TRIP annual report 2011

Hemovigilance

Extended version

TRIP
Hemo-en biovigilantie

TRIP annual report 2011

Hemovigilance

Extended version

The TRIP annual report 2011, extended version, concerning hemovigilance reports in the Netherlands in 2011 is published under editorial responsibility of TRIP Foundation (Transfusion Reactions In Patients). TRIP Foundation includes representatives of the various professional bodies involved in blood transfusion.

TRIP
Hemo- en biovigilantie

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Foreword

This is the extended version of the 2011 TRIP hemovigilance report, presenting findings of the ninth year of hemovigilance reporting to TRIP. It is an honour to write this foreword as Prof. René de Vries' successor as president of TRIP foundation.

TRIP's primary task is receiving and analysing reports and reporting publicly on findings. As in recent years we have published a short TRIP report presenting the key points for policy-makers and managers. This year the short report combined information on hemovigilance and tissue vigilance. The extended version - only published in digital form (on www.tripnet.nl) this year – is intended for professionals in the transfusion chain.

From the start of TRIP's work, in principle all the reports were assessed first by TRIP staff and additionally by the Expert Committee. Because of the improved quality of information in the majority of reports, as well as the increased number of reports, the TRIP board decided in 2011 to maintain the 100% verification standard only for the serious reports, and move to expert checks for only a sample of the nonserious reports. This procedure was followed for the 2011 data.

The 2011 findings show a slight continuing rise of the total number of reports, while the number of serious reports is similar to last year. Once again there were very few confirmed or highly likely reports of transfusion transmitted infections. There was however, for the first time in the Netherlands since 1969, a documented case of malarial transmission. There is an encouraging decline in the number of reported incorrect blood component transfused which carried a risk of ABO-incompatible transfusion. This category could be an indicator for the safety of the transfusion chain. Analysis of the hemovigilance data in the next years will be necessary to establish whether this reflects a true reduction of the risk of serious transfusion errors.

The TRIP office commenced its activities at the end of 2002. As its first director I had the challenge and the pleasure of shaping the national hemovigilance registry and later the tissue vigilance system, together with the other members of the office staff. We are aware that the success of such a registry depends on the involvement and collaboration of professionals in the hospitals and at Sanquin Blood Supply Organisation. Moreover the work would have been impossible without the inspiration and support of the members of the TRIP governing board, the Advisory board and the Expert Committee. Each of the members represents a professional group which is practically involved in one part or another of the transfusion. As the president of the foundation as well as the former director, I wish to express sincere thanks to all these people.

In July 2012 the statutes of TRIP Foundation were changed, so that the vigilance of substances of human origin, better described with the broader term biovigilance, is now a formal task of the Foundation. TRIP now stands for Transfusion and Transplantation Reactions in Patients. What has not changed is that TRIP works on behalf of the professionals in the field of transfusion.

Dr. Martin R. Schipperus
President, TRIP Foundation

Summary

Objectives and procedures of the TRIP Office (hemovigilance)

The objective of TRIP (Transfusion Reactions In Patients) Dutch National Hemovigilance Office is to collect information and report on the safety of clinical use of blood components. Reporting is anonymous as to patients and treating clinicians. Reports are assessed by the TRIP office staff and further questions may be asked. An Expert Committee of transfusion experts from different professional backgrounds assess all serious reports and scans the non-serious reports for incongruities.

In the framework of compulsory reporting under the European directive 2002/98/EC and the additional directive 2005/61/EC, TRIP analyses and supplies an annual overview of serious adverse reactions (grade 2 or higher) and events involving blood components for the European Commission on behalf of the Healthcare Inspectorate (Inspectie voor de Gezondheidszorg, IGZ). The reporter can make a report directly available to the IGZ and/or the blood supply organisation Sanquin via the TRIP digital reporting system.

Participation

In total, 96 (96%) of the 100 Dutch hospitals participated in the TRIP registration in 2011. Transfusion reactions were reported by 91 hospitals and five hospitals indicated that they did not have any transfusion reactions to report in the TRIP categories. The closing date for this annual report was February 1 2012.

The reports in 2011

The number of reports received in 2011 was 2601 in total (2010: 2590 including late reports). Of this total, 2298 involved reports of transfusion reactions and 299 were reports of incidents in the transfusion chain; four potentially serious reports could not be categorised for lack of information. Seventeen reported incidents were associated with transfusion reactions, which were recorded as additional categories. Out of all the reports, 2391 (92 %) were submitted electronically.

Categorisation according to severity and imputability

The number of reports received in 2011 was 2601 in total (2010: 2590 including late reports). Of this total, 2298 involved reports of transfusion reactions and 299 were reports of incidents in the transfusion chain; four potentially serious reports could not be categorised for lack of information. Seventeen reported incidents were associated with transfusion reactions, which were recorded as additional categories. Out of all the reports, 2391 (92 %) were submitted electronically.

The transfusion reactions were also evaluated for imputability: the likelihood that the observed symptoms or findings can be attributed to the transfusion. The imputability was listed for 2260 (97.6%) of the 2315 transfusion reactions reported in 2011. Of these, 351 reports (15.5%) were considered to be definitely related to the transfusion, 634 (28.1%) as probable, 1082 (47.9%) as possible, 183 (8.1%) as unlikely and 10 (0.4%) as definitely not. Among the grade 4 reports, one acute hemolytic transfusion reaction in a patient with anti-Wra, had a probable imputability; in the other grade 4 reports the relation between the patient's death and the transfusion reaction was deemed to be either (only) possible or unlikely. Among all the serious reports, 92 had a possible, probable or definite imputability to transfusion, a number which is in the range observed since 2006.

Types of reactions and incidents

The reported reactions are: non-hemolytic transfusion reaction 497, mild non-hemolytic febrile reaction 362, acute hemolytic transfusion reaction 15, delayed hemolytic transfusion reaction 9, transfusion-related acute lung injury (TRALI) 12, anaphylactic reaction 65, other allergic reaction 189, circulatory overload 38, post-transfusion purpura 2, post-transfusion viral infection 1, post-transfusion bacteremia/sepsis 60, hemosiderosis 2, other reaction 215 and new alloantibody formation 826.

The reported incidents include 44 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 six cases. TRIP also received 137 reports concerning other incidents, of which six were followed by transfusion reactions (one of grade 2) and 43 reports of near misses. There were 37 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 for a platelet concentrate was later found by Sanquin. Three of these reports stated that the patient had shown a nonserious transfusion reaction. The remaining incident reports were: positive bacterial screening of blood component 6 (in these cases no bacterial species was confirmed by Sanquin), look-back 30, hemolysed product 2 (this was unwashed drain blood intended for reinfusion).

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

In 2011, Sanquin supplied a total of 670,983 blood components to the hospitals. The total number of reports for 2011 was 2601. This gives an overall rate of 3.9 reports per 1000 distributed blood components. This is similar to 2010. In comparison to 2010 there was a higher number of reports of other reaction and other incident and a lower number of reports of incorrect blood component transfused, near miss and look-back.

Discussion and conclusions

Serious transfusion reactions

Among all the serious reactions with definite, probable or possible imputability the largest categories in 2011 were other reaction, anaphylactic reaction and circulatory overload, with 22, 20 and 18 reports respectively.

An acute hemolytic transfusion reaction with fatal outcome was probably caused by anti-Wra. In all there were 16 reports of grade 3 or 4 and definite, probable or possible imputability. Five of these concerned transfusion-associated circulatory overload (TACO). A clinician should specify the speed of administration when prescribing a transfusion and note down whether the patient has risk factors for TACO. For patients who are at risk prophylactic diuretics can be prescribed.

TRALI

The number of TRALI reports in 2011 was 12, among which eight (four of grade 2) with definite, probable or possible imputability. This number remains lower than it was before 2007, when the male-only plasma measure was introduced.

Other reaction

The number of reports registered as "other reaction" shows a rising trend. They are reports that do not meet the definitions for the specific categories. There was a cluster where breathing difficulties following transfusion were the main feature. These reactions should be adequately investigated including chest X-ray so that the patients can be diagnosed and treated appropriately.

Infectious complications

In 2011 there was one probable case of transfusion-transmitted bacterial infection, reported as post-transfusion bacteremia/sepsis. There was one report of confirmed malarial transmission (Plasmodium malariae); donor screening had been performed correctly. This case shows that the risk of malarial transmission can never be fully eliminated. There were no confirmed reports of transfusion-transmitted viral infection in 2011. There were cases where Sanquin notified hospitals about a look-back but received no reply about the patients in question.

Incorrect blood component transfused (IBCT)

The number of reports of IBCT (44) was lower than in any year since 2005. The number of cases where there was a risk of an ABO incompatible transfusion (17) is similar to 2011 but lower than the figures for 2008 and 2009 (the first years when TRIP performed the assessment of risk type), this could indicate an improvement in transfusion safety, but it is equally possible that there is underreporting of certain types of incidents.

Other incident

An important subcategory among the other incidents is that of reports of unnecessary administration of transfusions or of avoidable wastage of blood components. In order to minimise wastage of blood components, hospitals should have protocols which indicate how many components may be requested and issued at a time, as well as procedures for units which are issued but not actually transfused.

Transfusions and reports in patients under 21 years

The Dutch data about patients younger than 21 years of age appear to show higher incidences of allergic transfusion reactions and of febrile reactions, as well as of incidents. These incidences were calculated on the basis of the small number of reports in this age group and using extrapolated figures for numbers of administered blood components; moreover the differences are not statistically significant, so no firm conclusions can be drawn at present.

Blood management techniques (BMT)

The number of reports involving drain blood was almost twice as high in 2011 as in 2010. The extent of use of these techniques is still not known to numerous hospital transfusion committees. As recommended in the revised "CBO" national transfusion guideline (2011), hemovigilance should be extended to cover the use of autologous blood management techniques, with correct transfusion triggers and a procedure for reporting adverse reactions and incidents.

Other conclusions and recommendations

As recommended in the 2010 TRIP report on hemovigilance, hospitals should have clear procedures for tracing and investigating recipients of blood components which are later found to have possibly been infectious. The hospitals should document what steps are taken and report back to Sanquin, even if a decision is taken not to contact the patient.

In four reports, including three submitted as severity grades 2, 3 and 4 respectively, the hemovigilance officer in the reporting hospital (n=3) had no access to clinical information which was necessary to assess the type of transfusion reaction. Hospitals must ensure that the hemovigilance officer and hemovigilance assistant (transfusion safety officer) are provided with sufficient information for them to adequately assess the reactions which are reported. This matter requires particular attention where laboratory services are provided by an external organisation.

1 Introduction

Sound information of the nature and extent of adverse effects of blood transfusion is essential in order to detect known and previously unknown adverse effects of current or new blood components in a timely manner. The transfusion chain can be monitored by means of central registration of transfusion reactions (TR) and thus weak links in the chain can be identified.

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 managed the national reporting system for transfusion reactions in collaboration with contact persons in the hospitals and the blood service, Sanquin Blood Supply. Reporting to TRIP is anonymous and in principle voluntary. However, reporting to TRIP is considered the norm by the Healthcare Inspectorate (IGZ) and the CBO Guideline for Blood Transfusion (2004 and 2011 revisions). The digital reporting system was used actively by most of the hospitals in 2011.

Relevant findings of investigations and the degree of severity of the clinical symptoms should be included in the report. An assessment is also given of the imputability, the likelihood with which a reaction can be attributed to a blood transfusion that has been administered. If necessary, the TRIP physicians will ask the reporter for further explanations or additional data. This allows the TRIP staff to assess the coherence of the reports and to verify the reported category of (potentially) serious reports.

Reporting to TRIP is not linked to the provision of care and is also separate from other, non-voluntary reporting routes. Under the European directive 2002/98/EC there is an obligation to report to the competent authority, IGZ, serious undesirable 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 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 via the TRIP online reporting system; this is not automatic but remains the hospital's responsibility.

An Expert Committee appointed from the TRIP Governing Board assesses all serious reports and a sample of non-serious reports. Definitive inclusion in the TRIP report is subsequent to this review process.

Since August 2006 TRIP has also managed a national supporting system for serious adverse reactions and/or adverse events associated with the use of human tissues and cells. The TRIP annual tissue vigilance reports (available on www.tripnet.nl) describe this system and the findings.

2 Hemovigilance reports in 2011

2.1 Participation

The value of national registration and evaluation of transfusion reactions is determined by the level of participation and by the quality of the information submitted. In 2011, 96 of the 100 hospitals participated in the registration. Of these, 91 hospitals reported transfusion reactions and five hospitals indicated that there were no transfusion reactions to report. Data about blood use were received from 94 institutions. As in the past, it was the responsibility of the contact persons in the hospital to determine at which moment subsequent to a merger different locations have become sufficiently comparable to proceed under one reporting code. The total number of hospital contact addresses dropped from 103 in 2010 to 100 in 2011 because of two mergers and one small hospital ceasing to perform transfusions.

Every year, a number of hospitals do not send in data before the closing date: these hospitals have the status of non-participants in the TRIP report. The closing date for inclusion of reports from 2011 in this annual report was February 1 2012.

Additionally, Sanquin's central departments made summary data available to TRIP on serious reports and administered blood components for which positive bacterial screen results were subsequently obtained (see section 3.2). A number of reports were also received from contact persons in Sanquin's regional blood bank divisions. Annually, TRIP checks on double reports and merges these after discussing this with the reporters.

After the closing date for the 2010 report, 89 late submissions (3% of the final total) were received for 2010. The Expert Committee has since formally assessed these reports. Late information from previous years has been incorporated in all figures and tables of this report.

Figure 1 shows the level of participation over the years 2002 (baseline measurement) up to and including 2011.

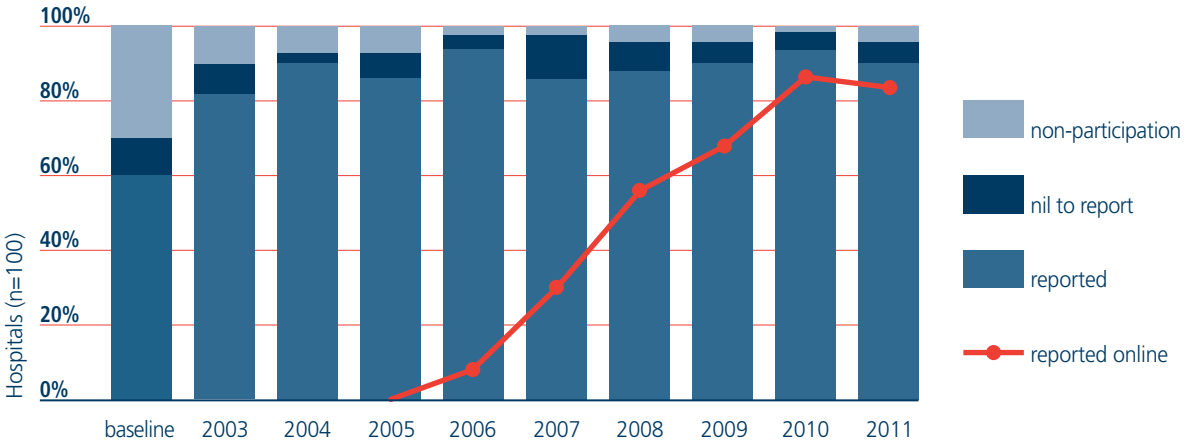


Figure 1 Participation per year

2.2 Summary of data regarding the reports for 2011

The TRIP hemovigilance definitions can be found at www.tripnet.nl.

Reports received

In total, 2601 reports of transfusion reactions and of incidents in the transfusion chain were received in 2011; these were submitted by 91 hospitals. There has been an increase of 0.4% compared to the final total for 2010. This increase concerns non-serious reactions and will be discussed further in the relevant sections of this report. Of all the reports, 2391 were submitted electronically (92%, 84 hospitals).

Following initial assessment by the TRIP office staff some 40 complex reports were discussed in a joint meeting of Expert Committee members and hospital reporters. All serious reports were reviewed by the Expert Committee members and the non-serious reports were checked in overview form. Subsequently reporters were asked supplementary questions in a number of cases (approximately 30 times in total). In some cases additional relevant information was forthcoming and in 16 cases consensus was reached to adjust the category, severity or imputability level.

Table 1 (transfusion reactions) and Table 2 (incidents) show the number of reports per category for the years 2003 up to and including 2011. The transfusion reactions that followed incidents are discussed separately in the paragraphs concerning incidents in chapter 3.3 and have not been included in Table 1.

Table 1 Transfusion reactions reported to TRIP, 2003–2011

Reaction	2003	2004	2005	2006	2007	2008	2009	2010	2011	Grade 2 or higher[#]	Hospitals with reports in 2011
NHTR	318	345	435	490	452	453	488	505	497	8	81
Mild febrile reaction	326	341	375	363	328	275	360	363	362	2	72
AHTR	8	14	9	19	11	18	18	21	15	8	12
DHTR	19	14	12	14	11	18	8	7	9	1	
TRALI	7	9	17	25	31	21	13	17	12	4	9
Anaphylactic reaction	8	21	26	19	54	65	71	73	65	20	24
Other allergic reaction	132	171	219	222	202	171	181	184	189	3	48
Circulatory overload	7	6	27	34	31	39	42	47	38	18	23
Post-transfusion purpura	0	0	0	0	0	1	0	0	2	2	2
TA-GVHD	0	0	0	0	0	1	0	0	0	0	0
Hemosiderosis	0	0	4	5	3	5	2	4	2	2	2
New allo-antibody	244	428	571	607	601	610	756	814	826	0	63
Other reaction	54	64	67	61	55	101	136	164	215	22	57
Post-tf bacteremia/sepsis[§]	9	5	10	7	19	37	55	41	60	3	31
Post-tf viral infection	5	7	8	7	7	7	4	1	5	1	1
Post-tf malaria									1	1	1
Total TR	**1137**	**1425**	**1780**	**1873**	**1805**	**1822**	**2134**	**2241**	**2298**	**95**	**91**
Total grade 2 or higher[#]	35	83	88	112	102	131	102	96	100	100	43
Insufficient information									4	1	3
Total reports*	**1268**	**1547**	**1985**	**2130**	**2081**	**2055**	**2412**	**2590**	**2601**	**101**	**91**

[#] *imputability certain, probable or possible*

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

* *total transfusion reactions and 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; TR = transfusion reaction*

Tabel 2 Incidents reported to TRIP, 2003–2011

Incident	2003	2004	2005	2006	2007	2008	2009	2010	2011	Hospitals with reports in 2011	Hospitals with reports ever*
Incorrect bc transfused	34	36	60	64	64	59	61	58	44	25	80
Near miss	31	62	79	77	74	55	72	68	43	17	45
Other incident	5	12	51	86	100	83	110	117	137	33	61
Look-back (info reported by hospital to TRIP)		2	2	1	4	9	6	50	30	14	30
Viral contamination of bc				2	0	2	1	4	0	0	4
Positive bacterial screen[$]	61	10	13	27	29	2	4	3	6	20	53
Bacterial contamination of bc[$]					5	23	22	40	37		
Hemolysed product									2	2	2
Total incidents	**131**	**122**	**205**	**257**	**276**	**233**	**278**	**349**	**299**	**56**	**87**

* *out of the 100 hospitals in 2012*

[$] *however no bacterial species confirmed. If confirmed bacterial contamination, included in bacterial contamination of bc.*

Abbreviations: *bc = blood component*

Severity 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. Severity and imputability are not relevant for incidents without clinical consequences. The total number of transfusion reactions, i.e. all reports in the categories of transfusion reaction (2298) plus the reactions that occurred in incidents and reports of bacterial contamination (17), was 2315, of which the severity was recorded in 2239 cases (97%). The severity was grade 0 for 772 reports (33%), grade 1 for 1344 reports (58%), grade 2 for 104 reports (4.5 %), grade 3 for 13 reports (0.6 %) and grade 4 for six reports (0.3 %). The grade 4 reports are discussed further in section 3.5.

Figure 2 shows the severity grades of transfusion reactions in 2003 - 2011. The total number of serious reports (grades 2-4) was 123. This figure has lain between 115 and 145 since 2006.

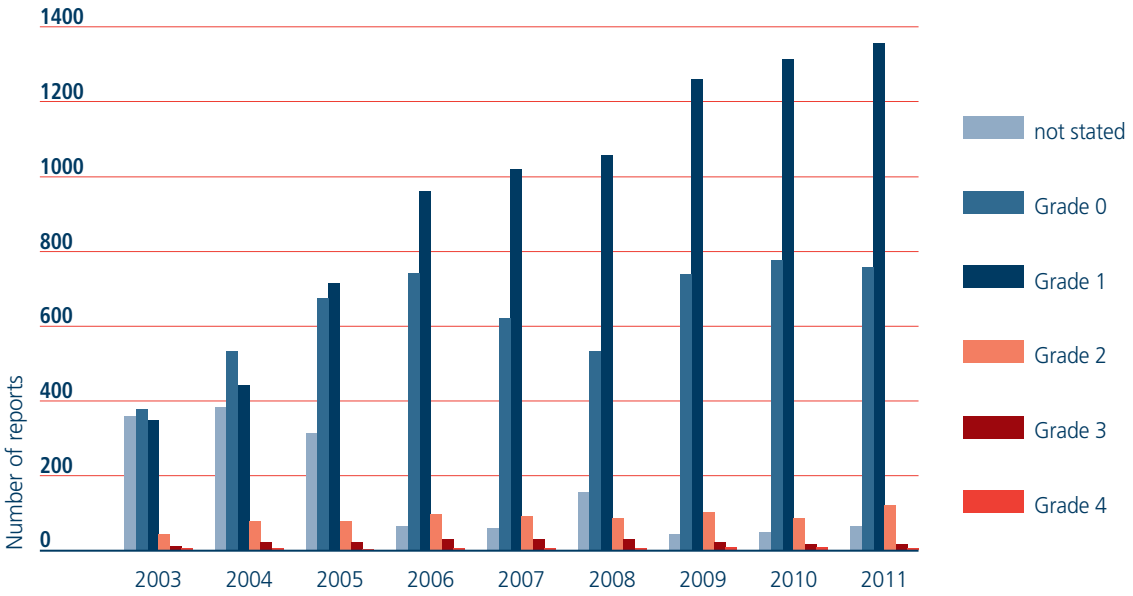


Figure 2 Severity of the transfusion reactions, 2003 – 2011

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 is only relevant if the patient experienced a reaction. Of the 2315 transfusion reactions reported in 2011, the imputability was listed for 2260 reports (98%). Of these, 351 reports (16%) were considered certainly related to the transfusion, 634 (28%) were probable, 1082 (48%) were possible, 183 (8.1%) were unlikely and 10 (0.4%) were excluded. Figure 3 shows the imputability of the 2315 transfusion reactions in 2011, compared to previous years. Of the 126 reports of severity grade 2 or higher, 100 were of certain, probable or possible imputability (2010: 97).

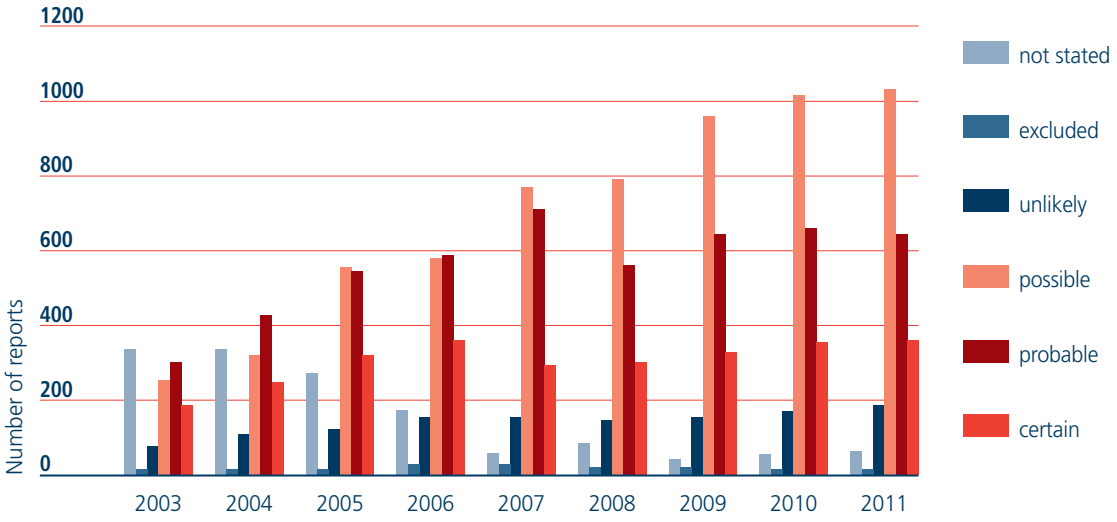


Figure 3 Imputability of the transfusion reactions, 2003 – 2011

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

In 2011, Sanquin supplied hospitals with a total of 670.983 blood components; this number does not include special components like lymphocytes and granulocytes.

The total number of reports for 2011 was 2601. Using the total number of distributed blood components as a denominator, that makes 3.88 reports per 1000 blood components distributed nationally, or 3.78 after exclusion of the reports relating to autologous blood management techniques (see section 3.4). 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 2010 and 2011

Type of blood component (bc)	2010					2011				
	Number of bc supplied	Reports; number per 1000 bc		Serious reports#; number per 1000 bc		Number of bc supplied	Reports; number per 1000 bc		Serious reports#; number per 1000 bc	
Red blood cell concentrate	529.840	1959	3,70	54	0,10	524.072	1958	3,73	59	0,11
Platelet concentrate	57.346	345	6,02	19	0,33	61.665	351	5,69	18	0,29
Fresh frozen plasma	83.274	84	1,01	7	0,08	85.246	79	0,93	11	0,13
Cell-saver and drain blood		38		2			64		1	
Other products		1*		1*			1*		0	
Combinations		90		11			91		10	
Not stated		74		0			57		0	
Total	**670.490**	**2590**	**3,86**	**92**	**0,18**	**670.983**	**2601**	**3,88**	**100**	**0,15**

Imputability certain, probable, possible

* *Reconstituted blood for intrauterine transfusion*

Figure 4 shows the number of reports per year and the number per 1000 units since the beginning of the TRIP registry. Data on 2002 were retrospectively collected in 2003; it can be seen that there was a ramp-up phase in 2003-5 and a subsequent slower increase which was interrupted by a dip in 2007-2008. In 2008 it became obligatory to report serious adverse reactions and serious adverse events (errors and incidents) to the Healthcare Inspectorate. The module in the TRIP digital reporting system allowing hemovigilance officers to send reports directly to the Inspectorate and/or to Sanquin was activated at the end of 2008. In 2008 also a number of

definitions were modified, notably that for grade 2 which was adjusted to capture reactions defined as serious by the European legislation. The ongoing increase is seen in the non-serious reports. This is discussed further under the relevant categories and in section 4.1 of this report.

Table 4 in parts A and B shows the distribution of the administered blood components per type of reaction or incident.

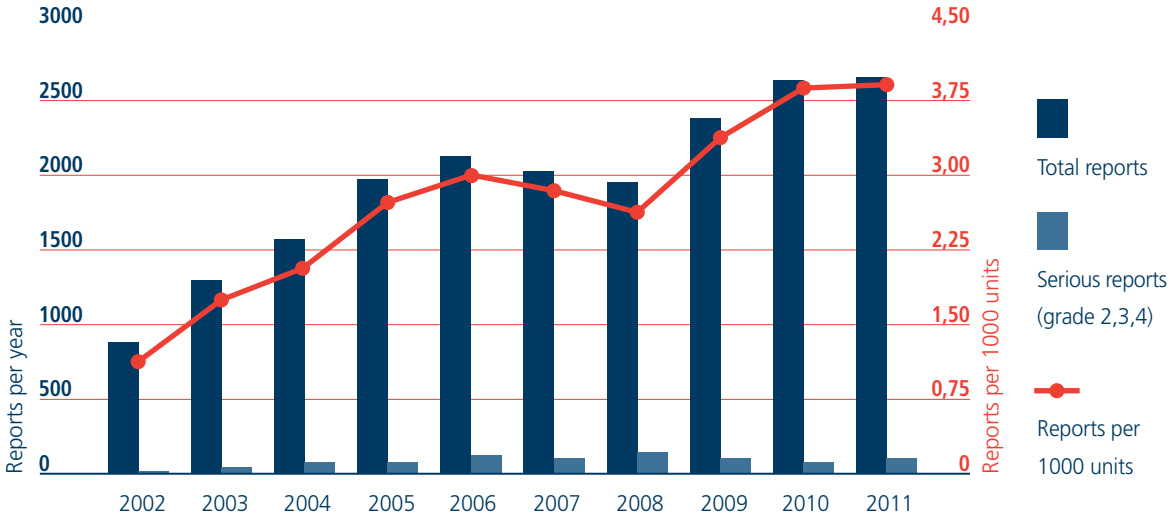


Figure 4 Number of reports per year, 2002 - 2011

Table 4 Distribution of types of blood components per category of report* in 2011

A. Reaction	RBCs	Platelets	Plasma	Combi-nation	Other#	Not stated
Non-hemolytic transfusion reaction	366	77	2	15	37	-
	73,6%	15,5%	0,4%	3,0%	7,4%	
Mild non-hemolytic febrile reaction	338	16	3	2	2	1
	93,4%	4,4%	0,8%	0,6%	0,6%	0,3%
Acute hemolytic transfusion reaction	15	-	-	-	-	-
	100%					
Delayed hemolytic transfusion reaction	9	-	-	-	-	-
	100%					
TRALI	8	3	-	1	-	-
	66,7%	25%		8,3%		
Anaphylactic reaction	15	26	17	6	1	-
	23,1%	40,0%	26,2%	9,2%	1,5%	
Other allergic reaction	37	103	40	9	-	-
	19,6%	54,5%	21,2%	4,8%		
Circulatory overload	32	2	-	4	-	-
	84,2%	5,3%		10,5%		
New allo-antibody	772	13	-	40	-	2
	93,5%	1,6%		4,8%		0,1%
Other reaction	152	36	7	6	14	-
	70,7%	16,7%	3,3%	2,8%	6,6%	
Post-transfusion bacteremia/sepsis	53	7	-	-	-	-
	88,3%	11,7%				
B. Incident						
Incorrect blood component transfused	33	3	3	1	-	4
	75,0%	6,8%	6,8%	2,3%		9,1%
Other incident	89	11	6	1	9	21
	65,0%	8,0%	4,4%	0,7%	6,6%	15,3%
Near miss	10	2	-	1	-	30
	23,3%	4,7%		2,3%		69,8%
Bacterially contaminated blood component	7	30	-	-	-	-
	18,9%	81,1%				
Look-back	16	14	-	-	-	-
	53,3%	46,7%				

* *Smallest categories not shown*

\# *Includes autologous blood management techniques*

2.3 Information about the patients

Table 5 gives an overview of the distribution of patients' age group and gender per transfusion reaction and incident category. Information collected in the "Proton" study on recipients of blood components in the Netherlands is included at the bottom of Table 5 for purposes of comparison.

Table 5 Distribution of age groups of patients per category of report* in 2011

A. Transfusion reactions	<1y		1-20		20-60		60-80		>80y		Not stated or N/A[1]
	M	F	M	F	M	F	M	F	M	F	
Non-hemolytic transfusion reaction	1	1	9	10	69	88	131	112	40	34	2
Mild non-hemolytic febrile reaction	1	1	9	4	44	48	117	72	34	31	1
Acute hemolytic transfusion reaction	-	-	1	-	2	1	1	4	2	4	-
Delayed hemolytic transfusion reaction	-	-	-	-	-	1	4	2	-	2	-
TRALI	-	-	1	1	1	3	3	2	1	-	-
Anaphylactic reaction	-	1	6	5	10	15	10	11	2	5	-
Other allergic reaction	1	1	22	8	49	52	26	17	4	9	-
Circulatory overload	1	-	-	-	2	2	9	9	8	6	1
New allo-antibody	-	1	6	5	58	130	191	257	55	123	-
Other reaction	1	2	5	4	17	35	43	63	25	20	-
Post-transfusion bacteremia/sepsis	1	-	2	1	6	9	14	12	8	7	-
Total (TR)	**6**	**7**	**61**	**38**	**262**	**388**	**550**	**561**	**179**	**241**	**5**
	0,6%		4%		28%		48%		18%		
B. Incidents											
Incorrect blood component transfused	1	2	-	2	3	8	7	14	3	4	-
Other incident	-	2	2	2	10	21	29	23	16	23	9
Near miss	-	1	-	-	5	11	9	12	2	1	2
Bacterially contaminated blood component	-	-	1	3	7	1	17	5	-	3	-
Look-back	-	-	-	2	7	2	4	5	4	3	3
Total (incidents)*	**1**	**5**	**3**	**9**	**34**	**43**	**70**	**60**	**25**	**35**	**14**
	2%		4%		27%		46%		21%		
Units transfused nationally[2]											
RBC	1,5%		2,9%		30,5%		50,6%		14,4%		
Platelets	4,4%		12,4%		46,2%		34,4%		2,8%		
Fresh frozen plasma	2,4%		5,4%		37,0%		50,4%		5,0%		

* *smallest categories not shown but included in totals*

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

[2] *The Proton study: profiles of transfusion recipients in The Netherlands in 1996-2006. Borkent-Raven et al. Vox Sang. 2010;99(1):54-64..*

Abbreviations: *TR = transfusion reaction(s); RBC = red blood cell concentrate.*

Blood transfusions and reported transfusion reactions in patients under 21 years of age

The 2010 TRIP hemovigilance report called for special attention to be paid to blood transfusions and reports involving pediatric patients. SHOT, the United Kingdom hemovigilance system, has for several years observed a relatively high number of reports in patients younger than 18 years of age, but lacks information on transfusions administered to patients in this age group. TRIP asked the hospitals to provide details of units transfused to patients below 21 years of age in 2011. The reason for going up to 20 years (in contrast to other systems including SHOT) is for comparability with the age groups applied in the PROTON study (Vox Sang. 2010

Jul;99(1):54-64). Fifty-one out of the 100 Dutch hospitals complied with this request, including four of the ten hospitals with neonatal intensive care units, two of the four cardiothoracic centres and the only fetal treatment centre.

In these 51 hospitals, a total of 6471 red blood cell concentrates, 1502 plasma units and 2960 platelet concentrates and 36 exchange units had been administered to patients under 21. The transfusions to patients below the age of 21 represented 2.5% of all red blood cell concentrates transfused in these hospitals, 4.4% of plasma and 11.2% of platelet units. Figure 5 shows the numbers of units according to the age of the recipients; it is seen that relatively large numbers of transfusions are administered to patients in the first month and in the rest of the first year of life. Note that each unit for transfusion has been counted once, thus a neonate receiving several pediatric portions from the same single donor unit will have the portions counted separately. Figure 6 shows the percentages of blood components which were transfused to patients below age 21 according to level of total blood use in the hospital.

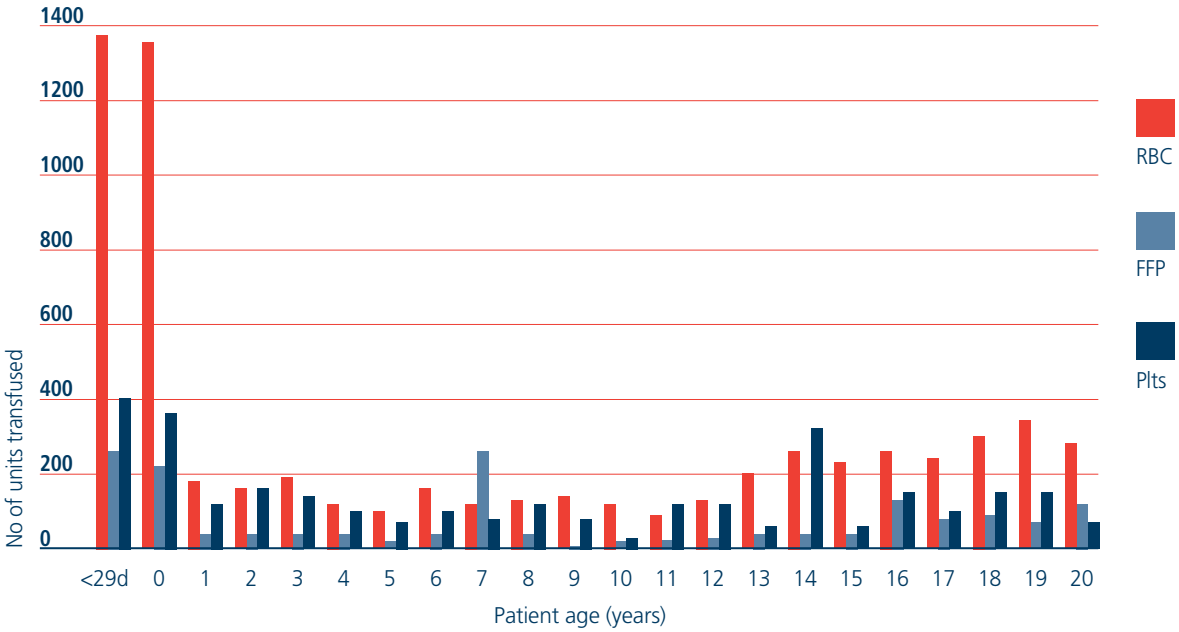
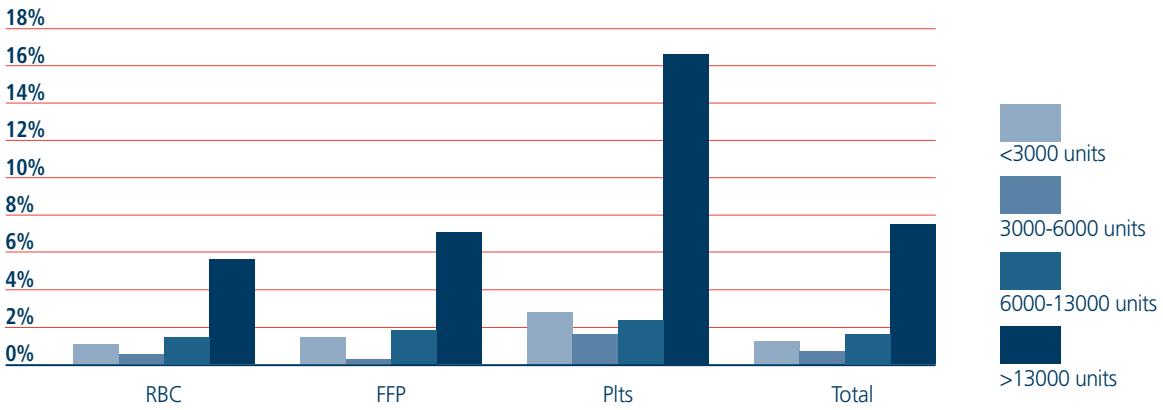


Figure 5 Units transfused to patients under 21 years (n=51 hospitals)



Abbreviations: *RBC = red blood cell concentrate; FFP = fresh frozen plasma; Plts = platelets*

Figure 6 Percentage of blood components administered to patients younger than 21 according to total hospital blood use (n=51).

In 2011 TRIP received 141 reports concerning patients younger than 21. An overview per age band is presented in Table 6 (transfusion reactions) and Table 7 (incidents). Age is calculated as the difference between transfusion date and date of birth. Twenty-nine of the 100 Dutch hospitals sent reports concerning this age group. Of the 29 reporting hospitals, 16 also submitted data on blood use in patients under 21 years. The number of reports ranged from 1 to 41. Of note, there were only few reports concerning neonates <29 days of age, the group that receives most transfusions. The annual number of reports in recipients under 21 was similar to previous years (see Table 8). Out of the total of 141 reports, 70 came from the 51 hospitals that supplied transfusion data for patients under 21. There were 71 reports concerning transfusion of RBCs, 45 for platelets, 18 for plasma, three for combinations, one report related to an intra-uterine transfusion and in three reports of incidents the type of blood component was not stated. The rate of reported transfusion reactions in patients under the age of 21 is 5.7 per 1000 transfused units if the transfusion data is extrapolated to obtain an estimated figure for all participating hospitals; it is 3.5 per 1000 units in adult transfusion practice. In order to verify these data the reporting rate was also calculated for the 51 hospitals that supplied data on blood use in patients under 21 years and comparable rates were obtained. Any differences in reporting rate were not statistically significant.

Table 6 Reported transfusion reactions in patients <21 years in 2011, per age group

Transfusion reaction	< 29 days	29 days to 1 year	1-11 years	11-21 years	Total
AHTR			1		1
Anaphylactic transfusion reaction		1	6	6	13
Other allergic reaction		1	22	14	37
Hemosiderosis				1	1
Mild non-hemolytic febrile reaction	1	1	9	4	15
Non-hemolytic transfusion reaction		1	11	10	22
New allo-antibody		1	2	10	13
Other reaction		3	6	3	12
Post-transfusion bacteraemia/sepsis		1	2	1	4
TRALI			2		2
TACO		1			1
Total	**1**	**10**	**61**	**49**	**121**

Table 7 Reported incidents involving patients <21 years in 2011, per age group

Incident	< 29 days	29 days to1 year	1-11 years	11-21 years	Total
Near miss	1				1
Bacterial contamination of blood component			2	2	4
Look back				2	2
Other incident	3		1	4	8
Incorrect blood component transfused	2	1	1	1	5
Total	**5**	**1**	**2**	**9**	**20**

Table 8 Reported transfusion reactions (TR) and incidents in pediatric recipients, 2008-2011

	2008	2009	2010	2011
Transfusion reactions	116	118	110	121
Incidents	19	11	30	20
Total	**135**	**129**	**140**	**141**

Six serious reactions were reported. One report in the category of other reaction of grade 4 severity and with possible imputability concerned a premature baby; the reporter noted a possible relationship between blood transfusion and necrotising enterocolitis (NEC). In the literature an association between the incidence of NEC and transfusion has been described in retrospective studies. SHOT for the first time reported two cases where there was a possible link between transfusion and necrotising enterocolitis in 2011 (category previously uncategorised complications of tranfusion, PUCT). The relationship and pathophysiology are unclear and should be investigated further. Four anaphylactic reactions were reported (1x severity grade 3 and 3x grade 2) after transfusion of plasma (3x) and platelets (1x); for all of these the imputability was probable. The sixth report was a TRALI with severity grade 2 with unlikely imputability. The percentage of severe reactions in patients under 21 years is comparable to that in the general TRIP data.

The largest number of reports (37) was in the category of other allergic reaction. Combined with anaphylactic reaction (13) they represent 41% of transfusion reactions reported in patients under 21 and 44% in patients aged >1 and <21 years. This is a larger proportion than in adult transfused patients (11%). In line with the total body of TRIP reports, the majority of these reports in patients <21 years of age concerned administration of platelets (26) or plasma (15). The rate of anaphylactic and other allergic transfusion reactions combined per 1000 blood components transfused (extrapolated to all participating hospitals) is 2.3 per 1000 (total) units transfused compared to 0.3 in adults; that of the allergic + anaphylactic reactions associated with plasma and platelets is 4.2 per 1000 units in patients under 21 in comparison to 1.3 in patients ≥ 21. Although the difference in rates does not reach statistical significance at the 95% level, the findings represent a trend towards higher rates, as has been cited in the SHOT report.

Non-hemolytic transfusion reaction and mild non-hemolytic febrile reaction combined (37) represent 31% compared to 39% in the adults. The majority of reports (30) concerned the administration of RBCs, as is the case in the general TRIP data. These figures correspond to estimated rates of 1.7 per 1000 (total) blood components transfused to patients <21 years and 2.4 per 1000 for reactions associated with transfusion of red blood cell concentrates, compared to 1.4 and 1.7 per 1000 respectively in adults.

New allo-antibody formation is relatively rare in children. The number of reports is relatively high owing to inclusion of five cases involving female patients who received a transfusion when they were less than 21 years of age and in whom the antibody was detected later. It cannot be excluded that the antibodies developed as a result of pregnancies. The remaining eight reports concerned six male and two female patients, in whom the following allo-antibodies were reported: anti-E (4x) anti-K, anti-Jkb, anti-Lea and anti-M in a six-month-old baby. It must be noted that anti-M, anti-E and anti-Lea may also arise spontaneously.

The number of incidents concerning patients under 21 years of age amounted to 20. Extrapolating transfusion data to all participating hospitals gives a calculated reporting rate of 0.9 per 1000 blood components in patients <21 compared to 0.5 in adults. Due to the small number of reports this is not statistically significant. The reports of incorrect blood component transfused (IBCT) and other incident are shown in the tables in chapter 3.3, broken down according to risk level and type of error.

Concluding remarks

The Dutch data on patients under 21 years of age show higher incidences of allergic and febrile transfusion reactions as well as of incidents. However the differences were not statistically significant. The incidences are based on a small number of reports and on blood use data supplied by 51 out of the 100 Dutch hospitals. At this time it is not possible to draw definite conclusions on the calculated differences of reporting rates. Prolongation of the special focus on transfusion reactions and incidents in patients under 21 in the TRIP annual report is recommended.

3 Discussion of reports by categories

3.1 Non-infectious transfusion reactions

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

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 temperature of >1°C (<2°) 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.

As in previous years the non-hemolytic transfusion reactions (NHTR) and the mild non-hemolytic febrile reactions (mild NHFR) make up approximately a third of the total number of reports. In 2011 497 non-hemolytic transfusion reactions were reported by 82 hospitals. The number of reported mild febrile reactions was 362. The latter came from 71 hospitals. It can be presumed that the true number of mild NHFR is actually higher because not all hospitals include these in their protocols for reporting and investigating transfusion reactions. There were 64 hospitals that reported both NHTR and mild NHFR.

Each year the NHTR and the mild NHFR together account for a number of serious reports, in most of which admission from day care for observation or a prolongation of hospital stay was the reason for rating as grade 2. There were 12 grade 2 reports in 2011 (nine with certain, probable or possible imputability) in these two categories and one report of mild NHFR grade 4 with unlikely imputability. All but one grade 2 reaction (plasma) occurred during or after transfusion of RBCs.

As in 2010 the contribution of platelet concentrates (77 = 16%) was relatively high in comparison to RBC concentrates (366 = 74%) for the NHTR, but relatively low for the reported mild NHFR (16 = 4% platelet concentrates compared to 338 = 93% RBC). The contribution of reports concerning drain blood is also much greater for the NHTR (37) than for mild NHFR (2). Breaking down the symptoms listed in the reports of NHTR and mild NHFR reveals that chills/rigors were present in 68 (73%) out of 93 reports involving platelets and in 37 (95%) out of 39 reports concerning drain blood. For the RBCs these figures are 213 (30%) out of 704 reports. Table 9 shows an overview of chills and rise in temperature in NHTR and mild NHFR reports. The difference in the pattern of symptoms could be explained by different mechanisms for the various blood components involved in causing the reaction.

Table 9 Chills and rise in temperature in NHTR and mild NHFR reports in 2011

Blood component	Subgroup Amount of temperature change	Chills/ rigors	no chills	Not stated*	Signs not recorded	Total
RBC		**213**	**327**	**135**	**29**	**704(30#)**
	<1°C	12	20(1#)			32
	>1°C<2°C	84(2#)	301(13#)	2		387
	≥2°C	85(5#)	1	128(9#)		214
	No rise in temperature	28				28
	Temperature not specified	4	5	5		14
Platelets		**68**	**16**	**7**	**2**	**93(6#)**
	<1°C	7(1#)				7
	>1°C<2°C	17(1#)	16			33
	≥2°C	22(1#)		7(1#)		29
	No rise in temperature	21(2#)				21
	Temperature not specified	1				1
Plasma		**1**	**3**	**1**		**5(1#)**
	>1°C<2°C		3(1#)			3
	≥2°C			1		1
	No rise in temperature	1				1
Other$		**37**	**2**			**39**
	<1°C	2				2
	>1°C<2°C	9	2			11
	≥2°C	7				7
	No rise in temperature	19				19
Combination		**10**	**2**	**4**	**2**	**18**
	>1°C<2°C	5	2			7
	≥2°C	3		4		7
	No rise in temperature	2				2

* *in NHTR reports*

\# *number of the total which occurred in patients <21 years of age*

$ *All cases involved re-infused drain blood*

Were bacterial factors excluded in NHTR reports?

From the start of digital reporting to TRIP in 2008 the number of reports including the results of patient blood cultures have increased. In 2011 68% of the NHTR reports gave the information that one or more patient blood cultures were performed and the results, 58% of the mild NHFR reports had culture results reported. A summary of reported positive culture results in NHTR reports can be found in Table 10.

In 2011 positive blood cultures in the patient were reported in 35 of 497 NHTR reports; in 24 of these pretransfusion cultures had also shown growth of the same bacteria. The hospital reported post-transfusion bacteremia/sepsis as an additional category in seven of the remaining 11 cases, in two cases the period between taking the blood culture and a positive result was considered too long and in the remaining two cases the hospital thought the positive culture result was false-positive (caused by artefactual contamination of the blood sample). During the 2010 Expert Committee meeting it was decided that a positive blood culture from the patient post-transfusion excludes the NHTR/mild NHFR category as an option, particularly if blood cultures before transfusion were negative or not performed. Instead the category post-transfusion bacteremia/sepsis is appropriate (this category exists since 2008). However, frequently patients who may well have already had a bacterial infection before transfusion have been reported to develop a febrile reaction to the transfusion. A documented pre-existing bacterial infection in the patient was recorded in 64 (13%) of the NHTR, 56 times

after transfusion of RBC concentrates and eight times after the transfusion of platelets. Of these 64, the culture after transfusion was negative in 33 cases and positive in 25 cases (no culture: six cases).

In 62% of the NHTR reports the results of a culture of the blood component were reported to TRIP. In 17 cases bacterial growth was found. This was interpreted as accidental contamination of the culture in 12 cases, while in the remaining five the additional category "bacterial contamination of the blood component" was recorded.

Tabel 10 Summary of NHTR with positive bacterial culture results in 2011

Blood component	Subgroup Result*			Total	Assessment of culture result				Additional category
	Sanquin Screening	Unit (hospital)	Patient blood culture		Patient's blood positive before Tf	Interval too long	Conta-minated sample	Unit not closed after halting Tf	
RBC				**41**	**20**	**1**	**7**	**3**	**10**
	0	0	+	7	5				2#
	0	-	+	21	15	1	1		4#
	0	+	-	12			5	3	4
	-	+	-	1			1		
Platelets				**10**	**4**	**1**	**3**		**2**
	0	0	+	4	2	1			1#
	0	-	+	3	2		1		
	0	+	0	1					1
	0	+	-	1			1		
	-	+	-	1			1		
Combination				**1**			**1**		
(RBC and plasma)	0	+	0	1			1		

* *0 = not reported/not performed, + = culture positive, - = culture negative*

Sanquin screening = if result known to hospital (reporters are only informed if result positive)

\# *Post-tf bacteremia/sepsis according to TRIP definitions*

For a number of reasons TRIP prefers the category post-transfusion bacteremia/sepsis to NHTR for those cases where a febrile reaction was found together with a positive culture of the patient's blood. Firstly, other symptoms besides fever and chills, such as dyspnea or hypotension, do not preclude the selection of this category; thus the scattering of such reports over several categories like NHTR, mild NHFR, anaphylactic reaction and other reactions is avoided. Secondly, capturing the report as post-transfusion bacteremia/sepsis shows that there is a plausible explanation for the observed signs/symptoms, namely bacteremia/sepsis, which may or may not be related to the transfusion. Finally, recording bacterial contamination of the blood component as an additional category identifies those cases where it is possible that a bacterial infection was indeed transmitted by transfusion.

Case histories NHTR

NHTR 1

A 75-year-old woman with acute myeloid leukemia, blood group B pos, is transfused with O positive platelets in plasma. 1:15 hours after the start of the transfusion, after the whole unit has been administered, the patient experiences chills. Culturing of the bag failed and the transfusion reaction wasn't investigated further. 24 hours after the transfusion, the Hb level had dropped slightly from 5.5 to 4.6 mmol/L, which was attributed to the chemotherapy treatment. A blood culture from the patient was positive for Streptococcus

oralis. However, it turned out that this culture was performed two days after the reaction, therefore it was concluded that the additional category "post-transfusion bacteremia/sepsis" was not applicable. Twelve days after the reaction HLA antibodies were detected in the patient.
Report: NHTR, severity grade 1, imputability possible.

NHTR 2
A 52-year-old man, admitted to the hospital with metastasized renal cell carcinoma, received an RBC concentrate because of a low Hb. After receiving 150 ml of this in half an hour he experiences chills and his temperature rises from 37.6 to 38.9°C. Blood group serology and biochemistry tests reveal no indication of hemolysis. The blood culture of the patient was positive for Klebsiella pneumoniae. The culture of the bag showed no bacterial growth. Because the same bacteria had already been found before transfusion, the category post-transfusion bacteremia/sepsis was not appropriate.
Report: NHTR, severity grade 1, imputability possible.

Acute hemolytic transfusion reaction (AHTR)

Symptoms of hemolysis occurring within a few minutes of commencement or 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.

In the reporting year 2011 TRIP registered 15 reports in the category acute hemolytic transfusion reaction following transfusion of RBCs, a number in line with previous reporting years. Acute hemolytic transfusion reaction was reported as an additional category in two reports of IBCT and one report of hemolysis of product (autologous drain blood) that are described in the relevant chapters.

This year one report of AHTR was assessed as severity grade 4 with imputability probable. This is the third report of a grade 4 acute hemolytic transfusion reaction since the start of the TRIP registration in 2002. In this case an acute hemolytic transfusion reaction was found to be due to an allo-anti-Wright-a (Wra) after administration of a Wra positive RBC. The patient developed dyspnea, hypotension and dark urine, was treated in the intensive care unit (ICU) and died of multi-organ failure the next day. Laboratory investigations confirmed hemolysis. Extensive investigations including autopsy revealed no other cause for the fatal outcome.

This case is remarkable because hitherto no fatal acute hemolytic transfusion reaction due to anti-Wra has been reported in the literature. One case report (NVB bulletin, September 2005, p. 21) concerned a baby who had cardiac surgery and developed hemolysis after subsequent transfusion of Wra positive RBCs and anti-Wra containing allogeneic plasma. The baby died of complications unrelated to transfusion. In line with national and international transfusion guidelines Wra is not present on irregular antibody screening panels as it is a low-frequency antigen. Consequently the occurrence of an acute hemolytic transfusion reaction due to anti-Wra is a calculated risk inherent to the type and screen transfusion practice. It is not deemed practical to add Wra to the screening panel as this would lead to many more positive screens that would need typing. An anti-Wra does not always give rise to a hemolytic reaction or the reaction may just be mild. As only 3% of the donor population has been typed for Wra at present it is currently not possible to exclude the few Wra positive donors from donating red cells. The case highlights the need for continued awareness of the small but serious risk of an acute hemolytic transfusion reaction due to irregular antibodies against a low-frequency antigen, particularly when type and screen is practised.

The remaining 14 AHTRs consisted of seven grade 2 reports and seven grade 1 reports. Imputability was assessed as certain (n=1), probable (n=6), possible (n=5) and unlikely (n=2). As in previous years the most often reported symptoms are non-specific namely fever and chills/rigors. In only four cases more specific symptoms

of AHTR were reported: hemoglobinuria and loin pain. In all cases hemolysis was substantiated by biochemical markers (LDH, bilirubin, haptoglobin) and/or absence of the expected rise in hemoglobin after transfusion. Blood group serology revealed an anti-Wra in another grade 2 report (due to prolongation of hospital stay), in two cases an antibody to a private antigen was suspected but could not be demonstrated. Three reports mentioned pre-existent hemolysis due to hemophagocytic syndrome or medication, where transfusion was chronologically related to increased hemolysis.

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.

In 2011 TRIP received nine reports of delayed hemolytic transfusion reaction, submitted by seven hospitals. On top of that ten hospitals sent 17 reports of new alloantibody formation that led to diagnosis of delayed hemolytic transfusion reaction that was added as an additional category. These numbers are in line with previous reporting years. Two cases of IBCT gave rise to DHTR (see relevant chapter).

As expected all reports related to transfusion of RBCs. All but one of the DHTR reported as main category were of severity grade 1 (imputability certain n=2, probable n=4, possible n=2). One DHTR was of grade 2 and certain imputability. The responsible antibodies were detected in eight out of the nine DHTR: anti-Jka (2x), anti-E (2x), anti-K (1x), anti-C (1x), a combination of anti-c + -E (1x) and a combination of anti-K, -Fya and -Jkb (1x). Notably this combination of allo-antibodies was found in a woman who had suffered twice from jaundice following a blood transfusion. Her history revealed jaundice after a Caesarean section and transfusion in the 1980s. TRIX (national database of irregular antibodies and crossmatch problems) could have prevented a second episode of jaundice which in this case led to readmission of the patient (severity grade 2).

Out of 17 reports of new alloantibody formation with additional category DHTR, 11 cases were reported as such by the hospital. In six cases targeted questions by TRIP led to the additional category DHTR being added by the reporter. The detected antibodies that were held responsible for hemolysis were: anti-K (4x), anti-E (3x), anti-C, anti-Cw, anti-Fya, anti-Fyb, anti-Jkb and combinations of anti-Jkb + -Fyb, anti-K + -Jka + -Wra, anti-e + -K + -Wra, anti-K + -M, anti-E +-Jka + -Wra.

In 2009 and 2010 TRIP systematically asked all reporters of clinically significant antibodies that were detected within three months of transfusion targeted questions about potential hemolysis. According to the literature the incidence of DHTR is 5-10 times higher than AHTR. This could not be substantiated in the Dutch hospitals by this method. In 2011 TRIP discontinued this practice of systematically asking about hemolysis. This did not lead to a drop in the number of reported DHTRs. There is now more awareness of hemovigilance staff of DHTR and often reports include information about hemolysis parameters and/or hemoglobin rise after transfusion.

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.

A total of 12 TRALI reports were received in 2011 and were deemed to meet the consensus criteria for this transfusion reaction: clinical features of hypoxia or dyspnea, interval less than six hours from the end of transfusion, findings of bilateral pulmonary infiltrates on chest X-ray. Circulatory overload must be excluded as a more likely cause for the clinical features. The assessment of the type of reaction requires full clinical information including laboratory and radiological results as well as the response to treatment. One additional

report was originally submitted as a TRALI but gave insufficient information for it to be assessed; no additional information could be obtained from the reporting hospital so the report has been removed from the TRALI category and only counted among the reports with insufficient information (Table 1). The TRALIs (n=8) with imputability definite, probable or possible are discussed further below. It is important to note that TRIP does not take account of the findings of leukocyte serological investigation when assessing the TRALI reports.

The total number of reports of TRALI has declined since approximately 2008. This may partly be the consequence of increasingly critical assessment of reactions which are initially suspected to be a TRALI. This is illustrated by the result that only eight out of the 13 initial reports of TRALI to Sanquin in 2011 are still registered in that category in the TRIP database. Out of the five initial TRALI reports to Sanquin, three were assessed as being more consistent with transfusion-associated circulatory overload and two were placed in the category of other reaction. Two TRALI reports to TRIP with definite, probable or possible imputability were not reported to Sanquin (or conceivably not accepted as such). In the section on other reaction it is described how a number of reports concern dyspnea as a predominant feature but the cases did not meet the TRALI definition – generally no chest X-ray was performed or the time interval was too long. These trends raise the suspicion that TRALI is in some cases less well investigated and/or possibly less well recognised than a few years ago. It is important to maintain awareness of TRALI and in any case perform chest X-ray so that patients can be diagnosed and treated appropriately.

Out of the eight definite, probable and possible TRALIs, five were associated with transfusion of red blood cells, two with platelets and one with both platelets and a red blood cell concentrate. Four of these reports were of severity grade 2 and four of grade 1. Four of the patients were men and four women; four were receiving treatment for hemato-oncological conditions, one each for COPD, post-partum blood loss, one had undergone hemithyroidectomy and one drain placement in connection with a hepatojejunostomy. The ages ranged from 4 to 90 years.

Figure 7 shows the blood components associated with definite, probable and possible TRALI since 2003. On the basis of the reports up to and including 2009, TRIP calculated that there has been a drop in the total TRALI burden by approximately one-third following the measure (effective in mid-2007) of exclusively distributing plasma from male, never transfused donors as fresh frozen quarantine plasma for transfusion. That corresponds to virtually all TRALI caused by plasma transfusions being prevented (Wiersum-Osselton et al. Transfusion 2011;51:1278-1283; Middelburg et al. Transfusion 2011;51(10):2111-7). A similar measure concerning the recovered plasma added to pooled platelet products (the standard platelet concentrate for all except the South-western region of The Netherlands) was implemented in November 2009. The reports after

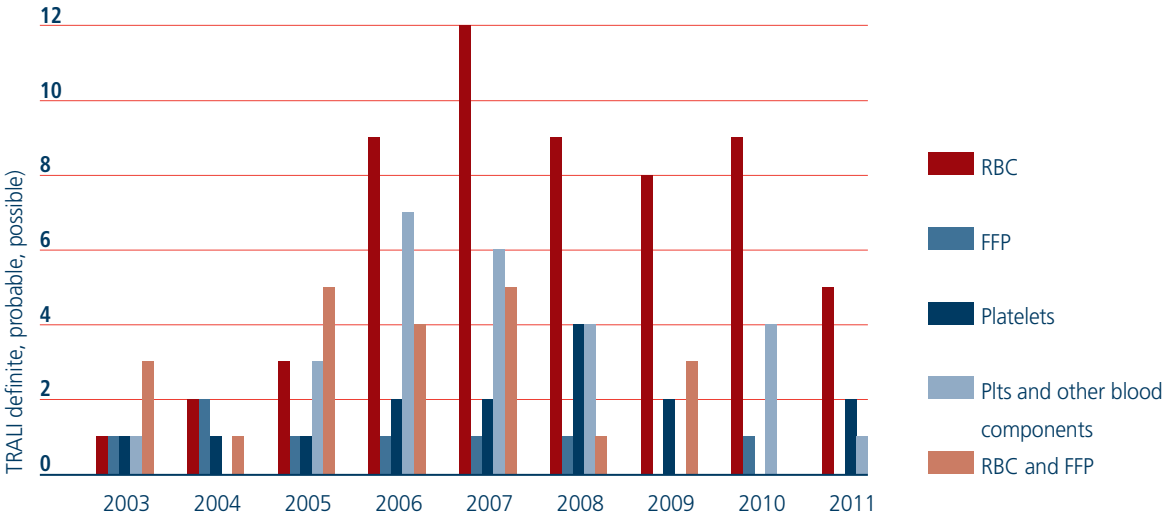


Figure 7 TRALI reports and associated blood components, 2003-2011

this date still include TRALI associated with platelets so at present the TRIP data cannot confirm a reduction in TRALI from the platelet measure. However, the reduced number of reports means that a longer period of monitoring will be needed.

Regarding the leukocyte serological investigations, these are known to have been performed in five out of the eight cases. In one the results are pending. In one case HLA antibodies were found in the patient and two out of five donors but there was no incompatibility; in the remaining three cases no leukocyte antibodies were found in patient or donors. Findings of leukocyte serology are not relevant for patient care but for guiding decisions about eligibility of a donor for future donations.

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 Hg systolic and/or diastolic, nausea or vomiting or diarrhoea, possibly with skin rash.

There were 65 reports of anaphylactic reactions in 2011, 20 being grade 2 or higher in severity: figures which are almost identical to those of previous years (Table 1). The anaphylactic reactions account for the largest cumulative number of serious reactions (with certain, probable or possible imputability to the transfusion) from the beginning of the TRIP registration. In Table 4 it can be seen that the largest number of anaphylactic reactions occurred during or after transfusion of platelets (39%) and fresh frozen plasma (26%). Nationally, the incidence of reported anaphylactic reactions is 0.42 per 1000 distributed units for platelet concentrates, 0.20 for fresh frozen plasma (FFP) and 0.03 for red blood cell concentrates. One of the 65 anaphylactic reactions occurred following the reinfusion of drain blood. In Table 5 it is seen that most anaphylactic and other allergic reactions occur in patients aged 20-60: 39% and 53% respectively, compared to 27% for all transfusion reactions. This is also the age group of patients receiving most platelet transfusions according to data from the PROTON study. Male and female patients are approximately equally affected.

The recorded symptoms in the anaphylactic reactions are shown in Figure 8. As expected the predominant features are respiratory, skin and systemic/cardiovascular symptoms. The figure also shows that (as previously noted, TRIP report 2009) a rise in temperature occurs in a significant proportion of patients, 17% in the combined data of 2010 and 2011 (with or without associated chills and rigors). For comparison the recorded features of 'other reaction' are presented. The considerable similarity suggests that some at least of those reports are in fact anaphylactic reactions. Currently there is no routinely available laboratory test to confirm an allergic etiology of a serious transfusion reaction.

Following an anaphylactic reaction, laboratory testing is recommended to investigate whether presence of anti-IgA in an IgA-deficient patient could be responsible for the reaction. Since 2003 this has only four times been confirmed as the cause of an anaphylactic transfusion reaction, in 2003, 2005 and 2011 (two in 2011). Out of the total of 416 reports, 84 record the finding of a normal IgA level and/or absence of anti-IgA or anti-IgA subclass.

The presence of HLA antibodies in blood components has not been specifically implicated in the patho-physiology of anaphylactic and allergic transfusion reaction. The implementation of measures for reasons of TRALI prevention presents an opportunity to observe whether there has been any change in the occurrence of these reactions. In The Netherlands male-only fresh frozen plasma (from donors who have never received a blood transfusion) has been supplied for transfusion from mid-2007 and a similar measure was introduced in November 2009 regarding the plasma which is added to pooled buffy coat platelet units. This ensures that the plasma is nearly always free of HLA antibodies. Table 11 shows the types of blood components transfused from 2007 to 2011 in association with the anaphylactic reaction reports. The data do not show any reduction in the relative involvement of FFP or of platelets units during these years.

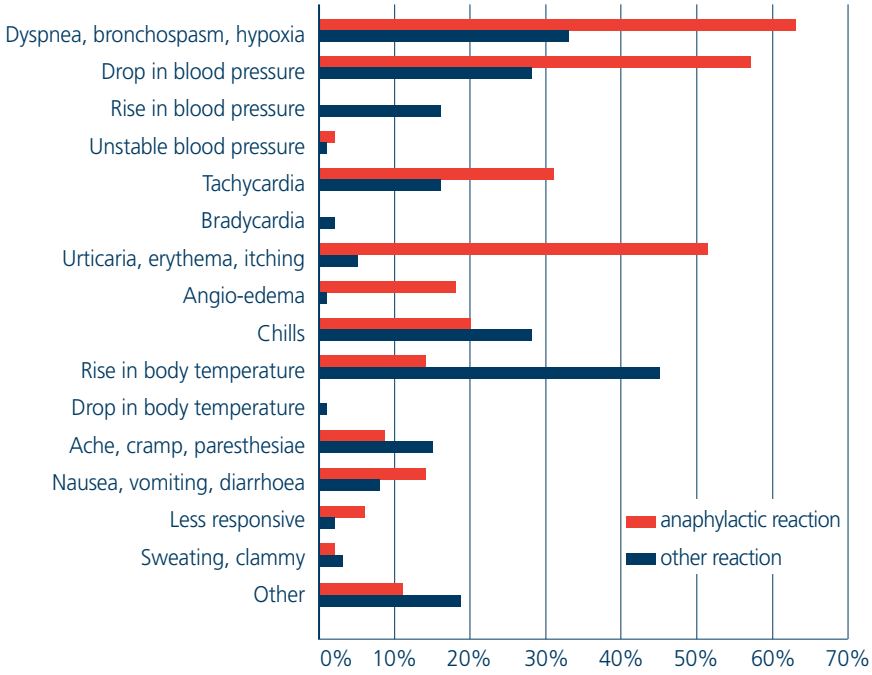


Figure 8A Signs and symptoms in reported anaphylactic reactions and other reactions in 2011

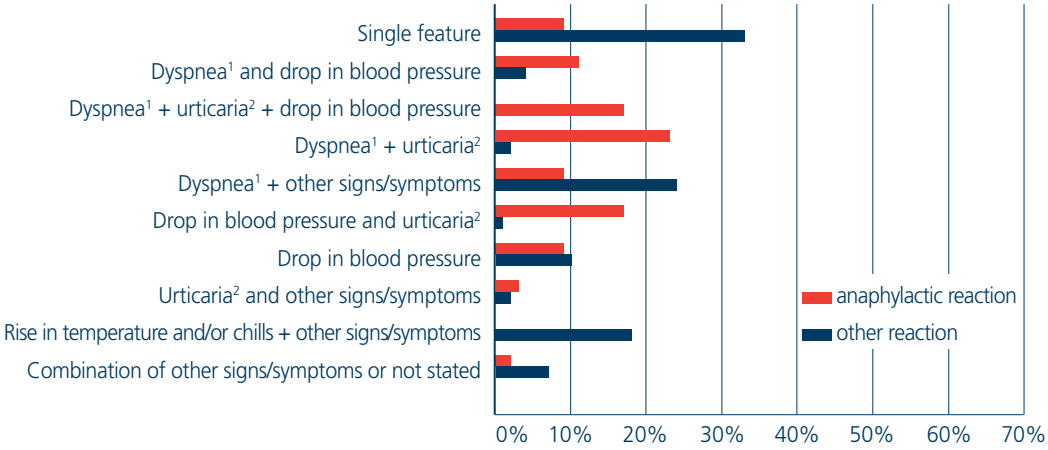


Figure 8B Single feature or cluster of symptoms/signs in anaphylactic reaction and other reaction in 2011

* *Cluster, sometimes combined with rise in body temperature, chills and/or other signs/symptoms*

[1] *Dyspnea, bronchospasm and/or hypoxia*

[2] *Urticaria, erythema, itching and/or angio-oedema*

It is known that certain patients suffer from recurrent allergic transfusion reactions. This is also seen in the TRIP data. In the years 2008 to 2011, six patients suffered from two or more serious anaphylactic transfusion reactions or from a serious anaphylactic reaction on one occasion and a serious other reaction or transfusion-associated circulatory overload on another. Taking just the years 2010 and 2011, a further five patients had 2-4 anaphylactic or allergic transfusion reactions.

In conclusion, as highlighted by TRIP in several annual reports, there is a need both for research into causes of serious anaphylactic or allergic transfusion reactions and for better investigation of individual cases. The starting point could be the development of a national recommended protocol for standard investigations in collaboration with Sanquin, as recommended in the 2010 TRIP report.

Table 11 Blood components in reports of anaphylactic reaction, 2007 – 2011

Anaphylactic reaction	2007		2008		2009		2010		2011	
	serious	all	serious	all	serious	all	serious	all	serious	all
Red blood cells	2	10	7	14	4	12	4	18	3	15
Platelets	9	26	14	30	7	31	10	37	7	26
Plasma	8	12	5	15	8	23	3	13	8	17
Platelets and RBCs and/or plasma	2	4	4	4	0	3	1	2	1	4
RBCs and plasma	1	1	0	2	0	0	0	1	1	2
Total	**22**	**54[1]**	**30**	**65**	**21[2]**	**71[2]**	**19[2]**	**72[3]**	**21[3]**	**65[3]**

[1] *Component type not specified in one report*

[2] *Two reports, one serious, involved the administration of unwashed autologous drain blood*

[3] *One serious report involved the administration of unwashed autologous drain blood*

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, 189, is similar to that in previous years. There were three reports of other allergic reaction of severity grade 2 or higher. The proportions of blood component types which were associated with other allergic reactions are virtually identical to those involved in anaphylactic reactions, which is consistent with there being common mechanisms at play. It can be seen in Table 5 that men and women are represented equally as is the case for anaphylactic reactions. Over half (70%) of the patients are below the age of 60, compared to 14% in the case of transfusion-associated circulatory overload and 33% overall among the reports.

Although other allergic reactions are generally benign they constitute the fourth largest category of transfusion reactions. In practice it is often possible to continue a transfusion after administering antihistamine medication to the patient. Many hospital protocols do not require further investigations. Thus among the 189 reports of other allergic transfusion reaction in 2011, 37 mention that there were no or no new abnormalities in blood group serology while 33 mention that this was not performed and the remaining reports enter no information in that box on the reporting form. Two reports record the detection of HLA antibodies, two record negative findings of testing for HLA antibodies and 15 note that this investigation was not applicable or not performed.

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.

The number of reports of transfusion-associated circulatory overload (TACO) in 2011 was 38, which is in line with the numbers since 2008. Among these, 18 of definite, probable or possible imputability were of grade 2 or higher (the third most frequent category, following anaphylactic reaction with 20 and other reaction with 22 serious reactions). Five of these, more than in any other category, were of grade 3 or 4. TACO has been highlighted as one of the chief causes of transfusion-associated mortality by several hemovigilance systems, including the French, Canadian and British (SHOT).

As in previous years, over two thirds of the reports of circulatory overload involved the administration of red blood cells (84%: Table 4). Most patients were in the older age groups, 49% being aged 60-80 years and 38%

over the age of 80. Male and female patients were equally affected. The median time interval from start of transfusion until noting symptoms of circulatory overload was 2 hours and 20 minutes (interquartile range 55 minutes to 3 hours and 15 minutes).

As in 2010, a noteworthy number of reports mentioned a rise in body temperature: this was the case in ten out of the 38 reports (26%). It might be queried whether this resulted from a patient mentioning or a nurse noticing dyspnea at the time of the routine temperature check after the first 10 minutes of transfusion, however only a minority of the reports with a rise in temperature were detected soon after the start of transfusion. Another possible explanation, suggested in the 2010 report, is that the increased circulatory demands in febrile patients can contribute to the occurrence of circulatory overload. An association of a rise in body temperature and TACO has also been noted by the French and Canadian hemovigilance systems (18.9% and 26% respectively, oral communications by Ph. Renaudier and G. Lambert, April 2012, Montreal).

In addition to the reports of transfusion-associated circulatory overload, six serious reports recorded TACO as an additional category. In the case of two reports classified as anaphylactic reaction and three as other reaction, the additional category has been used to signify diagnostic uncertainty. For instance, two of the other reactions presented dyspnea combined with pulmonary edema on the chest X-ray but this was combined with hypotension. In the case reported as TRALI, the respiratory symptoms persisted after diuresis and a combination of reactions is possible. It is encouraging that in all these complex cases, findings of chest X-ray and summary clinical information are provided.

Circulatory overload most often occurs in patients who have reduced cardiac reserve. The method of treatment is essentially with diuretics. If these are given pre-emptively (even before commencing transfusion) more cases could be prevented, thus avoiding patient morbidity and wastage of blood components. A possible approach is for hospital blood transfusion request forms to include a checklist where the prescribing doctor indicates whether a patient is at risk of circulatory overload; the doctor will then consider prescribing prophylactic diuretics and is triggered to indicate speed of transfusion. Other possible preventive measures are the prescription of plasma-reduced blood components and use of an infusion pump to prevent too-rapid administration.

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.

In 2011 there were two reports of post-transfusion purpura. Previously there had been only two reports of PTP, namely one in the baseline measurement year of 2002, not supported by clinical data, and one in 2008. In general, PTP only occurs very sporadically with the administration of leukodepleted blood components.

Both the reported cases in 2011 occurred in women aged 50-60 and followed transfusion (of red blood cells in one case and of platelets in the other case) by approximately eight days. The clinical manifestations were melena in one case and skin hemorrhages and cardiac tamponade in the other. One patient was found to have anti-HPA-1a, the commonest platelet antibody to cause PTP. The other had anti-HPA-1b and anti-HPA-3a as well as a number of HLA antibodies. Both patients recovered. After PTP patients should receive antigen-negative units if transfusion support is needed.

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 (non-irradiated) blood component.

As in previous years, there were no reports of TA-GVHD in 2011. Leukodepletion, as performed on all blood components in the Netherlands since the end of 2001, significantly reduces the occurrence of TA-GVHD. Despite a number of reports to TRIP each year of incorrect blood component transfused where a patient erroneously received non-irradiated blood components (approximately seven cases per year since 2009), no patient has developed TA-GVHD.

Hemosiderosis

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

In 2011 there were two reports of hemosiderosis in poly-transfused patients. One patient was male, the other - less usually - female. Both were hemato-oncological patients, recipients of hematopoietic stem cell transplants; the female patient was less than 21 years old at the time when she received multiple transfusions. One patient in addition had sickle cell disease, chronic graft versus host disease and reduced renal function. A further two reports mentioned hemosiderosis as an additional category, once with a report of post-transfusion bacteremia/ sepsis and once with new allo-antibody formation.

Since 2005 TRIP has received a total of 30 reports of hemosiderosis. In six of these it was an additional category, the iron overload having come to light in the course of investigations of the transfusion reaction. TRIP wishes to encourage the reporting of hemosiderosis, particularly since preventive medical treatment can be effective. Consistent reporting is necessary in order to gain insight into the national level of occurrence of hemosiderosis.

New allo-antibody

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 2011 there were 826 reports in the main category new allo-antibody, a 4% increase compared to 2010. This category has been the largest category since 2004 and increases annually, probably due to increased reporting levels. In 2011 two thirds of the Dutch hospitals (61) registered new allo-antibody reports. From the start of the TRIP registration 80% of hospitals have reported new allo-antibodies in one or more years. A delayed hemolytic transfusion reaction was added as additional category in 17 reports submitted in 2011 by 13 hospitals; in these cases the finding of an allo-antibody led to the diagnosis of a DHTR. Table 12 shows that the number of hospitals reporting a DHTR as additional category is not very high. A DHTR can be easily missed if no symptoms develop and no laboratory tests are done. In 72 cases, where a drop in Hb level and/or transfusion history pointed at the possibility of delayed hemolysis, TRIP specifically asked if hemolysis had been excluded. In three cases this led to recording an additional category of DHTR. One report was registered with the additional category IBCT: a patient with anti-K also developed an anti-E after transfusion in 2010. When the anti-E was detected in 2011 it was found that he had been given a Rhesus incompatible RBC contrary to hospital protocol that dictated transfusion of Rhesus compatible RBCs in patients with one or more antibodies.

Table 12 Numbers of hospitals and reports with additional category DHTR, 2008-2011

	Hospitals reporting additional category DHTR after finding new allo-antibody	New allo-antibody reports with additional category DHTR
2008	2	11
2009	13	17
2010	9	12
2011	13	17

New allo-antibody formation was reported as an additional category in 20 reports (please see relevant chapters): ICBT (1), other incident (1), DHTR (6), other reaction (6), non-hemolytic transfusion reaction (3), post-transfusion purpura (2) and other allergic reaction (1).

As expected the large majority of reports (772) of new allo-antibody formation were found after RBC transfusion. In thirteen cases only platelets were transfused and gave rise to Rhesus antibodies. One of these mentioned anti-Fya in a woman with a negative screening before transfusion; the allo-antibody may be due to the very small amount of red cells present in a platelet unit or could have been developed in pregnancy and boostered after platelet transfusion. The remainder of reports mentioned a combination of administered blood components: RBC and platelets (16), RBC and plasma (9), RBC, platelets and plasma (15) or unknown type of blood component. The reports concerned 310 male and 516 female patients. The female preponderance has been noted in the previous TRIP reports and can be explained by previous allo-exposure in pregnancy.

There were 138 reports (16%) of detection of more than one new allo-antibody. Two allo-antibodies were reported in 118 cases, three allo-antibodies in 16 cases and four antibodies in four cases; these numbers are comparable to 2010 (112, 15, 2). The reported antibodies, including those stated in reports with additional category new allo-antibody, are presented in Table 13. The group 'other' consists of anti-HLA (3), anti-HPA (3), anti-k (2), anti-P1 (2), anti-s (2) and one each of anti-f, anti-Fy5, anti-Jk3, anti-Leb, anti-H and anti-G.

Table 13 Reported antibodies and sex distribution in main and additional category new allo-antibody.

Antibody	Total	Male	Female
Anti-E	294	116	178
Anti-K	184	69	115
Anti-Jka	81	27	54
Anti-c	79	20	59
Anti-Fya	79	28	51
Anti-Lua	46	27	19
Anti-C	43	12	31
Anti-Cw	28	7	21
Anti-Wra	27	11	16
Anti-Jkb	24	7	17
Anti-S	20	8	12
Anti-D	19	10	9
Anti-Kpa	16	4	12
Anti-M	12	5	7
Anti-e	10	3	7
Anti-Lea	9	5	4
Anti-Fyb	7	2	5
Other	18	4	14
Total	**996**	**365**	**631**

Anti-D was reported 19 times. Apart from one report of IBCT and one other incident there were nine reports of anti-D following transfusion of Rhesus positive platelets administered to Rhesus negative patients (7 men and 2 women >45 years). There were also six reports of anti-D combined with anti-C following transfusion of RBCs; in these cases an anti-G antibody that mimics the combination of anti-D and anti-C in the irregular antibody screening is presumed as all administered blood components were Rhesus negative. In one case anti-D and anti-E were reported and presumed to be due to a Rhesus D variant. In one case anti-D was found in a Rhesus negative woman of childbearing age after transfusion for post-partum blood loss; no explanation was found as she was transfused with Rhesus negative RBCs and anti-D immunoglobulin was administered according to protocol.

Anti-K was reported in 184 cases. Five women of childbearing age developed anti-K; in all cases the K-positive transfusions were administered before the implementation of the K-negative transfusion policy for women of childbearing age. Five women of childbearing age developed anti-c and 25 women developed anti-E. TRIP advised in the 2006 report that Rhesus compatible transfusion for women of childbearing should be considered for prevention of hemolytic disease of the fetus and the newborn. This recommendation for women of childbearing potential to receive c and E compatible RBCs was included in the revised 2011 CBO blood transfusion guideline. To be able to monitor the implementation of this policy continued reporting of new allo-antibodies is advised.

Other transfusion reaction

Transfusion reaction that does not fit into the categories above.

In 2011 the number of reports of other transfusion reaction increased to 215, a 35% rise in comparison to 2010. Imputability was assessed as possible or higher in 181 of these reactions. Twenty-eight reports are of severity grade 2 or higher, 22 with possible, probable or certain imputability, whereas six of these reactions are assessed as unlikely in imputability. Products involved are RBCs (152), platelets (36), plasma (7), a combination of RBCs with platelets or plasma or both (6) and autologous drain blood (14).

Table 14 Overview of other reactions consisting of a single clinical sign or symptom

Clinical feature	Total	Blood component					Severity				
	70	RBC	Plts	FFP	other*	combi	0	1	2	3	4
Hypotension	30	22	2	3	3		1	26	3		
Rise in blood pressure	8	8						8			
Dyspnea/hypoxia	7	2	4			1		6	1		
Rise in temperature**	7(2#)	5	2				1	6			
Drop in temperature	1	1						1			
Pain/cramps or paraesthesia	6(1#)	4	1	1				6			
Tachy- and/or bradycardia	4	4						4			
Nausea/vomiting	2	1	1					2			
Chills/rigors**	3	1	2				2	1			
Sweating/clammy	1				1			1			
Confused	1	1						1			

* *All cases involved reinfusion of drain blood*

** *Not reported as NHTR/mild NHFR because of disqualifying finding such as late onset, persistence of raised temperature or positive culture result*

\# *Number out of total which involved patients <21 years*

The presence of clusters of reports with similar symptoms is examined each year. There were 70 reports in which only one symptom or two symptoms likely to be due to the same problem are listed, e.g. nausea and vomiting (Table 14). Notably, 38 of these reports mention (only) a rise or drop in blood pressure. In 139 reports there was a combination of clinical manifestations, while in six reports no symptoms were specified.

The other reactions with a certain combination of symptoms were examined further (Table 15). Firstly, there is a cluster of reports with hypotension, a decrease in blood pressure or a fluctuating blood pressure being an important feature, often combined with a rise in temperature and/or chills/rigors. Secondly, there is a cluster of reports with dyspnea or hypoxia as the main feature and generally combined with a rise in temperature and/or chills/rigors. In eight reports of other reaction there was a decrease in blood pressure as well as dyspnea and there was a similar number of reports with dyspnea in combination with a rise in blood pressure. A final noteworthy cluster is that of a rise in blood pressure without dyspnea, but often combined with a rise in temperature and/or chills/rigors.

Table 15 Overview of other reactions with combinations of symptoms

Main feature	Total	Subgroup	Blood component					Severity				
			RBC	Plts	FFP	other*	combi	0	1	2	3	4
Hypotension	**25(2#)**	**15**	**18**	**3**		**3**	**1**		**21**	**4**		
With temp ↑		7(1#)	5	1			1		6	1		
With chills/rigors		4	3	1					4			
With temp ↑ and chills/rigors		4	4						3	1		
Dyspnea/hypoxia	**47(2#)**	**41**	**32**	**11**	**1**	**2**	**1**		**38**	**8**	**1**	
With temp ↑		20	17	2			1		16	4		
With chills/rigors		6	1	4		1			5	1		
With temp ↑ and chills/rigors		15(1#)	10	4		1			12	2	1	
Hypotension and Dyspnea/hypoxia	**8(1#)**	**3**	**7**				**1**		**5**	**3**		
With temp ↑ and chills/rigors		3(1#)	3						2	1		
Rise in blood pressure	**20(2#)**	**18**	**15**	**2**		**3**			**17**	**3**		
With temp ↑		8(2#)	6	2					8			
With chills/rigors		1	1						1			
With temp ↑ and chills/rigors		9	6			3			7	2		
Rise in blood pressure and dyspnea/hypoxia	**7**	**5**	**4**	**2**	**1**				**6**	**1**		
With temp ↑		2	1		1				2			
With temp ↑ and chills/rigors		3	2	1					2	1		**1**
Other	**32(2#)**	**25**	**23**	**6**		**2**	**1**		**27**	**2**		
With temp ↑		12	10	1			1		11	1		
With chills/rigors		6	4	2					4			
With temp ↑ and chills/rigors		7	5	1		1			7			

* *All cases involved reinfusion of drain blood*

\# *Number out of total which involved patients <21 years*

Why was the category other reaction selected? In the reports submitted in this category from the start (115), the main reason is the presence of a single symptom or a combination with unusual symptoms without evidence that justifies the choice of a specific category (57). In some cases, TRIP staff asked questions to clarify the choice of a particular category, e.g. when symptoms are reported that could (also) indicate a different type of reaction. Sometimes this leads to a change of category. This year, TRIP examined in how many cases the reaction category was changed to other reaction after the initial submission of the report. The reason for the change was evaluated and an assessment was also made of whether the change to other reaction was

inevitable or a specific category could have been chosen but was not. It turned out that 100 out of 215 reports were first submitted for a different category, mostly NHTR (53) or mild NHKR (20). The presence of symptoms not accepted in this category, e.g. severe dyspnea, hypo- or hypertension, in combination with exclusion of a specific category such as TRALI, TACO or AHTR was the reason for a change to other reaction 47 times. Anaphylactic reaction was the category initially chosen in 12 reports: seven times only one symptom was noted (5x hypotension and 2x nausea and/or vomiting) and in the remaining five cases the combination of symptoms was assessed as not sufficiently convincing for anaphylaxis.

Case histories Other reaction

OR 1

A 77-year-old man receives red blood cells in day care because of chronic symptomatic anemia. On starting the transfusion at 15:50 hours his blood pressure is 148/70. After the whole unit has been given at 18:30 hours a rise in tension to 219/100 is noticed. There are no other signs or symptoms. After normalizing of his blood pressure the patient can go home the same evening.
Report: other reaction, severity grade 1, imputability possible.

OR 2

A 66-year-old man with lung cancer and postural hypotension, blood group B pos, receives a RBC because of Hb 4.4 mmol/L. At the start of the first RBC (B neg) at 08:50 hours his blood pressure is 161/78 in sitting position. At 09:15 hours the blood pressure is 99/48 lying down, it drops further: 92/43, 80/38, 84/38. The patient is conscious and has no symptoms. After transfusion of approximately 50 ml the transfusion is stopped and the patient receives two units of Voluven and Solucortef intravenously. The blood pressure rises to 111/50 and then remains stable. After recovery of the blood pressure another 2 RBCs are administered without problems. The Hb after the transfusions is 6.2 mmol/L. There is no evidence of hemolysis in biochemistry results. The blood culture of the patient remains sterile, and the culture of the remainder of the first RBC also gives negative results.
Report: other reaction, severity grade 1, imputability probable.

OR 3

A 64-year-old woman with known anti-Jka receives a blood transfusion because of anemia due to myelo-dysplastic syndrome. Ten minutes after the start of the RBC she feels dizzy and nauseous, and develops palpitations and visual disturbances. The transfusion is temporarily interrupted. Checking temperature, pulse and blood pressure does not reveal abnormalities. On recommencing transfusion following disappearance of the symptoms the same symptoms arise again. The transfusion of this unit is therefore permanently discontinued. Serology shows a positive DAT; no new antibodies in the eluate. There is no evidence of hemolysis. Culture of the blood component remains negative. The patient recovers completely from the reaction.
Report: other reaction, severity 1, imputability probable.

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 2011 Sanquin registered five reports from hospitals of post-transfusion viral infection that led to investigation into possible viral contamination of transfused blood components. The first case concerned HBV infection in a liver transplant patient who had multiple transfusions in 2008 and tested HBV negative at the time of the liver transplant. All donors were negative except for one donor, who had a high anti-HBs titre but could not be contacted for further investigation. Due to the fact that investigations could not be completed the imputability is assessed as possible.

Two patients developed hepatitis C virus infection and serious liver impairment after operations that necessitated several transfusions in the eighties and nineties of the last century. In the first case the patient died of hepatitis C; all involved donors repeatedly tested negative for hepatitis C. TRIP has no information on possible other sources of the infection and imputability is assessed as unlikely. The second patient developed liver cirrhosis due to chronic hepatitis C; investigations are still ongoing at the time of writing this report.

Two cases concerned Parvo virus B19 infection: a patient suffering from sickle cell anemia developed a Parvo B19 infection after exchange transfusion of Parvo B19 safe products. All donors were retested and negative. A heart transplant patient was diagnosed with Parvo B19 infection after multiple transfusions. The donors were either Parvo B19 safe (as previously tested) or tested negative for IgM and PCR and positive for IgG antibodies to Parvo B19; the heart donor was also Parvo B19 negative. In both cases there was no evidence for transmission by transfusion.

It is noteworthy that in 2011 all the reports of post-transfusion viral infection came to TRIP from Sanquin Blood Supply and not from the hospitals. Sanquin is primarily concerned with the investigation of blood products and the reporting of any serious adverse event to the healthcare inspectorate. Sanquin does not have access to full clinical and patient outcome information. In the interests of completeness and transparency it would be advisable for all hospitals and Sanquin to report using the TRIP online system. As TRIP does an annual check on duplicate reports it would be possible to link information and report comprehensively on results from the blood service and clinical patient outcome as supplied by the hospitals.

Bacterial contamination of blood component and report of positive bacterial screen

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.

In 2011, in total 43 reports for both categories were submitted. Six reports were in the category of positive bacterial screen and 37 reports were registered as bacterial contamination of a blood component. An overview

of the culture results is provided in Table 16. Bacterial contamination of a blood component was recorded as an additional category on 18 occasions, listed in Table 17.

The majority of the reports are reports from hospitals providing information on administered units of platelets (37) which had later given a positive result in the bacteriological screening performed by Sanquin. In two of those cases there were symptoms of (mild) fever in the patient. In one case it was noted that the increment of two units of platelets, of which one had a positive bacterial screening result, was minimal, whereas on other days the patient had a good increment after transfusion of platelets. Six times the report concerned RBCs related to a unit of platelets which had given a positive result in the Sanquin screening. One of those reports mentioned a mild rise in temperature in the patient. In 11 of the 43 cases a blood culture of the patient was performed; nine of these blood cultures were negative and two were found positive for different bacteria from those found in the screening of the blood component.

Table 16 Culture results listed in TRIP reports bacterial contamination of a blood component

Blood component	Subgroup Patient blood culture	Sanquin culture result* Sterile	Coryne bact sp	Micro cocc sp	Peptostrepto cocc sp	Propioni bact sp	Staphylo cocc sp	Gram + cocci	Anaerobic Gram -	Not stated
RBC					**1**	**3**		**1**		**1**
	Sterile					1				
	Not stated									1
	Not performed				1	2		1		
Plts		**6**	**4**	**2**		**20**	**2**	**1**	**1**	**1**
	Sterile	1				5	1			1
	Not stated	2	2	1		7	1	1		
	Not performed	3	2	1		6			1	
	Staphylo coccus sp					2				

* *Sterile: reporting category positive bacterial screening*

Culture positive: reporting category bacterial contamination blood component

Abbreviations: *: cocc = coccus; bact = bacterium; sp = species*

As well as the reports from the hospitals, each year Sanquin provides summary information on the results of the bacteriological screening of all platelet concentrates. In all, 321 platelet units showed an initial positive reaction in the screening and in 201 of these cases one or more components had been distributed. In 125 reports one or more components had already been transfused. The hospitals were asked to report back on any transfusion reactions which had occurred. A total of four reactions, all non-serious (grade 1), were reported to Sanquin. It is likely that these are the same reactions as reported to TRIP, but this cannot be verified using the data known to TRIP.

A total of 18 reports mentioned bacterial contamination of a blood component as an additional category. These cases relate to positive bacteriological findings by a hospital as part of investigations following a (possible) transfusion reaction. In three cases this was an addition to a report of post transfusion bacteremia/sepsis. The cases with a positive patient blood culture are described in the case histories in the section on post-transfusion bacteremia/sepsis. Reports of post transfusion bacteremia/sepsis combined with bacterial contamination of a blood component need to be assessed as to the likelihood that there was a transfusion transmitted bacterial infection (TTBI). In one case both the bacterial culture performed by Sanquin and the culture of the blood component in the hospital were positive. This case is described in more detail in the case history below.

Table 17 Culture results listed in TRIP reports with additional category bacterial contamination of a blood component 2011

Blood component	Subgroup*		Total	Hospital culture result on blood component								
Subgroup / Reporting category	Sanquin Screening	Pat. Blood culture		Staph cocc sp	Micro cocc sp	Salmonella B	Entero cocc sp	Coryne bact sp	E. coli	Propioni bact sp	Gram + rods	Other (soil bact)
RBC			**13**	**5**			**1**	**1**	**1**	**2**	**3**	**2**
Mild NHFR	0	0	1									x
	-	0	1	x								
NHTR	0	0	1	x								
	0	-	3	x							x	x
Post-Tf bact/sepsis	0	+	2	2x								
Other reaction	0	-	3				x		x	x	2x	
	0	+	2					x		x		
Platelets			**5**	**3**	**1**	**1**						
Anaphylactic reaction	+	0	1	x								
Other allergic reaction	-	-	1	x								
NHTR	0	0	1		x							
Post-Tf bact/sepsis	0	+	1			x						
Other reaction	0	-	1	x								

** 0 = not reported/not performed, + = culture positive, - = culture negative*

Sanquin screening = if result known to hospital (reporters are only informed if result positive)

Abbreviations: *cocc = coccus; bact = bacterium, bacteria, bacteremia; sp = species*

Case history Bacterial contamination of blood component

A 63-year-old woman with metastasized ovarian cancer complains about a tingling sensation of the mouth and tongue, and dyspnea, 3 minutes after the start of a platelet transfusion (platelets in plasma). 2 mg of Tavegil is administered. Repeated blood serology testing shows no abnormalities. There is no increment from the transfusion. No HLA antibodies are found.

Prior to transfusion the patient's blood culture had been found to show growth of Klebsiella pneumonia, for which the patient started antibiotics one day before transfusion (genta+cefuroxim). The transfusion reaction, without a rise of temperature or chills, does not warrant a further blood culture. After the reaction, the bag is cultured, showing a Staphylococcus species (caprae or capitis). The hospital receives a notification from Sanquin of a positive bacterial screening result on the unit, from which a Staphylococcus saccharolyticus was cultured. The Staphylococcus species found by the hospital and by Sanquin are different. No post-transfusion bacteremia/sepsis was shown in the patient. The reaction which arose soon after the start of transfusion was the reason for taking a bacterial culture of the blood component. The reporting category is therefore determined by the observed features (anaphylactic reaction). The positive culture of the unit is registered as an additional category: bacterial contamination of the blood component. In the absence of post-transfusion bacteremia consideration of transfusion transmitted bacterial infection is not applicable.

Report: anaphylactic reaction, severity grade 1, imputability probable; additional category bacterial contamination of the blood component.

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.

In 2011 TRIP received 60 reports regarding cases in which the hospital found a not previously known positive blood culture in a transfused patient on performing investigations because of signs or symptoms that could indicate a transfusion reaction. The administered blood components were RBCs in 53 reports and platelets in seven. The patients were mostly receiving transfusion for anemia or thrombocytopenia due to (hemato-) oncological problems, while in five cases acute bleeding was mentioned. Features that could indicate a pre-existing bacterial problem, e.g. fever before transfusion or positive urine or wound culture, were present in 26 patients. Four cases concern children while almost 70% of the patients were older than 60 years of age.

Table 18 summarizes the symptoms seen in post-transfusion bacteremia/sepsis reports. A rise in temperature is mentioned as a feature in 57 of these cases. In 24 cases (40%) there was a rise of more than 2°C while in four cases there was only a slight rise in temperature (<1°C), which in one case was accompanied by chills/rigors.

Table 18 Signs and symptoms in reports of post-transfusion bacteremia/sepsis by type of blood component

Blood component	*Subgroup* Rise in temperature	*Subgroup* Culture of the unit (hospital)*	Total	Accompanying symptoms chills/ rigors	Accompanying symptoms other symptoms	Pre-existing symptoms of infection
RBC			**53**	**33x**	**23x**	**24x**
	<1°C		**3**	**1x**		**2x**
		0	2			1x
		-	1	x		x
	>1°C<2°C		**25**	**13x**	**9x**	**10x**
		0	7	2x	1x	2x
		-	15	10x	6x	5x
		+	3	1x	2x	3x
	≥2°C		**20**	**15x**	**12x**	**9x**
		0	2	1x	1x	1x
		-	16	13x	9x	7x
		+	2	1x	2x	1x
	No rise in temperature		**3**	**3x**	**1x**	**2x**
		0	2	2x		2x
		-	1	x	x	
	Rise in temperature not specified		**2**	**1x**	**1x**	**1x**
		0	1		x	
		-	1	x		x
Platelets			**7**	**3x**	**6x**	**2x**
	<1°C		**1**		**1x**	**1x**
		0	1		x	x
	>1°C<2°C		**2**	**1x**	**1x**	**1x**
		-	1		x	
		+	1	x		x
	≥2°C		**4**	**2x**	**4x**	
		0	2	1x	2x	
		-	1		x	
		+	1	x	x	

** 0 = not reported/not performed, + = culture positive, - = culture negative*

None of the reports stated a positive Sanquin screening of the blood component

In the three remaining cases there were chills/rigors without a rise in temperature. The time interval between starting transfusion and the onset of symptoms in the patient was calculated in 53 cases: the mean interval was 2:43 hours. The time interval for reports with probable and certain imputability ranged from 10 minutes to $3^1/_2$ hours.

In the majority of cases of post-transfusion bacteremia/sepsis a culture of the unit had been performed with negative results. In many of these cases the bacteremia could have been caused by the underlying condition of the patient. The imputability of the post-transfusion bacteremia/sepsis reports was assessed as unlikely in 29 cases (almost 50%), once the relationship with transfusion was stated to be certain, three times probable and 27 times possible.

In six cases of post-transfusion bacteremia/sepsis the hospital found culture(s) of the unit to be positive. In three of these cases the positive culture was considered to be due to contamination of the culture during sampling. The three remaining cases were reported with the additional category bacterial contamination of a blood component. In one of the cases the blood culture of the patient and the culture of the blood component were positive for different bacteria species. Once the same type of bacteria was found but not further determined and once the bacteria were described as identical. The last three cases are described as case histories at the end of this section. Based on these findings the conclusion is that there was one probable and one possible case of TTBI in 2011.

Case histories post-transfusion bacteremia/sepsis

PTB 1

A 59 year-old hemato-oncology patient receives irradiated platelets. Approximately 1 hour after starting the transfusion symptoms arise that might indicate a transfusion reaction: temperature rise >2 °C, chills, rise in blood pressure, tachycardia, dyspnea, nausea and vomiting (vomiting blood). Investigation of the transfusion reaction reveals: results of serology and biochemistry show no abnormalities. The blood culture taken after the reaction and the blood culture of the next day are positive for Salmonella B. The culture of the bag is also positive for Salmonella B. The bacterial strains are classified as identical. Prior blood cultures from the patient (3 and 6 days in advance) revealed no growth of bacteria. The blood culture of five days after transfusion shows no growth of bacteria. The patient fully recovers from the reaction.

The bacteriological screening at Sanquin remained negative. Further testing of the donors gave no explanation for the infection. PCR testing of the donors' faeces gave negative results. Report: Post-transfusion bacteremia/sepsis, grade 2; additional category bacterial contamination of blood component. The imputability of post-transfusion reaction bacteremia/sepsis is rated as certain because the culture of the blood component yielded an identical strain. The source of the infection was not confirmed and it is therefore unknown at which moment the bacteria ended up in the bag. The likelihood of TTBI is therefore determined as probable.

PTB 2

A woman of 54, admitted for dyspnea with chronic anemia and infection (pneumonia and urinary tract infection) receives a transfusion of red blood cells. One hour and 30 minutes after the start of transfusion her temperature increases by >1<2 °C and chills, sweating and tachycardia are observed. Investigation of the reaction is performed: results of serology and biochemistry show no abnormalities. The aerobic blood culture taken after the reaction is positive: Staphylococcus epidermis. The culture of the bag is also positive for Staphylococcus epidermis aerobic/Corynebacterium species. The bacterial strains were not further identified. There is no positive bacterial screening of associated platelets by Sanquin. The patient fully recovered from the reaction. Report: post transfusion bacteremia/sepsis, severity grade 1, additional category bacterial contamination of a blood component.

The imputability of post-transfusion bacteremia/sepsis was assessed as probable. However, there is no evidence that the bacterial strains in the blood culture of the patient and in the culture of the bag are identical. Staphylococcus epidermis is a widely occurring type of bacterium, so there is a fair chance that the Staphylococcus epidermis in the blood culture of the patient and the Staphylococcus epidermis found in the culture of the blood component originate from different sources. The likelihood of TTBI is therefore determined as possible.

PTB 3

A 55-year-old woman receives a transfusion with two RBC because of anemia due to chemotherapy for lung cancer. More than nine hours after the start of the first RBC a rise in temperature ≥ 2 °C (up to 40 °C) accompanied by tachycardia occurs in this neutropenic patient. Investigation of the reaction is performed: results of serology and biochemistry show no abnormalities. A blood culture is taken and is found to be positive: Escherichia coli. A culture of one of the two units is positive for Staphylococcus warneri and the other unit remains negative. There is no reported positive bacteriological screening result of related platelets by Sanquin. The patient fully recovered from the reaction. Report: post-transfusion bacteremia/sepsis, severity grade 1, imputability possible, additional category bacterial contamination of a blood component.

In this case the bacteria cultured from the unit are different from the patient's blood culture result so there is no ground to suspect TTBI.

Post-transfusion malaria (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.

In 2011 TRIP received a report of post-transfusion malaria for the first time. A case of post-transfusion malaria from Plasmodium Malariae was diagnosed approximately seven weeks after perioperative transfusion of RBCs. Since the patient had no history of travel to a malaria-endemic area and had not been bitten by a mosquito in the vicinity of an international airport, there was a strong suspicion of transmission by transfusion. The PCR test in the donor was weakly positive. The donor did have a history of travel to malaria-endemic areas but this was more than three years before donation. The donor had never had suspicious symptoms. This case occurred despite correct application of the donor deferral periods following travel to malaria-endemic areas. The case shows that these deferral periods must be taken seriously but that the risk of malaria transmission cannot be fully removed.

3.3 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.

In 2011 there were 44 reports of incorrect blood component transfused (IBCT), of which four cases were judged to be cases of calculated risk, leaving 40 cases of true IBCT. These reports were submitted by 25 hospitals (30 in 2010). In comparison to previous years (since 2005 61 IBCT on average per year) there is a decline in the total number of this category. In five cases an IBCT led to clinical consequences and once taking a calculated risk (administration of uncrossmatched O neg RBCs) led to a delayed hemolytic reaction in a patient with irregular antibodies. An overview of these reactions is provided in Table 19. The number of cases with clinical consequences (6) is larger than last year when there were relatively few IBCT with clinical consequences. In percentage terms 2011 is not different from previous years: 15% of the IBCT in 2011 had clinical consequences whereas this ranged from 6% to 27% in earlier years. In 2011 there were also two reports (one NHTR and one new allo-antibody) with additional category IBCT. Both cases concerned failure to follow the preventive Rhesus phenotype compatible component selection policy for an at-risk patient. A short description of these cases has been included in the case histories at the end of this paragraph.

For all the reports in the category of IBCT TRIP assesses the greatest hazard to which the patient was exposed by administration of the blood component. For example, in a case resulting in patient X receiving the component intended for patient Y, the greatest risk is that of administration of an ABO incompatible component, although it may prove that by chance the transfused unit was actually compatible. As far as possible, the reports are classified according to the first error (in time) that resulted in the incorrect blood component being administered. The first error is broken down according to the type of error, e.g. identification error, communication error or selection error. The step in the transfusion chain where the first error occurred is also registered. A schematic representation of the steps in the transfusion chain and the description of the risk categories can be found on www.tripnet.nl, hemovigilance. If the first error did not occur in the reporting hospital but elsewhere, the first error was not analysed further. These types of errors are usually reported as component errors (e.g. the component was not B19-safe, even though this had been ordered). Table 20 provides an overview of the reports per risk type according to first error and step in the chain.

Table 19 Clinical consequences following transfusion of an incorrect blood component

IBCT risk type	Reaction	Total	Component	Severity grade*				
				0	1	2	3	4
ABO	Acute hemolytic transfusion reaction	2	2x RBC			2		
	Other reaction	1	RBC			1		
Irregular antibody	Delayed hemolytic transfusion reaction	1	RBC	1#				
Preventive selection policy	New allo-antibody	1	RBC					
Calculated risk	Delayed hemolytic transfusion reaction	1	RBC		1			

* *severity grade concerns the reaction*

\# *only minor changes in lab. results*

Of the 40 reports of incorrect blood component transfused 17 (43%) were assessed as ABO incompatibility risk. The number is almost the same as in 2010 (n=16, 28%), but the percentage is more comparable with 2008 (44%) and 2009 (50%). Among the 40 reports in 2011, identification errors constitute the largest group: 14, followed by errors in evaluation (judgement): 10. Compared with 2010 there is a drop in both communication and selection errors to five of each. As in previous years identification error is the most common error resulting in a potential ABO risk (13 out of 17) with this identification error taking place in the last check (bedside check) before administration of the blood component eight times.

Table 20 Nature of risk for the patient and first errors leading to IBCT in 2011

Risk	*Subgroup* *Step in transfusion chain where first error occurred*	Total	Type of first error						
			Adm	Evaluation	Comm	Ident	Lab proc	Selection	Other
ABO		**17(2#)**		**2**		**13**	**1**	**1**	
	Investigation for transfusion request	5		2		2	1#		
	Processing of request	1						1#	
	Issue	2				2			
	Transfusion	8				8			
	Hospital outside transfusion chain	1				1			
Irregular antibody		**9**	**1**	**4**	**2**		**2**		
	Investigation for transfusion request	6		3	1		2		
	Aanvraag	1			1				
	Processing of request	1		1					
	Hospital outside transfusion chain	1	1						
TA-GvHD		**6(1#)**		**3**	**3**				
	Request	3			3				
	Processing of request	1		1#					
	Transfusion advice	2		2					
Preventive selection policy		**6(1#)**		**1**			**1**	**3**	**1**
2x Irr.ab	Investigation for transfusion request	2		1					1
2x Irr.ab 2x B19	Processing of request	4					1	3(1#)	
Other		**2(1#)**				**1**		**1**	
	Processing of request	2				1		1#	

 # number out of total which involved patients <21 years of age

Abbreviations: *Adm = adminstrative; Comm = communication; Ident = identification; Lab proc = laboratory procedure; Irr.ab = irregular antibody*

The components that were administered in the 17 IBCT with ABO incompatibility risk were RBCs 15x and plasma twice. In four cases ABO incompatible RBC were transfused. In three of these cases a transfusion reaction was observed: once an other reaction after administration of an A pos RBC to a B pos immunosuppressed patient and twice an acute hemolytic transfusion reaction: once during administration of an A neg RBC to an O pos patient and once after administration of an A pos RBC to a B pos patient. A 78 year old, immune incompetent O pos patient with a very low titre of anti-A received an A neg RBC and no adverse reaction was observed. For the remaining 11 RBCs administered with an ABO risk but without a transfusion reaction being observed, by pure chance the unit was ABO compatible in nine cases. In one of these ABO compatible cases a Rhesus D positive RBC unit was administered to a Rhesus D negative elderly female recipient and there were no signs of a hemolytic transfusion reaction, nor did anti-D formation occur (up to a month after transfusion). Twice an ABO identical RBC was transfused to a patient whose blood group had not yet been confirmed by a second independent sample (this is the standard requirement in Dutch hospitals) but the blood group check afterwards showed the same blood group. One of the two cases with plasma concerned transfusion of O neg plasma to an A neg newborn child who showed no transfusion reaction, while in the other case the blood group of the plasma (A pos) was by chance identical to the patient's (A pos).

In 2011 nine reports were assessed as irregular antibody incompatibility risk, this number is slightly lower than that in 2008-2010 (10 each year). A DHTR was reported after administration of an E pos RBC to a patient with negative antibody screening but a positive history for irregular antibodies (anti E) in another hospital. Failure to follow the preventive component selection policy for an at-risk patient group (n= 4, 10%) was less often reported than in 2008-2010 (average 13) and only once led to a reaction (additional category). Formation of

anti D, anti C and anti E was detected after administration of a D pos RBC to a patient whose blood group had erroneously been determined as D pos. Unlike the IBCT reports with ABO risk there seems to be no particular error that causes the majority of these cases.

The number of IBCT with TA-GvHD risk in 2011 is six, which is almost the same as in previous years with the exception of 2010 (13). In contrast to previous years where in most cases errors in communication were the primary causes of administration of non-irradiated blood components, this year in 50% of the cases evaluation errors were mentioned as primary cause.

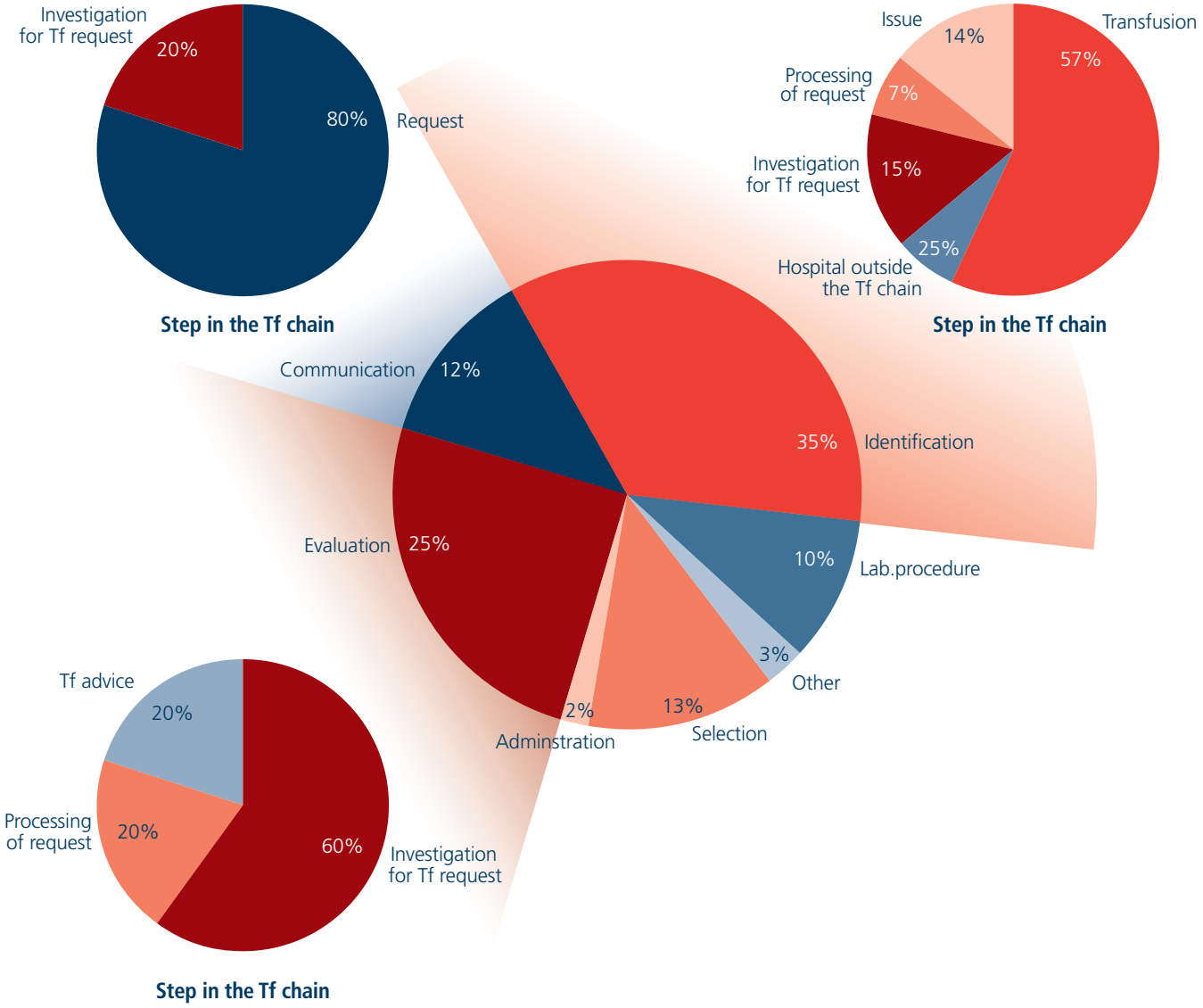


Figure 9 IBCT 2011. Type of first error; identification, communication and evaluation errors broken down according to step in the transfusion chain

The total number of IBCT is the lowest since 2005. The number of IBCT with ABO risk is about the same as in 2010, but much lower than 2009 and 2008 (the first years when risk assessment of IBCT reports was performed by TRIP). This could point to an improvement in this category, but it is not clear if this is due to enhanced vigilance and/or new patient safety measures or merely an effect of underreporting of certain cases.

Conclusion

The total number of IBCT reports has dropped from a highest level of 64 (2006 and 2007) to 40 and the number of IBCT with ABO risk has dropped from a highest number of 30 (2009) to 17.

Case histories Incorrect blood component transfused

IBCT 1

On the ward there are two patients, X and Y, who are for transfusion. The A neg RBC for patient X is checked at the desk. The nurse who will administer the transfusion is momentarily distracted before the transfusion can be started. Next the nurse goes with the checked RBC to Mr. Y, a 87-year-old urology patient with macroscopic haematuria, who has blood type O pos. No bedside identification is performed and the transfusion of the A neg RBC is started. After approximately 1h 15 mins, patient Y is found to be tachycardiac. The checks show that this blood component is being administered to the wrong patient and the transfusion is stopped immediately. Besides tachycardia patient Y has dyspnea, abdominal pain, nausea and vomiting. He is transferred to the IC unit for observation and remains hemodynamically stable. The hemolysis parameters are slightly increased after the reaction, the haptoglobin level is not reduced. Patient Y fully recovers from the reaction.
Report: IBCT with additional category AHTR, severity grade 2, imputability certain
Classified as: ABO risk, transfusion, identification error.

IBCT as additional category:

New allo-antibody

Patient A, a 76-year-old man, was admitted for urological surgery. Patient A was previously known to have anti-K and on screening for irregular antibodies, a newly formed allo-antibody is detected: anti-E. Looking back in the transfusion history of patient A shows that in 2010 an E pos RBC was administered. According to hospital policy this patient already had an indication for Rhesus phenotype identical RBCs at the time of transfusion in 2010 because of the presence of a clinically significant allo-antibody.
Reported: new allo-antibody, severity grade 0, imputability certain, additional category IBCT.

NHFTR

Patient B, a woman of 77, is being treated palliatively for acute myeloid leukemia and receives RBC transfusions for low Hb. During the second transfusion period (2 RBCs) in the day care unit patient B gets chills 1 hour (75 mL) after the start of the transfusion. Patient B is admitted to a ward and the reaction is further investigated.

Biochemistry: before/after transfusion: Hb 5.6/6.3 mmol/L, LDH 160/194; bilirubin 8/23; haptoglobin 1.4/1.3.
Blood group serology: direct Coombs before/after transfusion negative, antiglobulin crossmatch negative.
Previously known antibodies: allo anti-f, anti-Wra, HLA class 1, HTLA type Ch/Rg
Rhesus phenotype of patient: CCee (K negative).

It is found that the Rhesus phenotype of the administered RBC is not identical. According to hospital policy transfusion of blood components with identical Rh phenotyping is indicated since patient B will require multiple transfusions. The laboratory was not informed about the diagnosis/prognosis for the patient B in timely fashion, so the blood component was selected without taking into account the Rhesus phenotyping. Patient B did not develop any new allo-antibodies.
Reported: NHFTR, severity grade 2, imputability possible, additional category IBCT.

Other incident

Errors or incidents in the transfusion chain that do 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.

The number of reports of other incidents in 2011 (137) was higher than in previous years. Reports of other incidents were submitted by 34 hospitals, 15 of these hospitals reporting three or more other incidents. A reaction was observed in the patient in six of these reports. There were also 17 reports of transfusion reactions for which the additional category of other incident was reported. An overview is provided in Tables 21 and 22. The relationship between the incident and the patient's symptoms can be very different. In some cases it is likely that the incident led to the patient's reaction, whereas on other occasions an incident is discovered as a result of a reaction or the patient's reaction creates a situation in which an incident occurs.

Table 21 Clinical features with or after an other incident

Type of other incident	Reaction	Total	Blood component	Severity* 0	1	2	3	4
Pre Tf checks not properly performed	Mild NHKR	1	RBC		1			
Unnecessary Tf or failure to transfuse	Other reaction	1	RBC			1		
Unnecessary Tf	Circulatory overload	1	RBC		1			
Problem with IV line	Other reaction	2	2x RBC		2			
Tf advice not observed	New allo-antibody	1	Plts	1				

* *severity grade concerns the reaction*

Table 22 Transfusion reactions with additional category other incident

Reaction	Subgroup Type of other incident	Total	Blood component	Severity* 0	1	2	3	4
Mild NHFR		**4**			**2**			
	Not reported to BTL as TR	2	2x RBC					
	TR not investigated according to protocol	1	RBC		1			
	TR not correctly dealt with	1	RBC		1			
NHTR		**8(2#)**			**6**	**1**		
	TR not investigated according to protocol	2#	2x RBC		2			
	Not reported to BTL as TR	2	2x RBC			1		
	TR not correctly dealt with	1	RBC		1			
	Tf instruction not followed correctly	1	Plts		1			
	Pre Tf checks not properly performed	1	RBC		1			
	Maximum transfusion time exceeded	1	RBC		1			
Circulatory overload		**1**						
	Not reported to BTL as TR	1	RBC					1
Other allergic reaction		**2**			**2**			
	Tf unnecessarily stopped	2	RBC		2			
New allo-antibody		**1**						
	Unnecessary Tf	1	RBC	1				
Other reaction		**1**						
	Not reported to BTL as TR	1	RBC					

* *severity grade concerns the reaction*

number out of total which involved patients <21 years of age

Abbreviations: *BTL = blood transfusion laboratory*

The blood components involved in these other incidents were RBCs (95), platelets (12), plasma (6), autologous drain blood (8) and twice a combination of RBC and plasma. The other incidents with autologous blood are discussed in the section on blood management techniques. In ten reports the type of blood component involved in the incident was not specified but most likely concerned RBCs. In four cases the reported incident took place without a blood component being ordered.

Wastage of blood components

The number of reports regarding allogeneic blood components that became unsuitable for transfusion due to an other incident has risen over the past years. In 2011 the majority of other incidents (82 out of 129) were cases in which one or several blood products (a total number of 107 components) had to be destroyed. This year TRIP analysed whether this could have been avoided. In 55 cases involving 73 blood components the loss of blood components was considered to be avoidable.

In some of these cases it is obvious that the incident creates a situation in which it is inevitable that the blood component becomes unsuitable for transfusion, for example where the bag is accidentally punctured when attaching the drip line (14). However most reports concern cases where blood components were not returned to the laboratory or not returned in time after cancelling the transfusion (32). This is considered as avoidable, because in the reporting hospitals laboratory staff could have collected the blood component. In other cases it is difficult or impossible to assess whether disposal of blood components could have been avoided, e.g. when a patient is or seems to be bleeding severely and several blood components, including plasma, are ordered at one time. When it turns out that not all the units are needed and the components are returned to the laboratory in a timely manner, but have to be disposed of due to hospital policy and/or expiration of the (shortened) maximum storage time, it is considered unavoidable (7). TRIP has only counted the case as avoidable waste of blood components if it should have been clear that there was no indication for transfusion at the moment of ordering (3). Four reports mention forgetting to administer a blood component to the patient, in all of those cases the blood component had to be destroyed (considered avoidable), only once did the report state that the patient did not need another blood component instead. There were 13 reports where a problem led to (unnecessary) termination of the transfusion, e.g. a slight rise in patient's temperature, problems with the infusion system or removal of the infusion system by the patient, resulting in a large portion of the blood (a half bag or more) not being transfused. In reports of unnecessary termination of the transfusion this is regarded as avoidable wastage of blood components (11).

There were 20 reports where an unnecessary transfusion was administered or avoided just in time, e.g. following an unintended request (2) or a request for blood components for another patient than intended (5) or a request based on incorrect or misinterpreted lab results (11). Among the last 11 cases four were due to taking the blood sample from the drip arm and twice the Hb was not tested by the laboratory but elsewhere. In all, 13 patients unnecessarily received 27 blood components, with a maximum of four units administered to one patient.

Seven further reports mention the risk of unnecessary transfusion or blood needlessly becoming unsuitable for transfusion is, but in these cases it was possible either to start/continue transfusion after solving the problem or to take the unit back into stock and issue it again for another patient.

Among the remaining reports of other incident there were three reports concerning traceability and a number of problems concerning meeting a patient's special requirements. Twice irradiated blood was requested without this being indicated and twice the requirement for irradiated blood was omitted. Wrong or absent label information (not concerning the ABO blood group) on the blood component was also reported twice.

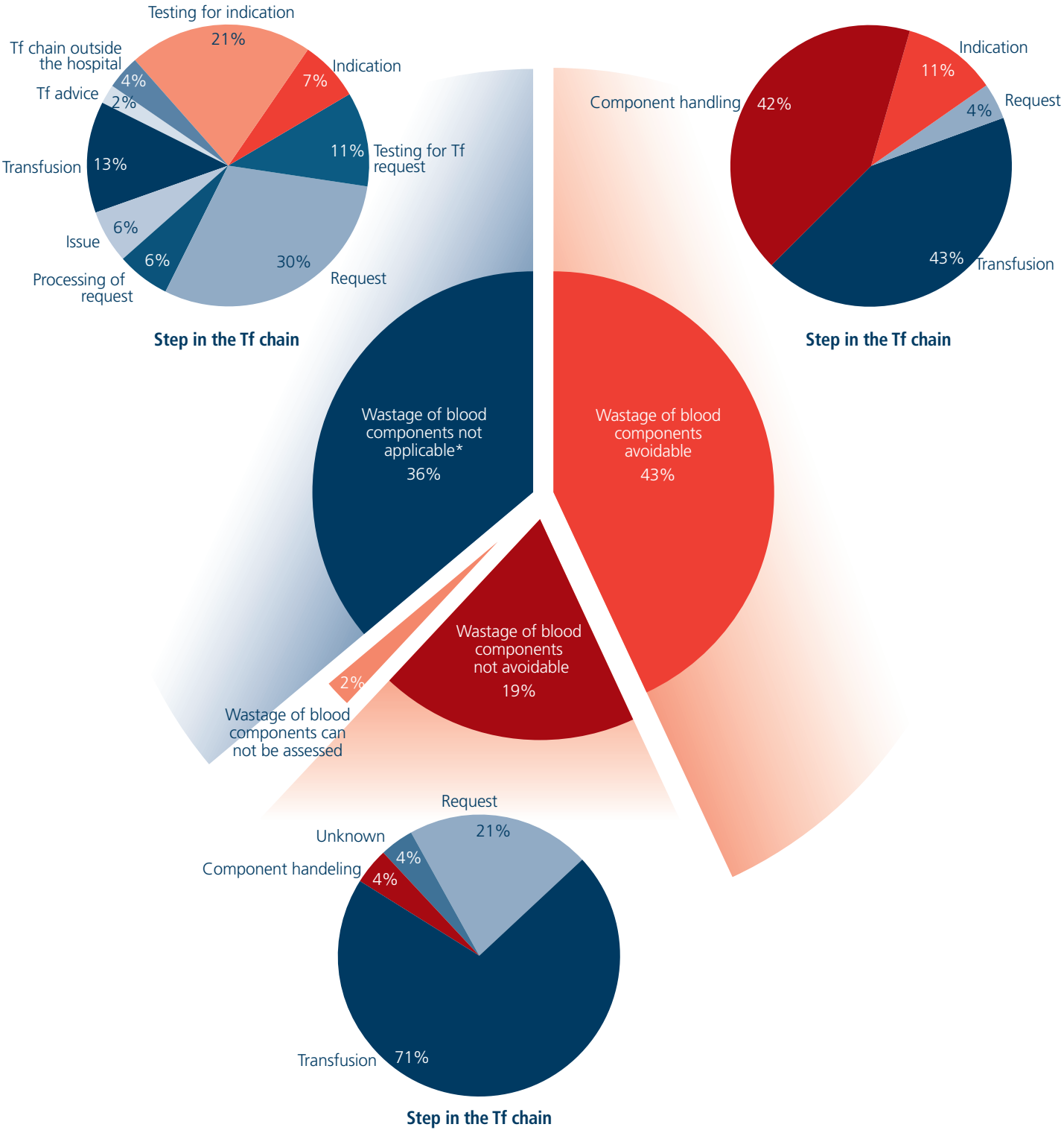


Figure 10 Other incidents in 2011 (n = 137) Wastage of blood components* and step in the chain where first error occurred

* *not applicable refers to reports were there was no blood component wastage, including the unnecessary transfusions and cases where component loss was avoided*

One or several blood components became unsuitable for transfusion in 64% of the reported other incidents (20% in 2010) and in approximately two thirds this was considered to be avoidable. Together the reports about unnecessary transfusion and the reports about avoidable loss of blood components represent 53% of the other incidents with allogeneic blood components. The total number of hospitals reporting other incidents has slightly risen in comparison to 2010 (34 vs 30), however the number of hospitals reporting on (avoidable)

wastage of blood components, 27 in 2011, is much higher than in 2010 (9). It is notable that there is a large variation in the number of submitted reports per hospital (from 1 to 28, mean 4, median 2) that cannot be explained by differences in blood use. It must be assumed that the same types of other incidents took place in some hospitals that did not submit these reports to TRIP, implying that there is probably underreporting. Hospital-wide awareness of the fact that blood ought to be regarded as a relatively scarce, delicate and precious human material is important and can probably help to prevent needless loss of blood components. Also clear agreements between the stakeholders and formal protocols are needed within a hospital, for instance about the appropriate number of components to request or to issue at one time and about procedures when issued blood components are not transfused. Hospital transfusion committees should verify whether adequate guidance is provided in their hospital.

Case histories other incident

OI 1

Patient A, a 76 year-old woman, has sepsis following laparotomy. Her Hb is 5.2 mmol/L so she receives a prophylactic RBC transfusion. Two days later the laboratory receives a notification of a rise in temperature to 39ºC with this transfusion. At the time the transfusion reaction protocol was not activated by the ward. There is no record of the baseline temperature before the transfusion so the degree of temperature increase cannot be determined. The patient had two blood culture results: one taken 5 days before the transfusion and one 3 days afterwards; both were negative. The Hb result, 3 days after the transfusion, showed a satisfactory rise to 6.7 mmol/L.
Report: other incident (baseline temperature not recorded, TR protocol not followed) with additional category mild NHFR

OI 2

Patient B, a 2 year-old with acute lymphoblastic leukemia, attends the outpatient clinic with a fracture (foot). The attending pediatrician assumes that the patient must have a low platelet count and requests a platelet concentrate without waiting for the blood results. After issue of the platelet unit but before the start of transfusion, the platelet count turns out to be 70. Consequently there is no indication for administration of a platelet concentrate and the transfusion is cancelled. The patient's Port-a-Cath has been needlessly spiked and the ward staff dispose of the platelet concentrate.

OI 3

An RBC transfusion has been requested for patient C, a man of 64, whose hemoglobin level is 5.3 mmol/L after a hip operation. At 6.40 am a nurse collects the blood for patient C from the laboratory. However the transfusion is not started and (contrary to the hospital protocol) the unit is placed in the non-validated ward refrigerator. At 11 am the hematology team leader is informed by the ward that a blood unit has been found in the fridge. The unit is declared unusable for transfusion.

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.

In 2011 43 near miss incidents were reported by 16 hospitals, the number per hospital varying from one up to seven reports, mean 2.69, median 2 (2010: 68 reports from 19 hospitals). The number of near miss reports in 2011 is the lowest since 2003. The first error was made in the steps of transfusion request (6) or pretransfusion testing (25) in 31 (72%) of the reported cases and 22 of these errors involved an error in the identification of the patient, blood sample and/or request form.

Routine checks and alertness of blood transfusion laboratory staff were responsible for preventing more serious incidents in the majority (26) of these near misses. In 20 of those cases (47%), a blood group discrepancy was the reason that an error was discovered. Only two reports mention discovery of an error through checking at issue by both lab staff member and nurse. Checking prior to transfusion on the ward or in the operating room picked up the error four times. Coincidence revealed six near miss cases and five reports did not describe how the error was discovered. In total the number of reported near misses in which nurses or other staff from clinical areas discovered an error is lower than in 2010, 6 (14%) was lower than in 2010.

An overview of the types of error in near miss events and the manner of discovery is provided in Tables 23 A and B. In Table 23A, the reports are categorised according to the type of the first error that was made. The right side of the table lists how the errors were discovered. Some cases involved both coincidence and staff vigilance. The event has been listed under coincidence if staff alertness alone would not have been enough to discover the error. This information was sometimes provided by the reporters themselves on the digital reporting form or stated in the explanation, in other cases it was assessed by TRIP staff on the basis of the description of the incident.

Table 23A Near miss: type of first error and manner of discovery

Type of error	Total	Planned safety measure	Personal vigilance	Coincidence	Not reported
Identification	27	21	1	2	3
Administrative	1			1	
Evaluation	3	3			
Laboratory procedure	3		1		2
Communication	5	4		1	
Selection of product	2(1[#])	1		1[#]	
Product	2	1		1	

[#] *number out of total which involved patients <21 years*

Table 23B Near miss and manner of discovery: planned safety measure

Type of safety measure	Subgroup	Total	Type of first error				
	Step where first error occurred		Identification	Communication	Evaluation	Selection	Product
2[nd] blood group determination		**20**	**17**	**2**	**1**		
	Testing for Tf request	18	17		1		
	Request	2		2			
Check of Tf history/ lab results		**2**		**1**	**1**		
	Request	2		1	1		
Check at issue		**2**		**1**		**1**	
	Request	1		1			
	Processing of request	1				1	
Pretransfusion check on ward		**4**	**4**				
	Processing of request	1	1				
	Issue	3	3				
Check on entering stock		**1**					**1**
	Tf chain outside hospital	1					1
Check of satellite fridge		**1**			**1**		
	Stock management	1			1		

Abbreviations: *Ident = identification; Comm = communication; Prod = product*

The majority of the errors were discovered due to a safety procedure (n=30), however, as last year almost 20% of errors involved in the reported near misses were discovered by coincidence and/or staff alertness.

It is noteworthy that as in previous years, the first errors in the reports of near miss were mainly identification errors: n = 27, 63% in 2011 (n = 48, 71% in 2010), whilst communication and selection errors together account for only seven (16%) of the near miss reports (in 2010 n = 12, 18%). If we compare this to the first errors in reports of an incorrect blood component being transfused, the percentage of identification errors in 2011 was 32% (14) which is similar to 2008 - 2010 (22% - 41%). The percentage of both reported communication errors and selection errors for IBCT in 2011 was 11% (n = 5 of each). The proportions of types of the first error in near miss, shown in figure 11, can be compared to figure 9 which gives the proportions for IBCT.

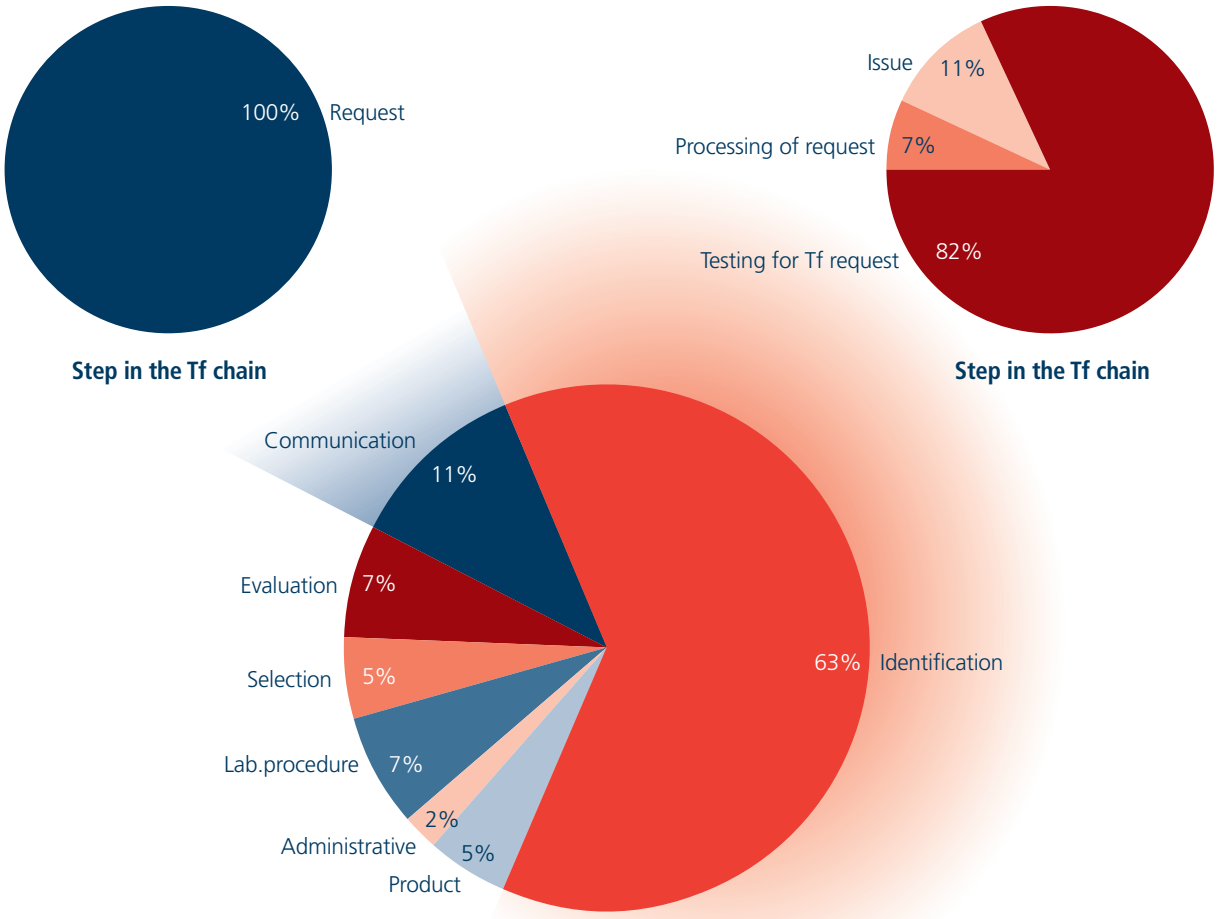


Figure 11 Near miss 2011: type of first error, identification and communication errors showed with step in the transfusion chain

It can be expected that the number of near miss events exceeds the number of IBCT. The three hospitals that reported the highest numbers of near miss indeed reported none or only one IBCT. Of the 26 hospitals that submitted reports in the category IBCT only seven reported one or more near miss incidents. Surprisingly two out of those seven hospitals reported less near miss incidents than IBCT. It is clear that the actual number of near miss incidents must be far higher than 43. TRIP wishes to encourage hospitals to report near miss, which will contribute to knowledge at the national level about risks and error-prone steps in the transfusion chain.

Case histories near miss

NM 1 (communication error, request)
The blood transfusion laboratory receives a request for two platelet concentrates for patient X, a man of 73 on the ICU. His platelet count is seen to be 285 so the laboratory enquires about the reason for the requested platelets. It transpires that not platelets but a RBC unit should have been requested for patient X.

NM2 (identification error, issue)
The reserved blood for patient Y, a 76 year-old woman with blood group O pos, is collected from the laboratory by a nurse. No discrepancies are noticed on issue of the RBC unit. A second nurse, who performs the bedside checks of patient Y's identity and the RBC unit, discovers that the unit is intended for another patient. This bag is returned to the laboratory and then the correct unit for patient Y is issued and transfused.

NM 3 (identification, testing for Tf request)
A preoperative blood sample has to be collected from patient Z. The barcode label for a crossmatch sample had become misplaced among the labels for patient A. The phlebotomist takes a ccrossmatch sample from patient A and sticks the label of patient Z on this tube. The error is discovered because the blood groups of patient A and patient Z are different. The results of the blood group determination for patient Z (determined on patient A's blood) produces a discrepancy with the historical record of patient Z's blood group in the laboratory system.

NM 4 (selection, processing request)
An RBC unit is requested and issued for a newborn baby. The child has an indication for "fresh" (<5 days) and irradiated blood (<24 hours before Tf). In the end, it is not necessary to administer blood. The ward sends the RBC back to the laboratory. Upon returning the RBC in the stock, it is noted that at issue the RBC was already older than 5 days and it had been irradiated more than 24 hours before issue.

Look-back by the blood service

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

During the 2011 reporting year 30 look-back procedures were reported by 14 hospitals; the number of reports per hospital varied from one to seven. Since the start of the TRIP registration the annual number of reported look-back procedures by hospitals was less than ten until 2010, when there was a rise due to the introduction of HBV-NAT testing by Sanquin to screen donors for occult hepatitis B infection (OBI), resulting in 44 reports. Look-back investigation in order to detect cases of possible viral transmission by blood components is sometimes hampered by the fact that hospitals are unable to or do not report to Sanquin on patient outcome.

This year 26 reports concerned look-back procedures into recipients of blood products of regular donors who were found to be carriers of an OBI by the HBV-NAT testing. In 2011 no transmission of HBV was found. In eight cases the recipient was checked and tested negative for HBV infection; nine recipients died before testing could be initiated, without having had symptoms that could be related to HBV infection. In the remaining reports testing was not initiated at the decision of the patient's doctor, because there were no symptoms suggestive of HBV infection. There is a very small risk of transmission by transfusion of hepatitis B from donors with OBI as was described in the 2010 TRIP report where transmission was reported to two recipients of blood components from one OBI donor. As the viral titre in an OBI fluctuates near the detection threshold donors may test negative several times before they are found to be carrying HBV. In mid-2011 Sanquin introduced donor screening for hepatitis B core antibodies. Anti-HBc is found in persons who have had hepatitis B in the past and this includes OBI donors. Individuals with anti-HBc antibodies will be permanently deferred unless they are demonstrated

to have immunity to hepatitis B (as shown by the presence of high titres of anti-HBs). It remains important for hospitals to be vigilant and have procedures in place to trace and test recipients of blood products of donors who have been found to be an OBI carrier or seroconverted for other infections. It is clear that there is under-reporting of look-back procedures to TRIP; hospitals may decide not to report a look-back procedure when the recipient was not apparently affected.

The four remaining reports on look-back related to possible transmission risks of syphilis, malaria, West Nile virus and HBV respectively. A regular donor tested positive for syphilis; an archived blood sample of the previous donation was retested and negative. The transmission risk was assessed to be very small. Three look-back procedures related to donors who should have been temporarily deferred, two following travel to risk areas for malaria and West Nile virus. In the third report, the donor had failed to mention a recent endoscopic procedure. None of the recipients was clinically affected.

3.4 Blood Management Techniques (BMT)

Data on application of blood management techniques in the Dutch hospitals are not well known. Since 2009 TRIP has annually request all hospitals to submit figures on various techniques. The numbers of hospitals supplying information and the data on numbers of applications are presented in Tables 24 and 25.

Table 24 Number of hospitals using blood management techniques, 2009-2011

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

* *In 2009 TRIP asked for figures on use of BMT for the first time; hospitals that did not submit any number on BMT in 2009 have not been counted*

\# *Preoperative autologous donation*

For most techniques the hemovigilance officers in over half of the hospitals are not aware of whether the method is applied in their hospital. Possibly these data are hard to obtain from the operating theatre. The 2011 revised CBO Blood Transfusion guideline specifically advises hemovigilance with BMT. The hemovigilance personnel now have this document to support the implementation of hemovigilance. Regarding the actual figures, incomplete as they are, it can be seen that drain blood procedures are used widely. Preoperative autologous donation (PAD) in The Netherlands is not used as a standard procedure as it may lead to wastage. In 2011 only 33% of PAD were transfused.

The reporting year 2011 showed a considerable increase in reports of adverse reactions and events with blood management techniques. Reports were submitted by eight hospitals and ranged from one to 26 reports per hospital. As in 2010 the majority of reports were sent by (the same) two reporting hospitals, which submitted: 26 and 23 reports respectively. With the exception of two grade 2 reports all were grade 1. Imputability was mostly rated as possible; it was probable in ten reports and certain in two reports. A comparison of the numbers of reports and reporting hospitals from year to year can be found in Table 26.

Table 25 Reported numbers of applications of blood management techniques, 2009-2011

Blood Management Technique	Total applications 2009*	Total applications 2010*	Total applications 2011*
Drain blood	7514	8821	11464
Cell saver	3033	5001	4282
PAD - patients referred	109	153	50
- units donated	208	289	113
- units transfused	187	224	38
Normovolemic hemodilution	122	1412	1250
Hypervolemic hemodilution	2	0	1172
ECC	2177	4430	5606
Fibrin glue	798	1056	1437
Thrombocyte gel	846	1225	510

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

Table 26 Reports to TRIP involving blood management techniques, 2006-2011

BMT reports (hospitals)	2006 (n= 6)	2007 (n=3)	2008 (n=9)	2009 (n=6)	2010 (n=5)	2011 (n=8)
Reactions	5	2	12	21	31	54
Incidents	1	1	13	12	6	10
Total	**6**	**3**	**25**	**33**	**37**	**64**

This year all 64 reports concerned non-mechanical auto-transfusion (drain blood). There were 54 transfusion reactions and ten incidents. Notably, among the latter there were two reports of hemolysis of drain blood that gave rise to a reaction in the patient. An overview of reactions and incidents is shown in Table 27. In previous years a small minority of reports concerned mechanical auto-transfusion (cell-saver blood) or pre-operative autologous donation whereas in 2011 only autologous drain blood gave rise to reports. In 13 reports drain blood was (partly) destroyed after a reaction or incident and nine of these specifically mention that the patient did not need an allogeneic transfusion.

Table 27 Reported reactions and incidents involving BMT, 2011

TRIP category	Autologous drain blood
Anaphylactic reaction	1
Non-hemolytic transfusion reaction	37
Mild non-hemolytic febrile reaction	2
Other reaction	14
Other incident	8
Hemolysis of product	2
Total	**64**

Again non-hemolytic transfusion reaction was the largest reported category (37), in all cases with orthopedic operations (mostly total knee replacements). The reports, sent by six hospitals, were all of grade 1. In 19 cases only rigors without fever were reported and in 17 cases a combination of fever and rigors was noted. In 20 cases cultures of drain blood were taken and all turned out negative. In only seven cases were blood cultures of the patient performed and these were also negative. Two mild non-hemolytic febrile reactions were reported.

There were 14 reports in the category of other reaction that did not meet criteria of the specific TRIP categories. In six reports isolated hypotension or a significant drop in blood pressure was the only symptom. One report mentioned severe sweating. The other reports concerned combinations of symptoms: rigors and significant rise in blood pressure (3x), rigors with a rise in temperature and drop in O^2 saturation (1x), rigors and drop in blood pressure (1x), rigors and hyperventilation (1x), chest pain combined with tingling sensation in arms (1x).

One anaphylactic reaction of severity grade 2 was reported. The patient developed fever and rigors, a drop in blood pressure and itchy skin that did not show objective abnormality.

Hemolysis of drain blood was registered in two cases, where the patient suffered a reaction. One patient became unwell with sweating and rigors without change in the vital parameters (other reaction). Two samples of drain blood were visually hemolytic. The hospital did not have facilities for determining free hemoglobin levels, but supplied photographs showing red serum in the blood sample tubes. In the other report an acute hemolytic transfusion reaction was recorded: the patient suffered rigors and rise in temperature. Free hemoglobin in the drain blood was 746 µmol/L; the patient had a significant rise of hemolysis parameters.

Eight other incidents relating to autologous unwashed drain blood were reported by one hospital. In four reports there was a technical problem with the system that led to (partial) loss of drain blood. Contrary to previous years only one report mentioned clotting. One report mentioned failure to re-infuse the drain blood within the set time of six hours. A patient was mistakenly re-infused via a standard intravenous line instead of an autotransfusion line with micro-aggregate filters. Finally one report mentioned the separation of drain blood in three distinct layers (red viscous layer, watery fluid, fatty layer) in a dialysis patient who had had a total knee replacement. Reinfusion of the red viscous substance was without incident until the time of discontinuing administration.

Conclusion

The number of reports with the use of drain blood doubled compared to 2010. In the majority of hospitals application numbers of drain blood are not known. Only 22 hospitals provided data on the use of non-mechanical autologous drain blood. Twenty-four hospitals reported they did not use drain blood. Two reports concerned hemolysis of drain blood that led to a reaction in the patients. The rates of reports of transfusion reactions and incidents relating to BMT from the two highest-reporting hospitals were 3.0% (23/760) and 3.4% (26/765) respectively.

3.5 Deceased patiënts and transfusion reactions (grade 4)

There were seven grade 4 reports in 2011, of which three were of definite, probable or possible imputability, the others unlikely. The reports are briefly presented in Table 28. Only one report, that of an acute hemolytic transfusion reaction (discussed in chapter 3.2), describes a case where the reaction clearly contributed to the patient's death. One of the grade 4 reports was reported by the doctor to the blood transfusion laboratory as an anaphylactic reaction but subsequently no further details were given. It is essential for clinical staff treating patients with serious (suspected) transfusion reactions to discuss the most likely diagnosis with the hemovigilance staff, even in cases where this is no longer relevant to the patient's treatment.

Table 28 Reports of patients who died following a transfusion reaction

Category of reaction	Age, gender	Imputability	Clinical situation
Acute hemolytic transfusion reaction	66, F	Probable	See chapter 3.2
Other reaction	4w, M	Possible	Neonate born at 28 weeks of gestation, anemic and metabolically unstable, developed necrotizing enterocolitis following transfusion.
TACO	83, F	Possible	RBC in anemic patient with myocardial ischemia prior to endoscopy: clinical deterioration and hypoxia
Mild non-hemolytic febrile reaction	70, M	Unlikely	Terminally ill patient with lung infection and on antibiotics, rise in temperature during RBC transfusion, patient declined further active treatment
Other reaction	82, M	Unlikely	Patient with terminal renal failure, anemia and poor cardiac function: cardiac arrest during RBC transfusion.
Post-transfusion bacteremia/sepsis	64, M	Unlikely	Hemato-oncological neutropenic patient: fever, respiratory infection, positive blood culture but unit negative
Insufficient information	69, F	Unlikely	Multiple units for major blood loss, doctor reported anaphylactic reaction to transfusion laboratory, no further clinical information available

Table 29 shows the grade 4 reports to TRIP with imputability certain, probable or possible since 2003. The largest three categories are TRALI (9), other reaction (7) and transfusion-associated circulatory overload (5).

Table 29 Reports of Grade 4 (imputability certain, probable or possible), 2003 – 2011

Reaction	Total	2003	2004	2005	2006	2007	2008	2009	2010	2011
AHTR	3	1	-	-	-	-	-	1	-	1
Anaphylactic reaction	2	-	-	1	-	1	-	-	-	-
Other reaction	6	-	-	1	-	-	1	-	3	1
Post-transfusion bacteremia/sepsis*	2	1	-	-	-	-	-	1	-	-
TRALI	9	-	-	1	2	3	-	1	2	-
Incorrect blood component transfused	2	-	-	-	-	1	1	-	-	-
Transfusion-associated circulatory overload	5	-	-	1	1	-	-	-	2	1

* *Before 2008: bacterial contamination*

3.6 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 30 shows the data for 2010 and 2011. The reactions about which insufficient information was available (n=1 with imputability rated as probable) have not been included.

Table 30 Number and imputability of reports of grade 2 or higher in 2010 and 2011

Type of reaction	Number of serious reports		Possible		Probable		Certain	
	2010	2011	2010	2011	2010	2011	2010	2011
Acute hemolytic TR	6	10	1	2	2	5	3	3
Delayed hemolytic TR	5	1	-	-	3	-	2	1
TRALI	12	4	6	4	6	-	-	-
Anaphylactic reaction	18	20	8	5	8	14	2	1
Other allergic reaction	-	3	-	2	-	1	-	-
Circulatory overload	18	18	10	11	6	5	2	2
Post-transfusion bacteremia/sepsis	4	3	3	2	-	-	1	1
Post-transfusion malaria	-	1	-	-	-	-	-	1
Post-transfusion purpura	-	2	-	1	-	1	-	-
Post-transfusion viral infection	1	1	-	1	1	-	-	-
Other serious reactions	29	35	17	23	9	6	3	6
Total	**93**	**98**	**45**	**51**	**35**	**32**	**13**	**15**

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

4 General considerations, conclusions and recommendations

4.1 The ninth TRIP report, what can be said about transfusion safety?

Once again the data show that there is generally a high level of transfusion safety in The Netherlands. The overall rate of transfusion reactions was less than 1 per 250 transfused units in 2011, the majority of reactions not being serious. Serious reactions occurred at a rate of 1 per 6700 units. Infectious complications are most feared but these are very rare indeed: the total number of proven or plausible cases amounted to one case of (definite) post-transfusion malaria, and two reports of post-transfusion bacteriemia/sepsis (one probable, one possible).

In 2011 the main trends were

- Little change in total number of non-serious transfusion reactions and serious reactions.
- Continued growth in the category of other reaction, this being apparently at the expense of anaphylactic reaction, TRALI and circulatory overload.
- Reduction in the number of reports of incorrect blood component transfused, the reports where there was an ABO incompatibility risk remaining at the level of last year, which was lower than in the previous years.

Transfusion safety can be seen as

1. Transparency and awareness regarding transfusion risks. The TRIP database and TRIP annual reports meet this need to a considerable extent. However there is a need for fuller investigations for some reports, so as to classify them in the most appropriate category. It is concerning that some serious reactions cannot be confirmed because hemovigilance staff lack clinical details.
2. Transfusions going to the right patient at the right time, following correct procedures. TRIP will continue to monitor and report on the incorrect transfusions. Despite the encouraging trend of reduction in incorrect transfusions with ABO incompatibility risk, it is not yet clear whether this truly represents an improvement in transfusion safety.
3. Absence of preventable reactions. Over the years the TRIP data have documented reduction of the risk of TRALI but that is the only category where clear improvement has been achieved since 2002. Among the serious reactions, cases of circulatory overload could potentially be reduced by clinical measures, notably prophylactic diuretics in susceptible patients. Serious allergic reactions remain under-researched and largely uninvestigated.
4. Avoidance of transfusions which were not strictly indicated. Hospitals have gone a long way in implementing and auditing the application of strict transfusion triggers. However analysis of some reports reveals that the transfusion may not have been necessary. Additionally, some reported incidents involve inappropriate or unnecessary transfusions. There is clearly still room for improvement.

The year 2011 was also the year in which the revised "CBO" national blood transfusion guideline was published. It contains recommendations which have also been made by TRIP, notably that of having a hemovigilance worker in all hospitals where blood transfusions are given. The guideline also presents draft quality indicators for transfusion practice. At the suggestion of the guideline group, TRIP requested and over 75% of hospitals submitted their data on these indicators. These are currently being analysed. The indicators may need further refinement, but will ultimately become a tool for hospitals to monitor the trends in their own blood use against national data.

4.2 Actions and developments following recommendations in previous TRIP reports

	Update on recommendations which are still current from TRIP reports 2003 - 2009	Comment
1.	Focus on blood transfusion and hemovigilance in the curriculum for the training of medical specialists (2007).	TRIP sends the annual report to training institutes for nurses and to those training specialists in the relevant disciplines. TRIP intends to make available teaching materials via website.
2.	Transfusion-associated circulatory overload also an important category (2006).	Action for clinical staff. See recommendation 4 in this report.
3.	Integration of activity within safety management system in hospital with hemovigilance activity (2006).	This point of concern remains current.
4.	Further research required on factors that influence the number of reports per hospital and their relationship to the safety of blood transfusion (2008).	TRIP continues to provide hospital blood transfusion committees with feedback on their reporting level. Analysis undertaken in 2011-12, Vox Sanguinis Epub 2012, DOI: 10.1111/j.1423-0410.2012.01642.x.
5.	Action on improved monitoring of patients at risk of transfusion-associated hemosiderosis (2006; 2008).	No actions undertaken, underreporting continues.
6.	Hospital blood transfusion committees should have insight into the scale of the use of blood management techniques. There should be a protocol for their use, with correct transfusion triggers and a procedure for reporting side effects and incidents. (2007, 2008, 2009).	Gradual improvement in providing figures, but not yet satisfactory. Recommendation included in revised national transfusion guideline.
7.	Recommendation for clinical scientific research on various blood component types with transfusion reactions as outcome measure. Alternative products to the 'male-only' FFP, such as SD plasma, should be prospectively investigated with respect to allergic and other reactions (2005, 2008).	Encouraging reducing trend of incidents with ABO-incompatibility risk, but it is too early for any definite conclusions. CBO indicators include question on use of electronic bedside identification.
8.	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 reducing trend of incidents with ABO-incompatibility risk, but it is too early for any definite conclusions. CBO indicators include question on use of electronic bedside identification.
9.	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 guideline can form a starting point for this (2009).	Pilot of proposed quality indicators in 2010-2011 with volunteer hospitals, (only) minor modifications to the indicators in the revised CBO transfusion guideline. In 2012 hospitals asked to provide data of adopted indicators, analysis of data ongoing.

	Update on recommendations from TRIP report 2010	Comments
10.	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 already existing TRIP categories (2009). TRIP should revise and refine the definitions for the current categories of transfusion reactions. New categories should be defined for hypotensive transfusion reactions and transfusion associated dyspnea (as recommended in 2009).	Definitions on bacterial complications have been reviewed. Draft definitions (based on ISBT definitions) for hypotensive transfusion reaction and transfusion-associated dyspnea to be subject of workshop in 2012-3.
11.	A classification is needed (similar to that in use by SHOT) for the link between a transfusion reaction, the patient's clinical condition and a fatal outcome in the patient.	Tool drafted and tested in "meet the Expert" meeting in March 2012.
12.	A standard protocol should be developed for the further investigation of serious anaphylactic transfusion reactions.	This project has not yet been picked up. *Action:* TRIP and Sanquin Clinical Advisory Service.
13.	In order to monitor optimal use of blood components, TRIP wishes to encourage reporting of incidents which lead to unnecessary transfusion or avoidable component loss.	Further cases are discussed in the present report.
14.	TRIP will collect figures concerning transfusions to infants and children in order to gain insight into the incidence of transfusion reactions in this patient group.	Data provided by over 50% of hospitals at the end of 2011, first findings presented in this report.
15.	Hospitals should have a defined procedure for investigation of recipients of blood components which retrospectively might have been infectious.	CBO guideline reiterates legal requirement for traceability (data retention 30 years) and includes an indicator for traceability.
16.	Action is required on the implementation of hemovigilance for Blood Management Techniques as recommended in 2009: the blood transfusion committees should ensure that a protocol is created for the use of blood management techniques, with correct transfusion triggers and a procedure for reporting side effects and incidents.	CBO blood transfusion guideline includes recommendation for hemovigilance of autologous blood management techniques. TRIP will continue to monitor.

4.3 Conclusions

1. There was an increase in reports of other reaction where dyspnea was the predominant feature.

2. A grade 4 acute hemolytic transfusion reaction was probably caused by anti-Wra.

3. Transfusion-associated circulatory overload accounted for five out of the sixteen grade 3 or 4 transfusion reactions in 2011 with definite, probable or possible imputability.

4. In look-back investigations by Sanquin Blood Supply in 2011, no new cases of post-transfusion viral infection were detected. A significant number of hospitals did not reply following notification that a transfused unit may have been infectious. Unless the investigations are fully pursued, cases of viral transmission may be missed.

5. The total number of reported incorrect blood components transfused reached a peak of 64 in 2006 and 2007 and has since declined to 44. The number of reports of incorrect blood transfused with an ABO risk reached its highest value of 30 in 2009 and has shown an encouraging reduction to 17 in 2011.

6. Reports of incidents leading to unnecessary transfusions or wastage of blood components constituted a major subgroup in the category of other incident.

7. The number of reports relating to the use of drain blood almost doubled in 2011 compared to 2010 and included two reports concerning hemolysis of drain blood. As 50 % of hospitals do not know if drain blood is used it is not possible to draw conclusions about incidence of transfusion reactions.

8. In four reports, including one each of grades 2, 3 and 4, the hemovigilance officer in the reporting hospital (n=3) had no access to clinical information necessary to diagnose the category of transfusion reaction.

4.4 Recommendations

A. Recommendations based on the 2011 TRIP Report

Recommendations	Action
1. 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.	Hospitals, hemovigilance officers
2. Serious reactions (in any case those of grades 3 and 4) should be discussed between laboratory and clinical staff to agree the most likely diagnosis.	Hospitals, hemovigilance officers
3. 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.	Clinical staff
4. 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.	Doctors
5. 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.	Hospitals
6. 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.	TRIP
7. 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.	Hospital transfusion committees
8. 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.	Sanquin Responsible Person, TRIP
B. General recommendation	
9. The hospitals should implement vigilance of blood management techniques as recommended in 2009; the blood transfusion committees should ensure that there are protocols for the use of these hospital techniques and a reporting procedure for adverse reactions and incidents.	Hospital transfusion committees

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
ECC	extracorporeal circulation
FFP	fresh frozen plasma
Hb	hemoglobin (level)
HBV	hepatitis B virus
HCV	hepatitis C virus
HLA	human leukocyte antigen
Hosp.	hospital
HPA	human platelet antigen
IBCT	incorrect blood component transfused
IBST	International Society for Blood Transfusion
ICU	intensive care unit
IGZ	Inspectie voor de Gezondheidszorg (Healthcare Inspectorate)
Mild NHFR	mild non-hemolytic febrile reaction
NAT	nucleic acid amplification test
NEC	necrotising enterocolitis
NHTR	non-hemolytic transfusion reaction
OBI	occult hepatitis B infection
PAD	preoperative autologous donation
PAS	platelet additive solution
PCR	polymerase chain reaction
Plt	platelet concentrate
PTP	post-transfusion purpura
PUCT	previously uncategorised complication of transfusion
RBC	red blood cell concentrate
RN	registered nurse
Sanquin	Sanquin Blood Supply Foundation
SD	solvent detergent (virus-reducing treatment)
SHOT	Serious Hazards of Transfusion (UK hemovigilance system)
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 for patient irregular antibodies, hematopoietic stem cell transplants and crossmatch difficulties
TTI	Transfusion-transmitted infection
Tx	transplantation

TRIP Hemovigilance and biovigilance office
P.O. Box 40551 | 2504 LN The Hague | Netherlands
Tel: 070 308 3120 | Email: info@tripnet.nl
www.tripnet.nl

TRIP
Hemo- en biovigilantie