TRIP annual report 2010
Hemovigilance
Extended version

Tulipa TRIP is owned by Prima Tulp B.V. TRIP wishes to thank Prima Tulp for naming and freely making Tulipa TRIP available to draw attention to the importance of hemo- and tissue vigilance.

The TRIP annual report 2010, extended version, concerning hemovigilance reports in the Netherlands in 2010 is published under editorial responsibility of the TRIP Foundation (Transfusion Reactions In Patients). The TRIP Foundation includes representatives of the various professional bodies involved in blood transfusion.

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Foreword

This is the 2010 TRIP annual hemovigilance report. It is also the last annual report for which I will write the foreword. As I am retiring, on 8th June 2011 I stepped down as president and resigned from the TRIP board. Dr. Martin Schipperus has been appointed as my successor.

In the first reporting year, 2003, 73 hospitals participated and a total of 1092 reports were received. Since 2006 we have seen a near-complete participation of approximately 96% each year, with a coverage of a slightly lower percentage of national blood use.
The annual number of reports has risen to approximately 2500 among which between 110 and 145 are classed as serious. Reports of incorrect blood component transfused have been at a stable level for a few years. Stable, but not reduced.

TRIP's primary task is to register and to report back to the professionals. Each year the findings are published in the now-familiar brochure format, and since 2007 there has been a short version with the key points for policy-makers and governors. The reports have been well-received and many of the recommendations have been adopted.

In the years since TRIP commenced its activities, a number of measures have been introduced by Sanquin Blood Supply. TRIP has documented a reduction in the number of plasma-related TRALI cases since the implementation of male-only plasma. The new nucleic acid amplification test for hepatitis B will bring about a further reduction in the already very low infectious risks of blood components in this country. Most transfusion reactions – even the subgroup of serious reactions – are not caused by unsafe blood components.

Many of the reactions cannot be prevented, but safety improvement can certainly be achieved by avoiding transfusions which are not clearly indicated and by preventing errors. Hospitals have worked to improve safety in the transfusion chain, but it is not easy to quantify the results. At this time I wish to mention the role of the transfusion safety officers who have been appointed under a variety of names in most of the hospitals. Not only do they compile the reports to TRIP, but they also perform a range of tasks in protocol development, training on blood transfusion and monitoring of blood use. TRIP's first recommendation (December 2002), that of appointing a hemovigilance assistant (transfusion safety officer) to perform practical tasks in the domain of hemovigilance, has been adopted in the 2011 revision of the national "CBO" transfusion guideline.

I have seen TRIP grow to an adult hemovigilance organisation which is also well known internationally. I am pleased and also a little proud to have been able to contribute to TRIP's development, and I particularly wish to thank my fellow TRIP board and steering group members for our enthusiastic and pleasant collaboration. TRIP is entering a new phase and this is not just because of a change of presidency. More importantly, tissue vigilance has become a permanent task for TRIP as from 2011. This will lead to renewal of the TRIP statutes and governance. What will not change is TRIP's commitment to working with the professionals to provide reporting which is as valid and useful as possible. I have pleasure in recommending this 2010 report to you and wish you every success in your work to improve the quality and safety of blood transfusion.

Prof. René R.P. de Vries
(Past) president, TRIP Foundation

Executive Summary

Goals and procedures of TRIP Office (hemovigilance)

The objective of TRIP (Transfusion Reactions In Patients) Dutch National Hemovigilance Office is to receive reports on side effects and incidents associated with the transfusion of labile blood products and to report publicly on transfusion safety. Both serious and non-serious adverse effects are reported as well as incidents. These are reported by the permanent contact persons (hemovigilance officers) in the Dutch hospitals. Both the patient and the treating physician remain anonymous in the report. Participation is voluntary, but is regarded as the professional standard by the national CBO Guideline for Blood Transfusion and the Healthcare Inspectorate (Inspectie voor de Gezondheidszorg, IGZ). TRIP also receives information from Sanquin Blood Supply about serious adverse reactions and events, in cases where Sanquin has detected an abnormality involving units which had been distributed to the hospitals. Following receipt of the reports they are assessed by the medical staff of the TRIP office and additional questions are asked if necessary. The reports are evaluated by an Expert Committee composed of transfusion experts from different professional backgrounds before being finalised and included in the report.

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 IGZ. The reporter can directly make a report available to the IGZ and/or Sanquin via the TRIP digital reporting system.

Participation

In total, 99 (94%) of the 103 Dutch hospitals participated in the TRIP registration in 2010. Transfusion reactions were reported by 91 hospitals and eight hospitals indicated that they did not have any transfusion reactions to report in the TRIP categories. The closing date for the report was 1 February 2011.

The reports in 2010

The number of reports received in 2010 was 2501 in total (2009: 2410 including late reports). Of this total, 2161 involved reports of transfusion reactions and 340 were reports of incidents in the transfusion chain. A transfusion reaction was reported as an additional category in 18 incidents (4x incorrect blood component transfused, 7x other incident and 7x infectious). Of all the reports, 2308 (92 %) were submitted electronically.

Categorisation according to severity and imputability

In accordance with international practices, transfusion reactions are categorised according to severity. The severity was listed for 2136 (98.0%) of the 2179 reactions reported in 2009: i.e. 2161 reported reactions as a main category and 18 reactions following incidents. The degree of severity was grade 0 for 757 reports (35.4 %), grade 1 for 1265 (59.2%), grade 2 for 88 (4.1%), grade 3 for 17 (0.8%) and grade 4 for 9 reports (0.4%). The total number of serious reports (grade 2 or higher) was 114, which almost identical to 2009 and lower than in 2006-8 when this was approximately 135 on average per year. Out of the serious reports, 92 were of definite, probable or possible imputability. The larger number of grade 4 reports (in comparison to 3 or 4 in past years) is caused by reports where the relation between the patient's demise and the transfusion reaction was improbable, possible or could not be excluded.

The transfusion reactions were also evaluated for imputability: the likelihood that the observed symptoms or findings can be attributed to the transfusion; it is known that symptoms experienced by a patient can be related to factors other than the transfusion. The imputability was listed for 2141 (98.3%) of the 2179 transfusion reactions reported in 2010. Of these, 339 reports (15.8%) were considered to be definitely related to the transfusion, 640 (29.9 %) as probable, 1010 (47.2%) as possible, 150 (7.0%) as unlikely and 2 (0.1%) as definitely not.

Types of reactions and incidents

The reported reactions are: non-hemolytic transfusion reaction 491, mild non-hemolytic febrile reaction 332, acute hemolytic transfusion reaction 20, delayed hemolytic transfusion reaction 7, transfusion-related acute lung injury (TRALI) 17, anaphylactic reaction 72, other allergic reaction 181, circulatory overload 47, post-transfusion viral infection 1, post-transfusion bacteremia / sepsis 41, hemosiderosis 4, other reaction 159 and new allo-antibody 789.

The reported incidents include 58 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 four cases. TRIP also received 117 reports concerning other incidents, of which seven were followed by transfusion reactions (two of grade 2 or higher) and 68 reports of near misses. There were 40 reports from hospitals concerning bacterial contamination of a blood component; three were related to culture findings following a transfusion reaction and the remainder concerned blood components that had already been administered and for which a positive bacterial screening result was later found by Sanquin. Finally, there were two reports of viral contamination of a blood components with an additional category of post-transfusion viral infection with hepatitis B. One report was of improbable imputability and the other was probable. These reports involved past donations by donors who were found to be carriers of an occult hepatitis B (OBI) infection through the recently implemented nucleic acid amplification test for that virus. There were also 50 reports from hospitals in the category of look-back, mainly concerning earlier donations from OBI donors.

Among the late 2009 reports there was one grade 4 report of post-transfusion bacteremia/sepsis, caused by a bacterially contaminated red blood cell concentrate (Y. Enterocolitica). In addition, look-back findings in 2009 led to the adjustment of the imputability of two 2008 reports of post-transfusion hepatitis B viral infection from excluded to definite.

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

In 2010, Sanquin supplied a total of 670,490 blood components to the hospitals. The total number of reports for 2010 was 2501. This gives an overall rate of 3.7 reports per 1000 distributed blood components. This is an increase compared to 2009 (3.4 per 1000), which can be attributed mainly to an increase in the categories of new allo-antibodies, other reaction and look-back.

Discussion and conclusions

TRALI

The number of TRALI reports in 2010 was 17, of which 12 were of definite, probable or possibility and could be verified as meeting the criteria of the TRALI case definition. Based on the data of 2002 up to and including 2009, TRIP has calculated that the total number of TRALI reports decreased by approximately one third following the implementation of the male-only plasma measure (effective from mid-2007). The 2010

findings are consistent with this. The effect of the additional measure (introduced late in 2009) of using only plasma from male, never-transfused donors as added conservation solution in pooled buffy-coat platelets, cannot be assessed yet.

Other reaction

There is a rising trend of reports in this category. They are reports that do not meet the definitions for the standard categories, including reports of hypotension and breathing difficulties following transfusion. For this reason TRIP will develop criteria so that in the future separate categories for transfusion-associated dyspnea and hypotensive reaction will be distinguished in the TRIP database.

Transfusion-associated circulatory overload (TACO)

In 2010 there were 47 reports of TACO, including 17 which were grade 2 or more and definite, probable or possible in imputability. This means that they are second only to anaphylactic reactions in number among the serious reactions. Measures to reduce the occurrence of TACO lie in the domain of the clinical care staff, particularly doctors and nurses.

Occult hepatitis B infection (OBI)

Sanquin Blood Supply introduced a nucleic acid amplification test for hepatitis B at the end of 2008. Since then several donors have been found to have occult hepatitis B infection. Look-back investigation of recipients of past donations from these donors led (in the present reporting period) to the retrospective diagnosis of probable or confirmed hepatitis B transmission to three patients. It is advisable for hospitals to have a defined procedure for contacting and conducting investigations of patients who were transfused with blood components which are later found to have possibly been virally contaminated.

Incorrect blood component transfused (IBCT)

The number of reports in this category is comparable to recent years. The cases where there was a risk of an ABO incompatible transfusion, 16 out of the total of 58 (28%), show a falling trend compared to 2008 and 2009 (44 and 50% respectively). Identification errors at the time of transfusion were the primary error in 10 of these 16 reports.

Other conclusions and recommendations

Anaphylactic reaction is the largest group among the serious reactions: TRIP recommends developing a national recommended protocol of investigations in these cases. Among all the reports to TRIP there may be under-reporting of reactions and incidents in pediatric transfusion. As yet in many hospitals the blood transfusion committee cannot find out how often blood management techniques are used, including perioperative blood salvage and reinfusion.

In the category of other incident, 24 (20%) of the reports concern unnecessary transfusions or excessive volume in consequence of various types of errors: TRIP calls on hemovigilance staff to pay special attention to these incidents. In addition to this, after publication of recommended quality indicators for the transfusion chain in the revised national transfusion guideline (2011), TRIP will request the hospitals to collaborate by submitting the indicator data along with the blood use data for 2011. This national audit will (at least once) be performed and analysed to permit benchmarking and feedback to the hospitals in order to support their efforts to optimise blood use.

1. | Introduction |

TRIP working method

Sound knowledge 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 the central registration of transfusion reactions (TR) and thus any 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 Bloedvoorziening. 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, revised version 2011). The digital reporting system that came into use in 2006 – initially in pilot form – was used actively by most of the hospitals in 2010.

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 degree of likelihood with which a reaction can be attributed to a blood transfusion that has been administered. If necessary, TRIP will ask the reporting party for further explanations or additional data. This allows the TRIP physicians to assess the coherence of the reports and to verify the reported category of (potentially) serious reports.

Reporting to TRIP is not linked to the provision of care and is also separate from other, non-voluntary reporting routes. Reports are made to the IGZ in case of calamities, to Sanquin in the case of possible consequences for the safety of the blood component or related components and within the hospital to the committee for Reporting of Incidents in Patient Care. The criteria of European directive 2002/98/EC stipulate that there is an obligation to report 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 competent authority IGZ. The reporting party remain responsible for submitting the report to the IGZ. Since the end of 2008 it has been possible to make serious reports directly available to the IGZ and where relevant to the Sanquin blood bank via the TRIP online reporting system.

An Expert Committee appointed from the TRIP Governing Board assesses all submitted reports. Definitive inclusion in the TRIP report is subsequent to approval by the Expert Committee.

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 2010 |

2.1 Participation

The value of national registration and evaluation of transfusion reactions is determined by the number of actively participating hospitals (level of participation) and by the quality of the information submitted. In 2010, 99 of the 103 (96 %) hospitals participated in the registration. Of these, 91 hospitals reported transfusion reactions and eight hospitals indicated that there were no transfusion reactions to report. Data about blood use were received from 99 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. 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 2010 in this annual report was 1 February 2011.

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 2009 report, 26 late submissions (1% of the final total) were received for 2009. 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 2010.

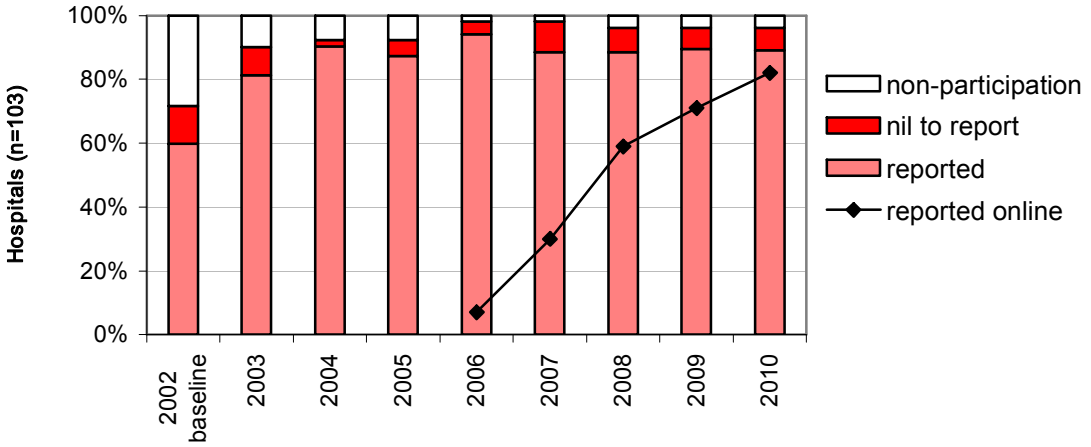

Figure 1 Participation per year

2.2 Summary of data regarding the reports for 2010

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

Reports received

In total, 2501 reports of transfusion reactions and of incidents in the transfusion chain were received in 2010; these arose in 91 hospitals. In 2009 the number was 2384 and ultimately, including late reports, 2410 from 93 hospitals. Therefore there has been an increase of 4 % compared to the final total of reports in 2009 (5% compared to the number included in the 2009 annual report). This increase concerns non-serious reactions and will be discussed further in the subsequent chapters of this report. Of all the reports, 2308 were submitted electronically (92%, 82 hospitals).

Following assessment by the Expert Committee, reporters were asked supplementary questions in a number of cases (approximately 40 times in total). In some 20 instances, after discussions with the reporter, the reporting category was amended. In other cases additional relevant information was forthcoming and in some instances consensus was reached to adjust the 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 2010. 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, 2003–2010

Reaction	2003	2004	2005	2006	2007	2008	2009	2010	Grade 2 or higher #	No. hospitals with reports in 2010
NHTR	318	345	435	490	452	453	488	491	6	77
Mild febrile reaction	326	341	375	363	328	275	359	332	4	66
AHTR	8	14	9	19	11	18	18	20	6	12
DHTR	19	14	12	14	11	18	8	7	5	6
TRALI	7	9	17	25	31	21	13	17	12	15
Anaphylactic reaction	8	21	26	19	54	65	71	72	18	27
Other allergic reaction	132	171	219	222	202	171	181	181	0	43
Circulatory overload	7	6	27	34	31	39	42	47	17	32
Post-transfusion purpura	0	0	0	0	0	1	0	0	0	0
TA-GVHD	0	0	0	0	0	1	0	0	0	0
Hemosiderosis	0	0	3	5	3	5	2	4	1	2
New allo-antibody	244	428	571	607	601	610	756	789	1	62
Other reaction	54	64	67	61	55	101	136	159	16	52
Post-tf bacteremia / sepsis§	9	5	10	7	19	37	55	41	4	25
Post-tf viral infection	5	7	8	7	7	7	4	1	0	1
Total TR	**1137**	**1425**	**1779**	**1873**	**1805**	**1819**	**2133**	**2161**	**90**	**90**
Total grade 2 or higher#	35	76	86	108	102	130	102	92	92	50
Total reports*	**1268**	**1547**	**1984**	**2130**	**2081**	**2052**	**2410**	**2501**	**92**	**91**

imputability certain, probable or possible
§ up to and including 2007: bacterial contamination; see remarks about revised definitions in section 3.2
* Total transfusion reactions and incidents

Table 2 Incidents reported to TRIP, 2003–2010

Incident	2003	2004	2005	2006	2007	2008	2009	2010	No. hospitals with reports in 2010
Incorrect bc transfused	34	36	60	64	64	59	61	58	30
Near miss	31	62	79	77	74	55	72	68	19
Other incident	5	12	51	86	100	83	110	117	30
Look-back (info reported by hospital to TRIP)		2	2	1	4	9	6	50	13
Viral contamination of bc				2	0	2	1	4	3
Positive bacterial screen[$]	61	10	13	27	29	2	4	3	3
Bacterial contamination of bc[$]					5	23	22	40	20
Total incidents	**131**	**122**	**205**	**257**	**276**	**233**	**277**	**340**	**54**

[$] see remarks about revised definitions in section 3.2
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 (2161) plus the reactions that occurred in incidents and reports of bacterial contamination (18), was 2179, of which the severity was recorded in 2136 cases (98.0 %). The severity was grade 0 for 757 reports (35.4 %), grade 1 for 1265 reports (59.2 %), grade 2 for 88 reports (4.1 %), grade 3 for 17 reports (0.8 %) and grade 4 for 9 reports (0.4 %).

Among the late reports from 2009 there were four of Grade 2 and higher: one anaphylactic reaction, one TACO and two post-transfusion bacteraemia/sepsis, which will be referred to where relevant under the specific headings.

Figure 2 shows the severity grades of transfusion reactions in 2003 - 2010. In 2010 there was an increase in the reports of grade 4 which will be discussed in the relevant paragraph. The total number of serious reports (grade 2 to 4) shows a falling trend since 2008 but this does not reach statistical significance.

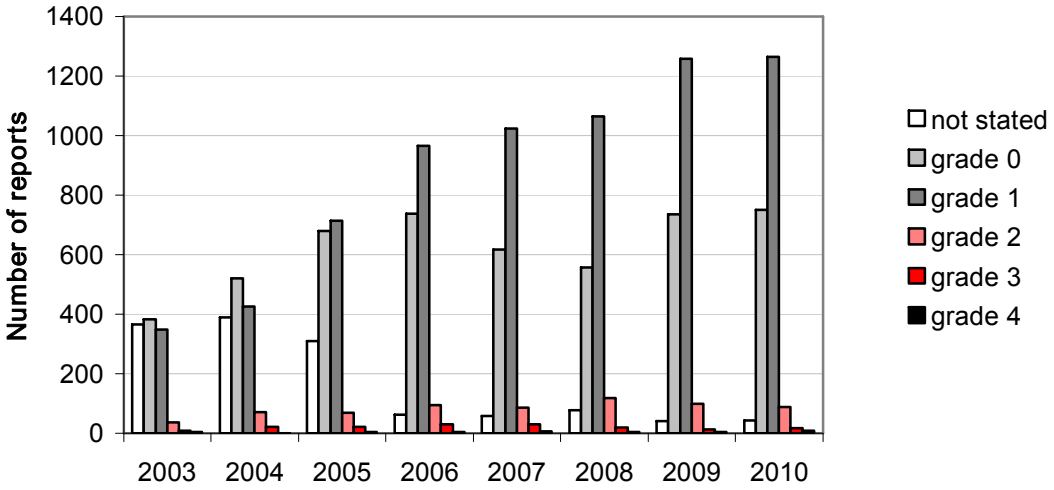

Figure 2 Severity of the transfusion reactions, 2003 – 2010

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 2179 transfusion reactions reported in 2010, the imputability was listed for 2141 reports (98.2%). Of these, 339 reports (15.8%) were considered certainly related to the transfusion, 640 (29.9%) were probable, 1010 (47.2%) were possible, 150 (7.0%) were unlikely and 2 (0.1%) were excluded). *Figure 3* shows the imputability of the 2179 transfusion reactions in 2010, compared to previous years. Of the 114 reports of severity grade 2 or higher, 92 were of certain, probable or possible imputability.

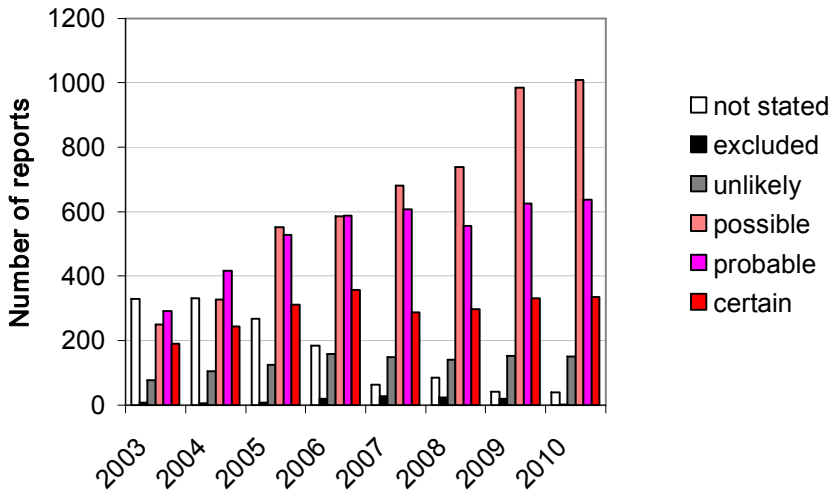

Figure 3 Imputability of the transfusion reactions, 2003 – 2010

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

In 2010, Sanquin supplied hospitals with a total of 670,490 blood components; this number does not include special components like lymphocytes and granulocytes. In contrast to previous years, the figures for apheresis platelet units are included. This explains the rise in the number of distributed components; information from the hospitals about numbers of transfused units shows that the use of platelet concentrates has remained stable in comparison to last year.

The total number of reports for 2010 was 2501. Using the total number of distributed blood components as a denominator, that makes 3.73 reports per 1000 blood components distributed nationally, or 3.67 after exclusion of the reports relating to autologous blood management techniques. *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 2009 and 2010

Type of blood component (bc)	2009					2010				
	Number of bc supplied	Reports; number	Reports; number per 1000 bc	Serious reports[#]; number	Serious reports[#]; number per 1000 bc	Number of bc supplied	Reports; number	Reports; number per 1000 bc	Serious reports[#]; number	Serious reports[#]; number per 1000 bc
Red blood cell concentrate	559,976	1831	3.27	64	0.11	529,840	1889	3.57	53	0.10
Platelet concentrate	49,354	305	6.18	19	0.38	57,346	333	5.81	19	0.33
Fresh frozen plasma	90,390	99	1.10	9	0.10	83,274	83	1.00	7	0.08
Cell-saver and drain blood		33		3			37		1	
Other products		0		0			1*		1*	
Combinations		73		8			87		11	
Not stated		69		0			71		0	
Total	**699,720**	**2410**	**3.44**	**103**	**0.15**	**670,490**	**2501**	**3.73**	**92**	**0.14**

[#] Imputability certain, probable, possible
* Reconstituted blood for intrauterine transfusion

Table 4 in parts A and B shows the distribution of the administered blood components per type of reaction or incident. *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 then the reports levelled out. In 2009 and 2010 there was a slight increase in the non-serious reports. This is discussed further under the relevant categories and in section 4.1 of this report.

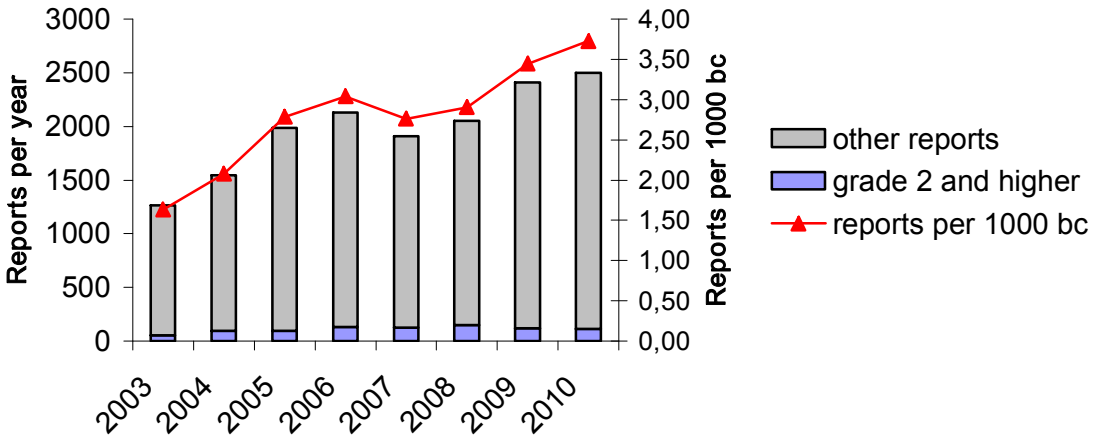

Figure 4 Number of reports per year, 2003 – 2010

Table 4 Distribution of types of blood components per category of report in 2010

A. Reaction	RBCs	Platelets	Plasma	Combi-nation	Other[#]	Not stated
Non-hemolytic transfusion reaction	373	74	9	16	18	1
	76.0 %	15.1 %	1.8 %	3.3 %	3.7 %	0.2 %
Mild non-hemolytic febrile reaction	312	14	1	5	-	1
	93.7 %	4.2 %	0.3 %	1.5 %	-	0.3%
Acute hemolytic transfusion reaction	20	-	-	-	-	-
	100.0 %					
Delayed hemolytic transfusion reaction	7	-	-	-	-	-
	100.0 %					
TRALI	11	-	1	5	-	-
	64.7 %	-	5.9 %	29.4 %		
Anaphylactic reaction	18	37	13	3	1	-
	25.0 %	51.4 %	18.1 %	4.2 %	1.4%	
Other allergic reaction	37	87	41	12	4	
	20.4 %	48.1 %	22.7 %	6.6 %	2.2 %	-
Circulatory overload	35	4	1	7	-	-
	74.5 %	8.5 %	2.1 %	14.9 %		
Hemosiderosis	1	-	-	3	-	-
	25.0 %			75.0 %		
New allo-antibody	733	20	-	21	-	15
	92.9 %	2.5 %		2.7 %		1.9 %
Other reaction	121	19	3	7	9	-
	76.1 %	11.9 %	1.9 %	4.4 %	5.7 %	
Post-transfusion bacteremia / sepsis	33	8	-	-	-	-
	80.5 %	19.5 %				
Post-transfusion viral infection		-	-	-	-	1
						50.0 %
B. Incident						
Incorrect blood component transfused	49	2	3	4	-	-
	84.5 %	3.4 %	5.2 %	6.9 %		
Other incident	81	16	8	1	6	5
	69.2 %	13,7 %	6.8 %	0.9 %	5.1 %	4.3 %
Near miss	15	2	1	2	-	48
	22.1 %	2.9 %	1.5 %	2.9 %		70.6 %
Bacterially contaminated blood component	5	35	-	-	-	-
	12.5 %	87.5 %				
Virally infected component	3	-	1	-	-	-
	75 %		25 %			
Pos. bacterial screen	-	3	-	-	-	-
		100.0 %				
Look-back	34	12	1	-	-	3
	68 %	24 %	2 %			6 %

[#] Includes autologous blood management techniques

Variation between hospitals

The number of transfusion reactions per 1000 administered blood components per hospital varies from 0 to 13.85 (the maximum in 2009 was 13.84; the median is 3.50). *Figures 5A* and *B* show the number of transfusion reaction reports related to the hospital's blood use. *Graph A* shows all reports. *Graph B* presents the transfusion reactions (imputability certain, probable and possible), with the exception of new allo-antibodies and mild non-hemolytic febrile reactions because those categories are not reported by all hospitals. One would expect the hospitals to show more uniform reporting rates in *Graph B* but the spread is still considerable. In an additional analysis TRIP has demonstrated that the reporting rate for transfusion reactions is fairly consistent in a hospital from year to year, i.e. that the variation in rate between hospitals is not merely a result of statistical variation (submitted for publication, J.C. Wiersum-Osselton et al).

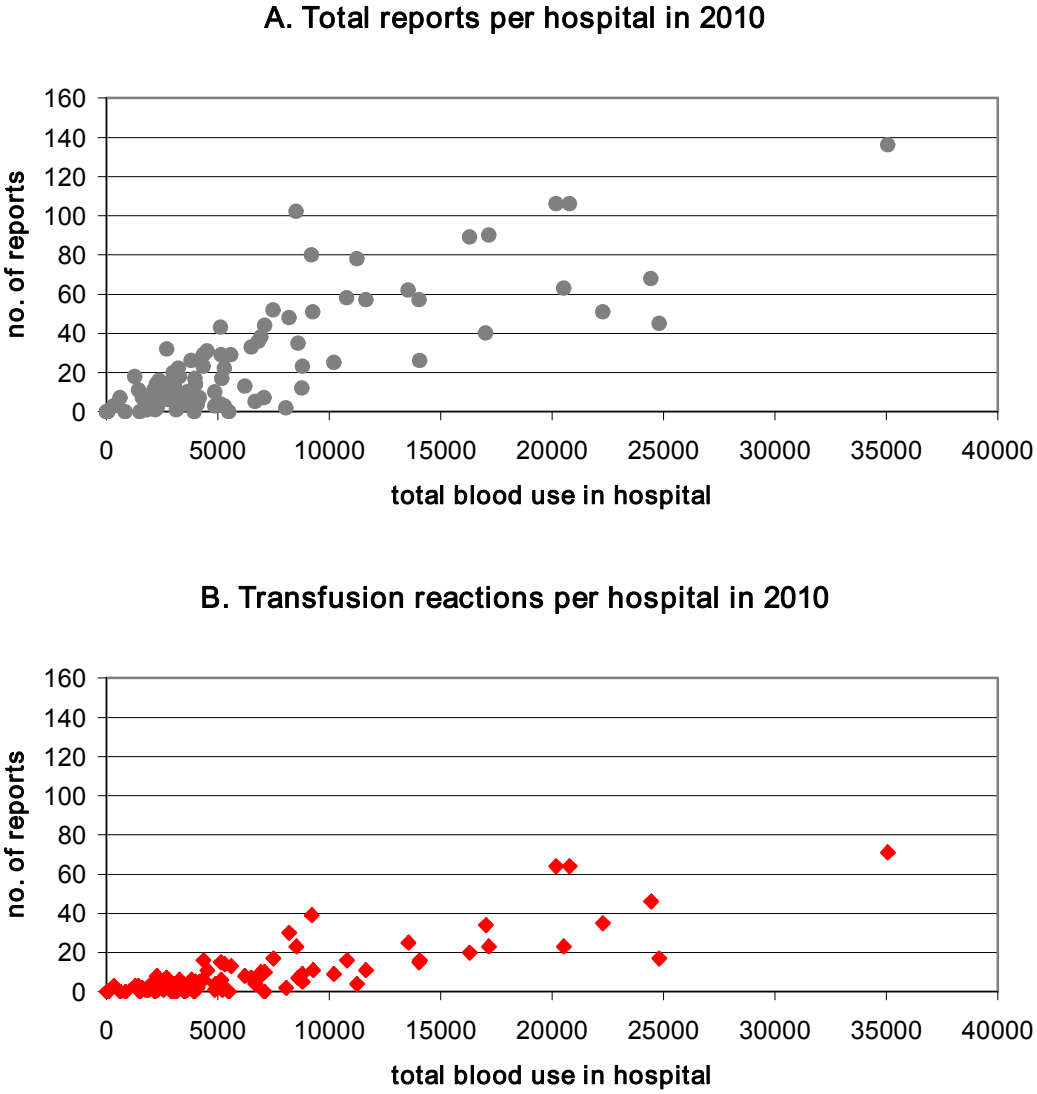

Figure 5 Number of reports per hospital against number of blood components transfused (A: total reports B: transfusion reactions with certain, probable and possible imputability, excluding new allo-antibodies and mild non-hemolytic febrile reactions)

Each year TRIP sends benchmarking graphs to the hospitals showing the level of their reports in relation to their blood use, compared to the national average in the various

reporting categories. At the level of the hospital blood transfusion committees it would be relevant to analyse within-hospital factors underlying the differences in reporting level. These probably include staff training in recognition of transfusion reactions and the hospital's safety and reporting culture. The revised (2011) national transfusion guideline includes a compact set of quality indicators for the blood transfusion chain. TRIP hopes to collect and analyse these at national level in order to provide feedback to hospitals in this area also.

2.3 Information about the patients

Each year TRIP checks for double reports, using date of birth and patient gender. This also highlights cases where patients suffered more than one transfusion reaction. In some cases the hospitals mention this in their reports; in other cases TRIP checks the information on patient's pathology and the hospital code. This makes it very unlikely that it will be a false assumption that two reactions concerned the same patient. It is more likely that in cases where a patient has suffered transfusion reactions in more than one hospital and different conditions were being treated it will not be recognised that there were multiple reactions from that patient. In 2010 transfusion reactions occurred in 90 patients who had had earlier transfusion reactions in 2008, 2009 or 2010; reports of new allo-antibodies were not taken into consideration in this analysis.

In each section of the report we comment briefly on the patients who suffered from transfusion reactions or adverse incidents. *Table 5* gives an overview of the distribution of patients' age group and gender per transfusion reaction and incident category. TRIP does not possess denominator data about transfused patients who did not have transfusion reactions. Information collected in the "Proton" study on recipients of blood components in the Netherlands is included at the bottom *Table 5* for purposes of comparison.

In the table a number of striking points emerge:

- There is a female predominance in the categories of delayed (but not acute) hemolytic transfusion reaction and new allo-antibodies: it can be presumed that this results from the allo-exposure of females during pregnancy.
- There are relatively few reports of transfusion reactions in patients aged <1year (0.4% of all transfusion reactions) but they account for a higher percentage of incidents (2.2%) reported to TRIP. There are also relatively few reports of transfusion reactions in patients aged 1 to 20 years. It is possible that transfusion reactions for certain age groups like neonates present differently and need adapted criteria. TRIP has no data on the total number of transfusions in the different age groups (neonates, infants, children, adolescents) so we miss a specific denominator for comparing rates in pediatric patients to those in adults and those reported internationally. In the SHOT (Serious Hazards of Transfusion, the United Kingdom hemovigilance office) registry a relatively high number of both incidents and transfusion reactions in pediatric patients is found (SHOT Annual Reports 2008, 2009, 2010, www.shotuk.org), however SHOT also lacks a specific denominator.

A number of further points are commented on in the sections concerning the different categories of reports.

Table 5 Distribution of age groups of patients category of report in 2010

A. Transfusion reactions	<1y		1-20		20-60		60-80		>80y		Not stated or N/A[1]
	M	V	M	V	M	V	M	V	M	V	
Non-hemolytic transfusion reaction	2	1	21	7	58	106	131	104	22	37	2
Mild non-hemolytic febrile reaction	2	1	6	6	39	54	90	49	42	43	-
Acute hemolytic transfusion reaction	-	-	-	-	4	3	4	3	4	2	-
Delayed hemolytic transfusion reaction	-	-	-	-	-	2	1	2	-	2	-
TRALI	-	-	1	1	6	3	2	3	-	-	1
Anaphylactic reaction	1	-	5	6	10	21	11	11	5	2	-
Other allergic reaction	1	-	21	15	40	43	22	27	8	4	-
Circulatory overload	-	-	1	-	2	5	11	10	5	13	-
Hemosiderosis	-	-	-	-	-	-	-	-	4	-	-
New allo-antibody	-	-	3	4	70	134	163	238	67	108	2
Other reaction	-	1	-	5	13	25	41	32	22	20	-
Post-transfusion bacteremia / sepsis	-	-	1	-	6	5	14	7	3	5	-
Post-transfusion viral infection	-	-	-	-	-	-	-	-	-	-	1
Total (TR)	**6**	**3**	**59**	**44**	**248**	**401**	**553**	**486**	**182**	**236**	**6**
	0.4%		**5%**		**30%**		**46%**		**19%**		
B. Incidents											
Incorrect blood component transfused	-	-	1	-	10	15	11	9	5	4	3
Other incident	1	2	3	6	11	13	32	19	8	17	6
Near miss	1	1	1	1	6	12	10	14	7	4	11
Bacterially contaminated blood component	-	1	8	-	5	3	9	11	1	2	-
Virally infected component	1	-	-	-	-	-	-	1	1	1	-
Pos. Bacterial screen	-	-	-	-	1	-	-	-	-	2	-
Look-back	-	-	-	1	7	7	15	7	4	8	1
Total (incidents)	**3**	**4**	**13**	**8**	**40**	**50**	**77**	**61**	**26**	**38**	**21**
	2%		**6%**		**28%**		**44%**		**19%**		
Units transfused nationally[2]											
RBC	1.5%		2.9%		30.5%		50.6%		14.4%		
Plts	4.4%		12.4%		46.2%		34.4%		2.8%		
FFP	2.4%		5.4%		37.0%		50.4%		5.0%		

[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. Appendix, Tables A-C. PhD thesis Utrecht 2010.

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

The number of reported non-hemolytic transfusion reactions in 2010 is 491 from 77 hospitals, roughly the same as 2009 (488). The number of mild febrile reactions (mild NHFR) is 332 in comparison to 359 in 2009. The latter come from 66 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. Together the non-hemolytic transfusion reactions and the mild febrile reactions make up approximately a third of the total number of reports.

Each year the NHTR and the mild NHFR together account a number of serious reports per year, in most of which admission from day care for observation or a prolongation of hospital admission was the reason for rating as grade 2. There were 14 reports in 2010 (10 with certain, probable or possible imputability) in these two categories, compared to 22 in 2009.

Table 4 shows that the contribution of platelet concentrates is relatively high in comparison to RBC concentrates for the NHTR, but relatively low for the reported mild NHFR. *Table 9* below shows the specialty which requested the transfusions, broken down according to type of blood component.

Table 9 Reports of febrile reactions: type of blood component and requesting specialty

A. Non-hemolytic transfusion reaction	RBC	Platelets	Plasma	Combi-nation	Other[#]	Not stated
Surgical	108	3	3	2	18	0
Medical	247	65	4	14	0	1
A&E, Intensive care or specialty not stated	18	6	2	0	0	0
B. Mild non-hemolytic febrile reaction						
Surgical	88	0	0	2	0	0
Medical	209	14	1	3	0	1
A&E, Intensive care or specialty not stated	14	0	0	0	0	0

[#]transfusion of drain blood

In cases where a platelet transfusion was followed by a febrile reaction, 85% of the reports concerned transfusion which had been requested by a medical specialty and this

was the case for all reports of mild NHFR. This probably reflects the specialties which prescribe platelet transfusions; in addition differences between the patient populations may explain this difference. TRIP lacks information about the total patient population which receives platelet transfusions, so it is not possible to propose an explanation.

In 2010 there was further improvement in the recording of observed symptoms; TRIP assumes that this has been facilitated by the progressive uptake of electronic reporting. It was discussed in the expert review meeting that there are cases where other symptoms are associated with a rise in body temperature, and that the phrase “without further relevant symptoms or signs” in the definition can be ambiguous. When does a clinical feature fit in with the rise in temperature, when is it a relevant finding which precludes the diagnosis of a non-hemolytic reaction? It was agreed that additional reporting guidance should be drafted to assist in optimising the quality of reports. *Case histories 1* describes some examples of febrile reactions where the reported symptoms led to further questions for clarification before the report was accepted in the febrile reaction category.

TRIP’s 2008 and 2009 annual reports identified an improvement in the number of reports in which a result was reported for blood culture performed on the patient following an NHTR: from 42% in 2006 to 46% in 2007 and 58% in 2008 and 2009. In 2010 this has increased to 66%. Regarding the assessment of febrile reaction, it was discussed in the expert meeting that a positive patient blood culture - notably if found after transfusion and not tested beforehand - essentially excludes the category of febrile reaction (NHTR or mild NHFR). Nevertheless there are many occasions when a patient who may have a bacterial infection receives a transfusion and may also develop a febrile reaction. If the blood culture is positive, the category post-transfusion bacteremia/sepsis (available since 2008) is appropriate. Use of this category by reporters is progressively improving. In two cases a (different) bacterial species was found in the remnant of the unit, and this was interpreted as contamination at sampling. These reports are however included in the tables in the section on infectious complications of blood transfusion in section 3.2. That section also contains a discussion of reports of post-transfusion bacteremia/sepsis or febrile reactions in patients who had no pre-transfusion blood cultures and who in some cases had documented pre-existing bacterial infections

Case histories 1 NHTR and mild NHFR

1. Following RBC transfusion to a hematological patient, a rise in temp from occurs (37 to 38.2°C) and blood pressure rises. Bacteriology and blood group serology reveal no abnormalities. Further questions from TRIP elicit the information that the blood pressure changed form 131/80 to 150/85. The report is registered in the category of mild NHFR.

2. A urology patient receives a RBC unit; three hours after it started a rise in temp of >1 <2°C was noted. The report states, “A positive blood culture is found, with a Gram-negative rod. Antibiotics prescribed. Temp was already 40.6°C before transfusion. The report was submitted in the category of mild NHFR, imputability improbable.
   Question from TRIP: When was the specimen taken which gave the positive culture: after transfusion or before? Answer: the positive blood culture was taken before transfusion. The report was registered as mild NHFR.

3. A female patient with acute myeloid leukemia receives a platelet transfusion. She has a rise in temperature of >2°C and shortness of breath/dyspnea. No bacteriology specimens are taken, but the report states there were no signs of hemolysis. The report is submitted as a non-hemolytic transfusion reaction, grade 1, imputability possible.

Question from TRIP: was dyspnea the predominant feature?
Answer: No Chest X-ray taken on the day of transfusion. On X-ray taken two days later (check following placement of pacemaker) no indication of volume overload or TRALI. Report: NHTR.

Acute hemolytic transfusion reaction (AHTR)

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

In 2010 TRIP received 20 reports from twelve hospitals regarding an acute hemolytic transfusion reaction, a number in line with previous reporting years. In only two cases the additional category new allo-antibody formation was stated. Severity grade and imputability, which are largely comparable to 2009 are shown in *Table 10.* All AHTR were observed after transfusion of RBCs.

Table 10 Severity and imputability of acute hemolytic transfusion reactions in 2010

Severity grade	Imputability certain	Imputability probable	Imputability possible	Imputability unlikely	Total
1	5	-	8	1	14
2	2	2	1	-	5
3	1	-	-	-	1
4	-	-	-	-	-

In *Table 11* reported clinical symptoms and signs are summarised. Symptoms and signs are largely non-specific; in only two cases more specific hemoglobinuria is reported.

Table 11 Clinical features of acute haemolytic transfusion reactions in 2010 (n=20)

Symptom/sign	Number of times reported
Rise in temperature ≥ 2 °C	8
Rise in temperature >1<2 °C	2
Chills/rigors	7
Tachycardia	6
Hemoglobinuria	2
Dyspnea	4
Nausea/vomiting	3
Drop in blood pressure	4
Increased blood pressure	4
Pain (head, chest, back)	3
No increase in Hb level	3

In all reports haemolysis could be substantiated by biochemical hemolysis parameters (LDH, bilirubin, haptoglobin). Blood group serological abnormalities were found in 12 reports. In five cases an antibody was demonstrated: anti-Yka, anti-Jkb, 2x anti-Wra, anti-AnWj. The last antibody caused four AHTRs in two months in a male patient, all registered with certain imputability (1x grade 3, 2x grade 2 and 1x grade 1); anti-AnWj is an antibody directed against a high frequency antigen and was finally identified by an international blood group reference laboratory. In six cases the patient had an underlying

hemolytic anemia and out of these three patients had an autoimmune hemolytic anemia. In these cases there was increased hemolysis temporally related to transfusion, so-called hyperhemolysis. In all these cases increased hemolysis was supported by laboratory investigations.

Furthermore one report mentioned new allo-antibody formation with an additional category AHTR. In this case a patient was given several uncrossmatched O negative RBC units in an emergency situation. A pre-transfusion sample showed an anti-C that was not known in the transfusion laboratory; the hospital does not participate in the TRIX (Transfusion Register for Irregular antibodies and Xmatch problems) national database for patient antibodies. Although no symptoms of an AHTR were seen levels of hemolysis parameters (LDH, bilirubin, haptoglobin) did show evidence of hemolysis. This is a calculated risk situation that some reporters prefer to report in the category other incident.

Delayed hemolytic transfusion reaction (DHTR)

> *Symptoms of hemolysis occurring longer than 24 hours after transfusion to a maximum of 28 days: unexplained drop in hemoglobin, dark urine, fever or chills etc; or biochemical hemolysis within the same period. Biochemical testing and blood group serology confirm this.*
> *If new antibodies are found without biochemical confirmation of hemolysis, report as new allo-antibody.*

In the reporting year 2010 TRIP received 20 reports in the category of delayed hemolytic transfusion reaction. Seven reports were submitted in the main category DHTR, another twelve DHTR were reported as an additional category to new allo-antibody formation and one was reported as an additional category to a NHTR (blood group serology and biochemistry were initially normal). A DHTR is reported as an additional category when the finding of a new allo-antibody or NHTR is the reason to check for DHTR. One DHTR was reported as an additional category to a report of incorrect blood component transfused (see chapter 3.3).

All DHTR occurred after transfusion of RBCs. Six reports were of severity grade 2 (imputability certain n=3, imputability probable n=3), nine grade 1 and five grade 0 (DHTR could only be demonstrated by means of laboratory parameters). In the cases of main category DHTR (5x grade 2, 1x grade 1) the responsible antibody was identified namely: anti-e, anti-E, anti-E + anti-Cob, anti-K + anti-Jka, anti-E + anti-c, anti-E + anti-S + anti-Lua. In only one case no responsible antibody could be demonstrated.

In 2010 TRIP continued the policy started in 2009 of asking reporters of clinically significant new allo-antibodies targeted questions about hemolysis. All reporters of clinically significant antibodies found within three months of a transfusion were asked if the patient had required a another transfusion and if so, whether there were signs of hemolysis e.g. an unexplained drop in Hb level and/or hemolysis demonstrated by the course of hemolysis parameters LDH, bilirubin and haptoglobine. Targeted questions about hemolysis were asked in 140 cases. In only two cases did this result in registering an additional category DHTR. The total number of DHTR (main and additional category) is slightly lower than in 2009 (29).

For two years running TRIP has attempted to test the DHTR incidence, stated in the literature to be 5 – 10 times higher than AHTR, against that in reporting practice. In 2008 the majority of reports of new allo-antibody formation with additional category DHTR had originated from one reporter, which could imply that DHTR were often missed. The higher incidence of DHTR compared to AHTR could not be demonstrated in the Dutch hospitals

by this method. Quite often reporters responded that there was no evidence of hemolysis. It is likely that cases are not diagnosed simply because there are no data that support the diagnosis DHTR. A DHTR may remain subclinical; biochemical hemolysis parameters are therefore not tested and in many cases the underlying illness in the patient can explain a drop in hemoglobin level. The TRIP policy of asking about hemolysis has led to increased awareness of DHTR among hemovigilance staff in hospitals. Many reports of new allo-antibody formation now include information about hemolysis parameters. Further questions about hemolysis in cases of new allo-antibody formation do not often lead to diagnosis of DHTR. In future TRIP will only ask about hemolysis in cases where a DHTR might be suspected from transfusion history, hemoglobin levels or biochemical hemolysis parameters.

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 17 TRALI reports were received in 2010 and of these 17, 16 were deemed to meet the consensus criteria for this transfusion reaction. The seventeenth report gave insufficient information for it to be assessed and no additional information was forthcoming from the reporter; it is not included in the discussion below.

A number of other reports were received where TRALI was initially considered but on examination of the full data the reporting hospital decided (either itself, or in discussion with TRIP) that another type of transfusion reaction was more likely and the reporting category was modified. The principal reason for this lies in the fact that TRALIs must be rapidly reported to the blood service, and information is not complete at this time. The assessment of the type of reaction requires full clinical information including laboratory and radiological results as well as the response to treatment. It is important to note that TRIP does not take account of the findings of leukocyte serological investigation when assessing the TRALI reports.

Out of the 16 TRALI reports which met the criteria, three were assessed as unlikely because the patient's underlying pathology could also, more plausibly explain the clinical features. In one there was insufficient information for reliable assessment of the imputability. The remaining 12 definite, probable and possible TRALIs were six times associated with transfusion of a red blood cell concentrate, once with plasma, once with platelets and four times with platelets as well as red blood cells and/or plasma. These twelve cases will be discussed in the remainder of this section. Two TRALI reports were of severity grade 4, both times in patients who were already seriously ill. One patient developed multi-organ failure and the other, with an incurable malignancy, was being treated for multiple postoperative complications.

In *Table 5* of this report it can be seen that the median age of patients suffering from TRALI is lower than that of patients with transfusion-associated circulatory overload. Out of the 12 cases, there is one postpartum patient, six received their transfusions for blood loss before, during or after surgery while five patients were medical (nephrology 1x, oncology 4x).

Figure 6 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 (33%,

95% confidence interval 9 – 51%) following the implementation of the measure (which became effective in mid-2007) of exclusively distributing plasma from male, never transfused donors as fresh frozen quarantine plasma for transfusion (Wiersum-Osselton et al., Transfusion 2011;51:1278-1283). The data from 2010 are consistent with this estimate. A similar measure concerning the recovered plasma added to pooled platelet products for conservation was introduced in November 2009. The data do not yet permit any conclusions to be drawn about the effect of this measure.

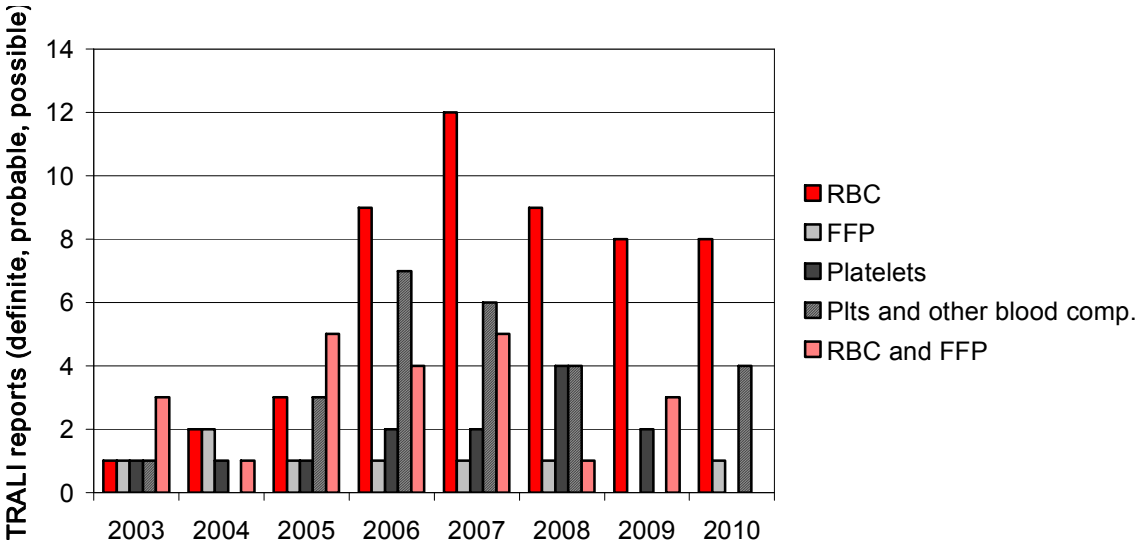

Figure 6 TRALI reports and associated blood components, 2003-2010

Regarding the leukocyte serological investigations, these are known to have been performed in ten cases. In two cases the results were not yet available. In two incompatibility was demonstrated between the patient's leukocytes and donor antibodies. In two cases one or more donors had HLA antibodies but crossmatch was negative or could not be performed. In the additional reports TRIP was informed by the reporting hospital that the leukocyte serological investigations gave no indication of an immune-mediated TRALI, or that no HLA antibodies had been found in the donors. Findings of leukocyte serology are not relevant for patient care but for guiding decisions about eligibility of a donor for future donations. Occasionally the diagnosis of TRALI is only considered some time after transfusion and this may – inappropriately - deter the hospital from reporting it to Sanquin Blood Supply. Even if full investigation is no longer possible (for instance, if a patient sample can no longer be obtained for HLA typing or for leukocyte crossmatch testing) the donor(s) can be flagged as having been associated with a TRALI.

Anaphylactic transfusion reaction

Rapidly developing reaction occurring within a few seconds to minutes after the start of transfusion, with features such as airway obstruction, in and expiratory stridor, fall in blood pressure ≥ 20mm Hb systolic and/or diastolic, nausea or vomiting or diarrhoea, possibly with skin rash.

Hemolysis testing and bacteriology negative, test for IgA and anti-IgA.

There were 72 reports of anaphylactic reactions in 2010, 19 being grade 2 in severity: figures which are almost identical to those of 2009. The anaphylactic reactions account for the largest number of serious reactions (with certain, probable or possible imputability to the transfusion), closely followed by transfusion-associated circulatory overload and then other reaction, TRALI and post-transfusion bacteremia/sepsis (*Table 1*).

The anaphylactic reactions occurred during or after transfusion of red blood cells in 18 cases (25%), platelets in 37 cases (51%) and plasma in 13 (18%). The incidence of anaphylactic reactions is highest for platelet concentrates, slightly lower for FFP and lower again for red blood cell concentrates. The proportions of types of blood components are very similar to those for other allergic reactions. The same is true of the age distribution of patients: most anaphylactic and other allergic reactions occur in patients aged 20-60: 43% and 46% respectively, compared to 29% for all transfusion reactions. This is also the age group of patients receiving most platelet transfusions according to data from the PROTON study (*Table 5*). In the future it would be relevant to investigate specific risk factors other than the type of blood component.

In last year's report we raised the question whether the implementation of male-only fresh frozen plasma (effective mid to late 2007) has led to a change in the incidence of anaphylactic reactions: the data do not indicate that there was any change. The same question could be asked concerning the pooled platelet units: has there been any change in the occurrence of anaphylactic reactions since the introduction (November 2009) of male-only plasma as added conservation solution for pooled buffy coat platelet units? In the Northwest, Northeast and Southeast regions of the Netherlands pooled platelet components with plasma are distributed as the standard product, whereas in the Southwestern region pooled units with platelet additive solution (PAS) are distributed as the standard product. *Table 12* shows the types of blood components from 2007 to 2010 in the anaphylactic reaction reports. The figures do not show a decrease in the involvement of platelet units after 2009.

Table 12 – Blood components in reports of anaphylactic reaction, 2006 – 2009

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

[1] product 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

Published data state that allergic transfusion reactions occur more often following transfusion of apheresis platelets (see for instance the French hemovigilance reports, www.afssaps.fr) and less frequently in association with platelets produced with platelet additive solution (PAS) than when plasma is added as conservation fluid. Thanks to online reporting to TRIP, the type of product is specified by a steadily increasing number of reporters. We studied the distribution of the types of platelet concentrates in the 2010 reports to see if the data are in agreement with the findings quoted above.

Table 13 shows the specification of the type of component per region for all reports of anaphylactic and other allergic reaction in 2010 where the component type involved was recorded as platelets. Note that in The Netherlands, apheresis platelets are used for special indications such as HLA-matched or neonatal platelet transfusions. It can be assumed that patient risk factors also play a role as well as a possible increase of risk from a particular product type. However TRIP has no information on denominators and cannot make any statement on the different factors.

Table 13 Reports of anaphylactic and other allergic transfusion reactions per type of platelet product

Region	Total platelets transfused[1]	Overall rate of allergic reactions[2]	Apheresis (single donor)		Pooled 5-D BC plts, plasma		Pooled 5-D BC plts, PAS		Type of platelet product not specified	
			Ana	other	Ana	other	Ana	other	Ana	other
NW	17353	2.48	1	2	*9	28	-	-	1	2
NE	6688	1.35	-	-	*2	2	-	-	2	3
SW	16697	2.16	2	4	#2	16	*5	5	2	0
SE	12846	2.80	1	1	*5	14	-	-	5	10

[1] platelet units transfused in hospitals which participated in 2010.
[2] rate per 1000 units transfused; note that only reactions ascribed to platelets as sole blood component have been included.
*standard product in this region
#some products are exchanged between regions prior to distribution, however this could also represent inaccurate information.

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 twice been confirmed as the cause of a transfusion reaction, in 2003 and in 2005. Out of the total of 338 reports, 72 others record the finding of a normal IgA level and/or absence of anti-IgA or anti-IgA subclass.

In 2010 one report of an anaphylactic reaction occurred in a patient with peanut allergy who received a pooled platelet unit. In this case (see Jacobs JFM et al. NEJM 2011;364:1981-2) evidence to support the allergic mechanism was found in an elevated mast cell tryptase and peanut-specific IgE was detected in the patient's serum. Three of the five donors had consumed peanuts the evening before donation. Since peanuts are commonly consumed, however, this is unlikely to be a frequent mechanism of allergic transfusion reactions. In another report the recipient of a red blood cell concentrate was known to be allergic to latex; in this case a urinary catheter was seen as the most likely cause of the reaction.

As highlighted by TRIP in several annual reports, there is a need for systematic investigation of serious allergic transfusion reactions in order to address the lack of knowledge about causative mechanisms and allergens which give rise to anaphylactic and other allergic reactions. Currently few are reported to the blood service although in the past the recommendation was to flag the donor following a serious allergic or anaphylactic reaction. Anaphylactic transfusion reactions remain numerically the largest category of serious transfusion reaction.

Other allergic reaction

Allergic phenomena such as itching, redness or urticaria but without respiratory, cardiovascular or gastrointestinal features, arising from a few minutes of starting transfusion until a few hours after its completion.

The number of reports of other allergic reactions is similar to the final total of last year (181 compared to 171 in 2008). In 2010 as in 2009 there were no 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.

As can be seen in *Table 5* men and women are represented equally which is also the case for anaphylactic reactions. Over half of the patients are below the age of 60, compared to 17% in the case of transfusion-associated circulatory overload and 35% overall among the reports.

Most other allergic transfusion reactions do not have a serious course. Many hospital protocols do not require further investigations. Among the 181 reports in this category, two reports record the detection of HLA antibodies and ten mention negative findings of testing for HLA antibodies.

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 circulatory overload (also called TACO: transfusion-associated circulatory overload) in 2010 was 47, which means that there is a slight rising trend in comparison with the last few years. In addition there were three reports where circulatory overload was recorded as an additional category following an other incident. Twenty reports were of grade 2 or higher: thirteen of grade 2, five of grade 3 and two of grade 4 (cited in section 3.5). As in previous years, over two thirds of the reports of circulatory overload involved the administration of red blood cells (37/47, 79%).

Female patients were involved in slightly over half of the patients (27/47, 59%). Six patients were aged 40 years or younger: a toddler and a man both of whom had undergone hematopoietic stem cell transplantation, a man who developed circulatory overload during therapeutic plasmapheresis, two postnatal and a woman who was receiving treatment for leukemia.

The distinction between TRALI and transfusion-associated circulatory overload is difficult. A number of reports of circulatory overload (eight, of which six were of grade 2 or higher) were initially thought to be a TRALI. In the Expert Committee meeting it was recognised that even after collating as much as possible relevant clinical information a clearcut decision about the nature (cause) of suspect symptoms is not always possible. *Case histories 2* describes a reports registered in this category where it is seen that a single unit of blood component can be enough to cause TACO in a vulnerable patient.

Case histories 2 – Transfusion-associated circulatory overload

TACO-1
A male cardiology patient aged 87 and with pneumonia, a history of ischemic cardiac disease and chronic anaemia, receives a transfusion of red blood cells. After one and a half hours his shortness of breath and orthopnea worsen. Intravenous furosemide produces diuresis. The unit had been transfused too quickly, in 1 hour instead of in 2-6 hours. Earlier on the same day the chest X-ray already showed pleural fluid and pulmonary infiltration, radiography was not repeated.
TRIP report: circulatory overload grade 1, imputability probable.

On assessing the reports of TACO in 2010, the TRIP reviewers noted a considerable number of reports, 14/47 (30%), where a rise in body temperature was mentioned. Fever as a feature of circulatory overload is not plausible. One can speculate whether the

increased circulatory demands in febrile patients can contribute to the occurrence of circulatory overload.

Post-transfusion purpura (PTP)

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

There were no reports of PTP in 2010. Since the start of the TRIP registration there have been only two reports of PTP, namely one in the baseline measurement year of 2002 and one in 2008. In general, PTP only occurs very sporadically with the administration of leukodepleted blood components.

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

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

No reports of TA-GVHD were received in 2010. Leukodepletion, as performed on all blood components in the Netherlands since the end of 2001, significantly reduces the occurrence of TA-GVHD. In addition, prophylactically irradiated components are used for high-risk patients.

TRIP receives occasional reports where the patient has incorrectly received a non-irradiated component. These incidents are included in the chapter on Incorrect Blood Component Transfused. To date, TA-GVHD has never been reported in these patients.

Hemosiderosis

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

In 2010, four reports were received about poly-transfused patients who had been diagnosed with hemosiderosis. The reports came from two hospitals. The patients concerned were all men with a history of multiple transfusions. Two out of four had previously received chelation therapy and responded to this; subsequently the ferritin had again increased above 1000 micrograms/l. Two out of four were chronically transfusion-dependent and the other two had received multiple transfusions in the course of chemotherapy for a malignant condition. In these four cases there was no evidence of organ damage.

It is clear that the finding of hemosiderosis is currently not well reported to TRIP. TRIP wishes to encourage the reporting of hemosiderosis, particularly since medical treatment can be given for the condition. Consistent reporting is necessary in order to gain insight at the national level in the rate of occurrence of this complication of blood transfusion.

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).

The reporting year 2010 showed a further 5% increase in the number of reports in the category of new allo-antibody formation, the largest TRIP category since 2004. TRIP received 789 reports that were submitted by 61 hospitals in the main category new allo-antibody formation (2009: 753 by 60 hospitals). This means that roughly two thirds of the Dutch hospitals report allo-antibody formation to TRIP. In twelve cases the additional category DHTR was reported i.e. the demonstration of a new allo-antibody leading to the diagnosis DHTR. Contrary to 2008, when most of these cases were reported by one hospital, in 2010 DHTR was reported as an additional category by nine hospitals. New allo-antibody formation was reported as an additional category in 17 reports: IBCT (n=4), AHTR (n=2), DHTR (n=6), NHTR (n=5). In one report, other incident was added as additional category because there was no documentation to ensure traceability of transfusion. For these reports please see relevant chapters.

The patients involved were 484 females and 305 males. In 20 reports the new allo-antibody was formed after transfusion of platelets, in 733 cases transfusion of RBCs was followed by allo-antibody formation. The remainder were reported after transfusion of a combination of RBCs and other blood components: RBCs, platelets and plasma (n=5), RBCs and plasma (n=6) and RBCs and platelets (n=10). Fifteen reports did not state the type of blood component administered.

The number of detected allo-antibodies per report varied from one to four. In 660 cases a single allo-antibody was reported in 2010, 112 reports stated two allo-antibodies and 15 mentioned three allo-antibodies. Two reports stated four allo-antibodies. An overview of reported allo-antibody specificities is presented in *Table 14.* The group of other antibodies represents less commonly reported antibodies i.e.: anti-M 17, anti-Lea 10, anti-Fyb 7, anti-P1 4, anti-s 4, anti-Leb 3, anti-G 3, anti-HLA 3, anti-Cob 3, anti-Bga 2 and one report each of: anti-Ch1, anti-IH, anti-Yka, anti-HPA, anti-Kna, anti-f and HTLA.

Platelets were implicated in the formation of anti-D in ten reports, in one of these combined with anti-C. In all of these cases Rhesus positive platelets had been administered to a man or a woman past childbearing age. Other allo-antibodies reported after platelet transfusion were anti-E in five cases, anti-c in two cases, anti-HPA (n=1), anti-Jka (n=1) and anti-S (n=1). Antibody formation to Rhesus antigens is well known after platelet administration as these antigens are expressed on platelets. The two latter antibodies are remarkable; reporters specifically indicated that only platelets were transfused and antibody formation was ascribed to the small amount of red cells that are present in platelet concentrates.

Table 14 Newly formed allo-antibodies and sex of the patient

Specificity of antibody	Number* Total	311 M	495 F
anti-E	288	101	187
anti-K	177	63	114
anti-Fya	71	26	45
anti-Jka	86	29	57
anti-c	73	27	46
anti-C	39	15	24
anti-Wra	26	13	13

anti-D	20	11	9
anti-Cw	26	12	14
anti-S	22	3	19
anti-Jkb	23	9	14
anti-Lua	16	13	3
anti-e	9	2	7
anti-Kpa	18	5	13
other	63	35	28
Total	**957**	**364**	**593**

***Including the patients and antibodies reported as an additional category associated with a transfusion reaction or incident; a patient with several antibodies is counted multiple times.

There was a total of 20 reports of anti-D formation involving nine men and eleven women past childbearing age: the ten cases transfusion (described above) after Rhesus positive platelets, nine after RBC transfusion and one after transfusion of RBCs, platelets and plasma. Seven reports mentioned a combination of anti-D en anti-C whereas no D positive component had been administered: these cases are assumed to involve an anti-G (an antibody that mimics anti-D combined with anti-C in irregular antibody screening). In three cases involving one male and two female patients no explanation was found as all administered components were D negative.

The number of reports stating anti-K was 177 of which 114 involved female patients. Only two of these concerned a woman of childbearing age. In both cases the patients were transfused before implementation of the K negative transfusion policy for women of childbearing age. Six women of childbearing age developed anti-c. Five were transfused after 2006 when TRIP advised that Rhesus compatible transfusion for women of childbearing should be considered for prevention of hemolytic disease of the fetus and the newborn. It is not known how many hospitals have implemented this preventive policy. The revised national transfusion guideline (2011) includes this recommendation.

Other transfusion reaction

Transfusion reaction that does not fit into the categories above.

In 2010 the number of reports of other transfusion reaction (159) increased still further in comparison to previous years: approximately 60 up to 2007, 101 in 2008 and 133 in 2009. Imputability was assessed as possible or higher in 129 of these reactions. Twenty-one reports are of severity grade 2 or higher, sixteen with possible or probable imputability, whereas five of these reactions are assessed as unlikely in imputability.

For the 129 other reactions with imputability possible or higher TRIP examined the files to see whether the reaction was originally assessed as other reaction by the reporting hospital or if there had been a change in category after questions from TRIP. The reporting hospital changed the category in 52 cases (40%). There can be different reasons why a reaction initially seemed to fit in a standard categories but this was later felt not to be appropriate. Some of these cases are not consistent with the definition of a standard category for example due to the interval being too long or because there is an unusual combination of symptoms. In other cases the clinical symptoms are consistent with the definition but category other reaction has to be chosen because further examinations give contradictory results or fail to provide sufficient evidence for the diagnosis of the standard category.

The presence of clusters of reports with similar symptoms is examined each year. There were 40 reports in which only one symptom or two symptoms likely to be due to the same

problem are listed, e.g. nausea and vomiting. In most of the remaining reports there was a combination of symptoms (117), twice no symptoms were listed.

Tables 15 A, B and C show an overview of the other reactions with imputability possible or higher. *Table 15A* shows solitary symptoms that were reported and *Tables 15B and C* show combinations of symptoms that were reported in this category. The distribution of the type of blood components and severity grade is presented alongside.

Table 15 Other transfusion reaction 2010, imputability possible (110), probable (19) or certain (0)

Table 15A Solitary symptom, possible (24), probable (5)

Symptom	Total	TAQ#	Product					Severity grade				
	29	9	EC	TC	FFP	other	combi	0	1	2	3	4
Decrease in blood pressure	8	4	7				1		5	3		
Unstable blood pressure	1		1						1			
Dyspnea/hypoxia	5	2	2	2			1		2	3		
Rise in temperature*	5	1	4				1		5			
Decrease in temperature	2		2						2			
Pain (lumbar/head/chest)	3	1	1	1	1				3			
Nausea/vomiting	2	1	2						2			
Tachycardia	2		1	1					2			
Chills/rigors*	1			1					1			

Category changed after questions from TRIP
* Not reported as NHTR e.g. because of time interval being too long or temperature remaining high too long or blood component tested positive for bacterial contamination

Based on the symptoms that were most frequently present as solitary symptom two groups of other reactions with a combination of symptoms were examined further. Firstly, there is a cluster of reports with hypotension or a decrease in blood pressure being an important feature (34), most of the time combined with a rise in temperature and/or chills/rigors (27x). Secondly, there is a cluster of reports with dyspnea as the main feature (33), also generally (29x) combined with a rise in temperature and/or chills/rigors. Another finding that was often present in association with dyspnea is a rise in blood pressure (6x). In three cases of other reaction there was a decrease in blood pressure as well as dyspnea. The last cluster that has to be mentioned is rise in blood pressure (14) without dyspnea, but often combined with rise in temperature and/or chills/rigors (12x)

Table 15B Combination of clinical symptoms consistent with definition of a standard category, possible (56), probable (8)

Major symptom	Total	TAQ#	Product					Severity grade				
	64		EC	TC	FFP	other	combi	0	1	2	3	4
Decrease in blood pressure	28	16	23			4*	1		26	2		
Dyspnea/hypoxia	29	15	22	6			1		25	3		1
Decrease in blood pressure and dyspnea/hypoxia	3	2	3						3			
Other	4	-	2	2					4			

Changed after questions from TRIP
* drain blood

Table 15C Combination of symptoms not consistent with definition of a standard category TR, possible (30), probable (6)

Major symptom	Total 36	TAQ[#]	Product					Severity grade				
			EC	TC	FFP	other	combi	0	1	2	3	4
Decrease in blood pressure	6	1	4			1	1		5	1		
Dyspnea/hypoxia	3	1	2	1					3			
Rise in blood pressure	14	5	10			3	1		13	1		
Other	13	4	8	2	1	1	1		11		1	1

[#] Changed after questions from TRIP

Case histories 3

OR-1
A 73-year-old male patient, with rectal bleeding and ileus, received a RBC. Start of transfusion at 22:30 hours. Five hours later the patient showed chills, dyspnea and a drop in saturation from 98% to 75%; there was also a slight rise in temperature. Blood cultures from the patient were taken and proved sterile. After administration of oxygen the dyspnea diminished and saturation went up again to 98%.

Against hospital protocol, the reaction was not immediately reported to the transfusion laboratory, so no culture of the RBC was taken and additional investigations concerning serology were performed.

The reaction was reported to TRIP as NHTR. Mild dyspnea is accepted in this category, but a decrease of saturation to 75% is not considered an usual accompanying symptom of NHTR. The symptoms could be consistent with several categories, e.g. TRALI, TACO or anaphylactic reaction. Questions asked by TRIP revealed that there were no other features suggestive of an allergic reaction. A chest X-ray taken after transfusion showed signs of pneumonia; there were no signs of circulatory overload. Considering these findings as well as the patient's clinical course, the category was changed to other reaction.

OR-2
A female patient, 83 years old, received drain blood after an orthopaedic hip operation. After 0:45 hour (225 ml) she started shivering and the systolic blood pressure dropped from 115/60 to 90/65 mm Hg. The reaction was reported as NHTR. The definition of NHTR states that except rigors/chills or rise in temperature during or in the first two hours after transfusion there may be no other relevant symptoms or signs. However in an adult a systolic tension below 95 – 90 mmHg is considered to be a serious sign which can point to developing shock. For this reason the category was changed to other reaction.

OR-3
Five minutes after the start of a platelet transfusion (A neg), a 7 year old child (ALL patient) complained about pain in the lumbar region and nausea, and she also vomited. The patient's blood group was B pos. Culture of the platelets remained sterile. There were no serological particularities. The reaction was reported and accepted as other reaction.

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 2010 four reports of viral contamination of blood component were received of which two had the additional category of post-transfusion viral infection. Three of these reports related to hepatitis B virus (HBV). Due to a new screening test that was introduced by the blood service in the autumn of 2008, which screens for HBV-DNA (HBV-NAT), it is now possible to detect donors with a so-called occult hepatitis B infection (OBI). A donor carrying an OBI will test negative for HbsAg, but may still transmit HBV due to viral DNA that is fluctuating near the detection threshold. A look-back procedure is performed by the blood service to investigate the recipients of these donors. In one case the recipient, transfused as a baby 17 years ago, tested positive for hepatitis B and this was registered as additional category post-transfusion viral infection, grade 2, imputability probable (viral typing could not unequivocally demonstrate the same virus after 17 years). The second case with additional category post-transfusion viral infection was registered as grade 4, imputability unlikely. It concerned an elderly patient who had received an RBC from a donor who was later found to have an OBI. Testing on an archived donation sample was shown to be HBV-NAT negative and anti-HBc positive. The recipient developed jaundice three months after transfusion, which at the time was attributed to a stone in the choledochal duct. After papillotomy and removal of the stone the patient did not improve and he died of unknown causes at home three weeks later. Testing for hepatitis B was not done. Liver function tests suggested post-hepatic jaundice, with very high bilirubin levels and only mildly elevated ASAT/ALAT; however a viral hepatitis cannot be fully excluded. The third case concerned another elderly patient without symptoms who did not undergo further testing. The fourth report of viral contamination of blood related to Epstein-Barr virus (EBV) in a donor from whom post-donation information was received about a confirmed EBV infection. The retained donation sample was not tested for EBV. The recipient showed no symptoms, had a positive EBV-Gig titre one day after transfusion and was considered to be immune to EBV.

Two reports of post-transfusion viral infection were received. A patient who had received multiple transfusions and a cord blood transplant for a hematological malignancy was diagnosed with hepatitis B. One year after diagnosis the possibility of a transfusion transmitted infection was considered. Investigations are ongoing at the writing of this report, so imputability is remains unclassifiable at this point. The second report (a late 2009 report) related to hepatitis E that according to the literature is likely to be transmissible by transfusion and transplantation. The recipient of a kidney transplant and three RBCs developed hepatitis E. All three donors and the kidney donor tested negative for hepatitis E and imputability was therefore assessed as excluded.

Table 16 shows the number of viral reports from the start of the TRIP registration up to and including 2010. The above-described case of hepatitis B, that traces back to a transfusion in 1993, has been added. Sanquin supplied additional information concerning a look-back procedure of an OBI donor and two recipients with previously reported post-transfusion hepatitis B after multiple transfusions in 2007 and 2008. At the time archived donation samples were negative. The imputability has changed from excluded to certain as viral typing was almost identical (Zaaijer et al., Infectious Diseases Bulletin 2010 no

4). These cases have been added in *Table 16*. , which also shows a rise in look-back procedures as described in chapter 3.3.

Table 16 Viral reports to TRIP, 2002 – 2010

Virus	Post-transfusion viral infection*	Number probable or certain	Number possible	Viral contamination of blood component or look-back°, no infection	Comment
Hepatitis B	15	6[#]	1	53	[#]Donations in 1993, 2006 and 2007
Hepatitis C	9	0	3	0	
B19	2	1	1	0	Components not B19-safe;no investigation
CMV	12	2	5	0	Several reports (in previous years) registered as certain/probable but never confirmed
EBV	6	0	1	0	
HAV	1	0	0	0	Report in 2006, Tf in 2003, no investigation by Sanquin
HIV	1	0	1[§]	4**	[§]Report from 2003, unconfirmed **Recipients died, no clinical signs of HIV
HTLV	0	0	0	1	Recipient died, no clinical signs

***** Prior to 2008 : Viral infection
° Reported to TRIP by hospital

Bacterial problems in relation to blood transfusion

Since reporting year 2008 TRIP has operated with definitions for bacterial problems which draw a distinction between bacterial contamination of a blood component and post-transfusion bacteremia/sepsis. With this breakdown, TRIP can distinguish between cases where a patient's symptoms were the reason for performing cultures and cases where a positive bacterial culture result was found (by Sanquin or the hospital). The reports of each type are discussed in the paragraphs below.

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 2010, 40 reports were registered in the category bacterial contamination of a blood component and bacterial contamination of a blood component was recorded as an additional category on 17 occasions.

The majority of the reports (n=39, plus three reports in the category positive bacterial screen) concerned reports from hospitals providing information on administered units which had later given a positive result in the bacteriological screening performed by Sanquin. The remaining reports of bacterial contamination of a blood component relate to positive bacteriological findings by a hospital, usually as part of investigations following a (possible) transfusion reaction. The findings are summarised in *Table 17A* (platelets) and *17B* (RBCs and plasma).

It can be seen (particularly in *Table 17B*) that several reporters preferred to classify febrile reactions as non-hemolytic transfusion reactions (as main category) despite the bacteriological findings. According to the definitions the febrile reactions are diagnosed by exclusion of other causes and can only be used if findings of bacteriological investigation are negative. A exception to this might be if there are reasons to believe that the positive culture result on the unit is false-positive.

Table 17A Bacteriological contamination of platelets (n=47)

Sanquin bacteriological screening	Hospital culture result on unit*	Patient blood culture*	Reporting category (if other than bacterial contamination of blood component) or symptoms*
Negative	Streptococcus dysgalactiae	Streptococcus dysgalactiae	Post-transfusion bacteremia/sepsis Gr 2, certain
Negative	Staphylococcus warneri	Staphylococcus warneri and Klebsiella oxytoca	Post-transfusion bacteremia/sepsis Gr 1, possible
Negative	Acinetobacter ursinii and Gram neg. rods	Acinetobacter ursinii	Post-transfusion bacteremia/sepsis Gr 1, probable
Negative	Gram neg. rods *NB split of same product as above*	-	Other reaction (additional category) Gr 1, improbable
Negative	St. Epidermidis	Enterococcus faecium	Post-transfusion bacteremia/sepsis Gr 1, possible
Negative; *findings from Q fever look-back procedure*	-	Pos. on PCR	Post-transfusion bacteremia/sepsis Gr 1, improbable
Negative	Micrococcus luteus St. Epidermidis	Negative	NHTR, Gr 1, probable NHTR, Gr 1, possible
	St. Hominis	2x neg	Other reaction, Gr 3, probable
	Str Oralis		Other reaction, Gr 1, possible
	Gram pos cocci	E. Coli	Post-transfusion bacteremia/sepsis Gr 1, improbable
Brevandimonas vesicularis	-	Negative	Other reaction, Gr 1, possible (additional category)
Peptostreptococcus sp.	-	Negative	Rise in temp >2°C, rigors
Micrococcus luteus	-	-	-
Clostridium clostridiforme gr 2	-	-	-
Gram + cocci	-	-	-
Gram neg rods (n=2)	-	-	-
Coagulase negative staphylococcus (n=2)	- -	-	-
Propioni bact. (n=20)	-	5 neg, 13 not cultured, 1 pos before and after	-
	-	-	Other reaction, Gr 1, possible
Propioni bact. and gram + rods (n=2)	-	1 neg. 1 not cultured	-
Pos, not specified (n=2)	1 neg. 1 not cultured	1 neg. 1 not cultured	-
Pos, no micro-organisms confirmed (n=3)	-	-	-

* - : no culture performed or no additional category

Table 17B Bacteriological contamination of RBC (n=13)

Sanquin bacteriological screening (associated platelet unit)	Hospital culture result on unit*	Patient blood culture*	Reporting category (if other than bacterial contamination of blood component) or symptoms*
Propioni bact. (n=2)	-	-	-
Micrococcus luteus	-	-	-
Pos, not specified	-	-	-
Gram neg rods	-	-	-
No report	St. Warneri	Negative	NHTR (additional category) Gr 1, possible
No report	St. epidermidis (n=2)	Negative	NHTR Gr 1, probable Mild NHFR Gr 1 possible
No report	Pseudomonas aeruginosa	Not cultured	Mild NHFR Gr 1 possible
No report	Brachybacterium sp	Not cultured	NHTR Gr 1, possible
No report	Rothia denticola and Str. Sanguinis	Negative	NHTR Gr 1, possible
No report	Citrobacter freundii	Negative	NHTR Gr 1, possible
No report	Coagulase negative staphylococcus	Negative	NHTR Gr 1, possible

The tables show that of the whole series, three reports (listed first in *Table 17A*) were associated with symptoms suggestive of bacteremia as well as positive bacteriology on the unit – in each case it involved platelets - and the patient's blood. In no case had there been a signal from the bacteriological screening system which is used by the blood service to screen all platelet concentrates. The report rated as certainly ascribable to the transfusion concerned a grade 2 transfusion reaction, with the patient showing rigors, a rise in temperature of over 2°C, a minor drop in blood pressure and a swollen feeling in the face. No investigations were performed to establish whether strains were identical. In the other two cases (both reported as Grade 1 reactions) a second bacterial species was also found in one of the culture specimens, raising the possibility of artefactual contamination during sampling.

One reports relates to a patient, resident in a Q-fever endemic area, who showed no relevant symptoms after receiving a platelet unit; one a donor in the Q-fever endemic area was later found to have seroconverted. When this became known and the patient was tested several months later, the patient showed positive Q-fever serology and PCR. Since the patient also lived in the endemic area, no conclusions can be drawn about transmission by the transfusion.

Sanquin provided an overview of the findings of the bacteriological screening of all platelet concentrates. In all, 332 platelet units showed an initial positive reaction in the screening, 197 platelet components or associated RBC units had been distributed at the time of the report. One hundred and six units had already been transfused. The hospitals were asked to report back on any transfusion reactions which had occurred. In seven cases minor (less than grade 2) symptoms were reported. Some of these seven cases are probably included in Table 17A. However hospitals do not always report to TRIP following findings of positive bacteria screening so TRIP and the Sanquin quality department have not exhaustively matched reports to determine the degree of overlap of these nonserious cases.

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 2010 TRIP received 41 reports in the category post-transfusion bacteremia/sepsis (2009: 50). The administered blood components were RBCs in 33 reports and platelets in eight. These reports are of cases where which the hospital found a positive blood culture after (stopping) transfusion following symptoms that could indicate a transfusion reaction. In the majority of cases a culture of the unit had been performed with negative results. With the exception of the three cases at the top of *Table 17A*, there were no results on the unit which demonstrated the same bacterial species as the patient's blood culture. Out of all the reports in this category, the imputability was recorded as certain once, probable three times, possible in 19 reports and unlikely in 18. In many such cases the bacteremia can be presumed to have occurred as a result of the patient's underlying condition. The clinical features recorded in the reports are summarised in *Table 18* below.

Table 18 Signs and symptoms in reports of post-transfusion bacteremia/sepsis

Clinical feature	No. of reports Total n=41	Number in Grade ≥2 reports (total n=7)
Rise in temp and chills/rigors	24	6
Rise in temp (no rigors)	14	1
Chills/rigors without rise in temp	2	-
Drop in blood pressure	5	3
Rise in blood pressure	3	-
Dyspnea	7	3
Increase in pulse rate	3	1
Clinical deterioration	2	1
Backache	2	1

In addition to the above reports, a late 2009 report of post-transfusion bacteremia/ sepsis described a fulminant septic reaction in the (already seriously ill) recipient of a red blood cell concentrate. Yersinia enterocolitica was cultured from the patient's blood and the remnant of the transfused unit; the donor was subsequently tested and showed serological results consistent with recent Yersinia infection.

As in 2008 and 2009, TRIP added a code to the report in the database if – based on the available information – the report involved a patient with a pre-existent bacterial infection. In the 2008 Annual report TRIP raised the issue of a possible interaction between blood transfusion and bacterial infection. Firstly it is possible that a blood component becomes contaminated with bacteria at the time of administration and that the recipient of this component therefore develops bacteremia/sepsis. Secondly, an intravenous procedure – such as infusion or transfusion – forms a risk for the occurrence of thrombophlebitis and/or bacteremia/sepsis. Thirdly, it is possible that the administration of blood components, particularly RBC concentrates with their iron content, can activate a bacterial infection which was already present. Regarding the third possibility, do the TRIP data give any indication that patients receiving RBC transfusions have a higher likelihood of developing a temperature? *Table 19* shows the distribution of the types of blood component for reports of NHTR and for mild non-hemolytic febrile transfusion reaction, subdivided according to whether the report mentioned a pre-existent infection. It is suggestive that the percentage of RBC transfusions among the reports is higher in cases where an infection was present, both for NHTR and mild NHFTR. It is also striking that the contribution of non-RBC transfusions is higher in NHTR than in mild NHFTR. As in

2008 and 2009, the available data from the reports are insufficient for definitive conclusions.

Table 19 Pre-existent infection and type of blood component with reports of NHTR

NHTR	RBCs	Platelets	Plasma	RBCs with other bc	Other bc
Infection present	68 87.2%	9 9.0%	1 1.3%	2 2.6%	-
Noninfectious diagnosis	232 70.9%	61 18.7%	7 2.1%	9 2.8%	17 5.2%
No diagnosis information	73 85.9%	6 7.1%	1 1.2%	4 4.7%	1 1.2%
Total	**76.3%**	**15.1%**	**1.8%**	**3.1%**	**3.7%**
Mild non-hemolytic febrile TR	**RBCs**	**Platelets**	**Plasma**	**RBCs with other bc**	**Other bc**
Infection present	49 96.9%	2 3.9%	-	-	-
Noninfectious diagnosis	187 91.7%	5 5.4%	1 0.5%	5 2.5%	-
No diagnosis information	75 100%	-	-	-	-
Total	**94%**	**3.9%**	**0.3%**	**1.5%**	

Concluding discussion on bacterial reports

As in previous years the number of transfusion complications where causation by bacterially contaminated blood components is proven or plausible is low. They are however serious: a fatal reaction confirmed to have been caused by Y. Enterocolitica in a red cell concentrate (a late 2009 report) and a Grade 2 probable reaction to a platelet transfusion, associated with Streptococcus dysgalactiae. The donor questionnaire and the constant process of bacteriological screening of platelet units with release “negative to date” do not completely eliminate the risk of transfusion-transmitted bacterial infection.

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 line with the numbers in previous years there were 58 reports submitted by 30 hospitals in this category in 2010; less than 15% submitted three or more IBCTs. In 2005 to 2008 the number of IBCTs compared to the total number of reports was about 3% and since 2008 there has been a gradual decline of the percentage of IBCTs: they accounted for 2,8% of all reports in 2008, 2,5% in 2009 (including late reports) and 2,3% in 2010 (without late reports). The number of incorrect blood components transfused which led to clinical consequences this year was rather low: 4; an overview of these reactions is provided in *Table 20*. A more detailed description of some of these reports has been included at the end of this paragraph (*Case histories 4*).

Table 20 Clinical symptoms following transfusion of an incorrect blood component

Nature of reaction	Total	Component	Severity grade				
			0	1	2	3	4
Delayed hemolytic transfusion reaction	1	RBC	1				
New antibody formation	2	2x RBC	2				
Other reaction	1	RBC		1			

As in previous years, for all the reports in the category of incorrect blood component transfused TRIP assessed the worst risk that the patient incurred by administration of the blood component. For example, for a patient switch resulting in patient X receiving the component intended for patient Y, the greatest risk is that of administration of an ABO incompatible component, irrespective of what the blood groups of patient X and patient Y actually were. As far as possible, the reports were classified according to the first error (in time) that resulted in the incorrect blood component being administered. The first error was evaluated for type of error, such as identification error, communication error or selection error. The step in the chain where the first error occurred was also registered; please refer to the diagram (*Figure 7*).

If the first error did not occur in the reporting hospital but elsewhere, the first error was not evaluated any further. These types of errors are usually reported as component errors (e.g. the component was not B19-safe, even though this was ordered from the blood service). An overview of the analysis according to risk and first error is provided in *Table 21*. The description of these categories can be found on www.tripnet.nl, hemovigilance page.

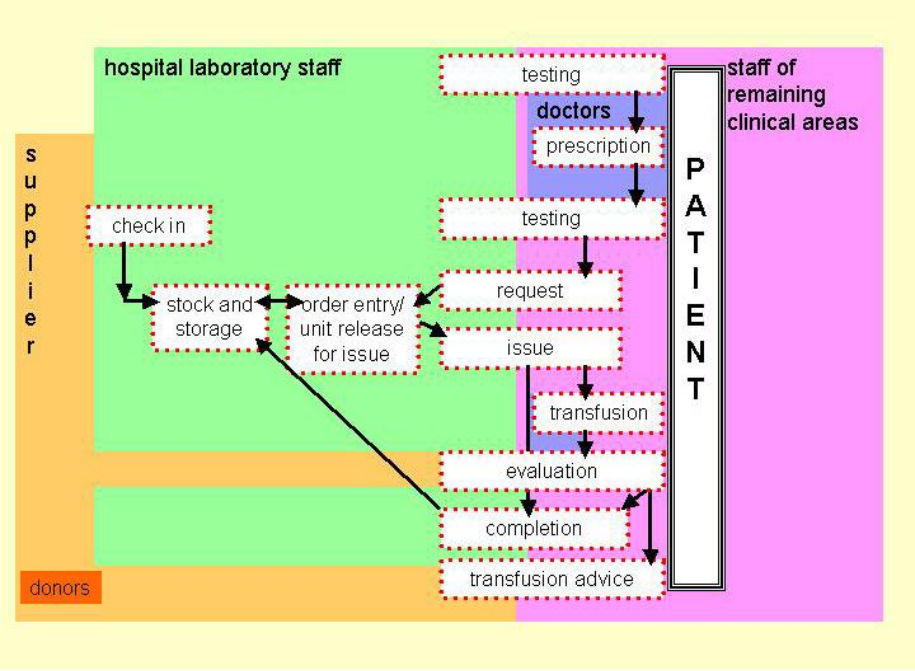

Figure 7 The transfusion chain

Table 21 Nature of risk for the patient and first errors leading to IBCT in 2010

Risk	Total	Step in transfusion chain where 1st error occurred		Type of 1st error	
ABO	16	Transfusion chain outside hospital	1	Not evaluated	
		Request	3	Identification	3
		Processing of request	2	Selection	1
				Lab procedure	1
		Transfusion	10	Identification	10
Irregular antibody	10	Transfusion chain outside hospital	1	Not evaluated	
		Investigation for Tf request	3	Evaluation	1
				Communication	1
				Lab procedure	1
		Request	3	Communication	2
				Other	1
		Processing of request	3	Evaluation	2
				Lab procedure	1
TA-GvHD in risk group	13	Request	11	Communication	8
				Selection	1
				Other	2
		Processing of request	2	Evaluation	1
				Lab. procedure	1
Preventive selection policy Irr. ab: 12 B19: 4	16	Request	2	Communication	2
		Processing of request	11	Selection	6
				Communication	2
				Administrative	1
				Evaluation	1
				Lab. procedure	1
		Issue	2	Selection	2
Contamination	1	Component handling	1	Communication	1
Clotting	2	Request	1	Evaluation	1
		Issue	1	Product	1

In 2010 communication errors are the largest group of errors (16) followed by identification errors (13) and selection errors (10). Identification error is still the most common error resulting in a potential ABO risk and the identification error took place in the last check (bedside check) before administration of the blood component ten times. Often these errors occur when the last check is not actually done at the bedside, but for instance at the desk. An overview of the type of risk for each type of first error is provided in *Figure 8*.

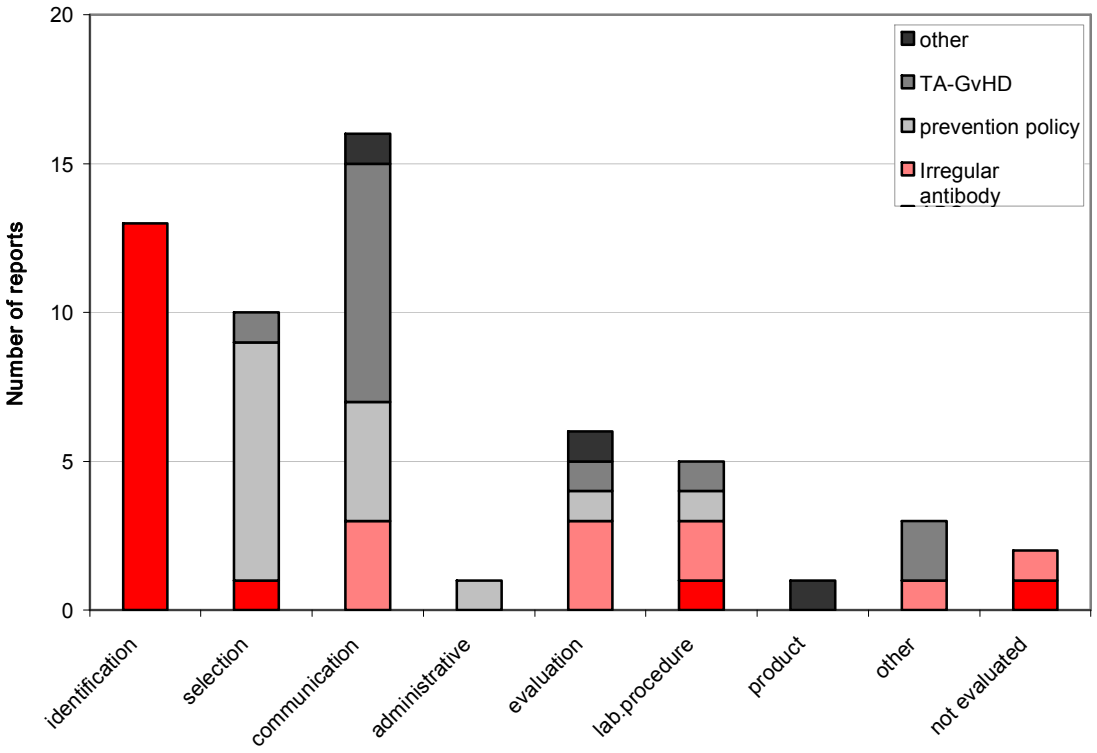

Figure 8 Type of risk per first error

Of the 58 reports of incorrect blood component transfused, only 16 (28%) were assessed as ABO incompatibility risk. This is a marked decline compared to 2008 (44%) and 2009 (50%). The components that were administered in these incidents were RBCs 15x and (O pos) plasma once.

For the 15 incorrect RBCs administered with ABO risk, five times the donor blood group was O, eight times A, once AB and once not specified but described as compatible. By pure chance the unit was ABO compatible in 12 cases. One A pos component was completely transfused to a patient whose former blood group was A pos, but who had changed to O pos after bone marrow transplantation. An elderly patient with blood group O pos received a small amount (10-30 ml) of an A pos RBC without clinical signs of hemolysis. A 68 year old A pos patient received an AB neg RBC and no adverse reaction was reported. In one of the ABO compatible cases a Rhesus D positive RBC unit was administered to a Rhesus D negative elderly female recipient, there were no signs of a hemolytic transfusion reaction or of anti-D formation (after a month).

Four reactions were reported in 10 reports (17% of the IBCTs) with irregular antibody incompatibility risk. A DHTR was reported after administration of three RBCs (2x c and E pos) to a patient with negative antibody screening but in whom anti-E and anti-c had been demonstrated in the past. Another patient felt unwell and developed tachycardia after receiving an RBC that was positive for antigen c. After the reaction it was established that the patient had a positive history for anti-c. There were two reports that mentioned new allo-antibody formation as reaction. On one occasion a patient, with a positive history for anti-E in another hospital, received E pos RBC after a negative screening result for irregular antibodies. There were no signs of hemolysis; two weeks later the reporting hospital also demonstrated ant-E. In this case boostering occurred rather than new allo-antibody formation. On another occasion a patient received five Jka pos RBCs because in the fax with preliminary results for alloantibodies anti-Jkb had

erroneously been written instead of anti-Jka. Hemolysis was not demonstrated in the following weeks, but after one week anti-E was found. Obviously this must not to be seen as the result of the incident. These last two reactions are not counted in *Table 20*.

On two occasions, failure to follow the preventive component selection policy for an at-risk patient group formed the reason for reporting an additional category. Once anti-K was detected after administration of a K pos RBC concentrate and once anti-E formation occurred after failure to follow preventive transfusion advice, both in women of childbearing age. In the first case however the hospital policy in the year when transfusion of the K pos RBC took place (2005) allowed administration of K pos blood to at-risk patients if K neg components were not available from hospital stock. This IBCT is probably not due to an error in processing the request but should be seen as a case of calculated risk; it is not further evaluated in *Table 21*.

The number of IBCT with TA-GvHD risk is unusually high compared to 2008 and 2009. In most cases errors in communication, e.g. not reporting an indication for irradiation to the blood transfusion laboratory, were the primary cause of administration of non-irradiated blood products.

Problems with clotting could have occurred in two cases. Once transfusion of plasma was cancelled because the product showed clotting and the filter to the IV line was totally blocked. In the other case plasma was erroneously ordered by a new administrative staff member and also administered to the patient, whereas platelets were indicated and had been ordered by the doctor. According to the national CBO transfusion guideline, even if administrative ward staff transmit the ordering physician's request, the physician is responsible and should personally sign the form. However signing a form becomes a problem when it concerns a digital request that does not require a signature, as was the case in this report.

Case histories 4

IBCT-1 (Irregular antibody formation risk, processing of request, selection)
Four RBCs are selected for a 41-year-old female patient because of elective surgery (pancreatic tail resection). According to national guidelines and hospital policy the RBCs should be K negative. However one of the selected RBCs is K positive and this unit is transfused. The error is not discovered till two days later (at second authorisation). It is not known whether the patient formed anti-K.

IBCT-2 (ABO risk, transfusion, identification)
Patient X, born in 1934, blood group B pos, needs transfusion. Early in the evening nurse 1 goes to the laboratory and collects a RBC for patient Y, born in 1924, who received RBCs the previous day. Back on the ward nurse 1 and nurse 2 together check the form and the RBC. Then nurse 1 goes to prepare iv antibiotics for patient Y and nurse 2 goes to start the transfusion. Nurse 2 knows that patient X is for transfusion today. No further bedside check of the identity of the patient is performed and transfusion is started.

When nurse 1 gives the medicine to patient Y, she notices that the transfusion has not been started. She asks her colleague, nurse 2, what has happened to the RBC. Then the error is discovered. Fortunately the blood group of patient Y is O pos.

IBCT-3 (contamination risk, dealing with component, communication)
Patient A, 26 years old, male, A negative, complained about chest pain and dyspnea almost immediately after the start of a platelet transfusion. Transfusion was stopped and the transfusion laboratory was consulted. It was arranged that blood samples and the platelets unit should be returned to the laboratory for further examination.

A few hours later when the laboratory started investigations on the platelets it turned out that the platelet unit had been issued for another patient, patient B, 64 years old, male, blood group A negative. Verification with the ward revealed that the unit had been transfused to patient B without problems. The nurse remembered that the second spike port had to be used, because the seal on the first had already been broken and replaced by a cap.

How did this happen? Instead of returning the unit directly to the transfusion laboratory, as was asked, the unit was returned to the issue area. The laboratory staff member did not know about the transfusion reaction and there was a misunderstanding about the fact that the product had been partly transfused. The unit was returned to the transfusion laboratory and was put back in stock. Some time later the platelets were released again. Throughout all these procedures it was not noticed that the seal of one of the spike port was broken and replaced by a cap.

IBCT-4 (ABO risk, transfusion, identification)
Through the pneumatic tube system on the ICU, nurse 1 receives a RBC. The blood is for patient X2, blood group O pos. Nurse 1 is taking care of patient X1, a male patient, blood group A pos, on the chest IC. Soon afterwards administration of the RBC to patient X1 is started.

A few minutes later nurse 2 arrives to collect a RBC unit for patient X2, a married female patient, blood group O pos, staying on the chest MC. Then it is discovered that the RBC was not meant for patient X1, there was not even a request for blood for patient X1. A correct check of patient name on the product should have made it clear that there must be two patients with the same surname, because patient X2 has also her maiden name.

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 2010 (117) is slightly higher than in 2009 (110). Reports of other incidents were submitted by 30 hospitals, more than 40% of these hospitals reported three or more other incidents. Symptoms were observed in the patient in seven of these reports. There were also nine reports of transfusion reactions for which the additional category of other incident was reported. An overview is provided in *Tables 22A and B,* and some examples are described in *Case histories 5*. It can be seen that the relationship between the incident and the patient's symptoms can be very different. In some cases it is likely that the incident caused the patient's reaction, sometimes an incident is discovered as a result of the reaction and in other cases the patient's reaction creates a situation in which an incident occurs.

Table 22A Clinical symptoms during or after an other incident

Nature of other incident	Reaction	Total	Product	Severity grade of reaction				
				0	1	2	3	4
TR not properly analysed (1)	Mild non-hemolytic febrile reaction	1	1x combi		1			
Unnecessary Tf (1) TR not properly analysed (1) Volume transfused too large (1)	Circulatory overload	3	2x RBC 1x platelets		2	 1		
Unnecessary Tf (1) TR not properly analysed (1)	Other allergic reaction	2	1x RBC 1x platelets		1 1			
Unnecessary Tf	Other reaction	1	1x RBC		1			

Table 22B Reports of transfusion reactions with additional category other incident

Reaction	Nature of other incident	Total	Product	Severity grade of reaction				
				0	1	2	3	4
Mild non-hemolytic febrile reaction	Tf unnecessarily discontinued (1) TR not properly analysed (1)	2	2x RBC		2			
Non-hemolytic transfusion reaction	TR not properly analysed (2)	2	1x RBC 1x platelets		1 1			
New allo-antibody	Traceability	1	1x RBC	1				
Post-transfusion bacteremia	TR not properly analysed	1	1x RBC		1			
Other reaction	TR not properly analysed (2)	2	2x RBC		2			
Bacterially contaminated blood component	Incident not properly handled	1	1x platelets	1				

The products involved in these other incidents were RBCs (81x), platelets (16x), once a combination of platelets and RBC, plasma (8x) and autologous drain blood (6x). The other incidents with autologous blood are discussed in the section on blood management techniques. In two reports the type of product involved in the incident was not listed. In three cases the reported incident took place without a blood component being ordered. A short summary is provided below of the important groups of other incidents that can be distinguished.

There were 13 reports of request of a blood component based on incorrect or preliminary lab results. Nine of these were cases where a sample was collected from the arm where infusion fluids were also being administered, three where the blood for Hb or platelet determination was processed under the name of another patient and in one case a low platelet count turned out to be a pseudothrombocytopenia. In one of the cases due to an incorrect lab result not only an unnecessary transfusion was given but also two other RBCs became unsuitable for transfusion. Five times a blood component was administered in error to a patient for whom blood had to be ordered only in case of low Hb or platelet counts and three times blood was ordered for a different patient from the one intended. On four occasions more RBCs than indicated were administered to a patient, resulting in a high hemoglobin level. An infant received erroneously a complete bag of platelets instead of 90 ml. Altogether there were 24 cases of the patient being given an unnecessary blood transfusion or too large a volume of blood products compared to only two reports of other incident when a request for blood for someone other than the intended patient was discovered in time. An overview of the type of first error in these cases is provided in *Figure 9*. In four of the 24 cases where unnecessary or too much blood was transfused a transfusion reaction was reported: twice circulatory overload, an other allergic reaction and an other reaction.

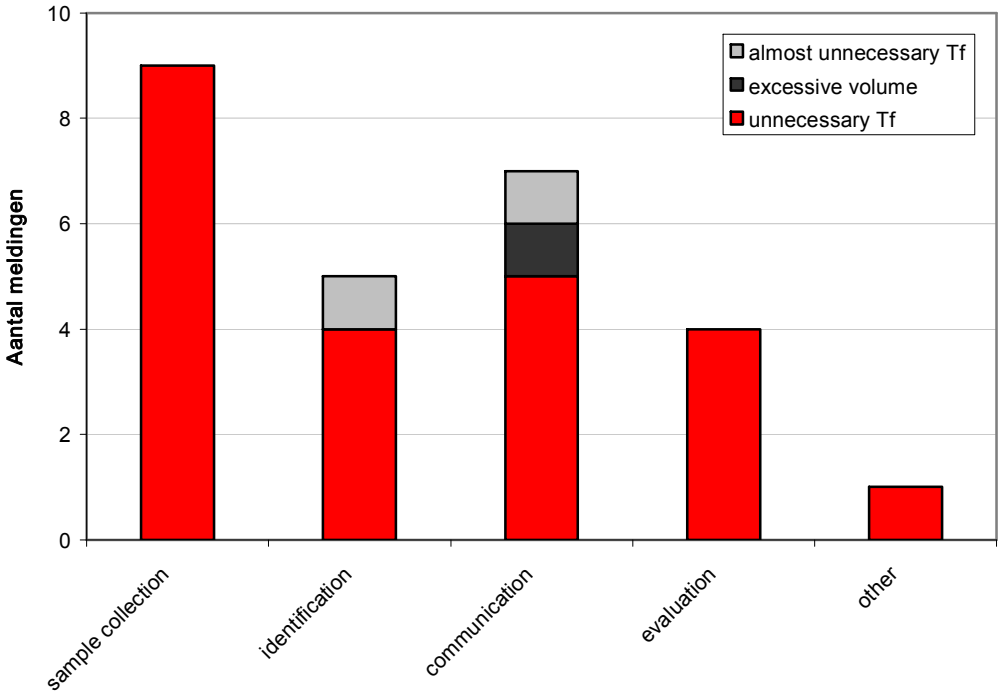

Figure 9 Type of 1st error in (almost) unnecessary transfusion or excessive volume

Eight other incidents were reported in which someone forgot to request blood (2) and/or blood group determination (1) for a scheduled procedure or where problems concerning a request for blood components (5) resulted in a delay in patient treatment. Three times the laboratory received a request for irradiated blood components for a patient who did not have an indication for irradiated blood. In two of these cases the patient was transfused with a non-irradiated blood component due to subsequent errors.

There were 10 reports of problems during the transfusion resulting in the blood not being completely transfused and a (higher) risk of contamination: leakage of the bag (2), problems with the infusion system (6) or removal of the infusion system by the patient (2).

Not transfusing properly, e.g. wrong setting of the infusion speed (1) or using the same infusion system for blood and medication (3), resulted in five reports.

In 2010 there were 31 reports of other incidents involving cases in which the allogeneic blood product became unsuitable for administration and this was discovered before or at the start of the transfusion. In four of these events it was unavoidable that the blood component became unusable, e.g. puncturing of the bag when attaching the drip line. One report describes a case where forgetting to open the valve led to unnecessary loss of a unit of platelets. Three reports mention forgetting to administer one or several blood components to the patient, in one of which the second of two required blood components was left in a cooler box for six days. In 21 of these cases the blood component was returned too late to the laboratory after the transfusion was cancelled; twice plasma was actually returned in time, but after 24 hours it had to be disposed due to expiration of the maximum storage time. Compared to 2009 (5 cases of forgetting to administer the blood component and 28 cases of returning the blood too late after cancelling the transfusion) there seems to be an improvement. *Figure 10* shows the nature of the first error for these reports and the step in the chain where the error was made. There were also three

reports of other incident were pre-transfusion checks were not done and transfusion was discontinued shortly after starting the administration, e.g. because checks after 5 minutes showed a raised temperature.

Comparison of the blood use in the nine hospitals (six of these hospitals also reported avoidable loss of blood products in 2009) that submitted these reports of avoidable loss of blood components shows that it involves 0.07% of the RBCs, 0.05% of the platelets and 0.06% of the plasma units. In 4 hospitals (44%) it concerned avoidable loss of 0.06% or more of the total amount of blood products, in 2 hospitals (22%) it concerned less than 0.01%.

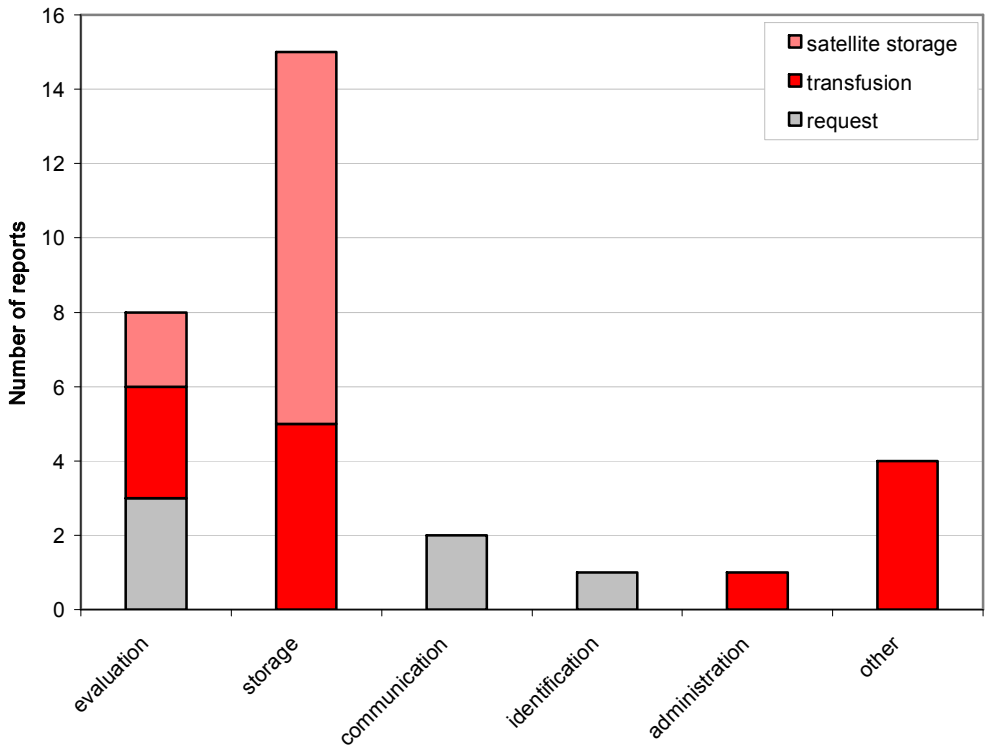

Figure 10 Type of 1st error in cases where blood became unsuitable for transfusion

Seven reports of other incident concern traceability and/or communication about patients' results, observations or symptoms during transfusion. For instance, two reports concerned administration of blood components that were transferred with the patient from another hospital without notifying the responsible laboratory. On another occasion 2 patients were present in the emergency room at the same time, both received several O neg uncrossmatched RBCs in an emergency situation and proper documentation failed.

Product errors that were detected before transfusion resulted in nine reports. Usually hospitals report product errors as other incident if the relevant product has been issued, with or without subsequent transfusion. For instance, three reports pertain to bags in which ward staff noticed clotting in the thawed plasma. Twice there were folds in bags of platelets. Two reports concern product-related problems that were discovered after (partial) transfusion. In one a little leak in a bag of RBCs was noticed half an hour after starting the transfusion and once an unexpected positive crossmatch was found due to passive transfer of anti-A by a unit of platelets some days earlier.

Case histories 5

OI-1 (investigations for indication, sample collection)
Patient A's haemoglobin level was found to be 2.1 mmol/l. It turned out that the blood sample was taken from the drip arm. A new sample was taken from the leg and showed a haemoglobin level of 2.9 mmol/l. Based on this haemoglobin level the doctor prescribed 3 RBC units.

The haemoglobin level went up to 8,1 mmol/l and a day after transfusion the chest X ray showed signs of circulatory overload. Probably the second blood sample was also unreliable, perhaps because the patient's ankles showed significant oedema. The patient had no known heart condition and there were no signs of circulatory overload before transfusion.

OI-2 (transfusion, evaluation)
A 47-year-old male patient received 2 irradiated RBCs at the daycare unit. After transfusion he had a rash in his neck. Against hospital policy the nurse failed to inform the doctor and sent the patient home with the advice to keep an eye on it.

OI-3 (transfusion, evaluation)
Transfusion of RBC to patient B is stopped after 150 ml. The transfusion laboratory is informed that the patient showed a mild rise in temperature and the doctor asks for further investigation. Hospital policy concerning mild febrile reactions however states that no further investigation is necessary and no laboratory investigation is initiated.

Afterwards it became clear that during the reaction the patient's main problem was dyspnea, but the doctor did not realize that this could also be a symptom of a transfusion reaction so the dyspnea was not mentioned in the request for investigation. The reaction was assessed as TACO.

OI-4 (indication, communication)
Patient X, an 88-year-old male, is receiving treatment for non-Hodgkin lymphoma. According to hospital policy a schedule for transfusion is drawn up for use in the event that the hemoglobin level becomes too low during chemotherapy.

Some time later it is discovered that patient X has unnecessarily received 2 units of RBC on 2 different occasions. The first time the pretransfusion Hb was 8.2 and the second time 10.4 mmol/l. After the second transfusion patient X showed a hematoma in the arm and had bleeding from his mouth.

The Hb level was tested before transfusion as usual, but the doctor was not familiar with the procedure, so it happened that nobody checked whether blood transfusion was actually necessary.

OI-5 (transfusion, administration)
Some time after starting transfusion of platelets to patient Y it is noticed that the drip has stopped. It is assumed that the IV-line is blocked and due to time limitations staff decide to discontinue the transfusion. Afterwards it is discovered that the valve had not been opened.

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 2010 there were 68 near miss incidents reported by 19 hospitals (72 in 2009 by 16 hospitals), varying in number from one to 15 reports.

The first error in almost 80% of the reported cases was made in the steps of transfusion request (5) or pretransfusion testing (48) and 43 of these 53 errors involved an error in identification of the patient, blood sample and/or request form.

Checks and vigilance by employees of the blood transfusion laboratory were responsible for preventing more serious incidents in the majority (48) of these near misses. In 24 cases (35%), 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. The number of reported near misses in which an error was discovered by nurses or other staff from clinical areas (n=13, 19 %) e.g. by checking prior to transfusion on the ward or in the operating room is the same as in 2009. However there seem to be more cases were an error like mislabelling a tube and/or a form is detected before the blood is processed in the laboratory.

An overview of the type of errors in near miss events is provided in *Table 23*. In the table, the reports are categorised according to the type of error that was made first in time. 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. The majority of the errors were discovered due to a safety procedure (70%), but as in previous years, a number of errors involved in the near misses were not detected by planned safety measures but by coincidence. Unfortunately nine reports did not describe how the error was discovered.

Table 23 Near miss in 2010: type of first error and manner of discovery

Type of error	Total	Planned safety measure	Personal vigilance	Coincidence	Not reported
Identification	48	34	4	1	9
Administrative	2	2			
Performing test	1		1		
Laboratory procedure	1	1			
Communication	5	2	1	2	
Selection of product	7	5		2	
Technical failure	1			1	
Product	1	1			
Evaluation	2	1		1	

It is noteworthy that the first errors in the reports of a near misses – the errors that were discovered in a timely manner – were mainly identification errors (71%), whilst communication and selection errors together account for only 12 (15%) of the near miss reports. If we compare this to the first errors in reports of an incorrect blood component being transfused, the a percentage of identification errors in 2010 was 22% (13) which is almost the same as in 2008 (23%), while in 2009 there were more identification errors leading to IBCT (41%). The percentage of reported communication errors for incorrect blood component transfused (28%) is higher than in 2008 (23 %) and 2009 (10%), whilst the percentage of selection errors shows less variation between the last years: 17 % in 2010, 16 % (2008) and 22% (2009). The distribution of the types of errors in near accidents in *Figure 11* can be compared to *Figure 12*, type of errors for incorrect blood component transfused.

Case histories 6

BO-1 (hospital outside Tf chain, identification)
When a married female patient was admitted to hospital her husband's details were entered in the hospital computer system, because he had showed his own health insurance card at the desk. The error was discovered only after blood samples for blood group determination had been taken.

BO-2 (processing of request, selection)
Three units of RBC were selected and crossmatched for a patient with recorded transfusion advice that E and K negative should be selected. When the nurse came to collect the blood, checking the products together with a member of the lab. staff revealed that two of the units did not meet the transfusion advice.

BO-3 (processing of request, identification)
In an emergency situation during delivery O neg RBCs and AB pos plasma are requested for patient X1 by phone. The name of the patient is checked in the transfusion laboratory and blood is selected and issued for patient X2, a male patient with the same surname. The error is discovered in the operating room when the identity of the patient is checked against the patient details on the blood products before transfusion.

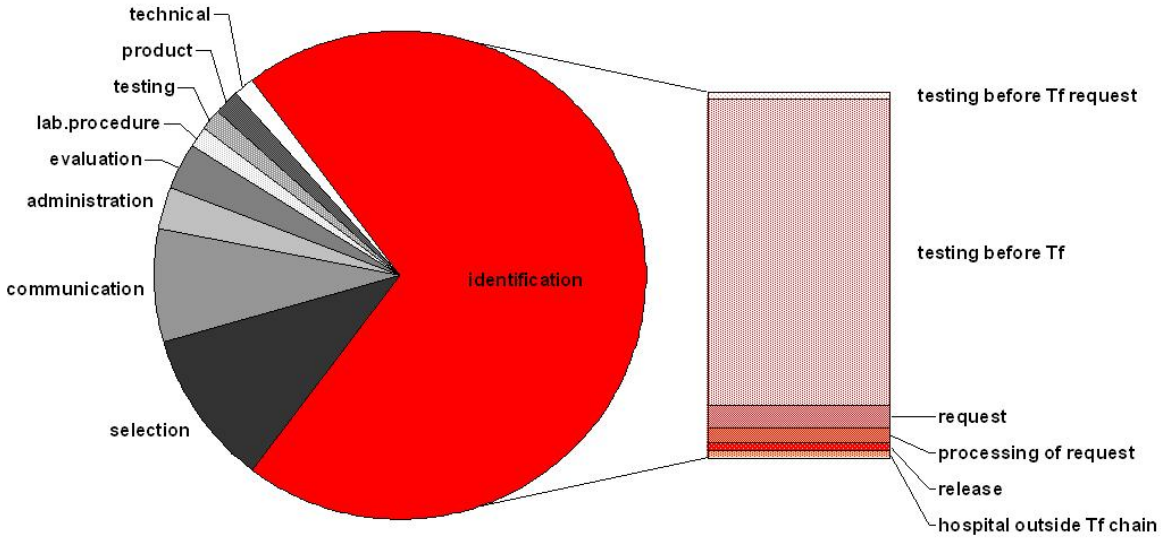

Figure 11 Near miss 2010
Type of error, identification error subdivided according to step in the chain

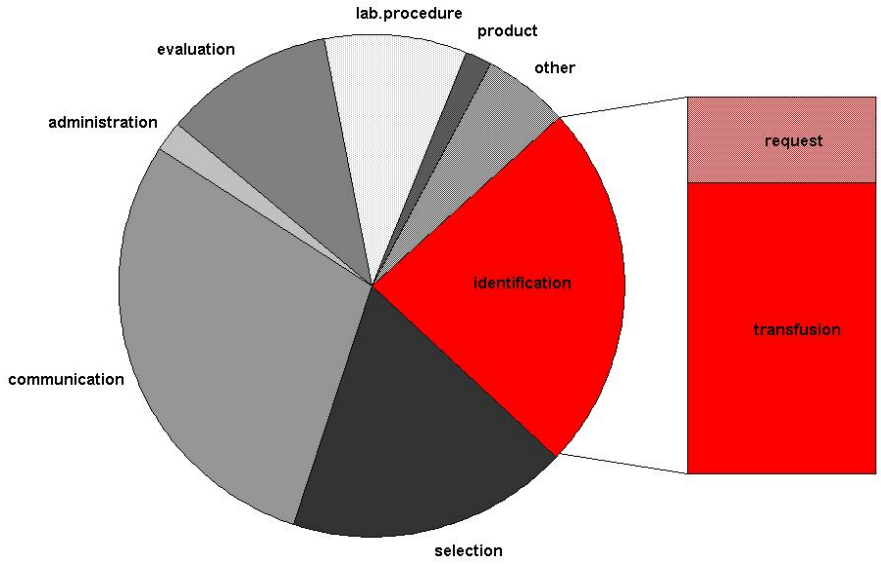

Figure 12 Incorrect blood component transfused 2010
Type of error, identification error subdivided according to step in the chain

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.

In 2010, 50 look-back procedures were reported by ten hospitals. This constitutes a rise in comparison to previous years. The majority of reports (44) related to hepatitis B, where the donor was found to have an occult hepatitis B infection (OBI) that came to light after the introduction of the HBV-NAT testing by Sanquin in autumn 2008. In only twelve of these reported cases the recipient was tested and was found to be negative. Two cases of transmission of hepatitis B from one donor, discussed in chapter 3.2, were demonstrated in the investigations concluded after the closing date for the 2009 report. All other recipients died before investigations could be started. As far as could be ascertained none of these recipients showed symptoms related to hepatitis B infection. It can be expected that the number of look-backs will gradually drop when the donor population has been screened by HBV-NAT testing and donors with OBI have been counselled and deferred; however the characteristic of OBI is that the viral titre is very low or undetectable, hence donors may be tested several times before they are found to be carriers.

There were two look-back procedures reported involving recipients of donors who showed HIV seroconversion in a subsequent donation. In one case the retained specimen of the donation tested negative for HIV-RNA, transmission was therefore thought to be unlikely. The other retained specimen was positive for HIV-RNA. Both recipients did not show clinical signs of HIV and died before testing could be initiated. Fortunately HIV seroconversions of donors are extremely rare, only four look-back procedures into HIV have been registered in the TRIP database.

There was one look-back procedure relating syphilis: a regular donor had been found shown to have a primary infection. Another donor had an HTLV-1 infection. Archived samples of previous donations tested negative in both cases. No recipient had any symptoms. One report concerned recall of a blood component of a donor implicated in a transfusion reaction in another hospital. The component had already been administered

without adverse effects. A further report arose from post-donation information from a donor who was investigated for Q fever and Lyme disease. The RBCs had already been transfused. Again, no recipient had relevant symptoms.

In conclusion the number of look-back procedures rose in 2010 due to OBI, owing to the introduction of the HBV-NAT test. Although not all recipients are alive, in 2010 and the late 2009 information three probable or confirmed transmissions of hepatitis B in the past were documented. Hospitals are advised to have a clear procedure for investigating recipients when the blood service gives notice of a look-back investigation.

3.4 Blood Management Techniques (BMT)

In 2010 for the second year in succession hospitals were asked to supply data on the use of autologous blood management techniques. These data are instrumental in determining the frequency of adverse reactions and incidents. Since the publication of the Guideline on Hemovigilance and Blood Management Techniques by the TRIP Board on the website TRIP has advocated hemovigilance with these techniques. The TRIP Annual Report 2009 concluded that BMT are widely used but exact data are hard to obtain from hospitals. In *Table 24* the data for 2010 are presented (2009 figures in brackets). In 2009 it was the first time that hospitals were asked to provide data; in that year hospitals which did not send data were not counted. The 2010 figures do include all 103 Dutch hospitals; if they did not submit data they are included in 'hospitals without data'. Judging from the number of hospitals that were able to supply figures for use of BMT, this information is still not widely available to hemovigilance staff in hospitals.

Table 24 Use of blood management techniques

Technique	Total applications		Number of hospitals		Hospitals BMT not used		Hospitals without data	
	2010	(2009)	2010	(2009)	2010	(2009)	2010	(2009)
Non-mechanical auto-transfusion (administration of drain blood)	8821*	(7514)	21[o]	(18)	24	(20)	58	(57)
Mechanical auto-transfusion (administration of cell-saver blood)	5001	(3033)	21	(18)	23	(25)	59	(50)
Pre-operative autologous donation			9	(8)	47	(58)	47	
- patients referred	153	(109)						
- units collected	289	(208)						
- units transfused	224	(187)						
Normovolemic hemodilution	1412[$]	(122)	3	(6)	32	(28)	68	(58)
Hypervolemic hemodilution	0		1[#]	(2)	31	(30)	71	(60)
Extracorporeal circulation	4430	(2177)	4	(2)	47	(39)	52	(52)
Fibrin glue	1056	(798)	15[&]	(12)	24	(21)	64	(59)
Platelet gel	1225	(846)	4[o]	(5)	37	(33)	62	(51)

* One hospital reports several hundreds, but no exact data. One hospital reports 1180 applications on the basis of the number of systems ordered.
[#] One hospital reports "daily use" but no numbers
[&] Two hospitals report use but no numbers
[o] One hospital reports use but no numbers
[&] Three hospitals report use but no numbers

In 2010 a total of 37 reports (2009: 33) concerning blood management techniques were sent in by five hospitals. The majority of reports came from two hospitals: 19 and 13 reports respectively. One hospital submitted a report but supplied no application data. The severity grade of the reaction was graded as 3 in one report, all other reactions were severity grade 1. Imputability was reported as possible in 28 reports, and was judged probable in three reports. The remaining six reports were of other incidents without clinical consequences for the patients, therefore imputability is not applicable. In *Table 25* an overview of reports per TRIP category per type of BMT is presented. As in previous

years the majority of reactions reported involved the reinfusion of drain blood. In 2010 contrary to previous years there were no reports involving pre-operative autologous donation (PAD). The most striking reaction with BMT was reported in the category of anaphylactic reaction with severity grade 3. This life-threatening reaction is described in *Case History 8.*

Table 25 Reports with use of BMT

TRIP category	Drain blood	Cell-saver	Total
Anaphylactic reaction	1	-	1
Other allergic reaction	1	3	4
Non-hemolytic transfusion reaction	18	-	18
Other reaction	8	-	8
Other incident	6	-	6
Total	**34**	**3**	**37**

Approximately half of the reports involved a non-hemolytic transfusion reaction during or after reinfusion of unwashed drain blood. All 18 reports were graded severity 1 and imputability possible. Seventeen reports mentioned chills/rigors, which in only four reports were accompanied by a rise in temperature; only one report mentioned fever exclusively. It is remarkable that 17 reports of NHTR were sent by one hospital. Cultures of drain blood were found to be negative in five cases, in all other cases no culture was done and in none of the cases were patient blood cultures performed. In four cases the patient and drain blood were investigated for hemolysis, which was negative.

Eight reports were sent in by three hospitals and registered as other reaction. They mention combinations of symptoms temporally related to reinfusion that do not fit another category. In five cases there was a significant drop in blood pressure combined with chills/rigors while in two cases a significant increase in blood pressure was observed, also in combination with chills/rigors.

Four reports of other allergic reaction were received, mentioning localised redness of skin, in two cases in combination with urticaria. All three reports concerning the reinfusion of cell-saver blood were in this category. It is possible that this reaction is caused by activated cytokines in the cell-saver blood.

All six other incidents were reported by one hospital and involved non-mechanical autotransfusion to orthopedic surgery patients. In five cases drain blood could (in part) not be reinfused due to: e.g. clotting (3), failure to reinfuse within 6 hours (1). Only two patients were subsequently transfused with allogeneic RBCs.

Case history 8 BMT, unwashed drain blood
anaphylactic reaction, grade 3, imputability possible

A woman, 61 years old, undergoes a lumbar fusion procedure (L3-L5). During the uncomplicated surgery two units of RBC are transfused and a drain for non-mechanical autologous transfusion is put in place. As soon as reinfusion is started on the ward (within the 6 hour period as per protocol) she experiences a bad taste, then feels unwell. She develops hypotension and bradycardia followed by loss of consciousness and apnea. There is frothing around the mouth. Despite successful intubation she goes into circulatory arrest. The drain blood reinfusion is stopped. The patient is resuscitated and responds well to vasopressors. After transfer to the ICU she arrests and is resuscitated again. Whole body CT scan is performed to rule out bleeding. One hour after resuscitation she develops oedematous lips and swollen tongue that are treated with clemastine and corticosteroids. Apart from blood grouping to rule out misidentification no investigations are performed on the drain blood. The patient's serologic and biochemical parameters are unremarkable. She makes a complete recovery. The autotransfusion set is returned to the

manufacturer for further investigation but no feedback is received by the hospital. After investigation of the reaction it turns out that the patient had a pre-existent cardiac condition (ASA II) that could also explain this serious reaction. According to her case notes she had been asymptomatic for 8 years and her cardiac history was not mentioned when the report was first submitted to TRIP. Consequently imputability was lowered from probable to possible. Hemovigilance for BMT was set-up in the reporting hospital.

In conclusion it can be stated that Blood Management Techniques are widely used in the hospitals, but in roughly 50 % of hospitals hemovigilance staff do not know if BMT are being used. Denominator data are badly documented. Unfortunately there is hardly any increase in the hospitals that are able to submit application data of BMT in comparison to 2009. It is likely that these data are registered in operating theatres, but these are not readily accessible for hemovigilance purposes. Reporting over the years shows that transfusion reactions and incidents can also occur with administration of autologous blood. The total number of reactions and incidents reported seems to have stabilised, but as reports originate from five hospitals only, it is possible that there is considerable underreporting. It is conceivable that reactions in operating theatres and recovery are not reported due to the fact that hemovigilance with BMT is not well implemented and the non-specific clinical picture could also be explained by the operation or other patient factors. Investigations on drain or cell-saver blood are not often undertaken. These factors determine that imputability is often assessed as possible. There was a marked drop in the number of reported other incidents from twelve in 2009 to five in 2010, all originating from one hospital. The nature of these incidents however are not necessarily exclusive to this one hospital. It is also apparent from the reports that transfusion triggers are not consistently used to determine if the patient needs reinfusion. The revised 2011 CBO blood transfusion guideline recommends that BMT are to be included in hemovigilance. It is hoped that full denominator data will become available for hospital hemovigilance staff and the hemovigilance system for allogeneic transfusion can be extended to include BMT in all hospitals.

3.5 Deceased patients and transfusion reactions (grade 4)

There were nine grade 4 reports in 2010, compared with approximately four per year in 2003-2009. The reports are briefly presented in *Table 26*. On studying the reports it is seen that only one report, the late grade 4 report from 2009 which is discussed in chapter 3.2, describes a patient whose clinical deterioration (from post-transfusion bacteremia/sepsis) can be clearly related to the transfusion. In most of the other cases the patients, generally frail and with complex or incurable pathology, were not intensively investigated or treated. The transfusion reaction may have increased the likelihood of death, but the patient was already at risk of dying through their clinical condition. The increased number of reports assigned to grade 4 is probably in part due to the item “clinical outcome” on the reporting form: this was added in 2008 because the information is required for the EU reporting. .

At the annual TRIP meeting with the expert reviewers, there was debate on the difficulty of classifying severity and imputability of reports where the patient died following a transfusion reaction which would not normally have been fatal. “SHOT” (Serious Hazards of Transfusion, the hemovigilance office in the United Kingdom, see www.shotuk.org) gives a separate classification of these cases to indicate the degree to which death can be attributed to the transfusion reaction. In previous years, for the Netherlands it was not felt necessary to introduce such a classification. Given the larger number of cases in 2010, the expert panel has mandated TRIP to draft criteria for levels, similar to those in use by SHOT.

Table 26 Reports of patients who died following a transfusion reaction

Category of reaction	Age, gender	Imputability	Clinical situation
Post-transfusion bacteremia/sepsis	75, M	Certain	See chapter 3.2
Non-hemolytic transfusion reaction and TACO	63, M	Unlikely	Disseminated malignancy, O_2-dependent; dyspnea and rigors during palliative tf despite prior diuretic.
Other reaction	81, F	Unlikely	COPD, admitted for worsening dyspnea and investigation of leukocytosis, diagnosed postmortem as CML with leukostasis
Other reaction	84, M	Possible	COPD and malignancy, cough and probable chest infection, clinical deterioration during day case transfusion
Other reaction	Fetus	Possible	Intra-uterine fetal death within 30 mins of intra-uterine transfusion, no explanation found.
TRALI	69, M	Possible	Inoperable malignancy, postoperative complications, respiratory deterioration, poor response to therapy
TRALI	53, M	Possible	Cardiac patient, kidney recipient, hemorrhage from GI malignancy, respiratory deterioration following tf.
Viral contamination of blood component	92, M	Unlikely	Anemia of unknown origin and not actively investigated; jaundice 3w after discharge and died several weeks later. Donor later found to have occult hepatitis B.
TACO	72, F	Possible	Myelofibrosis, pre-tf CXR already showed some oedema or infiltration
TACO	87, F	Possible	Anemia and recent myocardial infarction

Table 27 shows the grade 4 reports to TRIP with imputability certain, probable or possible since 2003. The largest three categories are TRALI (9), other reaction (4) and transfusion-associated circulatory overload (4).

Table 27 Reports of Grade 4 (imputability certain, probable or possible) 2003 – 2010

Category	Number	Year	Imputability
Acute hemolytic transfusion reaction	1	2003	Probable
	1	2009	Possible
Anaphylactic reaction	1	2005	Possible
	1	2007	Probable
Post-transfusion bacteremia/sepsis (pre-2008: bacterial contamination)	1	2003	Possible
	1	2009	Certain
Other reaction	1	2005	Possible
	1	2008	Probable
	2	2010	Possible
TRALI	1	2005	Certain
	2	2006	Possible
	3	2007	1 Probable, 2 Possible
	1	2009	Possible
	2	2010	Possible
Circulatory overload	1	2005	Possible
	1	2006	Possible
	2	2010	Possible
Incorrect blood component transfused	1	2007	Possible
	1	2008	Probable

3.6 Mandatory reports of serious adverse reactions in the transfusion chain

In accordance with the Common Approach drawn up by the European Commission in the spring of 2009, 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 29* shows the data for 2009 and 2010.

Table 29 Number and imputability of reports of grade 2 or higher in 2009 and 2010

Type of reaction	Number of serious reports		Possible		Probable		Certain	
	2009	2010	2009	2010	2009	2010	2009	2010
Acute hemolytic TR	11	6	3	1	1	2	7	3
Delayed hemolytic TR	3	5	-	-	1	3	2	2
TRALI	13	12	6	6	5	6	2	-
Anaphylactic reaction	21	18	7	8	11	8	3	2
Other allergic reaction	-	-	-	-	-	-	-	-
Circulatory overload	16	17	5	10	8	6	3	2
Post-transfusion bacteremia/sepsis	2	4	-	3	1	-	1	1
Post-transfusion purpura	-	-	-	-		-	-	-
Post-transfusion viral infection	1	2	-	1	1	1	-	-
Transfusion-associated GvHD	-	-	-	-	-	-	-	-
Other serious reactions	36	28	22	16	13	9	1	3
Total	**103**	**92**	**43**	**44**	**41**	**35**	**19**	**13**

4. | General considerations, conclusions and recommendations |

4.1 Trends in 2010, what do they signify as regards transfusion safety?

The main trends – not statistically significant - in this year's report in comparison to 2009 are

- further slight increase in reports of nonserious transfusion reactions,
- larger number of grade 4 reports
- a smaller number of incorrect blood component transfused where there was a risk of ABO incompatibility.

Are these real changes, reflecting a change in transfusion safety, or just "noise"?

The increase of nonserious reports is primarily caused by the larger number of reports of new allo-antibody formation. TRIP welcomes the reports of nonserious transfusion reactions, because these provide information on the common hazards of transfusion and show that the system is alert. It is possible that digital reporting has facilitated this increase. The increase also reflects modest rises in the reports of allergic reactions, transfusion-associated circulatory overload and of other reaction, as discussed in the relevant sections of this annual report. As discussed earlier in this report, the increase of Grade 4 reports does not represent a real increase of risk associated with receiving a blood transfusion. In future reports TRIP will adopt a further breakdown of the relation of the patient's demise to the transfusion reaction, allowing more relevant monitoring of adverse consequences of transfusion.

The smaller number of IBCT reports with ABO incompatibility is encouraging. If the reducing trend continues, it cannot be ascribed to widespread introduction of IT support of the patient identification procedures since these methods are hardly in use in The Netherlands. As noted above, France and the United Kingdom have demonstrated a gradual decline of ABO incompatible transfusions in the most recent reporting years, i.e. several years after the rise of national hemovigilance reporting. Any improvement in The Netherlands must be attributed to the diligent work of hemovigilance staff in the hospitals - including the blood transfusion laboratories – and the general focus on transfusion safety. This work must be continued, a real challenge in the current times of financial constraint.

4.2 Actions and developments following recommendations in previous TRIP reports

	Update on recommendations which are still current from TRIP reports 2003 - 2008	Comment C=concluded
1.	*Digital reports to TRIP and making reports available electronically to IGZ (2007).*	85% of reports in 2009, 92% in 2010. Electronic availability to IGZ and to the blood service is functional. (C)
2.	*Transfusion safety officer (hemovigilance assistant) in every hospital: an important task is the training of doctors and nurses (2007).*	Recommendation adopted in revised national transfusion guideline. (C)
3.	*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. Further action for professional groups and TRIP.
4.	*For women younger than 45 years, in addition to Kell negative, also select Rhesus phenotype-compatible erythrocytes in order to prevent hemolytic disease in newborns (2007).*	Recommendation for c compatible transfusion adopted in revised national transfusion guideline. (C)
5.	Transfusion-associated circulatory overload also *an important category (2006).*	Action for clinical staff.
6.	*Integration of activity within safety management system in hospital with hemovigilance activity (2006).*	This point of concern remains current.
7.	*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.
8.	*Each report in the category of other reaction to be accompanied by clinical and investigation data. Finding of hypertensive reaction of unclear significance, to be examined in future reports of this symptom (2008).*	2010: no evidence of hypertensive reaction representing a specific cluster. (C)
9.	*For all transfusion reactions suspected of having a bacterial cause, cultures to be taken from remnant of blood component and the patient, findings to be included in the report to TRIP (2007; 2008).*	Steady slight increase in inclusion of culture results in reports to TRIP. Recommendation reinforced in revised national transfusion guideline. (C)
10.	*Action on improved monitoring of patients at risk of transfusion-associated hemosiderosis (2006; 2008).*	No actions undertaken, underreporting continues.
11.	*Hospital blood transfusion committees should have insight into the scale of the use of blood management techniques. There should 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.
12.	*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).*	As present no funding available.. Allergic reactions remain largely uninvestigated. See recommendation in this report.

	Update on recommendations from TRIP report 2009	Comments
13.	*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 (also 2007; 2008 re staff training).*	Encouraging reducing trend of incidents with ABO-incompatibility risk, but it is too early for any definite conclusions.
14.	*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.*	Need again apparent in assessment of 2010 reports; TRIP to take action.
15.	*TRIP should be able to initiate and conduct research – independently and in cooperation with stakeholders in the field of blood transfusion – to promote the safety of blood transfusions.*	Several small projects (abstracts in 2010 and 2011) on additional analysis related to data in TRIP database. (C)
16.	*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.*	TRIP and a group of volunteer hospitals piloted the proposed quality indicators in 2010-2011. Adapted indicators will be included in the revised CBO transfusion guideline.

4.3 Conclusions

1. Anaphylactic reaction is now the largest category of serious transfusion reaction. These reactions are not systematically investigated.

2. There was a higher number of Grade 4 reports than in previous years. In the majority of these cases the reaction could have contributed to the fatal outcome but there were other relevant factors.

3 The number of reports classified as other reaction has risen. There are clear clusters of hypotensive reactions and transfusion-associated dyspnea which are increasingly being recognised.

4. There is a rise in numbers of reports relating to look-back procedures following demonstration of occult hepatitis B infection (OBI) in donors by the recently introduced HBV-NAT testing.

5. For the first time since 2003 there were two reports from hospitals relating to look-back procedures after HIV seroconversion in a donor. No transmission was demonstrated.

6. Autologous Blood Management Techniques are widely used but figures on the application of these methods known to hemovigilance personnel in only half the hospitals.

7. Compared to 2008 and 2009 there were fewer of IBCT with ABO incompatibility risk but the difference is not statistically significant. This is an encouraging trend, however the total number of IBCT reports is unchanged.

8. In the category of other incidents 24 reports (20%) involved unnecessary transfusion. In four cases symptoms of a transfusion reaction were reported.

9. Relatively few transfusion reactions seem to be reported in infants and children in comparison to blood use. It is not known whether this is due to a lower incidence or perhaps in part to poor recognition, possibly because of different clinical manifestations in pediatric patients.

4.4 Recommendations

A. Recommendations based on the 2010 TRIP Report

	Recommendation	Who?
1.	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).	TRIP
2.	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.	TRIP
3.	A standard protocol should be developed for the further investigation of serious anaphylactic transfusion reactions.	TRIP and Sanquin clinical advisory service
4.	In order to monitor optimal use of blood components, TRIP wishes to encourage reporting of incidents which lead to unnecessary transfusion or avoidable product loss.	Hospital transfusion committees and hemovigilance staff
5.	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..	TRIP and hemovigilance staff
6.	Hospitals should have a defined procedure for investigation of recipients of blood components which retrospectively might have been infectious.	Hospital transfusion committees and hemovigilance staff

B. General recommendations

7.	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.	Hospital transfusion committees and hemovigilance staff

List of terms and abbreviations

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