dutch donor. The second report was of post-transfusion hepatitis C, several years after transfusion; further testing of the donors was performed and showed that the infection had not been transmitted by the transfused blood components.

Table 11 gives an overview of all reports of viral infections in patients (possibly transmitted by transfusion) from 2002 up to and including 2012.

Table 11 Viral reports to TRIP, 2002 – 2012

Virus	Post-transfusion viral infection* total	Number probable or certain	Number possible	Comment
Hepatitis B	15	7[#]	3[#]	[#]Donations in 1991, 1993, 2006-2008, infections detected through look-back investigations by Sanquin
Hepatitis C	9	0	3[$]	[$]"Old" infections reported in 2005
HAV	1	0	0	Report in 2006, Tf in 2003, no investigation by Sanquin
B19	2[+]	1	1	[+]Components not B19-safe; no investigation
CMV	12	2	5	Not confirmed; components not requested as CMV-safe and/or other source of infection likely
EBV	6	0	1[§]	[§]Report in 2003, other source possible, long interval
HIV	2	0	1[¶]	[¶]Report from 2003, unconfirmed
HTLV	0	0	0	

** Prior to 2008 : Viral infection*

Abbreviations: *B19=Parvovirus B19; CMV=cytomegalovirus; EBV=Epstein Barr virus; HIV=human T-cell lymphotropic virus*

Bacterial problems in relation to blood transfusion

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 in the approved way with laboratory techniques, preferably including typing of the bacterial strain or strains.

Positive bacterial screen

The blood service reports a positive bacteriological screen, but bacterial contamination of the relevant material is not confirmed by a positive culture result on the same material or other products made from the same donation.

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 relation to the administered blood component.

Table 12. Overview of reports from hospitals of bacterial problems related to transfusion 2008-2012

	2008	2009	2010	2011	2012
Bacterial contamination of a blood component	23	22	41	37	34
Bacterial contamination of a blood component as additional category*	7	22	17	19	15
Positive bacterial screen	2	4	3	6	8
Positive bacterial screen as additional category*					1
Post-transfusion bacteremia/sepsis	37	55	41	61	49
Post-transfusion bacteremia/sepsis as additional category*	1	8	17	13	14

** an additional category is recorded if the problem is noticed following another transfusion reaction or incident*

Table 13. Positive bacterial screen of platelet units, summary figures from Sanquin 2008-2012

Total	2008	2009	2010	2011	2012
Platelets with initial positive result	Not asked	325	332	321	238
Number of units transfused prior to positive screening result (platelets and associated RBCs)	102	108	106	125	90#

Information from Sanquin: one serious adverse reaction was reported in 2012 (imputability unlikely)

Abbreviations: *RBC = red blood cell concentrate*

Table 14. Overview of post-transfusion bacteremia/sepsis culture results 2008-2012

Positive patient blood culture found after transfusion:	2008	2009	2010	2011	2012
Hospital culture on blood component: identical bacteria	1	1	2	1	1*
Hospital culture on blood component: same type of bacteria, not sub-typed			1	1	
Hospital culture on blood component: same type of bacteria, strain not identical	1				
Hospital culture on blood component: different type of bacteria			4	4	2
Hospital culture on blood component: not performed	10	18	9	20	15
Hospital culture on blood component: negative	25	36	25	34	31
Total	**37**	**55**	**41**	**60**	**49**

* *further information in section on post-transfusion bacteremia/sepsis*

Bacterial contamination of a blood component and Positive bacterial screen 2012

- 34 reports of bacterial contamination of blood component were received from 18 hospitals; these reports concern patients who were transfused with a blood component which later gave a positive bacterial screening result which was subsequently confirmed by a positive culture at Sanquin
- 4x a (non-serious) reaction was observed and reported to TRIP, all with imputability possible (Table 15)
- 8 reports of positive bacterial screen were received from 5 hospitals; in four cases the blood component had already been administered to a patient
- Bacterial contamination of a blood component was also registered 15x as an additional category in cases where a positive culture of the blood component was found by the hospital on analysing a transfusion reaction (Figure 9)

Table 15. Overview of reactions reported to TRIP in 2012 in patients who received a blood component which subsequently gave a positive bacterial screening result at Sanquin

Type of reaction Blood component	Non-hemolytic transfusion reaction	Other allergic reaction	Other reaction*	No reaction	Total
Platelets	1		2	25	**28**
RBC		1		4	**5**
Not specified				1	**1**
Total	**1**	**1**	**2**	**30**	**34**

* *in both cases: rise in temperature >2°C not normalising within 24 hours*

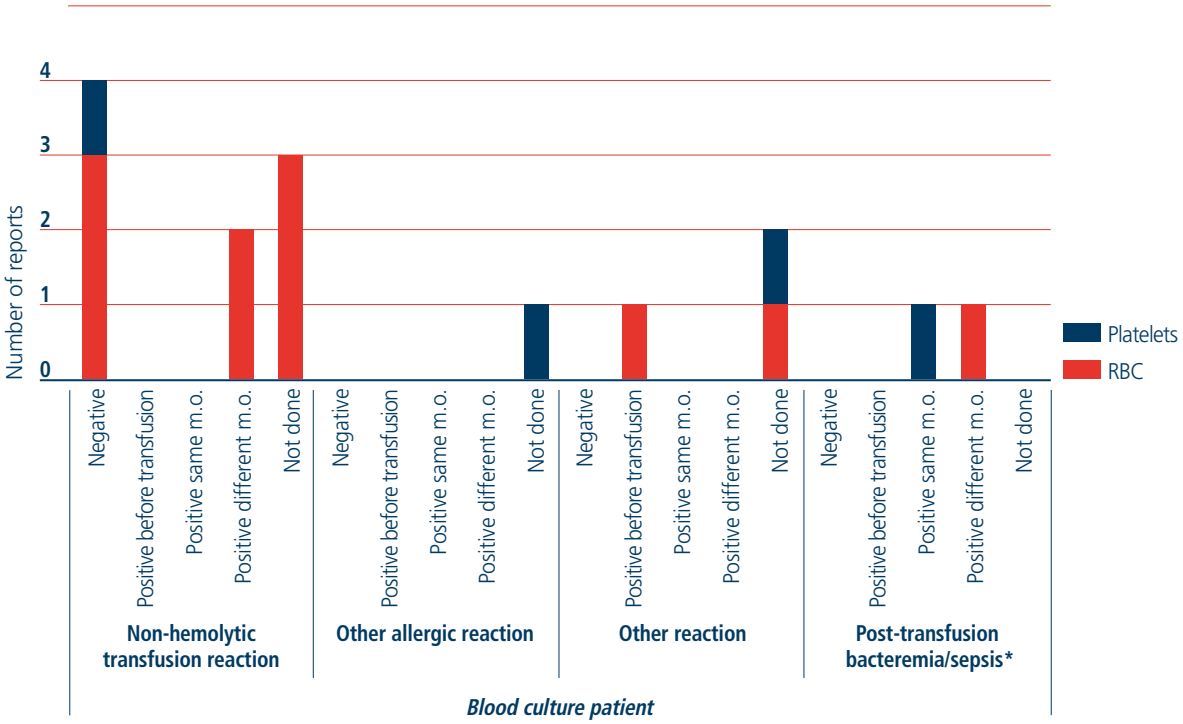


Figure 9 Blood culture findings in patients with reactions and positive culture of the blood component

* *further information in section on post-transfusion bacteremia/sepsis*

Abbreviations: *Tf=transfusion; m.o.=micro-organism*

Post-transfusion bacteremia/sepsis in 2012

- 49 reports of post-transfusion bacteremia/sepsis received from 37 hospitals
- 2x with additional category of bacterial contamination of a blood component (hospital culture results on blood component : see Figure 9)
  - haemolytic streptococci group C found in patient blood culture and in culture on platelets
  - E. coli found in patient blood culture and Enterococcus faecalis found in culture on RBC
- 1x with additional category of positive bacterial screen
  - Sanquin culture result: no anaerobic micro-organism found
  - Hospital culture results: Enterococcus sp. in patient blood culture and also Enterococcus sp. in culture from patient's CVC; no culture of RBC in hospital because there was not enough material
- 1x with additional category of other incident: reaction reported to the laboratory too late; RBC unit not sealed and sent for culture 20 hours later, findings (Streptococcus sobrinus and Staphylococcus epidermidis) regarded as contamination, Staphylococcus aureus found in patient blood culture

Conclusion: in 2012 there was one case of transfusion transmitted bacterial infection (TTBI) with hemolytic streptococci through transfusion of a platelet concentrate.

Post-transfusion malaria

Other post-transfusion other infection

Any case of infection other than with a virus or bacteria, e.g. a parasitic infection or variant Creutzfeldt Jakob Disease) which has been demonstrated within a relevant time interval following a blood transfusion.

Since the (confirmed) report of post-transfusion malaria in 2011 there have been no further reports in this category.

3.3 Non-infectious transfusion reactions

Non-hemolytic transfusion reactions (NHTR) and mild non-hemolytic 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

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.

In 2012, 447 reports of non-hemolytic transfusion reactions (NHTR) and 377 reports of mild non-hemolytic febrile reactions (mild NHFR) were submitted. Of these, 400 NHTR reactions and 335 mild NHFR were of certain, probable or possible imputability. The reports were of grade 1 with the exception of 10 NHTR and six mild NHFR reactions which were of grade 2 severity, most often because the reaction necessitated hospital admission or prolongation of hospital stay.

Table 4 on page 15 shows the distribution of blood components associated with febrile reactions. As in past years, transfusions of platelets and of drain blood were relatively often associated with NHTR in comparison to mild NHFR.

In a number of reports TRIP has examined the possibility of an association between the type of blood component administered and the presence of pre-existing infection in the patient, and the occurrence of an NHTR or mild NHFR. Table 16 shows the data for 2011 and 2012. Among the recipients of red blood cell concentrates who had febrile reactions, a relatively high proportion of reports recorded the presence of a pre-existing infection in comparison to other types of blood component. However, because TRIP has no information about patients who do not develop transfusion reactions, it cannot be concluded that red blood cell transfusion increases the likelihood of febrile reactions in patients harbouring infections.

Table 16 Pre-existent infection and transfused blood component associated with reports of non-hemolytic transfusion reactions, 2011-2012

NHTR 2011	RBC		Platelets		Plasma		RBC and other bc		Drain blood
Infection present	81	89%	9	10%	1	1%	0	0%	0
	22%		12%		50%				
Non-infectious	245	76%	61	19%	1	0%	14	4%	36
diagnosis	66%		78%		50%				
No information	46	84%	8	15%	0	0%	1	2%	1
on diagnosis	12%		10%						
Total	**372**	**80%**	**78**	**17%**	**2**	**0%**	**15**	**3%**	**37**
NHTR 2012									
Infection present	103	95%	5	5%	0	0%	0	0%	0
	28%		11%						
Non-infectious	204	83%	34	14%	4	2%	3	1%	21
diagnosis	55%		77%		80%				
No information	63	90%	5	7%	1	1%	1	1%	3
on diagnosis	17%		11%		20%				
Total	**370**	**87%**	**44**	**10%**	**5**	**1%**	**4**	**1%**	**24**
% of the total number of distributed blood components	**78%**		**10%**		**12%**				**Not applicable**

In cases where other more serious types of transfusion reactions have been excluded, non-hemolytic transfusion reactions and mild non-hemolytic febrile reactions by definition have a non-serious course but they cause morbidity, halting of transfusions and extra costs. Besides the hospital investigations and assessment of these reactions, it is irrelevant to monitor their occurrence nationally (at least of the NHTR) when there are changes in the specifications of blood components.

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 17. Acute hemolytic transfusion reactions, 2006-2012

	AHTR total	Patient gender F	M	Reports with certain, probable or possible imputability	Severity grade 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
Total	**110**	**66***	**43***	**103**		**64**	**33**	**3**	**3**

**1 x gender not stated*

In 2012 there were seven reports of acute hemolytic transfusion reactions (no significant difference compared to previous years). The annual number of reports was stable in 2006-2011.

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 alloantibody.

In 2012 there seemed to be a lower number of registered delayed hemolytic transfusion reactions (total of DHTR as main or additional category). Due to progressive implementation of TRIX (registry for irregular antibodies and cross (X) match problems) in the hospitals the number of potentially avoidable DHTR should decrease. However as patients are not systematically monitored for irregular antibody formation after a transfusion there is always a small risk that an irregular antibody will be missed at pre-transfusion screening if it has dropped below the detection threshold.

Since 2008 TRIP has followed the practice of systematically registering a report according to the reaction which was first noted (this is the main category). Since 2008 about half of reported DHTR were diagnosed after finding a new irregular allo antibody where laboratory hemolysis parameters and/or an unexplained drop in hemoglobin level led to the diagnosis of DHTR (Table 18, 3rd column); DHTR was registered as an additional category in these cases. Furthermore in all reporting years (with the exception of 2007) a small number of registered DHTR were caused by the administration of an incorrect blood component.

In the reporting years 2009 and 2010 TRIP systematically asked questions about hemolysis following reports of clinically relevant allo antibodies. This led to recording of DHTR as an additional category in only a few reports. These targeted questions could not substantiate the 5-10 x higher frequency of DHTR compared to AHTR that is shown in literature in the data collected by TRIP.

Table 18. Delayed hemolytic transfusion reactions (DHTR), 2006-2012

	Main category DHTR	New allo antibody + additional category DHTR	Another main category + DHTR		Total DHTR, main + additional category	Main category DHTR + additional category new allo antibody
2006	14	-	Other reaction	1	19	9
			Other incident	1		
			IBCT	3		
2007	11	3		-	14	5
2008	18	11	IBCT	2	31	13
2009	8	19	IBCT	1	28	6
2010	7	12	NHTR	1	21	6
			IBCT	1		
2011	9	17	IBCT	2	28	6
2012	8	7	IBCT	3	18	6
Total	**75**	**69**		**15**	**159**	**51**

Abbreviations: *DHTR=delayed hemolytic transfusion reaction; IBCT=incorrect blood component transfused; NHTR=non-hemolytic transfusion reaction*

Of all reports of DHTR a substantial proportion (42%) was registered as severity grade 2 (Table 19, 2006-2012 data). The number of serious reports showed a downward trend.

Table 19. Severity of delayed hemolytic transfusion reactions (DHTR), 2006-2012

	Main category DHTR	Severity grade			Main category new allo antibody formation + additional category DHTR	Severity grade		
		2	1	0		2	1	0
2006	14	8	5	-	-	-	-	-
2007	11	4	4	1	3	-	1	2
2008	18	4	6	5	11	1	8	2
2009	8	3	5	-	19	1	7	11
2010	7	5	2	-	12	1	6	5
2011	9	1	8	-	17	-	12	5
2012	8	1	5	1	7	1	5	1
Total	**75**	**26**	**35**	**7**	**69**	**4**	**39**	**26**

TRALI (transfusion-related acute lung injury)

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.

Nine reports in 2012 met the (clinical) criteria and were accepted as TRALI. All were of grade 2 or higher and the imputability was assessed as definite, probable or possible. Seven were associated with transfusion of red blood cell concentrates and two with platelet concentrates, in both cases these were pooled buffy coat platelets with plasma as added conservation fluid (from male donors). The reports came from five hospitals.

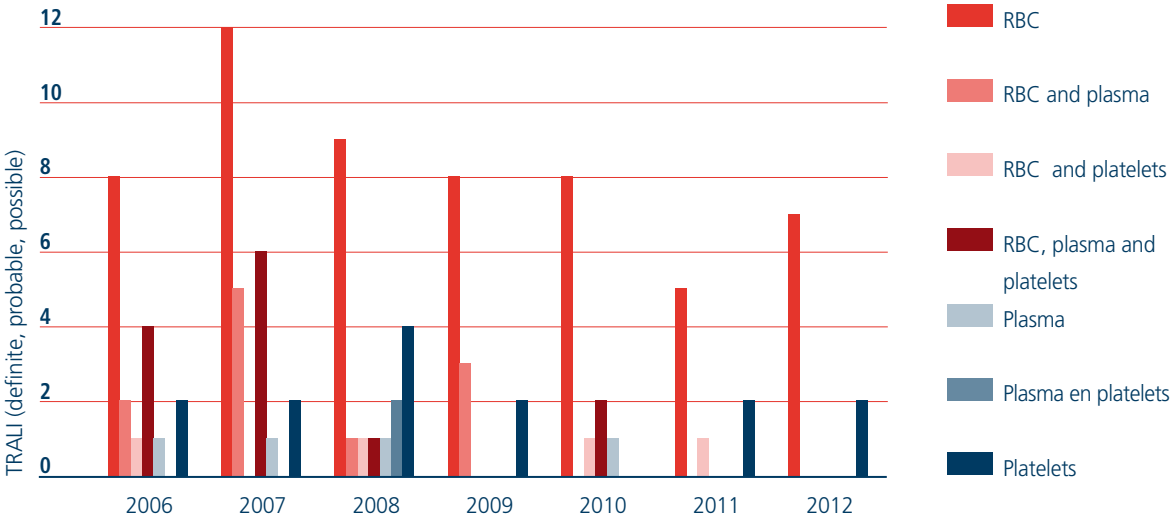


Figure 10 Blood components associated with reported TRALI, 2006-2012.

Figure 10 shows the types of blood components which were associated with the TRALI reports of definite, probable and possible imputability in 2006-2012. The annual number of TRALI reports has declined since approximately 2008, after the implementation (effective for units distributed from mid-2007) of the male-only plasma measure (fresh frozen plasma for transfusion sourced from male donors who have never themselves received a blood transfusion). A similar measure for platelets was implemented in November 2009 for the plasma which is added to pooled platelet units as conservation fluid; this is the standard type of platelets distributed in all regions of the country with the exception of the Southwest, where platelet additive solution (PAS) is used. This measure is based on minimising the exposure to plasma which might possibly contain HLA-antibodies: this is because TRALI can be caused by incompatibility between HLA/HNA antibodies in transfused plasma and the patient's HLA/HNA antigens. The data do not provide evidence for a further reduction of TRALI through the platelet measure. In 2012, investigations were performed to find a possible immunological cause. In two cases donor HLA/HNA antibodies were found (1x class 1, 1x class 2), however no leukocyte crossmatch test could be performed because the patient had died.

The number of TRALI reports was stable in comparison to 2011 but in the last two years it was lower than in 2006-2009. In 2011 it was suggested that (possible) cases of TRALI might have been less well recognised than previously. It is important to remain aware of this adverse reaction and to order chest radiography if patients have suspicious signs and symptoms so that they can be appropriately diagnosed and treated. Several times in 2012 (approximately 15) a reaction was first reported to Sanquin as suspected TRALI and subsequently reclassified because a different reaction was found to fit better (circulatory overload, anaphylaxis, other 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 ≥ 20mm Hb systolic and/or diastolic, nausea or vomiting or diarrhoea, possibly with skin rash.
Hemolysis testing and bacteriology negative, test for IgA and anti-IgA.

In 2012 a total of 57 reports were received in the category of anaphylactic reaction, 14 being of severity grade 2 or higher and definite, probable or possible imputability. These numbers are similar to those in previous years.

Table 20 gives an overview of the numbers of different types of blood components which had been transfused to the patients with anaphylactic reactions in 2008 up to and including 2012. In the literature it has been reported that allergic reactions occur more frequently with single-donor apheresis platelet units than with pooled products (Ansm rapport d'activité hémovigilance 2011, the French hemovigilance report) and are

reduced by the use of platelet additive solution (PAS) as added conservation fluid. The table shows the numbers of reports for the different types of platelet concentrate. In 2012 the distributed units were approximately 10% apheresis platelets, 70% of pooled five-donor buffy coat platelets with plasma from one of the five donors and 20% pooled buffy coat platelets with PAS. At present, the figures emerging from the reports to TRIP do not allow any conclusions to be drawn about the type of platelet concentrate and the risk of anaphylactic reactions. Not all reports give information about the product type and moreover, the choice of component is partly determined on the basis of a patient's history of previous reactions.

Table 20 Type of blood component associated with anaphylactic reactions, 2008-2012

Anaphylactic reaction	2008		2009		2010		2011		2012	
	serious	all	serious	all	serious	all	serious	all	serious	all
RBC	7	14	4	12	4	18	3	15	1	9
Platelets	14	30	7	31	10	38	7	27	7	23
Pool, plasma	*2*	*11*	*4*	*16*	*6*	*18*	*4*	*14*	*5*	*13*
Pool, PAS	*2*	*4*	*2*	*4*	*1*	*5*	*1*	*3*	*0*	*0*
Apheresis	*3*	*5*	*0*	*4*	*0*	*4*	*0*	*3*	*0*	*2*
Not stated	*7*	*10*	*1*	*7*	*3*	*11*	*2*	*7*	*2*	*8*
Plasma	5	15	8	23	3	13	8	18	5	20
Platelets and RBCs and/or plasma	4	4	0	3	1	2	1	4	0	2
RBC and plasma	0	2	0	0	0	1	1	2	1	3
Other[1]	0	0	1	2	1	1	1	1	0	0
Total	**30**	**65**	**20**	**71**	**19**	**72**	**21**	**65**	**14**	**57**

[1] *Unwashed drain blood*

Abbreviations: *RBC=red blood cells; PAS=platelet additive solution*

The national transfusion guideline recommends that following a serious anaphylactic reaction the possibility of causation by anti-IgA in an IgA-deficient patient should be investigated. In 2003 up to and including 2012 this was demonstrated in a total of four cases of anaphylactic reactions which were reported to TRIP. Among the 2012 reports, four mention that IgA deficiency and/or presence of anti-IgA was excluded and once it was recorded that these investigations were unnecessary because of subsequent uneventful transfusions. One report mentioned the possibility of causation by pharmaceutical agents which were also administered to the patient at the time of the reaction.

As in previous TRIP reports, anaphylactic reactions are one of the most important causes of serious morbidity. Some patients have more than one reaction (see previous TRIP reports, 2012 data similar but not shown). A cause is seldomly found.

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.

The number of reports of other allergic reactions, 177, and the relative contributions of different types blood components were comparable to previous years. In the majority of reactions no further investigations were pursued; ten reports in 2012 stated that the IgA level was normal.

Table 21 Type of blood component associated with other allergic reactions, 2008-2012

Other allergic reaction	2008	2009	2010	2011	2012
RBC	31	41	39	37	35
Platelets	85	86	88	105	81
Pool, plasma	*35*	*52*	*60*	*60*	*46*
Pool, PAS	*22*	*10*	*6*	*15*	*2*
Apheresis	*8*	*7*	*7*	*7*	*7*
Not stated	*20*	*17*	*15*	*11*	*26*
Plasma	44	44	41	40	50
Platelets and RBC and/or plasma	7	8	7	7	5
RBC and plasma	4	0	5	2	5
Other or not stated	0	2[1]	4[1]	0	1[2]
Total	**171**	**181**	**184**	**191**	**177**

[1] *unwashed drain blood*

[2] *SD-plasma (Octaplas)*

Abbreviations: *RBC=red blood cells; PAS=platelet additive solution*

Although most of these allergic reactions are not associated with serious morbidity they are numerically an important category. Some patients suffer from repeated reactions or may display both anaphylactic and other allergic reactions to blood transfusions.

Transfusion-associated circulatory overload (TACO)

Dyspnea, orthopnoea, 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.

Table 22 shows an overview of the TACO reports in 2008 – 2012. Among the serious reports in 2012 TACO accounted for the highest number. Figure 11 shows the reported information about risk factors for TACO in the patients.

Table 22. Overview Transfusion-associated circulatory overload 2008-2012

	2008	2009	2010	2011	2012
RBC	33	28	35	32	49
Platelets	3	7	4	2	2
Plasma	1	4	1		1
Combination	2	2	7	4	4
Other		1			
Total	**39**	**42**	**47**	**38**	**56**
Severity grade 1	22	26	27	20	29
Severity grade 2	15	13	13	13	22
Severity grade 3	2	3	5	4	2
Severity grade 4			2	1	2

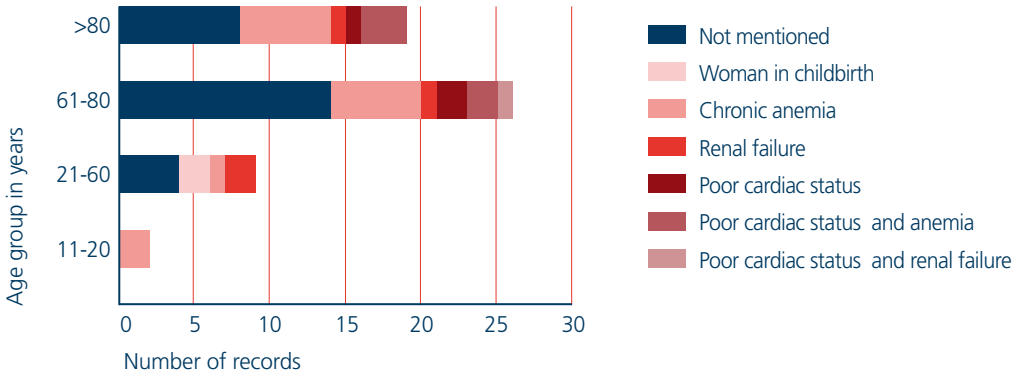


Figure 11 Transfusion-associated circulatory overload in 2012: risk factors in patients according to age group

Post-transfusion purpura (PTP)

Serious self-limiting thrombocytopenia possibly with bleeding manifestations (skin, nose, gastrointestinal, urinary tract, other mucous membranes, brain) 1-24 days after a transfusion of a red cell or platelet concentrate, usually in a patient who has been pregnant. Investigations: HPA antibodies and HPA typing of patient.

In the reporting year 2012 there was one report regarding post-transfusion purpura. All reports of PTP in the TRIP registration concerned female patients. The typical symptoms are bleeding (the 2012 report: nasal bleed and hematoma) due to thrombocytopenia. The demonstration of HPA antibodies (most frequently HPA-1A antibodies) support the diagnosis of PTP. PTP is only sporadically found after administration of leukodepleted blood components.

Transfusion-associated graft versus host disease (TA-GvHD)

Clinical features of graft versus host disease such as erythema which starts centrally, watery diarrhoea, fever and rise in liver enzymes 1-6 weeks (usually 8-10 days) after transfusion of a T-cell containing (nonirradiated) blood component. Skin (and liver) biopsies can support diagnosis.

As in previous reporting years there was no report in the category TA-GVHD. Leukodepletion, as performed on all blood components in the Netherlands since the end of 2001, significantly reduces the occurrence of TA-GVHD.

Hemosiderosis

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

There were no reports of post-transfusion hemosiderosis in 2012. This is despite several attempts by TRIP to encourage reporting of hemosiderosis in order to obtain a national overview of the incidence of hemosiderosis. Prescription of preventive medication can be effective and is essential to avert morbidity.

New alloantibody

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).

In 2012 the total number of antibodies reported was 977 in 816 reports, which is similar to previous years. Table 23 shows the antibodies reported in 2012. In 24 reports a transfusion of platelets was presumed to be the cause. For anti-D, this was the case in 10 of the 19 reports; in four of these and most of the nine remaining cases a combination of anti-C and anti-D was reported, suggesting that it was actually anti-G.

Table 23 New alloantibodies reported in 2012

Antibody	Number reported in women in 2012	Number reported in men in 2012	Total reported in 2012
Anti-E	153	107	260
Anti-K	129	81	210
Anti-Fya	64	24	88
Anti-c	47	27	74
Anti-Jka	30	25	55
Anti-C	27	20	47
Anti-Wra	28	17	45
Anti-Lua	12	32	44
Anti-Cw	14	12	26
Anti-S	19	4	23
Anti-Jkb	13	7	20
Anti-D	12	7	19
Anti-Kpa	13	2	15
Anti-M	8	4	12
Anti-e	4	4	8
Anti-Lea	2	6	8
Anti-Fyb	4	0	4
Anti-Leb	1	2	3
Anti-Jsa	2	1	3
Other antibodies *	10	3	13

* *Other antibodies: anti-N, anti-Cob and anti-f were each reported twice. Anti-s, anti-Ch1, anti-A, anti-Yta, anti-Doa, anti-Vw, anti-k were each reported once.*

In October 2011 the revised Dutch CBO national transfusion guideline recommended selection of c- and E-compatible red blood cells for women younger than 45 years of age, on top of the earlier recommendation to transfuse Kell-compatible red blood cells. Figure 12 shows the numbers of anti-c, anti-E and anti-Kell antibodies reported to TRIP in women who were younger than 45 at the time of transfusion. Note that the reports are sorted by year of transfusion.

New alloantibodies may be detected and reported years after the transfusion. The numbers for newly formed anti-c, anti-E and anti-Kell following transfusions in 2012 are not final. However, about 65% of all reported new antibodies are notified to TRIP within six months of the transfusion date, so it might well be that the total number of anti-c, anti-E and anti-Kell antibodies following transfusions in 2012 will remain low. The current numbers suggest that the new guideline is effective in reducing these newly-developed alloantibodies in women under 45, however the rates must be monitored for a longer period before any conclusions can be drawn.

New alloantibody formation in women under 45

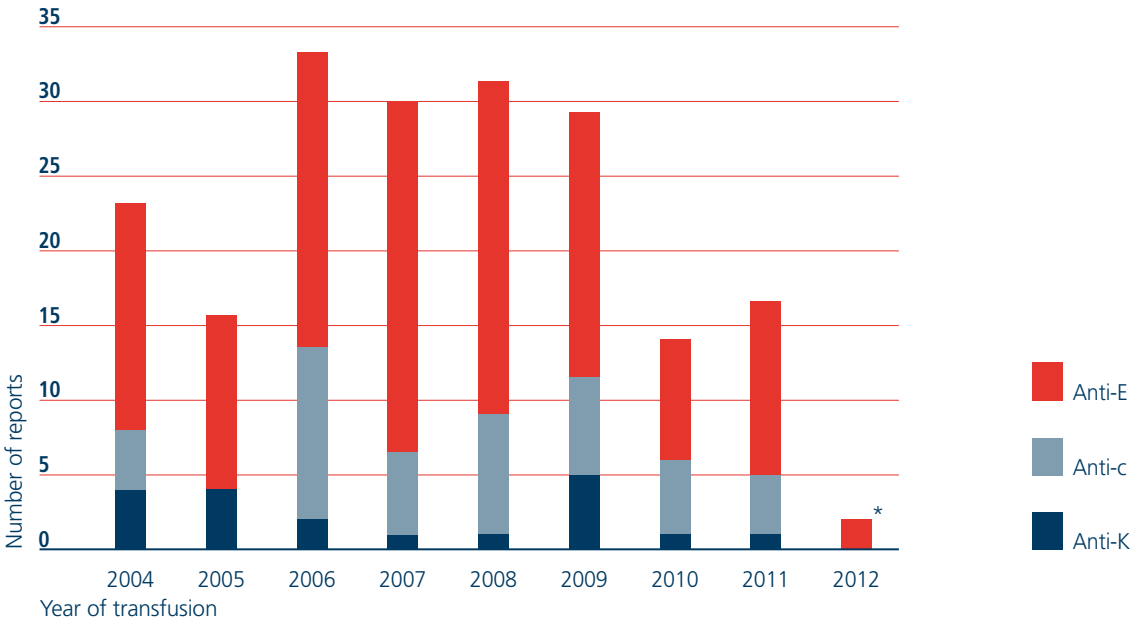


Figure 12 Reports of anti-c, anti-E and anti-Kell antibodies in women under 45 years of age at the time of transfusion (reports sorted by year of transfusion)

* *So far, two reports have been received about women of childbearing potential developing anti-E antibodies after a transfusion in 2012. The first report concerned a woman who received E-positive red blood cells in January 2012 in a hospital that hadn't yet implemented the new transfusion guidelines. The second report involved platelets from an E-positive donor.*

Other transfusion reaction

Transfusion reaction that does not fit into the categories above.

The number of reports of other reaction in 2012 was similar to last year. The category of other reaction is intended firstly for reactions which have not previously been detected and described (for instance necrotising enterocolitis in 2011). Next, for a number of years two clusters have been observed in this category which are specifically defined in some other hemovigilance systems: hypotensive transfusion reaction and transfusion-associated dyspnea (TAD). TRIP intends to introduce separate definitions for these reactions (as recommended in the 2010 and 2011 TRIP reports). In other reactions there may be various reasons why other reaction is the most appropriate reporting category. Table 24 provides an overview of the reports of other reaction in 2012.

Table 24 Types of report classified as other reaction

Type of reaction	Total number	Number definite/ probable	Number possible	Number ≥2*	Remarks
Hypotensive reaction	42	13	25	3	Bp drop specified in 27 cases; in n=11 the criteria for hypotensive reaction were met (ISBT definition)
Reactions with dyspnea	30	8	18	4	N=14 reports stated that dyspnea was the predominant feature
Rise in bp	14	3	11	-	Bp increase specified in 12 reports, median 43 mm Hg systolic
(Possible) cardiac signs/ symptoms	10	1	8	1	Including tachycardia as sole manifestation
Did not fit standard criteria	63	16	39	5	E.g. interval too long after Tf, late normalisation of temp, pt with positive DAT or blood culture before Tf
Solitary sign/symptom or combination of features, possibly in part due to clinical condition	57	7	33	3	Without demonstrable transfusion-related cause
Total	**216**	**49**	**129**	**16**	

* *Severity grade 2 or higher*

Abbreviations: *bp=blood pressure; Tf=transfusion; ISBT=International Society for Blood Transfusion; DAT=direct antiglobulin test*

Subgroup: hypotensive transfusion reaction

> *Draft definition based on ISBT definition: Drop in systolic blood pressure of ≥ 30 mm Hg occurring during or within one hour of completing transfusion and a systolic blood pressure is ≤ 80 mm Hg.*
> *Most reactions occur very rapidly after the start of the transfusion (within minutes). Hypotension is usually the sole manifestation but facial flushing and gastrointestinal symptoms may occur. All other categories of adverse reactions presenting with hypotension, especially anaphylactic or other allergic reactions, must have been excluded. The underlying condition of the patient must also have been excluded as a possible explanation for the hypotension*

Out of the 42 reactions where a drop in blood pressure or hypotension was the only or the most prominent feature, the decrease was quantified in 27 reports. The international (ISBT) definition for this category specifies a drop of ≥30 mm Hg and a systolic blood pressure ≤80 mm Hg. Eleven reports met these criteria: three with drain blood, 7 associated with red blood cells and one with platelets. The definition also requires other causes for hypotension to have been excluded, including the clinical condition of the patient, as (more likely) cause. This could not be verified in the reports. The median interval between the start of transfusion and the hypotension was 25 minutes, which can explain the generally high imputability rating. In seven of the 42 reports (including 3 of the 11 with profound hypotension) a rise in body temperature and/or chills and rigors were also reported. According to the literature bradykinin may play a role in the pathophysiology of hypotensive reactions, particularly in patients who are on ACE inhibitor medication, in whom bradykinin is broken down too slowly.

Subgroup: transfusion-associated dyspnea (TAD)

> *Draft definition based on ISBT definition of TAD: Respiratory distress or hypoxia during or within 24 hours of transfusion that does not meet the criteria of TRALI, transfusion-associated circulatory overload or anaphylactic reaction. Respiratory distress is the most prominent clinical feature and should not be explained by the patient's underlying condition or any other known cause.*

In the 2012 reports with dyspnea it was not always possible to verify that dyspnea was the most prominent feature. If a new reporting category of TAD is introduced, reporters will need to assess this. Further investigations are also necessary to (reasonably) exclude TRALI, TACO or anaphylaxis.

Remainder of reported other reactions

In 2012 there were a few reports of other reaction where the most prominent feature was a rise in blood pressure, sometimes accompanied by a rise in body temperature. In a few of these reports the patient was treated as for circulatory overload, however that diagnosis was not sufficiently supported by investigations or further clinical information. In the 2008 TRIP report a number of reports of hypertension were described and it was suggested that these might represent a specific cluster. However, reports with hypertension in subsequent years have been accompanied by vague symptoms, without remarkable findings of investigations or clinical course.

The remainder of the other reactions, as in 2011 (see Tables 14 and 15 of the extended TRIP hemovigilance report) involved either solitary signs or combinations of features which did not fit in any of the standard categories of transfusion reactions. In 2012 no cases of necrotising enterocolitis were reported. Because of the atypical features of most other reactions it is not surprising that the imputability, with the exception of hypotensive reactions and reactions with dyspnea, is rated as rather low: for 83% this was assessed as definite, probable or possible, in comparison with 92% for all transfusion reaction reports.

3.4 Blood Management Techniques (BMT)

Table 25. Reports regarding blood management techniques 2008-2012

Blood management technique	M	F	Number of reports drain blood	Number of reports Cell saver	Number of reports PAD [$]	Total	Reports of severity ≥ 2	Number of hospitals sumitting reports
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	-	-	51	3	8
Total	**89***	**120***	**196[#]**	**12**	**2**	**210**	**10**	**20**

[$] *preoperative autologous donation*

* *1 gender not stated*

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

Table 26. Reporting category in drain blood procedures, 2008-2012

Trip category	2008	2009	2010	2011	2012	Total	Number of hospitals submitting reports
Anaphylactic reaction		2	1	1		4	3
Other allergic reaction			1			1	1
Hemolysis of product				2		2	2
Mild non-hemolytic febrile reaction				2	4	6	3
Non-hemolytic febrile reaction	6	9	18	37	24	94	10
Other incident	9	12	6	8	4	39	4
Other reaction	5	4	8	14	17	48	8
Post-transfusion bacteraemia/sepsis					1	1	1
Circulatory overload		1				1	1
Total	**20**	**28**	**34**	**64**	**50**	**196**	**18**

- The number of reports concerning blood management techniques showed an increase up to and including 2011; in 2012 numbers of reports were lower but not statistically significant.
- Every year only a small number of hospitals reported transfusion reactions and incident concerning blood management techniques. Out of the total number of reports 154 were submitted by three hospitals (91, 46 an d 17 reports). This could point to underreporting.
- The majority of reports concerned the administration of drain blood.
- A small number of reports is serious.
- Almost 50% of reports concerning drain blood were submitted in category non-hemolytic transfusion reaction. Category other reaction is numerically second; in this category there were 21 reports that mentioned hypotension (three of severity grade 2).

Table 27. Number of hospitals that apply blood management techniques, 2009-2012

BMT technique	2009*			2010			2011			2012		
Number of hospitals	yes	no	?	yes	no	?	yes	no	?	yes	no	?
Drain blood	18	20	57	21	24	58	23	20	57	23	20	55
Cell saver	18	25	50	21	23	59	22	21	57	24	21	53
PAD#	8	58	20	9	47	47	10	52	38	11	62	25
Normovolemic hemodilution	6	28	58	3	32	68	3	33	64	2	28	68
Hypervolemic hemodilution	2	30	60	1	31	71	4	32	64	2	26	70
Extracorporeal circulation	2	39	52	4	47	52	4	46	50	4	40	54
Fibrin glue	12	21	59	15	24	64	20	25	55	12	22	64
Platelet gel	5	33	51	4	37	62	1	45	54	1	38	59

* *In 2009 hospitals which did not send data were not counted as it was the first time they were asked to provide data.*

\# *Preoperative autologous donation*

Table 28. Reported numbers of applications of blood management techniques 2009-2012

BMT technique	Total applications 2009*	Total applications 2010	Total applications 2011	Total applications 2012
Drain blood	7514	8821	11464	7162
Cell saver	3033	5001	4282	3801
PAD#				
- patients referred	109	153	59	26
- units donated	208	289	113	51
- units administered	187	24	38	34
Normovolemic hemodilution	122	1412	1250	?*
Hypervolemic hemodilution	2	0	1172	?*
Extracorporeal circulation	2177	4430	5606	3981
Fibrin glue	798	1056	1437	384
Platelet gel	846	1225	510	30

* *Some hospitals report approximations or state that they do apply BMT but do not submit numbers.*

\# *Preoperative autologous donation*

- In 2012 the information from hospitals regarding application of BMT is still incomplete. The number of hospitals where hemovigilance staff or transfusion safety officers do not know which BMT, if any, is applied in their institution is not declining, despite recommendations in the 2011 Blood Transfusion Guideline regarding hemovigilance concerning blood management techniques.
- All BMT application numbers were lower in 2012 compared to 2011. With regard to the application of drain blood lower application numbers could result from better observance of Hb triggers and/or a gradual decrease in the use of drain blood procedures as they are not cost effective (C. So-Osman: thesis Leiden 2012 Patient Blood Management in Elective Orthopaedic Surgery: Chapter 7).
- One hospital stated they administer unwashed drain blood peroperatively (instead of postoperatively); this technique is not recommended according to the 2011 Blood Transfusion Guideline.

3.5 Deceased patients and transfusion reactions (grade 4)

In 2012 there was a total of ten reports of severity grade 4; out of those five were assessed to be of certain, probable or possible imputability. The report are summarised in Table 29. In two reports, i.e. acute hemolytic transfusion reaction and TRALI, the transfusion reaction contributed to the patient's death.

Table 29 Reports of patients who died following a transfusion reaction

Categorie reactie	Leeftijd, geslacht	Bloedproduct	Imputabiliteit	Aard onderliggende pathologie
Acute hemolytic transfusion reaction	68, F	RBC + platelets + Plasma	Probable	Resuscitation and surgery for ruptured aortic aneurysm, transfusion of multiple uncross-matched units compatible for known alloantibody, patient developed intestinal necrosis an multi-organ failure
TRALI	26, F	RBC	Probable	ALL and viral infection
TACO	88, F	RBC	Possible	Patient declining analysis of iron deficiency anemia, admitted for dyspnea that worsened during transfusion
Post-transfusion bacteremia/sepsis	75, M	RBC	Possible	Hemodialysis patient, during transfusion developed fever, hypotension and somnolence
Other reaction	76, F	RBC	Possible	Admission for analysis of iron deficiency anemia in patient with MGUS; fever and positive blood cultures 1 day after transfusion (Str. Pneumomiae)
TACO	80, M	RBC	Unlikely	Admission for analysis of cognitive deterioration, dyspnea and hematuria in alcoholic patient; possible MDS, TTP or liver cirrhosis. Evidence for pneumonia; developed atrial fibrillation. After transfusion severe dyspnea/drop in saturation
Other reaction	51, F	platelets	Unlikely	Clinical presentation of typhlitis and sepsis in neutropenic patient who became unconscious and arrested
Other reaction	53, F	RBC	Unlikely	Day care curettage, lung embolism that evening
Other reaction	72, F	RBC	Unlikely	Peritonitis following gall bladder surgery; clinical deterioration and drop in blood pressure during transfusion
Other reaction	47, F	Plasma	Unlikely	TTP; sudden death at end of plasmapheresis procedure

Abbreviations: *ALL=acute lymphatic leukemia, MGUS=monoclonal gammopathy of unknown origin, MDS= myelodysplastic syndrome, TTP= thrombotic thrombocytopenic purpura*

Table 30 gives an overview of grade 4 reports to TRIP of certain, probable and possible imputability since 2006. The largest categories are TRALI (9), other reaction (6) and TACO (5).

Table 30 Reports of Grade 4 (imputability certain, probable or possible) 2006 – 2012

Category	2006	2007	2008	2009	2010	2011	2012	Totaal
Acute hemolytic transfusion reaction				1		1	1	3
Anaphylactic reaction		1						1
Other reaction			1		3	1	1	6
Post-transfusion bacteremia/sepsis*				1			1	2
TRALI	2	3		1	2		1	9
Incorrect blood component transfused		1	1					2
Circulatory overload	1				2	1	1	5
Total	**3**	**5**	**2**	**3**	**7**	**3**	**5**	**28**

* *Pre-2008: bacterial contamination*

3.6 Reports and transfusions in patients under 21 years of age

In 2012 TRIP received 135 reports concerning patients younger than 21 (2011: 141). Table 31 presents an overview of these reports. The reports were submitted by 31 hospitals. Of all transfusion reactions in this age group, seven were assessed to be serious – all were of severity grade 2 in patients over one year of age. These serious reactions were NHTR and TRALI in patients one to ten years of age, TACO and anaphylactic reaction in patients one tot ten years of age and TACO, anaphylactic reaction and mild non-hemolytic febrile reaction in patients aged 11-20 years.

Table 31. Reports in patients < 21 years in 2012, per age category

	<29 days	29 days <1 year	1-10 year	11-20 year	Total
Incidents					
Incorrect blood component transfused	2	1	1	1	5
Near miss	1	0	0	1	2
Other incident	2	1	0	1	4
Bacterial contamination of blood component	1	0	0	1	2
Total (Incidents)	**6**	**2**	**1**	**4**	**13**
Transfusion reactions					
Anaphylactic reaction	1	1	2	10	14
Other allergic reactiom	0	1	16	21	38
Mild non-hemolytic febrile reaction	1	1	12	6	20
Non-hemolytic transfusion reaction	0	0	16	11	27
New alloantibody	0	1	5	3	9
Other reaction	2	0	3	2	7
Post-transfusion bacteremia/sepsis	0	0	2	1	3
TRALI	0	0	1	0	1
TACO	0	0	0	2	2
Total (transfusion reactions)	**4**	**4**	**57**	**56**	**122**

Table 32. Reported transfusion reactions and incidents in patients < 21 years, 2008-2012

	2008	2009	2010	2011	2012
Reports					
Transfusion reactions	116	118	110	121	122
Incidents	19	11	30	20	13
Incidents excluding look-back and bacterial contamination of blood component	*18*	*11*	*17*	*14*	*11*
Total	**135**	**129**	**140**	**141**	**135**

In order to be able to relate the number of reports to the total number of administered transfusions to patients younger than 21 years of age, TRIP requested hospitals to provide this information. In 2012 62 hospitals provided their data. Figure 13 shows the total number of transfused blood components in the different age groups.

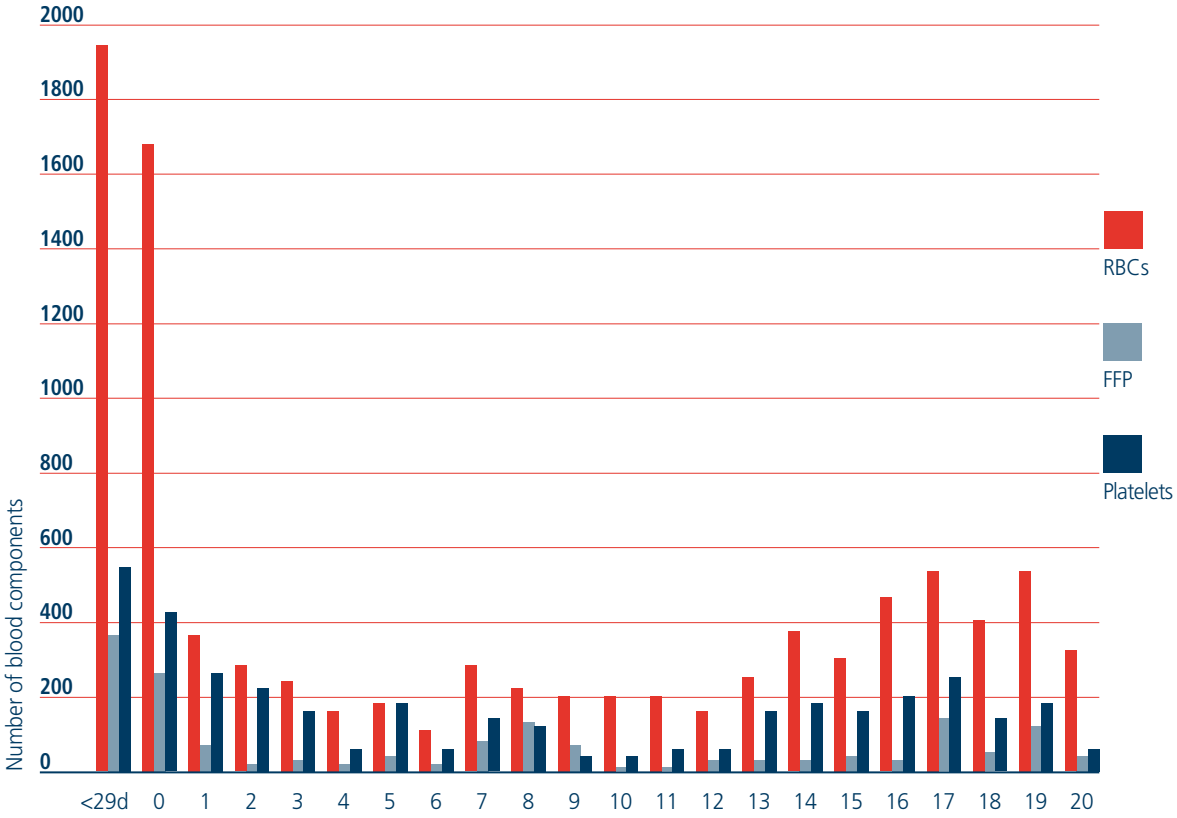


Figure 13 Number of blood components administered to patients <21 years of age in 2012 (n=62 hospitals)

Table 33. Numbers of units transfused and reports in patients under 21 in comparison to the total

Transfused blood components	All ages[$]		Patients <21 years (extrapolated)		Hospitals providing data regarding transfusion <21 years	
RBCs	441994		14141		9368	
FFP	63141[#]		2550		1614	
Platelets	54259		6295		3664	
All TR; rate per 1000 BP	2267	4,1	121	5,2	90	6,1
Febrile reactions (NHTR and mild NHFR)	824	1,5	47	2,0	37	2,5
Febrile reactions with RBCs	719	1,6	38	2,7	29	3,1
Anaphylactic and other allergic reactions	234	0,4	52	2,2	33	2,3
Anaphylactic and other allergic reactions, FFP/platelets	174	1,5	42	4,7	25	4,7
All incidents	286	0,5	14	0,6	12	0,8

[$] *Sum of all provided data from 96 hospitals*

[#] *In 2012 two hospitals informed TRIP they administered Octaplas (total 1237 units in patients < 21, 1 report). Octaplas figure not included with FFP, only in the total number of blood products.*

Abbreviations: *TR = transfusion reaction; NHTR = non-hemolytic transfusion reaction; mild NHFR = mild non-hemolytic febrile reaction.*

Table 33 summarises the data on transfusion reactions and transfused blood components in patients under 21 years of age. The calculated rates of transfusion reactions are higher than in adult patients. However, confidence intervals are wide and data are not homogeneous. Notably rates for anaphylactic and other allergic reactions per 1000 administered components are higher. These reactions are rarely reported in patients under 1 year of age, who are relatively often transfused (Table 31). The relatively high frequency of transfusion reactions in patients over 1 year old might be related to their morbidity and frequency of transfusion in this age group. Apart from age group variation there is also variation between hospitals in the number of reported transfusion reactions. Therefore reliable conclusions cannot be drawn from these data. TRIP is cooperating with international groups in the field of hemovigilance in (very) young patients.

3.7 Mandatory reports of serious adverse reactions

In accordance with the Common Approach drawn up by the European Commission, only reports with imputability certain, probable or possible 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 34 shows the data for 2011 and 2012; one reaction reported in 2011 was unclassifiable owing to insufficient information and has not been included.

Table 34 Number and imputability of reports of grade 2 or higher in 2011 and 2012

Type of reaction	Number of serious reports		Possible		Possible		Certain	
	2011	2012	2011	2012	2011	2012	2011	2012
Acute hemolytic TR	11	3	3	1	5	2	3	-
Delayed hemolytic TR	1	4	-	1	-	1	1	2
TRALI	4	9	4	5	-	4	-	-
Anaphylactic reaction	20	13	5	3	14	7	1	3
Other allergic reaction	3	1	2	-	1	-	-	1
Circulatory overload	18	26	11	13	5	7	2	6
Post-transfusion bacteremia/sepsis	3	7	2	4	-	2	1	1
Post-transfusion malaria	1	-	-	-	-	-	1	-
Post-transfusion purpura	2	1	1	-	1	1	-	-
Post-transfusion viral infection	1	-	1	-	-	-	-	-
Other serious reactions	36	36	23	25	7	8	6	3
Total	**100**	**100**	**52**	**52**	**33**	**32**	**15**	**16**

Abbreviations: *TR=transfusion reaction, TRALI=transfusion related acute lung injury*

4. General considerations, conclusions and recommendations

4.1 The 10th TRIP report: has transfusion safety improved?

Collecting hemovigilance reports on a national level is meant to be a tool for improvement of transfusion safety. Ten years of hemovigilance give a picture of what is happening. In general there is a high level of transfusion safety in The Netherlands. In 2012 there were four reports of adverse reactions or incidents per 1000 distributed blood components (1 report per 250 units), and the majority of reactions was non-serious. The incidence of reported serious reactions was 0.16 per 1000 distributed blood components (1 per 6400 units). The number of transfused red cell concentrates continues to show a slight decrease. Infectious complications are the most feared, but these are rare. Certain or probable transmission of infection was limited to one report of post-transfusion bacteremia/sepsis that was assessed to be a transfusion-transmitted bacterial infection. There were no cases of transfusion-transmitted viral infections.

Since the start of reporting to TRIP registration a drop in reports has been seen due to implementation of two blood policy changes:

- Male only plasma for TRALI prevention
- Selection of K-negative and (since 2011) Rhesus phenotype compatible RBCs for women of childbearing potential (< 45 years of age)

There is increased awareness of the risk of transfusion-associated cardiac overload. Specific actions to reduce the risk for TACO still need to be taken.

With regard to transfusion errors, although there seems to be a downward trend in the number of reports of incorrect blood component transfused, it is not yet possible to draw conclusions regarding improvement of transfusion safety. Errors occurring when identifying patients and errors during laboratory procedures still lead to serious transfusion reactions. Correct execution of existing protocols and procedures can in principle prevent these errors. It is however clear that circumstances like emergency situations or working under pressure may cause mistakes in following procedures and consequently lead to selection and/or administration of an incorrect blood component.

Part of TRIP's mission is to monitor the efficacy of the reporting system. Are all the required data for effective recommendations for prevention of transfusion reactions and transfusion errors captured? Or would it be feasible to register non-serious reactions in less detail as some of these details do not add value to the analyses? These questions are also relevant in the light of voluntary reporting and the administrative burden of such a reporting system for the hospitals. The findings of the TRIP reports will form the basis for an upgrading project of the TRIP reporting system. The basic principle will continue to be that of collecting and collating reliable data for further improvement of transfusion safety in The Netherlands.

4.2 Actions and developments following recommendations in previous TRIP reports

	Update on recommendations which are still current from reports 2003 - 2010	Comment
1.	Focus on blood transfusion and hemovigilance in the curriculum for the training of medical specialists (2007).	TRIP sends annual report to training institutes for nurses and to those training specialists in the relevant disciplines. TRIP intends to make available training materials on the website
2.	Transfusion-associated circulatory overload also an important category (2006). Doctors prescribing blood transfusion should specify speed of administration and record any patient risk factors for circulatory overload. Patients at risk should receive prophylactic diuretics.	Action for clinical staff. See recommendation 3 (this report)
3.	Integration of activity within hospital safety management system with hemovigilance activity (2006).	This continues to be a point of concern.
4.	Action on improved monitoring of patients at risk of transfusion-associated hemosiderosis (2006; 2008).	No actions undertaken, underreporting continues.
5.	Hospital blood transfusion committees should have insight into the scale of the use of blood management techniques. There should be a protocol for the their use, with correct transfusion triggers and a procedure for reporting side effects and incidents (2007, 2008, 2009).	Recommendation included in 2011 revised national transfusion guideline.
6.	Recommendation for clinical scientific research on various blood components with transfusion reactions as outcome measure. Alternative products to the 'male-only' FFP, such as SD plasma, should be investigated in a prospective study of allergic and other reactions (2005, 2008, 2010).	Allergic reactions remain largely uninvestigated. Recommendation reiterated in 2010.
7.	Measures are required to make identification procedures more robust. This could include electronic systems to support the procedures. This will serve not only the safety of blood transfusions, but also patient safety in other areas (2009, also 2007; 2008 re staff training).	Encouraging trend towards reduction of incidents with ABO-incompatibility risk, but it is too early for any definite conclusions. The quality indicators in the revised transfusion guideline incorporate a question about use of electronic identification at the bedside.
8.	It is useful to record information about the transfusion chain in a standardised manner, allowing for comparisons of transfusion practice and outcomes. The indicators included in the revised CBO guidelines can form a starting point for this (2009).	The hospitals were requested to supply the indicator data for 2011 and 2012. Data has been analysed, information on TRIP website and publication in preparation
9.	Criteria must be set that allow for the inclusion of new TRIP categories 'transfusion-associated dyspnea' and 'hypotensive transfusion reaction' in the TRIP database. These categories must be clearly distinguished from the existing TRIP categories (2009). TRIP should revise the definitions for the categories of transfusion reaction and make them clearer where necessary. New categories of hypotensive transfusion reaction and transfusion-associated dyspnoea should be defined (as recommended in the 2009 and 2010 reports).	Definitions for bacterial complications revised. Draft definitions (based on ISBT definitions) will be discussed in workshop in 2013.
10.	A classification is needed (similar to that in use by SHOT) for the link between a transfusion reaction and a fatal outcome in the patient.	A (draft) tool was presented and discussed in the "Meet the expert" session in March 2012

11.	A standard protocol should be developed for the further investigation of serious anaphylactic transfusion reactions (2010).	No steps taken. Action: TRIP and the Sanquin Transfusion Medicine Unit
12.	In order to monitor optimal use of blood components, hospital hemovigilance staff are encouraged to report incidents which lead to unnecessary transfusion or avoidable component wastage.	This report again presents findings on unnecessary transfusions and avoidable component wastage: there was a rise in reports
13.	In order to investigate the incidence of transfusion reactions and incidents in neonates and children, TRIP will request information from hospitals on numbers of transfusions administered to neonates and children.	Over 50% of hospitals provided data at the end of 2011; findings about 2012 presented in this report.
14.	Hospitals are recommended to have effective procedures for investigating recipients of blood components which later were found to have possibly been infectious (2010).	The national transfusion guideline reiterates the obligation of retaining traceability data (for 30 years) and includes a quality indicator asking about the percentage of blood components for which the final destination has been confirmed.
15.	The hospitals should implement hemovigilance of blood management techniques as recommended in 2009: the blood transfusion committees should ensure that application of salvaged autologous blood is laid down in protocols with correct transfusion triggers and a procedure for reporting adverse reactions and incidents (2010)	The national transfusion guideline recommends hemovigilance covering the application of autologous blood management techniques. TRIP will continue to collect this information.

	Update on the recommendations in the 2011 TRIP report	**Comment**
16.	Hospitals should have arrangements to ensure that the hemovigilance staff are provided with sufficient information to assess transfusion reactions. This requires special attention when laboratory services are contracted out.	TRIP and the haemovigilance advisory board will take steps to make the reporting system more effective and to promote adoption of the recommendations by stakeholders. This recommendation will be included in the process.
17.	Serious reactions should be discussed between laboratory and clinical staff to agree the most likely diagnosis.	No specific projects known to TRIP. In 2012 - unlike in 2011 - there were no serious reports which could not be registered for lack of information.
18.	All transfusion reactions should be investigated according to hospital protocols. In serious reactions with dyspnea or hypoxia adequate evaluation including chest X-ray is necessary so that patients can be diagnosed and treated appropriately.	Besides the guidance included in hospital protocols, TRIP intends to include this aspect in the upgrading of the digital reporting system, so that it becomes clearer what supporting data is relevant for each reporting category.
19.	At the time of ordering a blood transfusion the doctor should also prescribe the speed of administration and indicate on the form whether a patient is at risk for TACO. At-risk patients should receive prophylactic diuretics.	No specific projects known to TRIP. See recommendation 3.
20.	As recommended in the TRIP 2010 annual report, hospitals should have a clear protocol for investigating recipients of blood components which in retrospect may have been infectious. Hospitals should record their actions and provide feedback to Sanquin in all cases, even if it was decided not to contact the patient.	No specific projects known to TRIP.

21.	TRIP should further analyse the reports of incorrect blood component transfused, other incident and near miss to investigate whether the declining trends represent a true improvement in transfusion safety.	The figures in 2012 are similar to 2011. Developments will be monitored.
22.	There should be formal protocols within hospitals concerning number of components which may be requested and number of components issued simultaneously as well as procedures for issued blood components that are not transfused.	This issue remains current, particularly in the light of the 30 minute rule in the CBO national transfusion guideline.
23.	In order to ensure completeness and transparency of reports regarding post-transfusion viral infections, Sanquin and TRIP should collaborate to ensure that the final conclusions of investigations are included in the TRIP database. This could be facilitated if all hospitals and also Sanquin report using the TRIP online system.	This point will be included in the upgrade of the TRIP reporting system and the instructions. In 2012 there were fewer reports of look-back and post-transfusion viral infection.

4.3 Conclusions

1. The numbers of reports in the various categories in 2012 were stable in comparison to 2010 and 2011.

2. Administration of an incorrect blood component remains a cause of avoidable morbidity in patients. The reports of incorrect blood component transfused in 2012 once again demonstrate the danger of identification errors, not only when hanging up a blood component but also at earlier steps of the transfusion chain. Incorrect transfusions can also result from not properly following the laboratory procedures for irregular antibody screening and for selecting antibody compatible blood components.

3. The analysis of the reported near misses showed that the routine checks play a major role in detecting and correcting errors.

4. Transfusion-associated circulatory overload accounted for the largest number of the serious reports.

5. The reports of newly formed anti-K, anti-c and anti-E among females younger than 45 at the time of transfusion shows a declining trend.

6. In 2012 there was one case of transfusion-transmitted bacterial infection (TTBI), grade 2 in severity, caused by a platelet concentrate.

7. The number of reports involving the use of salvaged drain blood was comparable to 2011; it is likely that there is still under-reporting of reactions and incidents associated with autologous blood management techniques.

4.4 Recommendations

A. Recommendations based on the 2012 TRIP Report

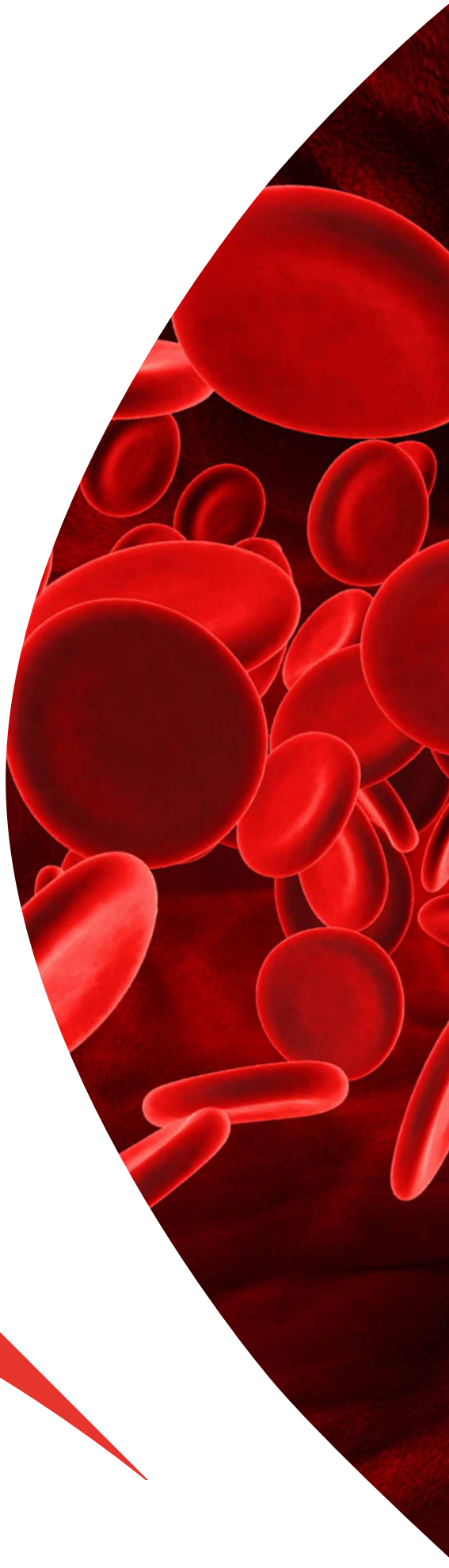
Recommendation	Who?
1. To promote and strengthen awareness of the importance of correctly adhering to protocols for identification of patients at all stages in the transfusion chain.	Hospital blood transfusion committees, hemovigilance officers and assistants, TRIP
2. Constant attention is needed for all laboratory procedures for irregular antibody screening and for selection of antibody-compatible blood components.	Hospital laboratory managers and biomedical scientists; hospital blood transfusion committees, TRIP
3. TRIP recommends that a procedure should be developed so that clinicians prescribing blood transfusion can assess whether a patient has risk factors for transfusion-associated circulatory overload.	Hospital blood transfusion committees

B. General recommendations

4. In cooperation with the hemovigilance advisory board and the professionals, TRIP should build on the acquired knowledge and experience and optimise the user-friendliness, monitor and where possible improve the effectiveness of the reporting system; the primary objective of reporting, that of increasing the safety of blood transfusion, should remain the guiding principle of this process.	TRIP, hemovigilance advisory board

List of terms and abbreviations

AHTR	acute hemolytic transfusion reaction
a.b.	antibody (formation)
BMT	blood management techniques
Bc	blood component
CBO	CBO quality organisation in healthcare
DHTR	delayed hemolytic transfusion reaction
FFP	fresh frozen plasma
Hosp	hospital
IBCT	incorrect blood component transfused
ICU	intensive care unit
IGZ	Inspectie voor de Gezondheidszorg (Healthcare Inspectorate)
NAT	nucleic acid amplification test
NHTR	non-hemolytic transfusion reaction
OBI	occult hepatitis B infection
PAS	platelet additive solution
PCR	polymerase chain reaction
PTP	post-transfusion purpura
RBC	red blood cell concentrate
RN	registered nurse
Sanquin	Sanquin Blood Supply Foundation
SD	solvent detergent (virus-reducing treatment)
TA-GvHD	Transfusion-associated graft versus host disease
TACO	Transfusion-associated circulatory overload,
Tf	transfusion
TR	transfusion reaction
TRALI	Transfusion-related acute lung injury
TRIP	TRIP Foundation (Transfusion Reactions In Patients)
TRIX	Dutch National database covering patient antibodies, hematopoietic stem cell transplants and crossmatch difficulties
Plt	platelet concentrate
Tx	transplantation



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