TRIP annual report 2009
Hemovigilance
Extended version

The TRIP annual report 2009, extended version, concerning hemovigilance reports in the Netherlands in 2009 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 TRIP annual report 2009, extended version. There are two versions of the TRIP hemovigilance report 2009: a standard version and an extended version. The extended version includes – among other things – detailed discussions of the various categories of reports and is particularly aimed at hemovigilance officers and hemovigilance assistants. Since last year, a separate report has been published concerning tissue vigilance in the Netherlands.

A number of remarks on important conclusions and recommendations of the report: the number of serious reactions has decreased, in part due to a decrease in the number of reports of TRALI (transfusion-related acute lung injury) and severe anaphylactic reactions. The decrease in the number of reports of TRALI is probably the result of the measure implemented by Sanquin, that of to supplying hospitals with plasma obtained exclusively from male donors.

Anaphylactic reactions are the most common serious reaction and it is good to emphasise that these reactions cannot be prevented by hospital employees, but that rapid detection and adequate treatment are a matter of life and death in this case.

There were only two reports of suspected transmission of infections via blood components: one bacterial infection and one viral infection, both in the imputability category probable. Therefore, the labile blood components supplied by Sanquin are very safe.

The number of errors made in the hospital when requesting blood components, processing the requests and administering blood components has not decreased. Therefore, I want to emphasise the first recommendation once more: “Measures to make the identification procedures more robust are required. This could include electronic systems to support the procedures.”

Finally, I wish to draw your attention specifically to Recommendation 5: “It would be sensible to record data about the transfusion chain in a standardised manner, so that comparisons of transfusion practice and outcomes becomes possible. The revised CBO guideline could form a starting point for this.” The revised CBO Guidelines for Blood Transfusion will be published during 2011 and TRIP will lead a pilot project, in which the listed quality indicators will be evaluated.

Hemovigilance is an international activity. We can learn a lot from the experiences and data from other countries. Therefore, I am pleased to invite you to attend the 13th International Hemovigilance Seminar, which will take place in Amsterdam from 9 to 11 February 2011. For more information and registration, please visit www.ihn-org.net.

I would like to thank all the staff of the TRIP Office, the members of the Expert Committee who checked all the reports and the members of the TRIP Governing Board who commented critically on this report.

Finally: I warmly recommend this report to you and hope that reading it will contribute to the further improvement of the quality and safety of blood transfusion in the Netherlands.

Prof. René R.P. de Vries
President, TRIP Foundation

Executive Summary

Goals and procedures of TRIP Office (hemovigilance)

The TRIP (Transfusion Reactions In Patients) National Hemovigilance Office aims to receive reports on side effects and incidents associated with the transfusion of labile blood products and to report publicly on transfusion safety. The registration concerns both serious and non-serious adverse effects and incidents. These are reported by the permanent contact person (hemovigilance officer) in the Dutch hospitals. Both the patient and the treating physician remain anonymous in the report. Participation is voluntary, but is considered to be the professional standard according to the national CBO Guidelines for Blood Transfusion and the Healthcare Inspectorate (Inspectie voor de Gezondheidszorg, IGZ). TRIP also receives information from the blood supply organisation Sanquin 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 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 overiew 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 make a report available to the IGZ and/or Sanquin via the TRIP digital reporting system.

Participation

In total, 99 (96 %) of the 103 Dutch hospitals participated in the TRIP registration in 2009. Transfusion reactions were reported by 92 hospitals and seven hospitals indicated that they did not have any transfusion reactions to report in the TRIP categories. The closing date for the report was 1 March 2010.

The reports in 2009

The number of reports received in 2009 was 2384 in total (2008: 2052 including late reports). Of this total, 2109 involved reports of transfusion reactions and 275 were reports of incidents in the transfusion chain. A transfusion reaction was reported as a subsidiary category in 25 incidents (13x incorrect blood component transfused, 7x other incident and 5x infectious). Of all the reports, 2019 (85 %) 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 2093 cases of the reactions reported in 2009: this is 98.1 % of the total of 2134 reactions, namely 2109 reported reactions as a main category and 25 reactions following incidents. The degree of severity was grade 0 for 732 reports (35.0 %), grade 1 for 1248 (59.6 %), grade 2 for 97 (4.6 %), grade 3 for 13 (0.6 %) and grade 4 for 3 reports (0.1 %). The number of serious reports (grade 2 or higher) formed a total of 113, which is lower than the annual average of 135 for 2006 – 2008.

The transfusion reactions were also evaluated for imputability: the likelihood that the symptoms observed can be attributed to the transfusion. After all, symptoms

experienced by a patient can be related to factors other than the transfusion. The imputability was listed for 2093 (98.1 %) of the 2134 transfusion reactions reported in 2009. Of these, 330 reports (15.8 %) were considered to be definitely related to the transfusion, 623 (29.8 %) as probable, 975 (46.6 %) as possible, 145 (6.9 %) as unlikely and 20 (1.0 %) as definitely not. Among the serious reports, 98 had an imputability of possible, probable or certain.

Types of reactions and incidents

The reported reactions are: non-hemolytic transfusion reaction 485, mild febrile reaction 357, acute hemolytic transfusion reaction 18, delayed hemolytic transfusion reaction 8, transfusion-related acute lung injury (TRALI) 12, anaphylactic reaction 69, other allergic reaction 180, circulatory overload 41, post-transfusion viral infection 2, post-transfusion bacteremia / sepsis 50, hemosiderosis 2, other reaction 132 and new allo-antibody 753. The reported incidents include 60 reports of administration of the incorrect blood component (component intended for another patient or not meeting appropriate specifications for that patient), with a subsequent clinical reaction (five of grade 2) in 13 cases. TRIP also received 110 reports concerning other incidents and 72 reports of near miss incidents. There were 26 reports from hospitals concerning bacterial contamination of a blood component; three related to culture findings following a transfusion reaction and the remainder were related to blood components that had already been administered and for which Sanquin later detected a positive bacterial screening. Finally, there was one report of viral contamination of a blood component, with an additional category of post-transfusion viral infection with hepatitis B, imputability probable: this concerned an earlier donation by a donor who was found to be a carrier of an occult hepatitis B infection upon implementation of a new test for that virus.

Number of reports in relation to the number of blood components supplied and administered

In 2009, Sanquin supplied a total of 699,720 blood components to the hospitals. The total number of reports for 2009 was 2384. This gives an overall rate of 3.4 reports per 1000 distributed blood components. This is an increase compared to 2008 (2.9 per 1000), which can be attributed mainly to an increase in the categories of febrile reactions and new allo-antibodies.

Discussion and conclusions

TRALI

The number of TRALI reports in 2009 was 12, which is lower than in previous years. From mid-2007, Sanquin has only distributed plasma from male, never-transfused donors for transfusion purposes, with the aim of reducing the risk of TRALI from transfused plasma. From this time on there have been fewer reports of TRALI following plasma administration. An additional calculation demonstrated that the total number of TRALI reports decreased by approximately one third.

Increase in other reactions

The category of other reaction, in which there is an increase, includes reports that do not meet the definitions for the standard categories, including reports of hypotension and breathing difficulties following transfusion. It is useful to distinguish clinical and research findings on which the diagnosis needs to be based, in order to create separate categories for transfusion-associated dyspnoea and hypotensive reaction in the TRIP database.

Blood Management Techniques (BMT)

In 2009, 33 reports were received (from six hospitals) of transfusion reactions (20) and incidents involving the application of blood management techniques. There were three grade 2 reports. Only a minority of the hospitals was able to inform TRIP about the number of times that these techniques were applied in 2009. Blood transfusion committees should ensure that there are adequate protocols and vigilance procedures in place for BMT.

Reflection on transfusion safety

As in previous years, the number of suspected or proven cases of transmission of infection by blood transfusion was extremely low. Only one report shows that it was likely that there were clinical symptoms due to a bacterially contaminated blood component. There was one report of suspected transmission of hepatitis B in a previous year, detected retrospectively.

The number of reported incidents in the transfusion chain increased from the start of the TRIP registration up to 2007. There was a decrease in the number of reported incidents in 2008, but the figures for 2009 are similar to those of 2007. Electronic blood tracking systems can contribute to the prevention of incorrect transfusions / administration of an incorrect blood component.

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 supply service Sanquin. 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 Guidelines for Blood Transfusion (2004). The digital reporting system that came into use in 2006 – initially in pilot form – was used actively by the majority of the hospitals in 2009.

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 extent of certainty 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 also separate from not linked to any other non-voluntary reporting routes: 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 effects and incidents that may be associated with the quality and/or safety of blood components. TRIP ensures the analysis and reporting of these serious (grade 2 or higher) reactions on behalf of the competent authority IGZ. The reporting party is still responsible for submitting the report to the IGZ. At the end of 2008, the hospitals were informed in a combined circular from the Inspectorate and TRIP about the option of making serious reports 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 undesirable adverse effects and/or incidents associated with the use of human tissues and cells. The TRIP tissue vigilance report 2009 (available on www.tripnet.nl) describes this system and the findings.

2. | Hemovigilance reports in 2009 |

2.1 Participation

The value of national registration and evaluation of transfusion reactions is determined by the number of actively participating hospitals (degree of participation) and by the quality of the information submitted. In 2009, 99 of the 103 (96 %) hospitals participated in the registration. Of these, 92 hospitals reported transfusion reactions and seven hospitals indicated that there were no transfusion reactions to report. Data about blood use were received from 100 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 became 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 'non-participants' in the TRIP report. The closing date for inclusion of reports during 2009 in this report was 1 March 2010.

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 2008 report, 102 late submissions (5 % of the final total) were received for 2008, of which 8 reports (two of 'other reaction', one anaphylactic reaction, one transfusion-associated circulatory overload, one TRALI, one hemosiderosis and two non-hemolytic transfusion reactions) were of severity grade 2 or higher. 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 2009.

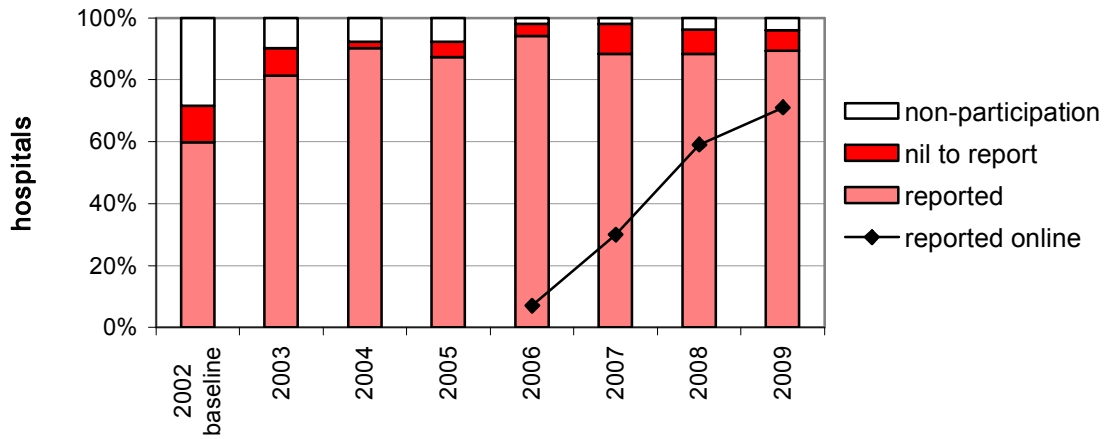

Figure 1 Participation per year

2.2 Summary of data regarding the reports for 2009

Readers can find all definitions used at www.tripnet.nl. At the beginning of 2008, TRIP distributed revised definitions, which came into force on 1 January 2008.

Reports received

In total, 2384 reports of transfusion reactions were received in 2009; these arose from 92 hospitals. In 2008, the number was 1950 and ultimately, including late reports, 2052 from 92 hospitals. Therefore, there has been an increase of 16 % compared to the final total of reports in 2008. This increase is discussed further in the subsequent chapters of this report. Of all the reports, 2019 were submitted electronically (85 %, 71 hospitals).

There are some non-serious categories that, until now, have been regarded as optional for reporting: mild febrile reactions, near accidents and information (from the hospitals) about positive bacterial screening and other component incidents. TRIP sees it as useful to register these events and has not distinguished any optional categories since 2008. After all, reporting is seen as the professional standard for all categories. Despite these efforts, the risk of under-reporting still exists in certain categories. This is regrettable, as the registered information can identify bottlenecks in practice or possible new problems. Of the total number of reports, 549 reports from 76 hospitals fall into this group (2008: 424 reports from 73 hospitals).

Following assessment by the Expert Committee, reporters were asked supplementary questions in a number of cases (a total of approximately 30 times). Discussions with the reporter led to seven instances of amending the reporting category. 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 2002 up to and including 2009. 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, 2003–2009

Reaction	2003	2004	2005	2006	2007	2008	2009	Grade 2 or higher #	No. hospitals with reports in 2009
NHTR	318	345	435	490	452	453	485	15	79
Mild febrile reaction	326	341	375	363	328	275	357	4	68
AHTR	8	14	9	19	11	18	18	6	16
DHTR	19	14	12	14	11	18	8	3	8
TRALI	7	9	17	25	31	21	12	12	10
Anaphylactic reaction	8	21	26	19	54	65	69	19	31
Other allergic reaction	132	171	219	222	202	171	180	0	48
Circulatory overload	7	6	27	34	31	39	41	14	22
Post-transfusion 1819purpura	0	0	0	0	0	1	0	0	0
TA-GVHD	0	0	0	0	0	1	0	0	0
Hemosiderosis	0	0	3	5	3	5	2	0	1
New allo-antibody	244	428	571	607	601	607	753	2	60
Other reaction	54	64	67	61	55	101	132	15	45
Post-tf bacteremia / sepsis§	9	5	10	7	19	37	50	0	34
Post-tf viral infection	5	7	8	7	7	7	2	0	2
Total TR	**1137**	**1425**	**1779**	**1873**	**1805**	**1819**	**2109**	**90**	**92**
Total reports*	**1268**	**1547**	**1984**	**2130**	**2081**	**2052**	**2384**	**98 ***	**92**

imputability certain, probable or possible
§ up to and including 2007: bacterial contamination; see definitions on www.tripnet.nl
* Total transfusion reactions and incidents

Table 2 Incidents per year, 2003–2009

Incident	2003	2004	2005	2006	2007	2008	2009	No. hospitals with reports in 2009
Incorrect bc transfused	34	36	60	64	64	59	60	32
Near miss	31	62	79	77	74	55	72	19
Other incident	5	12	51	86	100	83	110	22
Look-back (info reported by hospital to TRIP)		2	2	1	4	9	6	4
Virally infected component				2	0	2	1	0
Positive bacterial screen[$]	61	10	13	27	29	2	4	4
Bacterial contamination[$]					5	23	22	11
Total	**131**	**122**	**205**	**257**	**276**	**233**	**275**	**48**

[$] Amended definitions as of 2008, see www.tripnet.nl
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 (2109) plus the reactions that occurred in incidents and reports of bacterial contamination (25), was 2134, of which the severity was recorded in 2093 cases (98.1 %). The severity was grade 0 for 732 reports (35.0 %), grade 1 for 1248 reports (59.6 %), grade 2 for 97 reports (4.6 %), grade 3 for 13 reports (0.6 %) and grade 4 for 3 reports (0.1 %).

Figure 2 shows the severity grades of clinical transfusion reactions from 2002 up to and including 2009. In 2009, there was an increase in the reports of grade 0: this is explained by the higher number of reports of new allo-antibody formation. There was also an increase in the number of grade 1 reports – this can be attributed mainly to the higher number of non-hemolytic transfusion reactions and mild non-hemolytic febrile reactions.

There was also a lower number of serious reports (grade 2 to 4), namely 113 compared to an average of over 130 for the years 2006 – 2008. The definition remained unchanged during this period. Taking into consideration the overall increase in the number of reports, it is unlikely that hospital staff became less vigilant. The difference could be attributed to several factors, such as:

- a decrease in the risk of severe transfusion reactions
- a change in the reporting behaviour and/or assessment of severity.

This point will be discussed again further in the report.

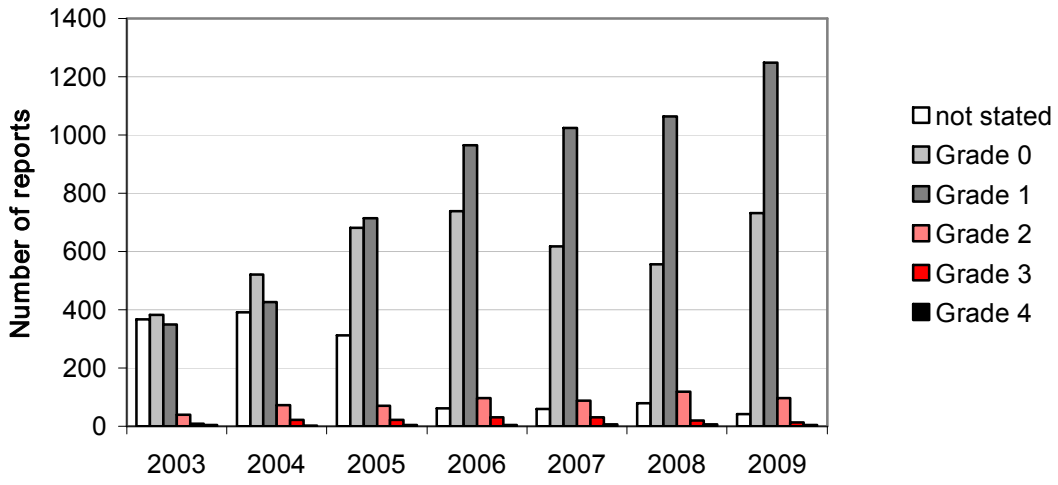

Figure 2 Severity of the transfusion reactions, 2002 – 2009

Relationship to the blood transfusion (imputability)

Imputability	*Definition*
	(Imputability is applicable to clinical 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; a measure of probability that the reaction resulted from the transfusion. The reporting of imputability is also only relevant if the patient experienced a reaction. Of the 2134 transfusion reactions reported in 2009, the imputability was listed for 2093 reports (98.1 %). Of these, 330 reports (15.8 %) were considered certainly related to the transfusion, 623 (29.8 %) were probable, 975 (46.6 %) were possible, 145 (6.9 %) were unlikely and 20 (1.0 %) were excluded). *Figure 3* shows imputability of the 2134 transfusion reactions in 2009, compared to previous years. For the 113 reports of severity grade 2 or higher, 98 had an imputability of certain, probable or possible.

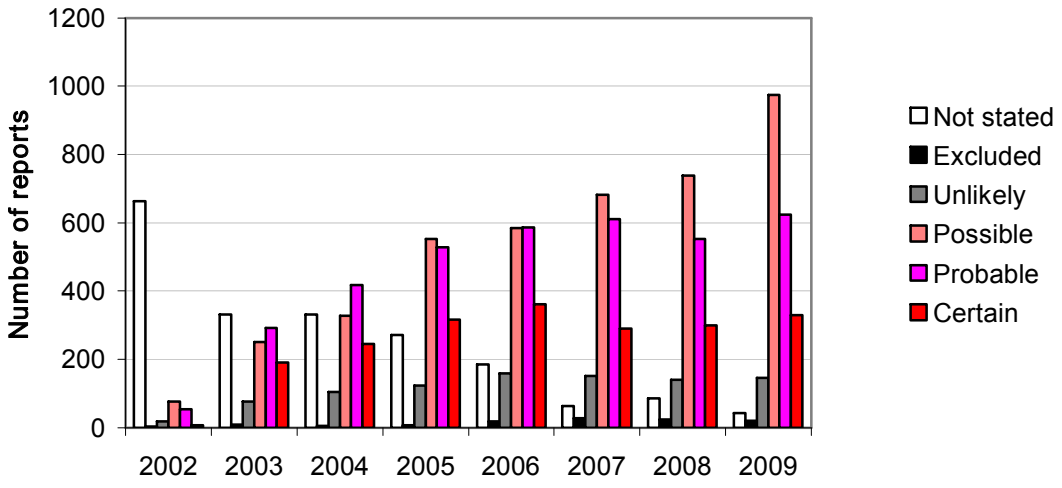

Figure 3 Imputability of the transfusion reactions 2002 – 2009

Number of reports in relationship to the number of supplied blood components

In 2009, Sanquin supplied hospitals with a total of 699,720 blood components; this number does not include special components like lymphocytes and granulocytes. The total number of reports for 2009 was 2384. On average, that is 3.41 reports per 1000 blood components distributed nationally, or 3.36 after exclusion of the reports relating to blood management techniques. *Table 3* shows the relationship between supplied blood components and the number of reports.

Table 3 Number of reports per type of blood component in 2008 and 2009

Type of blood component (bc)	2008 Number of bc supplied	2008 Reports; number per 1000 bc		2008 Serious reports[#]; number per 1000 bc		2009 Number of bc supplied	2009 Reports; number per 1000 bc		2009 Serious reports[#]; number per 1000 bc	
Red blood cell concentrate	559,372	1518	2.71	79	0.14	559,976	1812	3.24	63	0.11
Platelet concentrate	50,784	262	5.16	26	0.51	49,354	302	6.12	18	0.36
Fresh frozen plasma	96,622	81	0.84	11	0.11	90,390	99	1.10	8	0.09
Autologous (RBCs, pre-deposit)	110 dona-tions	1		0		No info	1		0	
Cell-saver and drain blood		24		1			32		3	
Other products		4		0			0		0	
Combinations		95		14			70		6	
Not stated		79		1			68		0	
Total	**706,868**	**2053**	**2.90**	**132**	**0.19**	**699,720**	**2384**	**3.41**	**98**	**0.14**

[#] Imputability certain, probable, possible

The number of reports per 1000 units has remained approximately stable at 2.9 since the reporting year 2005. *Figure 4* shows the course from 2002 up to and including 2009. In 2009 there was an increase of 0.44 reports per 1000 nationally distributed blood components. The 95 % confidence interval for this can be calculated as 0.28 to 0.59. However, this simple calculation does not pick up on the differences between categories of transfusion reactions and the fact that transfusion practice is not homogenous. The number of serious reports is 113: this corresponds to 0.16 reports per 1000 or approximately 1 in 6200 blood components. This in comparison to the average of 0.19 for 2006 – 2008 (difference 0.031, 95 % CI -0.005 to 0.066). *Table 4* in parts A and B shows the distribution of the administered blood components per type of reaction or incident.

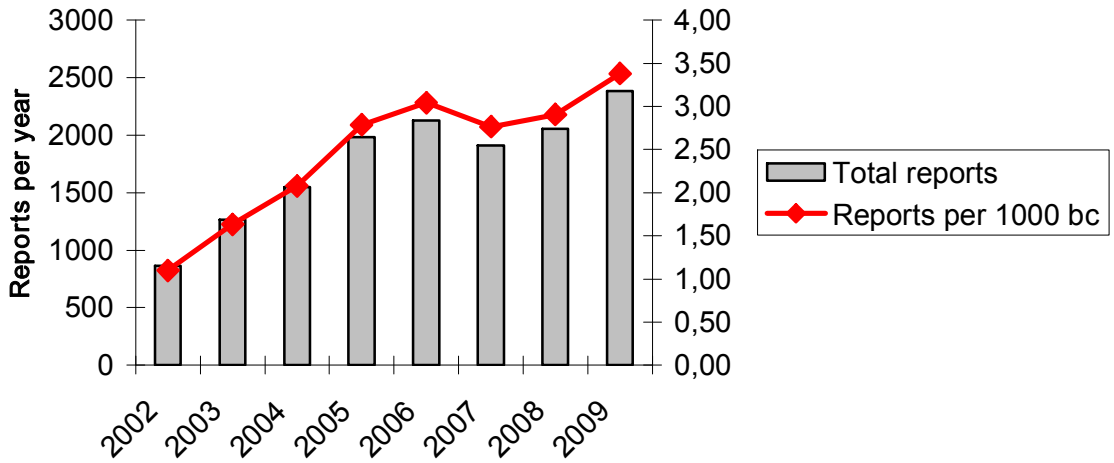

Figure 4 Number of reports per year, 2002 – 2009

Table 4 Distribution of types of blood components per category of report in 2009

A. Reaction	RBCs	Platelets	Plasma	Combi	Other	Not stated
Non-hemolytic transfusion reaction	389 80.2 %	70 14.4 %	2 0.4 %	13 2.7 %	11 2.3 %	-
Mild non-hemolytic febrile reaction	331 92.7 %	21 5.9 %	1 0.3 %	4 1.1 %	-	-
Acute hemolytic transfusion reaction	17 94.4 %	-	-	1 5.6 %	-	-
Delayed hemolytic transfusion reaction	7 87.5 %	-	-	1 12.5 %	-	-
TRALI	8 66.7 %	2 16.7 %		2 16.7 %	-	-
Anaphylactic reaction	11 15.9 %	31 44.9 %	22 31.9 %	3 4.3 %	2 2.9 %	-
Other allergic reaction	41 22.8 %	85 47.2 %	44 24.4 %	8 4.4 %	2 1.1 %	2 1.1 %
Circulatory overload	28 68.3 %	6 14.6 %	4 9.8 %	2 4.9 %	2 2.4 %	-
Post-transfusion purpura	-	-	-	1 100 %	-	-
Hemosiderosis	1 50.0 %	-	-	1 50.0 %	-	-
New allo-antibody	696 92.4 %	21 2.8 %	-	25 3.3 %	1 0.1 %	10 1.3 %
Other reaction	97 73.5 %	24 18.2 %	3 2.3 %	4 3.0 %	4 3.0 %	-
Post-transfusion bacteremia	47 94.0 %	2 4.0 %	-	1 2.0 %	-	-
Post-transfusion viral infection	1 50.0 %	-	-	1 50.0 %	-	-
B. Incident						
Incorrect blood component transfused	44 73.3 %	7 11.7 %	6 10.0 %	3 5.0 %	-	-
Other incident	78 70.9 %	6 5.5 %	11 10.0 %	1 0.8 %	12 10.9 %	2 1.8 %
Near miss	11 15.3 %	3 4.2 %	3 4.2 %	-	-	55 76.4 %
Bacterially contaminated blood component	1 4.5 %	20 90.9 %	1 4.5 %	-	-	-
Pos. Bacterial screen	1 25 %	3 75 %	-	-	-	-

Variation among hospitals

The number of transfusion reactions per 1000 administered blood components per hospital varies from 0 to 13.84 (the maximum in 2008 was 11.14, the maximum in 2007 was 9.45); the median is 3.18. *Figure 5* shows the distribution of number of reports related to the hospital's blood use. As expected, the distribution decreases as a hospital's blood use increases.

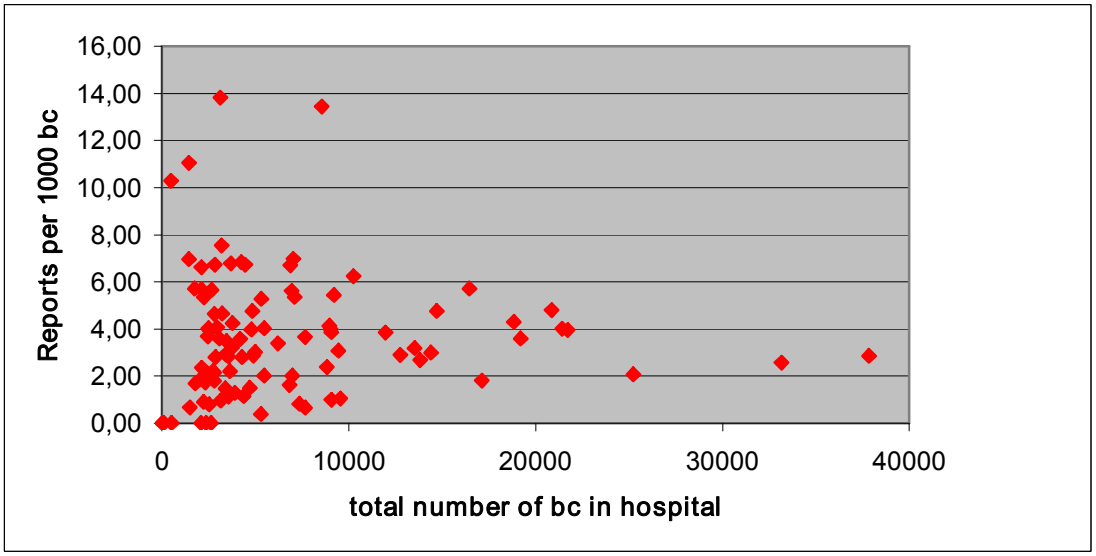

Figure 5 Reports per 1000 bc in 2009 according to number of blood components administered

Logically, a (small) portion of the variation in the number of reports per hospital can be explained by differences in the ratios of types of blood components. The number of reports per 1000 units is higher for platelet concentrates than for red blood cells and these in turn result in a higher number of reports than units of fresh frozen plasma. The number of reports per type of blood component, calculated according to national distribution numbers are presented in *Figure 6* below. The calculated number per type of component is an under-estimation, because a number of reactions and incidents are observed following administration of several types of blood components, or the type of blood component is not stated. In the case of incidents, these cannot always be linked to a specific type of blood component. A reaction can occur during the administration of 'other' blood components, notably salvaged autologous blood (see the paragraph on blood management techniques, page 54).

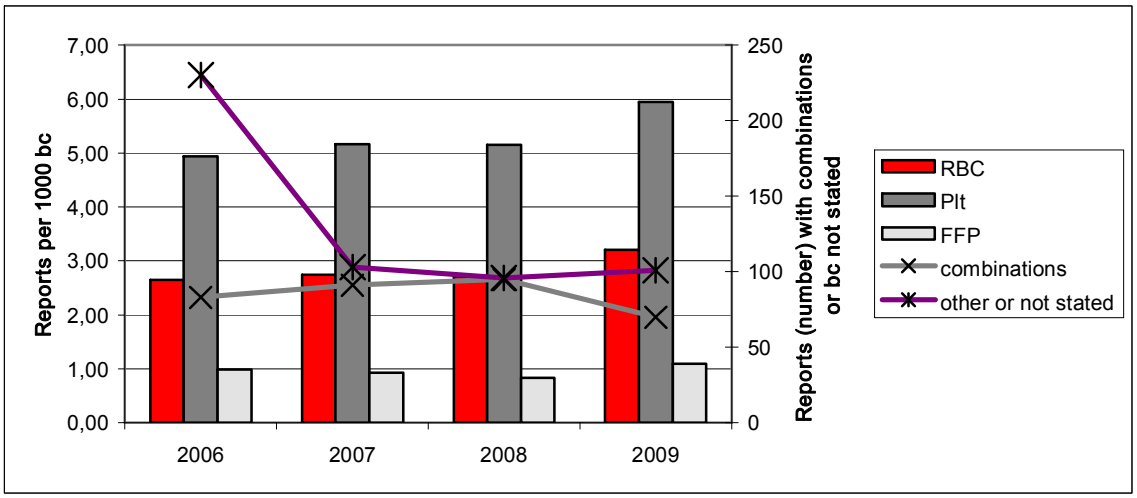

Figure 6 Number of reports per type of blood component, 2006 – 2009

In the annual feedback to hospitals about their reports in 2008 compared to the national average, an adjustment was made for the proportions of the various types of blood components. The blood transfusion committees will probably consider possible factors to explain a relatively high or low number of reports, such as staff training on recognition of transfusion reactions or the hospital's "reporting culture". It is useful to record data about the transfusion chain in a standardised manner so that comparisons of transfusion practice and results become possible.

2.3 Medical specialty requesting the transfusion

Since 2007 there has been a data entry box in the digital reporting form for the medical specialty of the physician requesting the transfusion. Since 2008, this information is requested for all reports whether submitted electronically or on paper forms. *Figure 7* shows the proportion of the surgical versus the non-surgical specialisms among the specialists requesting the transfusions which gave rise to reports to TRIP. *Figure 8* shows the relevant types of blood components for the reports (2008 and 2009 combined) submitted to TRIP. In the figures, anaesthesiology has been included in the surgical specialisms and the Intensive Care Unit (ICU) and Accident & Emergency (A&E) department have been included under specialism unknown.

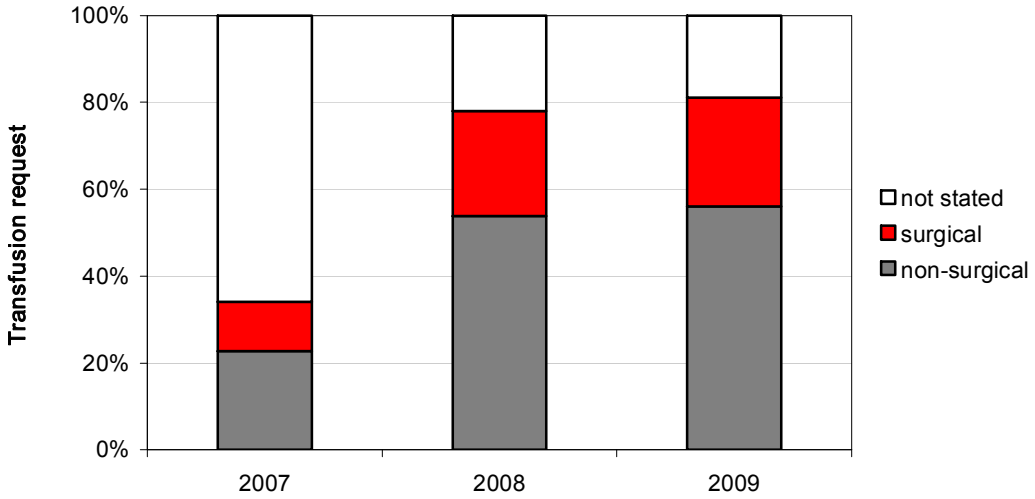

Figure 7 Specialty requesting transfusion in TRIP for reports 2007 – 2009

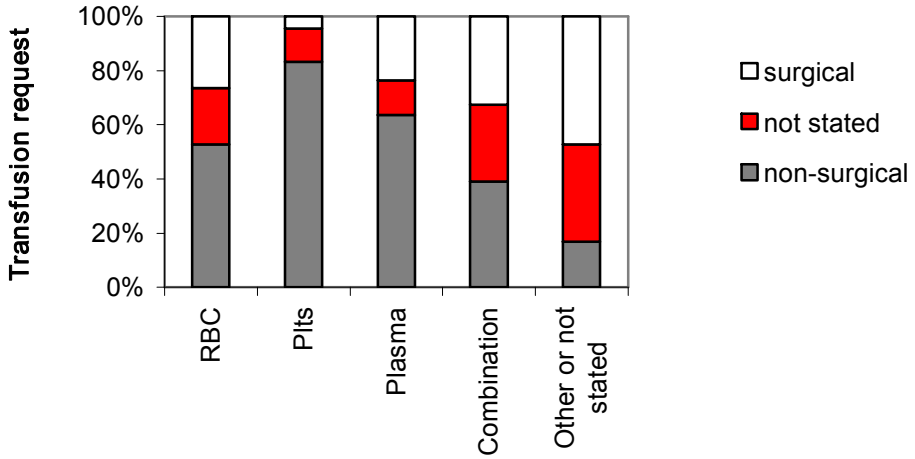

Figure 8 Distribution of types of blood components for TRIP reports, 2008 – 2009

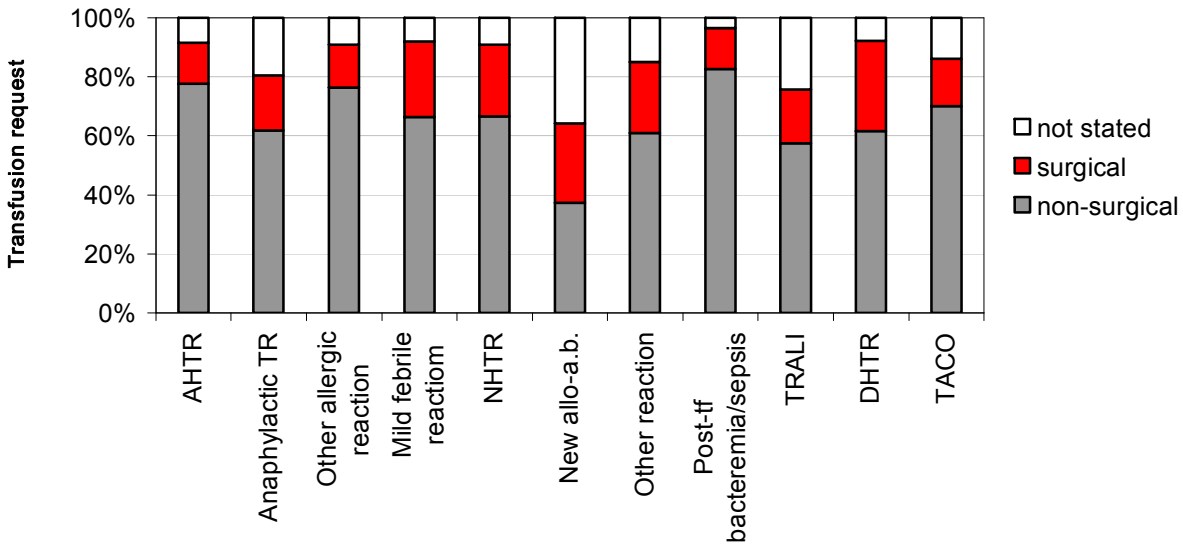

Figure 9 Type of TR in relation to specialty requesting transfusion

The type of transfusion reaction is displayed in *Figure 9* in relation to the transfusion had been requested by a medical or surgical specialist. The graph shows some variations that should be viewed in relationship to the differences in types of blood components administered. Based on the available data, it is not possible to draw any conclusions on relationships between certain patient groups and types of transfusion reactions. It is also important to remember that denominator data concerning the absolute numbers of administered blood components to various patient groups are essential.

3. | Discussion of reports by categories |

3.1 Non-infectious transfusion reactions

Non-hemolytic transfusion reactions (NHTR) and mild 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 2009 is 485, compared to 453 in 2008. The number of mild febrile reactions (mild NHFR) is 357 in comparison to 275 in 2008. Together, these make up a generous third of the total number of reports. *Figure 10* shows the number of reports of febrile reactions and allergic reactions from year to year. Among the febrile reactions, the number of NHTR is fairly stable. For the mild non-hemolytic febrile reactions, that are not reported by all hospitals, there was a dip from 2007 to 2008.

Since 2006, when the definition of severity grade 2 was amended in accordance with EU legislation, the NHTR and the mild NHFR together have accounted for approximately 20 serious reports per year. There were 22 reports in 2009 (19 with certain, probable or possible imputability), compared to 24 in 2008. Severity grade 2 in these categories usually applies because the patient was admitted for observation or under the criterion of “prolongation of illness”.

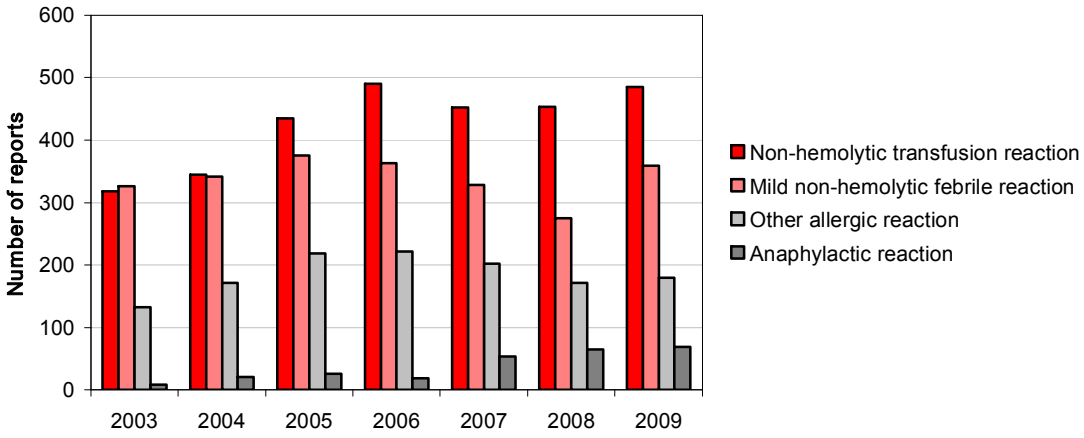

Figure 10 Number of reports of febrile reactions and allergic reactions per year, 2003 – 2009

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. TRIP does not have sufficient data yet to explain the difference in numbers of these reactions in relationship to the administered blood components. It would appear useful to perform further research in this area.

Some points stand out when studying the reports of febrile reactions. Firstly, the imputability is evaluated as relatively low. This can be explained by the fact that there can be various reasons for a transfusion recipient to develop a fever, whilst the differential diagnosis for allergic reactions is mainly limited to medication use. *Figure 11* below shows the imputability of the febrile reactions in comparison to that of allergic reactions.

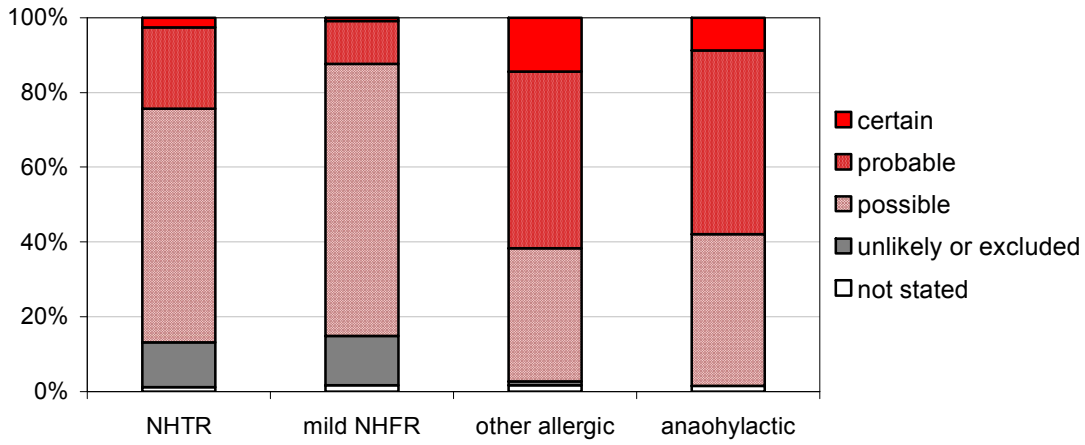

Figure 11 Imputability of the reports of febrile reactions and allergic reactions in 2009

The TRIP annual report 2008 identified an improvement in the number of reports in which a result was reported for blood culture performed on the patient: from 42 % in 2006 to 46 % in 2007 and 58 % in 2008. In 2009, a result for the blood culture was again reported in 58 % of the reports of NHTR. In 11 of the 276 reports of a negative result, the reporter indicated that the material from a segment of tubing of the blood component was used. However, the small volume in a sealed segment can give (false) negative results even though bacteria are cultured from a larger sample from the bag.

For seven of the reports registered as NHTR, a positive culture result was found in the hospital in the administered unit, but the hospital judged it to be not relevant, possibly resulting from contamination during collection of the culture sample. Where the result is *not* in doubt, the event should be reported as bacterial contamination of a blood component in accordance with the 2008 definitions.

Blood group serology results are reported for a lower percentage of the reports. In accordance with the CBO Blood Transfusion Guidelines (2004), these investigations should be performed. In order to limit the burden on the reporters, TRIP limits the number of additional questions asked for non-serious reports. However, if a report is not clear, if for example it is submitted as unlikely without any supporting information, additional information about study findings is required to validate the coherence of the report.

On examining the reports, a number of more technical aspects are noted:

1. In several reports it was noted that a patient received a transfusion despite of having fever. However, fever as such is not a reason for refraining from tranfusing a patient.

2. Various reports contain a comment that the symptom of a temperature increase of more than 2 ºC was not reported to the blood transfusion laboratory and only later became known to the hemovigilance employee upon inspection of the transfusion form.
3. Reports that are not a TRIP report. Several reports were submitted (n=14) in which the rise in temperature was less than 1 ºC and there were no rigors/chills. Such reports were included for the time being under the most suitable category, that of mild non-hemolytic febrile reaction. Another two were submitted in the category of other reaction. The observation is relevant for the hospital, but it does not fit into any of the TRIP categories. Such a report is a signal for both the hospital and TRIP that the reporting system is functional. TRIP should consider introducing a separate category, so that reports are registered but do not contaminate the official categories.
4. The observed symptoms were reported in the relevant fields for the majority of reports submitted electronically. This is an improvement in comparison to the reports submitted using paper forms, where TRIP sometimes has to conclude (and assume) from the choice of category that there has been a temperature increase. The analysis could be simplified by separate digital coding per symptom.

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; bloodgroup serological testing possibly positive; bacteriology negative.

In reporting year 2009, 18 reports of acute hemolytic transfusion reaction were submitted, with three of these reporting the formation of a new allo-antibody formation as additional category. This number of AHTR is comparable to previous reporting years. A further eight cases of acute hemolytic transfusion reaction as a result of the administration of the wrong blood component were identified and these reports are described in the paragraps on incorrect blood component transfused.

All acute hemolytic transfusion reactions occurred after the administration of red blood cells. The male to female ratio was 1 to 3.25 (gender not reported once). The male/female ratio for all reports to TRIP in 2009 was 1:1.2. The severity grade and imputability are presented in *Table 5*. The grade 3 AHTR is described as Case 1 on page 22. The grade 4 AHTR is discussed in the relevant chapter (3.5).

Table 5 – Severity grade and imputability of the AHTR in 2009

Severity grade	Imputability certain	Imputability probable	Imputability possible	Imputability unlikely	Total
1	5	3	3	1	12
2	2	1	1		4
3			1		1
4			1		1

Case history 1 Report of AHTR
The reported AHTR of grade 3 severity and possible imputability concerns a woman in sickle cell crisis who required a transfusion. She was known to have anti-C, anti-E, anti-Fya, anti-S and anti-Wra antibodies as well as non-specific warm auto-antibodies, cold antibodies, monophasic warm hemolysins and monophasic cold hemolysins. Because no bed was available she could not be admitted to the hospital where she was normally treated. The reference laboratory performed extensive investigations to exclude antibodies against high-frequency antigens. The patient was essentially un-transfusable and was transfused with the best-matched unit. A reaction occurred 90 minutes after the transfusion: > 2 °C rise in temperature, shivering and tachycardia with tea-coloured urine, a decrease in Hb compared to Hb before transfusion, elevated LDH and bilirubin. The patient was transferred to her usual hospital later that day, where she appeared to stabilise. Follow-up of hemolysis parameters were not determined. This was most probably a case of hyperhemolysis. The patient died 8 days later after a new sickling crisis. The relationship between her death and the transfusion cannot be evaluated in this case.

The reported clinical symptoms are presented in *Table 6*. More than one clinical symptom is reported for the majority of the reports. It is generally recognised that there are no specific symptoms of AHTR and it can be difficult to distinguish from the underlying disease of the patient.

Table 6 – Reported clinical symptoms for AHTR (N = 18)

Symptom	Number of times reported
Increase in temperature ≥ 2°C	11
Increase in temperature >1 < 2°C	7
Shivering	7
Increased heart rate / tachycardia	4
Hemoglobinuria	2
Dyspnea	2
Nausea / vomiting	2
Decreased blood pressure	2
Confusion	2
Increased blood pressure	1

In five reports hemolytic anemia was already present (auto-immune hemolytic anemia n=3), with the report of AHTR being based on symptoms and increase of hemolysis in relation to the transfusion. Such a reaction was registered in the category of other reaction in two further cases where the reporter did not wish to label a worsening of the underlying hemolysis as an acute hemolytic transfusion reaction.

In 17 cases, the reporter was able to substantiate the hemolysis with biochemical parameters (LDH, bilirubin, haptoglobin) and in one case AHTR was reported based on the clinical symptoms and subsequently discovered antibodies. The serology was not investigated extensively in all cases and even if extensive investigation was performed, it did not always provide an explanation for the hemolysis. The responsible antibody was identified in five of the eighteen reports, namely anti-Jkb + anti-s, anti-K, anti-Wra, anti-E, auto-anti-e + non-specific cold auto-antibodies.

There was one report of a weakly positive eluate without specificity and one report of a positive DAT. For one report, the blood service reference laboratory was able to identify anti-Jkb and anti-s antibodies after transfusion, which the hospital was unable

to demonstrate. This patient, with pre-existent jaundice from pancreatic cancer, developed a mild febrile reaction: this reaction was reported as AHTR (with unlikely imputability) and additional category of new allo-antibody formation.

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 2009, TRIP received 28 reports of a delayed hemolytic transfusion reaction: eight reports of DHTR were submitted as the main category, 19 reports were submitted as 'new antibody formation' with DHTR as an additional category and one report concerned DHTR after administration of the wrong blood component (see section on Incorrect Blood Component Transfused). In reports submitted as new allo-antibody formation with an additional category of DHTR, the new allo-antibody was the reason for diagnosing DHTR. The reports of main and additional category DHTR were submitted by 20 different hospitals. In reporting year 2009, TRIP attempted to test the DHTR incidence found in the literature (5 – 10 times higher than AHTR) against that in reporting practice by asking targeted questions about hemolysis following reports of new allo-antibody formation. For reports of new clinically relevant allo-antibodies – demonstrated within three months after transfusion according to the reporter's data – the TRIP Office asked the reporter whether there was still a need for transfusion on the date on which the antibody was discovered and if so, whether the patient was monitored for symptoms of hemolysis (course of hemolysis parameters and/or unexplained decrease in Hb). In 2009, this question following new antibody formation was asked 118 times and this resulted in only five cases of DHTR. The total number of DHTR (main and additional category) cases is similar to that in 2008 (18 + 11).

All delayed hemolytic transfusion reactions occurred after the administration of red blood cells. DHTR was diagnosed in twenty female patients and eight male patients. Four cases were of grade 2, thirteen cases were grade 1 and eleven cases were grade 0 (delayed hemolysis could only be demonstrated by means of laboratory parameters). The following antibodies were detected for the eight reports of DHTR as a main category (three of severity grade 2, five grade 1): anti-C + anti-E + anti-Jka, anti-E, anti-Jka, anti-Fya, anti-E + anti-S + anti-Fya, anti-CW + anti-Jkb. In two cases, no antibodies were detected even after extensive investigation. One case is described below (*Case history 2, below*).

Case history 2 – Report of DHTR

A 77-year-old woman with myelofibrosis has been receiving transfusions for 2 years. She is Rhesus phenotype ccdee and has had anti-K, anti-C and auto-anti-I antibodies for one year. She receives C, E and K negative transfusions. The anti-C is now no longer detectable. On 13 February she received two units of packed RBCs for an Hb value of 5.6. Her Hb was 5.0 on 3 March. The DAT at that time was 1+, non-specific reactions were found in the eluate and all clinically important antibodies were excluded. On 6 March she again received two units of packed cells. On 8 March she visited her GP because she looked yellow. No examinations were performed. On 16 March her Hb was 4.4 (DAT 1+), for which she again received a transfusion of two units of packed cells. On 20 March the hematologist decided to perform investigations because she looked jaundiced. This revealed a bilirubin level of 43 and an LDH of 419. Anti-K was detected in the eluate, but auto-anti-I is no

longer detectable. All transfused units were checked again and ere also checked again by the blood service: all units were K negative. Private anti-Kpa and anti-Wra antibodies were ruled out. Unfortunately, a blood test was not performed at the moment that the patient indicated that she thought she looked yellow.
On 16 March, the Hb value was the lowest ever measured for this patient and as a result, a report was submitted to TRIP: DHTR, severity grade 1, imputability possible.

TRALI (transfusion-related acute lung injury)

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

A total of 12 TRALIs were reported in 2009, all with imputability certain, probable or possible. This number is slightly lower than in 2008 (21, out of which 19 were of certain, probable or possible imputability). The number of reports of TRALI had increased from 2003 to 2007, probably due to increased national and international focus on this transfusion reaction. As in previous years, we critically examined whether the reports satisfied the national definition of a TRALI (which is consistent with the international definition) and the evaluated the imputability independently of the results of the leukocyte serology investigation by the blood service.

Eight (67 %) of the reactions occurred with the administration of RBC concentrates, two with platelets and two with plasma as well as RBC and/or platelets. Eight reports were of severity grade 2, three reports were grade 3 and one report was grade 4. There were eight male patients (age 2.4 – 71.4, median 59.2) and four female patients (age 24.6 – 89.4, median 55.3).

At the end of 2006, Sanquin implemented the measure that only plasma from male, never-transfused donors can be used for the preparation of quarantine fresh frozen plasma for transfusion purposes (generally referred to in this country simply as fresh frozen plasma or FFP). As in other countries, the reason for this measure lies in the fact that leukocyte antigens are found more often in female plasma and some TRALIs are observed following transfusion of plasma-containing blood components that contain antibodies targeted against HLA (class I or II) characteristics or other leukocyte antigens in the recipient. As of July 2007, only male FFP was supplied to hospitals. Units supplied to the hospitals before this measure came into force remained in stock and were used. An additional measure was implemented at the end of 2009, namely in the preparation of platelet pools to which donor plasma is added (platelet additive solution – PAS – instead of platelet storage solution). From now on, only plasma from male donors will be used for the added plasma.

Figure 12 presents the number of TRALIs (with imputability certain, probable or possible) per reporting year in relation to the blood components administered. It is clear that the number of reports decreased after the peak year of 2007. Based on the data registered by TRIP, the last plasma-related reports (all types of transfusion reactions included), using plasma obtained before the new measures, occurred in November 2007. The reports in which plasma (with or without other types of blood components) was administered have decreased since 1 December 2007 (up to the implementation of the ‘platelet measure’) compared to reports in which only red blood cells and/or platelets were administered in the six hours prior to the symptoms. It was calculated in an additional analysis that the decrease corresponds to approximately

33 % (95 % confidence interval, 9 % - 51 %) of the total number of reports before implementation of this measure (Wiersum-Osselton et al., Transfusion, accepted for publication).

Is the decrease a real decrease or is it merely due to the fact that suspected cases are evaluated differently since the implementation of the plasma rule: is the report now placed in a different category if there is any doubt about the diagnosis? A total of 17 reports (11 other reaction [of which eight were grade 2 or 3], three circulatory overload [1x grade 3], one anaphylactic TR [grade 2], one NHTR and one other allergic reaction [both grade 1]) were initially thought to be a TRALI. The same applied to 20 reports each in 2007 and 2008, but also to 16 in 2006. (In 2002 – 2005: total 19, however, less supporting information was submitted in the early reporting years).

Another possible explanation could be a decrease in general vigilance. This seems unlikely, taking into account the general increase in reports to TRIP in 2009.

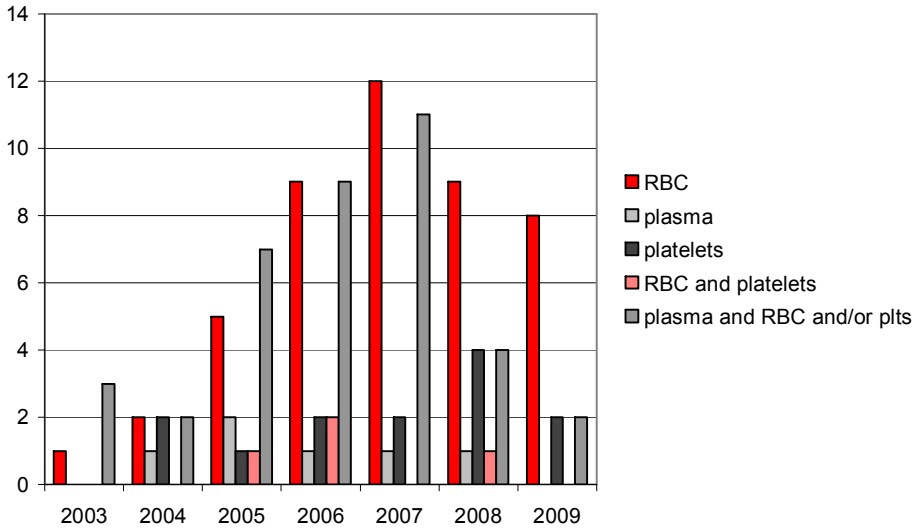

Figure 12 Type of blood component with TRALI reports

As usual, Sanquin examines leukocyte incompatibility in the case of TRALI reports that meet the clinical definition. In 2009, to the best of our knowledge at TRIP, this investigation was performed for 11 TRALI reports: the results from eight were submitted to TRIP and the results were negative in five cases. In four reports, HLA antibodies were found in donors and two cases of incompatibility with HLA characteristics of the recipient were demonstrated on two occasions (a platelet component was involved in both cases).

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 69 reports of anaphylaxis in 2009, with 19 of grade 2 (2008: 65, 30 serious). *Table 1* shows that anaphylaxis, TRALI and circulatory overload are the most important categories of the serious reports.

Of the reports, 11 were associated with administration of RBCs, 22 with plasma, 31 with platelet concentrates, three with several types of blood components and one with autologous blood from a drain. The risk of an anaphylactic reaction is greatest for a unit of platelet concentrate, slightly lower for a unit of FFP and lower again for a unit of red blood cell concentrate. The total number of reports of anaphylactic reaction is slightly higher than last year, but fewer of these reports were deemed serious (19 of the 30 in 2008 with imputability certain, probable or possible). Could the implementation of male fresh frozen plasma have affected the anaphylactic reactions? *Table 7* shows the distribution of blood components from year to year in anaphylactic reactions. There is no indication of a decrease in the involvement of fresh frozen plasma after 2006 – 2007.

Table 7 – Blood components in reports of anaphylactic reaction, 2006 – 2009

	2006		2007		2008		2009	
Anaphylactic	serious	all	serious	all	serious	all	serious	all
Red blood cells	2	5	2	10	7	14	4	11
Platelets	4	5	9	26	14	30	7	31
Plasma	5	7	8	12	5	15	7	22
Plasma and RBCs and/or platelets	1	1	2	2	3	5	0	3
RBCs and platelets	1	1	1	3	1	1	0	0
Total	**13**	**19**	**22**	**53**	**30**	**65**	**18**	**67***

* two reports involved the administration of unwashed blood from a drain

When evaluating the reports – if looking only at the reported symptoms – there is an overlap between the symptoms mentioned in reports of NHTR, mild non-hemolytic febrile reaction, anaphylactic reaction and other allergic reaction. This is illustrated in *Table 8* for the most reported symptoms. This table all amounts of rise in temperature or blood pressure decrease, without threshold level, because the degree of change was not specified in all cases.

Table 8 – Symptoms accompanying febrile and allergic reactions

Symptom	Anaphylactic	Other allergic	NHTR	Mild NHFR	Type of blood components			
					EC	TC	Plasma	O/C*
Total	69	180	486	358				
Increase in temperature	8	17	400	325[$]	646	74	7	23
Shivering	10	1	317	2	238	70	2	20
Increase in temperature / shivering	16	18	459[$]	326	679	112	8	30
Dyspnoea or bronchospasm	36	2	27	10	39	24	10	2
Temp / shivering with dyspnoea	8	0	27	10	36	8	0	2
Skin reaction / itching	41	169[#]	4	9	49	100	57	17
Nausea / vomiting / diarrhoea	10	1	7	28	31	6	4	5
Decrease in blood pressure	29	2	3	7	13	13	11	4
Increase in blood pressure	2	1	1	10	11	1	2	0
Poor yield	3	2	1	9	0	15	0	0

*other blood components or a combination of types of blood components
$no other symptoms reported, temperature increase is assumed for the remaining reports due to choice of category
#no other specific symptoms reported, skin rash assumed for the remaining reports due to choice of category

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.
Hemolysis testing and bacteriology negative if performed.

The number of reports of other allergic reactions is similar to the final total of last year (180 compared to 171 in 2008), but slightly lower than the average number of 210 for 2005 – 2007. The "missing" reports were probably reported in the category anaphylactic reaction in accordance with the request by TRIP to categorise allergic reactions with more than just skin symptoms in this category. In 2009, there were no reports of other allergic reaction of severity grade 2 or higher, in contrast to the previous years (five in 2008).

In the Netherlands, the standard platelet component (accounting for over 85 % of all distributed platelet units) is a pooled 5-donor unit that is prepared from five buffy coats with the same ABO blood group. One of the following is added to the unit: either platelet additive solution (PAS) or plasma from one of the five donors (since November 2009, plasma from a male donor who has never received a transfusion is always used). For the Sanquin regions, the pooled platelet concentrate with PAS is the standard component in the South-West region, whilst the pooled component to which plasma has been added is the standard component for the other regions. It has been suggested that PAS results in fewer allergic reactions. *Figure 13* shows the rates per region of reported allergic reactions (anaphylactic and other allergic reactions) associated with a platelet component, in relation to the total platelet use (data from 2006-8): there is no indication of a lower number of reports from the South-West region. An underlying difference also cannot be excluded due to a broad variation between hospitals in the number of reports compared to blood use.

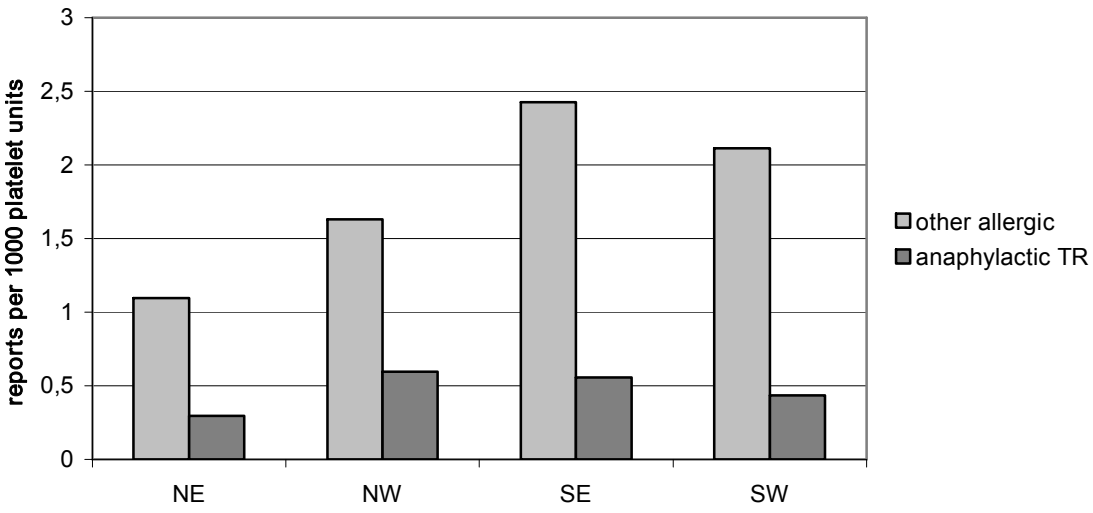

Figure 13– Rate of reports per region of allergic transfusion reactions with platelet concentrates (2006 – 2009)

As is the case for anaphylactic reactions, men and women are represented equally. A total of 47 % of the other allergic reactions is associated with the administration of

a platelet concentrate and 23 % with plasma. In comparison to the patients with other types of transfusion reactions, the patients are relatively young, probably reflecting the patient population receiving these types of blood components: the median age is 50.6. Of these patients, 22 (12 %) had previously suffered one or more allergic, febrile or other transfusion reactions which had been reported to TRIP.

Transfusion-associated circulatory overload (TACO)

Dyspnoea, 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 2009 was 39, meaning that a stable level has been maintained compared to the previous years. Two reports were grade 3 and thirteen were grade 2, also similar to the previous years. Over two thirds of the reports of circulatory overload involved the administration of red blood cells only (27/39, 69 %).

The majority of the patients was female (27/39, 69 %). There were some relatively young patients of 40 years or younger: a man who developed circulatory overload twice when undergoing therapeutic plasmapheresis; also nine women – four of whom developed the reaction after receiving a transfusion shortly after childbirth and one for nephrotic syndrome; two patients suffered from hemoglobinopathy. Circulatory overload in patients with renal failure or in post-partum patients was also observed in previous TRIP years. An increased risk is plausible in these situations. However, information about the total number of transfusions in these patient groups would be required to substantiate this. One of the patients developed circulatory overload following administration of autologous blood (see relevant chapter).

A number of reports of circulatory overload were initially thought to be a TRALI. The clinical distinction between circulatory overload and TRALI remains difficult, even when a chest X-ray is present. In the Expert Committee meeting those present recognised that the information accompanying reports does not always lead to in a clear decision about the nature (cause) of suspect symptoms. In general, a report is placed in the most suitable TRIP category, but a additional category can be added in the digital reporting form. Is “a bit” of circulatory overload an explanation for dyspnoea in a patient who (also) has another type of reaction? TRIP deems it important to verify that the diagnosis of circulatory overload was properly substantiated. The evidence could come from in the patient’s history / pathology, the clinical observations (including chest X-ray and fluid balance) and the patient’s response to starting or increasing diuretic therapy. *Case histories 3* describes three reports registered in this category. TRIP attemps to find a reasonable balance between asking additional questions to confirm a report while minimising the burden on reporting hospitals.

Case histories 3 – Transfusion-associated circulatory overload

TACO-1 54-year-old woman, “heart patient”, joint surgery
Administration of 2 RBCs. Two hours after start she developed temperature increase (38.5 ºC), cyanosis, increase in blood pressure from 124/70 to 180/80. Chest X-ray after transfusion: bilateral pulmonary oedema. appearances of cardiac asthma with blotchy consolidations in all lung fields, not present on previous X-rays. Comment in report: Sanquin was unable to confirm TRALI in serology. Reported as grade 3, probable.

Comment: Report probably OK. Information about the nature of the cardiac pathology and the response to therapy could be more convincing.

TACO-2 39-year-old male nephrology patient, therapeutic plasmapheresis
Headache, trembling and sweating; tendency to collapse; shortness of breath / dyspnoea; rigors. He was on diuretics because of hypertension. Halting the plasmapheresis was followed by recovery. Chest X-ray: appearances of circulatory overload. Plasmapheresis was restarted the following day. Reported as: grade 1, probable.

TACO-3 84-year-old woman, anemia due to malignancy
Half an hour after the start of 1 unit of RBCs she developed dyspnoea, vomiting, tachycardia, blood pressure increase from 129/69 to 170/110 (administration stopped), O2 saturation 98 %, bilateral wheezing. No chest X-ray performed. Blood group serology and CRP revealed no abnormalities. Report as grade 1, certain.

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: HPAantibodies and HPA typing of patient.

There were no reports of PTP in 2009. 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 leuko-depleted 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 2009. 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 on 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. Fortunately, TA-GVHD has never been reported in these patients.

Hemosiderosis

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

In 2009, two reports were received about poly-transfused patients who had been diagnosed with hemosiderosis. As in former annual reports, the reports were received from the same hospital. One of the reports describes a patient who received more than 35 RBC concentrates over six months and whose ferritin concentration

increased from normal to over 3500, without any infection that could have resulted in this increase.

Hemosiderosis was listed as an additional category in two other reports from different hospitals. In both cases the condition was already being treated. TRIP welcomes the reporting of this information, as many reports provide little or no information about the clinical condition of patients. Normally, the additional category is used to identify a reaction that is observed at that particular moment.

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).

There were 753 reports of new allo-antibody formation in the reporting year 2009. This makes it the largest reporting category (31.6 %) once again. The reports were received from 60 hospitals (20 % more than last year), which means that just under two thirds of the participating hospitals reported this category to TRIP.

There were 485 female patients and 267 male patients, with the gender not being reported in one case. The number of allo-antibodies found simultaneously during screening varied from one (615x) to six (1x). An overview of the most detected new antibodies, split according to age group and gender, is provided in *Table 9*. New antibodies that were detected less than 10 times in total are reported as 'other', these include anti-M (9), anti-Fyb (6), anti-Lea (6), anti-G (3), anti-Leb (2), anti-Cob, anti-I, anti-s, anti-Ytb, anti-Jsa, anti-Csa and anti-f (all 1). For 27 patients, a new antibody was detected several times in 2009 and this was reported to TRIP. There were three reports – by two different hospitals – of the same new antibody in the same patient. Following the standard TRIP procedures to remove the doubles and further inquiries by TRIP, the antibody was included in the count once only. There were two cases of passive transfer of anti-A by administration of platelets from blood group O (not included in the table).

Table 9 Newly formed antibodies and age of the patient

Type of antibody	Number*												
	Total			0 – 12 years		13 – 20 years		21 – 40 years		41 – 60 years		Older than 60 years	
		269 M	492 F	0 M	2 F	2 M	5 F	10 M	43 F	47 M	99 F	206 M	339 F
anti-E*	280	101	178	-	-	2	2	7	15	15	31	77	130
anti-K	171	59	112	-	-	-	-	1	41	8	35	40	73
anti-Fya*	84	37	47	-	-	-	-	1	9	7	7	29	31
anti-Jka*	71	31	40	-	-	-	1	-	3	5	11	26	25
anti-c	58	17	41	-	-	1	-	-	7	2	4	14	30
anti-C*	41	15	26	-	-	-	1	-	2	1	4	14	19
anti-Wra	33	8	25	-	-	-	-	1	1	1	5	6	19
anti-D	31	15	16	-	-	-	-	-	3	4	4	11	9
anti-CW	24	7	17	-	1	-	1	1	1	1	3	5	11
anti-S*	22	6	16	-	-	-	1	-	2	-	2	6	11
anti-Jkb*	22	2	20	-	-	-	1	-	3	-	3	2	13
anti-Lua	17	7	10	-	1	-	-	-	1	2	4	5	4
anti-e	13	8	5	-	-	-	-	-	-	1	1	7	4
anti-Kpa	13	-	13	-	-	-	-	-	1	-	2	-	10
other	50	14	36	-	-	-	-	2	2	2	4	10	30
Total	904	318	585	-	2	3	7	12	53	57	117	246	406

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

There were 696 reports of a RBC concentrate being the last administered blood components that could have triggered the new antibody formation, 21 reports of

administration of platelets, 25 cases of a combination of blood components being administered (including RBCs) and 10 reports that did not state the type of blood components administered. The interval between administration and detection could not be determined in 34 reports, because the date of administration (25x) and/or the date of detection (13x) is missing. For the other reports, the interval varied from less than 24 hours (1x) to 41 years (1x), with 120 reports having an interval longer than two years. The interval was shorter than six months for over 66 % of the reports.

For 24 reports of new allo-antibody formation, received from 12 different hospitals this year, an additional category was mentioned: 1x AHTR, 19x DHTR and 4x other reaction. The hemolytic TRs were all observed after administration of one or more RBC concentrates. In 19 patients, there had been at least two transfusion episodes prior to the new antibody formation. In one reported case of DHTR, it was reported that an elderly female patient had no history of transfusions and also had not experienced any pregnancies. After an interval of 55 days, three allo-antibodies (anti-C, anti-K and anti-Wra) and one auto-anti-e were detected. In three other reports with sub-category DHTR (two involving a female patient), the answer “unknown” was given to the question “transfusion in the past”. The antibodies involved here are: anti-f (detected after an interval of 6 days in a patient with known anti-Fya), anti-Jka (interval 47 days) and anti-E (interval 23 days). An overview of the antibodies in patients with additional transfusion reactions is provided in *Table 10*. Multiple antibodies were demonstrated in seven cases. A more extensive discussion of the reactions has been included in the relevant chapters.

Table 10 – New antibodies in patients who also exhibited an additional reaction

New allo-antibody Specificity of antibody	Additional category AHTR	Additional category DHTR	Additional category Other reaction
Anti-D anti-E anti-K		1	
Anti-C anti-K anti-Wra		1	
Anti-c		1	
Anti-c anti-E		1	
Anti-E		6	1
Anti-E anti-K		1	
Anti-E anti-CW		1	
Anti-f		1	
Anti-Jka		3	
Anti-Jka anti-Fya		1	
Anti-Jkb		1	
Anti-M anti-Lea		1	
Anti-Wra	1		1
HLA antibody			1
Anti-E anti-S			1

New allo-antibody formation was reported as an additional category for two reports of AHTR and six reports of DHTR. Several new antibodies were detected in four cases. *Table 11* provides an overview of these new antibodies. There had been two or more transfusion episodes prior to the reaction in seven patients and for one patient it was not known whether a previous transfusion had taken place. The interval varied from < 24 hours in AHTR to between 3.5 days (80 hours) and 18 days for DHTR.

Table 11 Antibodies detected after a hemolytic transfusion reaction

AHTR	DHTR	New allo-antibody
1		Anti-Jkb anti-s
1		Anti-K
	1	Anti-c anti-Jka anti-E
	1	Anti-Cw anti-Jkb anti-S
	1	Anti-E anti-s anti-Fya
	1	Anti-Fya
	1	Anti-Jka
	1	Anti-E

There were six reports of incorrect blood component transfused where there was new allo-antibody formation. A DHTR was observed once following administration of an E positive RBC concentrate to a patient with a weakly positive anti-E in the pre-transfusion screening. In the second case, a unit of Fya negative, Rh D positive RBCs had to be administered in an emergency situation to an Rh D negative patient with a strong anti-Fya, resulting in anti-D formation. Formation of anti-Cw was detected after failure to follow preventive transfusion advice (C-, D-, E- and K-neg). Failing to type or incorrectly typing the antibody after a positive screening resulted in the administration of an incorrect blood component on two occasions. Lack of clarity in the working instructions regarding the selection of K negative components for women of childbearing age resulted in a report of new antibody formation, which was later changed to a report of incorrect blood component transfused with sub-category new antibody formation.

Other transfusion reaction

Transfusion reaction that does not fit into the categories above.

The number of reports of other transfusion reaction increased further in 2009 to 133 in comparison to approximately 60 in 2004 to 2007 and 101 in 2008. Fifteen reports are of severity grade 2 or higher. This group is used for reports that do not fit into the more specific TRIP categories. The presence of clusters of reports with similar symptoms is examined each year. What has caused the increase compared to previous years?

Table 12 shows which symptoms were reported in the reports in this category (tachycardia is not scored separately, but was often listed with temperature increase, chills/rigors, hypertension or hypotension). The distribution of the type of blood components is presented alongside.

Table 12 Symptoms recorded with other reactions in 2009

Symptom	Number of reports	Number of serious reports	Blood components			
			EC	TC	Plasma	O/C*
Rise in temperature	54	6	42	11	-	1
Chills/rigors	36	5	23	11	-	2
Rise in temperature and/or chills/rigors	66	9	50	14	-	2
Dyspnoea	42	8	26	11	2	3
Decrease in blood pressure	45	4	36	1	3	5
Chest pain/pressure or arrhythmia	12	1	8	4	-	-
Skin reaction	7	-	2	4	-	1
Nausea/vomiting/diarrhoea	15	3	10	3	-	2
Increase in blood pressure	18	3	14	3	-	1
Non-specific feeling 'unwell'	10	1	10	-	-	-
Bronchospasm	6	-	3	1	-	2
Lumbago	4	2	3	1	-	-
Other reaction (all reports)	131	17	97	24	3	8

* other blood components, a combination of types of blood components or blood component not sspecified

Firstly, there is the cluster of reports with dyspnoea being the main complaint, but not consistent with the definition of TRALI or circulatory overload, for example due to absence of a chest X-ray or due to the interval being too long. Eight of these reports were initially thought to be a TRALI. For the 42 reports in which dyspnoea or hypoxia were reported, 27 cases also reported an increase in temperature and/or shivering. In some of these cases other symptoms were also reported and formed the reason for this reaction no longer fitting in a standard category (lumbago in four reports, increase in blood pressure in five reports, one skin reaction and two cases of nausea / vomiting). The combination of dyspnoea and an increase in temperature without other symptoms made up a total of 15 reports in the category of other reaction. We also know from the reports of NHTR and mild non-hemolytic febrile reaction that the combination with dyspnoea is sometimes registered under this category (n = 37), as well as under anaphylactic reaction (36) and other allergic reaction (2). Due to the absence of specific laboratory tests that can provide positive proof of a NHTR or an allergic transfusion reaction – despite the fixed definitions based on clinical criteria – it is sometimes difficult to decide the category in which a report belongs.

Secondly, there is a cluster of 22 reports (2008: 17) with hypotension as the only or main feature, associated on one occasion with a strange sensation and on another occasion with nausea and vomiting. Two of these reports were serious reactions (1x grade 2, 1x grade 3). A number of international hemovigilance systems place hypotensive reaction in a separate category. For 23 further reports of other reaction, a decrease in blood pressure was one of several symptoms listed.

The TRIP 2008 report referred to the symptom of increased blood pressure: "Three reports mention isolated increases in blood pressure and in five these are combined with fever and/or chills and sometimes other features, but these do not suggest circulatory overload." In 2009 again there are a number of reports in which an increase in blood pressure is mentioned. The extent of the increase in blood pressure

is not mentioned in all cases. More specific information is required to be able to decide in future whether this is a phenomenon that requires further study.

For reports that are hard to diagnose and particularly in the category of other transfusion reactions, information about the clinical situation, the patient's disease and results of additional tests are essential to evaluate the nature of a reaction. Increased awareness of transfusion reactions among clinical staff is desirable.

As in previous years, an additional category of other reaction sometimes indicates that a platelet transfusion produced insufficient yield. This was the case for six reports. The same symptom is reported in the explanatory text of 11 other reports. It would be useful to agree upon criteria for this and to encourage routinely mentioning the yield.

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.

There was one report in 2009 in the category viral contamination of blood component. As from the autumn of 2008, Sanquin tests all donations in mini pools using a combined NAT test for HIV, HCV and HBV. NAT tests for HCV and HIV were already in use. The new tests aim to increase the safety particularly in relation to hepatitis B. In addition to slightly earlier detection of a prior infection, people with a so-called occult hepatitis B (OBI) can also be traced, where following an infection that has (almost) cleared and with a negative test for HbsAg a low titre of HBV DNA is sometimes detected but not detectable on other occasions. The report in question pertains to a regular donor who showed a positive result in the HBV NAT. One previous recipient was found to have experienced a hepatitis B infection (imputability probable, as it is not possible to perform research into the genetic identity of the virus). The GP of a second, geriatric recipient with no relevant symptoms and who has been discharged from hospital treatment, had been informed.

Two reports were received in 2009 in the category post-transfusion viral infection. One report relates to a cytomegalovirus infection (confirmed by PCR testing) in an immuno-compromised adult transfusion recipient with extensive transfusion history. The imputability is listed as unlikely. The second report relates to an acute hepatitis B infection, 11 weeks after the patient was transfused with a RBC concentrate after surgery. Further investigation by Sanquin reveals that the imputability is excluded. The patient's history revealed no other sources of infection; findings of an investigation by the hospital hygiene department are not known to TRIP.

Table 13 shows the number of reports from 2002 up to and including 2009 per type of viral infection. It can be seen that a need to perform further investigation of one or more donors or patients arises every year. The number of probable or confirmed

cases of transmission of a viral infection through blood transfusion is extremely low and limited to 3 cases of hepatitis B.

Table 13 Viral reports to TRIP, 2002 – 2009

Infection	Post-transfusion viral infection*	Number probable or certain	Number possible	Viral contamination of blood component or look-back, no infection	Comment
Hepatitis B	13	3[#]	1	9	[#]Donations in 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	5	0	1	0	
HAV	1	0	0	0	Report in 2006, Tf in 2003, no investigation by Sanquin
HIV	1	0	1[§]	2	[§]Report from 2003, not confirmed

* Prior to 2008: Viral contamination

Bacterial problems in relation to blood transfusion

In 2009, we worked for the second year with the new definitions and with the categories of bacterial contamination of a blood component' and 'post-transfusion bacteremia/sepsis'. They have been summarised in the table below (*Table 14*).

Table 14 – Use of the categories for (suspected) bacterial contamination of a blood component

Category		
Post-transfusion bacteremia/sepsis	Required: positive blood culture after transfusion, not present before. If blood culture was positive before transfusion, select a different category.	*With consistent clinical image. *If positive culture by hospital (or Sanquin) on unit with the same bacteria, high imputability (probable/certain if identical strains)
Bacterial contamination of a blood component	(A) Detected by Sanquin, report bacteria found.	Report any clinical symptoms (in that case: select sub-category, list severity and imputability) and result of patient blood culture or list 'not performed'.
Bacterial contamination of a blood component	(B) Detected by hospital	Report as sub-category if symptoms are absent

With this modification, TRIP aims to achieve better distinction between cases where patient symptoms formed the reason for performing cultures and cases where a positive bacterial culture result was found (by Sanquin or the hospital), but where there may not be any relationship to patient symptoms or a positive blood culture result. The reports per individual category are discussed in the paragraphs below. Use of the amended categories has been almost seamless in this second year.

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 2009, 22 reports were registered in the category bacterial contamination of a blood component and the category was registered as an additional category on one occasion. The majority of the reports (n=19, plus four 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 an investigation into a (possible) transfusion reaction. The findings are summarised in *Table 15A* (platelets) and *15B* (RBCs and plasma).

Table 15A Bacteriological contamination of platelets

Sanquin bacteriological screening	Hospital culture result on unit*	Patient blood culture*	Reporting category (if other than bacterial contamination of blood component) or symptoms*
Negative	Staph. epidermidis	Staph. epidermidis	Post-transfusion bacteremia/sepsis (grade 2 prob., sub-cat); increased temp / rigors
Propioni bact. (n=10)	-	- or negative	- 1x: no blood culture; pseudomonas in sputum culture and possible catheter tip culture; 3w prophylactic AB
Staph. epidermidis	-	-	-
Peptococci	-	-	-
Corynebacterium urealyticum	-	-	-
(Aerobic) Kocuria cristinea	-	negative	Temp. increase >1<2ºC after 20 hours, recovered after AB
Gram neg. rods	-	-	-
Streptococcus saccharolyticus	-	negative	-
Gram pos. rods	-	Staphylococcus aureus	Post-transfusion bacteremia/sepsis (sub-cat.), no symptoms, imputability unlikely
Micrococcus luteus	-	-	-
Micrococcus luteus	-	negative	NHTR (grade 1 poss.) (patient already septic)
No report	Staphylococcus epidermidis	negative	Other reaction (grade 1 poss.): shortness of breath, increased temp.
No report	Staphylococcus epidermidis (in regional lab)	-	Other reaction (grade 1 poss.): nausea, shortness of breath (patient with cardiac decompensation)
No report	-	Staph. aureus	Other allergic reaction (grade 1, poss.)
No report	Coagulase negative staphylococcus	-	Other allergic reaction (grade 1, poss.)

* - : no culture performed or no additional-category

Table 15B Bacteriological contamination of RBCs or plasma

Sanquin bacteriological screening	Hospital culture result on unit*	Patient blood culture*	Reporting category (if other than bacterial contamination of blood component) or symptoms*	Type of blood component
Bacteroides from fragilis group	-	-	-	RBCs
Propioni bact.	-	-	Mild NHFR (grade 1, poss.)	RBCs
Not confirmed	-	-	Positive bacterial screen	RBCs
None	enterococcus species, coagulase negative staphylococcus	negative	NHTR (grade 1, poss.) Patient under dialysis and AB, had previously had fever spikes, but no pos. blood cultures	RBCs
N/A	Staph. epidermidis	From line: negative	Rash	Plasma

The tables show that of the whole series, only one report (listed first) was associated with suspicious symptomsas well as with corresponding findings in cultures of both the platelet unit and the patient's blood (S. epidermidis), however there was no investigation for or proof of identical strains.

Sanquin provided an overview of the findings of the bacteriological screening of all platelet concentrates. A positive result was obtained 325 times (21 apheresis platelet units, 307 pooled products). At least 1 component had been released for more than half of these reports (n=170, 162 concerning pools) and a recall was performed. At least 1 component had already been administered in 98 of these reports (93 pools): 88 platelet concentrates and 20 RBC concentrates. No serious adverse reactions occurred.

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 2009, we received 50 reports in the category post-transfusion bacteremia/sepsis (2008: 37). The administered blood components were RBCs 47 times, twice platelets and once a combination of platelets and RBCs. 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 nearly all cases, the observed clinical symptoms involved temperature increase and/or rigors, associated in several cases with drop in blood pressure or dyspnoea. One case of general malaise is described (imputability unlikely); two cases of localised urticaria were recorded, which are unlikely to be related to the positive blood culture (1x coagulase negative staphylococcus, 1x S. aureus; administered

component RBC and a platelet concentrate respectively; in the latter case the blood service bacteriological screening had not flagged up a report).

A negative culture result was obtained from the unit in 33 cases (tubing had to be used in three cases), the unit was not cultured in 13 cases and information about this is missing in four cases. Thus, no case of post-transfusion bacteremia/sepsis could be ascribed with any certainty to a bacterially contaminated blood component.

In addition to the above-mentioned 50 reports, post-transfusion bacteremia/sepsis was also registered as an additional category in a total of six other transfusion reactions (4x febrile reaction with RBC, 1x other allergic reaction with platelet concentrate, 1x circulatory overload following five RBCs and two FFP). In these cases it is also unlikely that the administered units formed the source of the bacterial growth that was found, as the cultures on the unit were negative and there was no report of a positive bacteriological screening. Although a relationship to the clinical symptoms could be plausible for the four febrile reactions; the reporters of three of these cases deemed other causes to be more likely and therefore preferred to use the additional category. There was only one case in which the same type of bacteria – Staphyococcus epidermidis – was found in the patient's blood culture. The bacterial screening by Sanquin remained negative and strain analysis was not performed by the hospital.

In addition, as in 2008, TRIP has added a certain code to the report in the office database – based on the available information – if the case involved a transfusion reaction in a patient with a pre-existent bacterial infection. The 2008 report raised the question of the effects that transfusion and bacterial contamination/infection can have on each other. 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 (particularly an iron-containing) blood components such as a RBC concentrate can activate a bacterial infection. An analysis of the relative contributions of the types of blood components was again performed for the 2009 reports. *Table 16* shows the distribution of the type of blood component for reports of NHTR, according to notification of a pre-existent infection. As in 2008, the available data from the reports provide insufficient grounds for any conclusions.

Table 16 Pre-existent infection and type of blood component with reports of NHTR

	RBCs	Platelets	Plasma	RBCs with other bc	Other bc
Infection present	53 88.3 %	5 8.3 %	0 0 %	2 3.3 %	0 0 %
Infection unknown	221 77.0 %	47 16.4 %	2 0.7 %	8 2.8 %	9 3.1 %
No diagnosis information	211 90.2 %	18 7.7 %	0 0 %	3 1.3 %	2 0.9 %
Total	485 83.5 %	70 12.0 %	2 0.3 %	13 2.2 %	11 1.9 %

Concluding discussion on bacterial reports

From the above discussion we can conclude that the new definitions were used more effectively in 2009 than in 2008. Out of 55 reports of post-transfusion bacteremia and 43 reports of bacterial contamination of a blood component as main category or

additional category, only one case reports clinical symptoms with a likely relationship to microbiologically confirmed bacterial contamination of a blood component. In the reports of manufacturer look-back (see the relevant section in chapter 3.3) with three reports relating to Q fever, no proof was found for transmission of infection by blood transfusion.

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. TRIP requests institutions to report these cases, even if there are no adverse consequences for the patient.

There were 60 reports in this category in 2009. The number of incorrect blood components transfused for which clinical symptoms were observed this year was 13; an overview of these reactions is provided in *Table 17*. A more detailed description of some of these reports has been included at the end of this paragraph (*Case histories 4)*.

Table 17 Clinical symptoms following transfusion of an incorrect blood component

Nature of reaction	Total	Component	Severity grade				
			0	1	2	3	4
Acute hemolytic transfusion reaction	7	7x RBCs		2	5		
Delayed hemolytic transfusion reaction	1	RBCs		1			
New antibody formation	4	4x RBCs	2	2			
Other reaction	1	RBCs		1			

As in 2008, 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 group 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 according to 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 below (*Figure 14)*. If the first error did not occur in the reporting hospital but elsewhere, the 1st 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). An overview of the analysis according to risk and 1st error is provided in *Table 18*. The description of these categories can be found on www.tripnet.nl, hemovigilance page. For two of the 60 reports of incorrect blood component transfused, there was a calculated risk in which Rh D negative female patients received Rh D positive blood components in emergency situations. In one of these cases a woman of childbearing age received platelets, anti-D immunoglobulin was administered and follow-up five months later showed no antibodies. The other case involved massive blood loss in a 50 year-old woman with strong Fya antibodies. She received 4 units of Rh D positive RBC concentrates (a total of 25 RBC concentrates, 24 plasma units and 4 platelet concentrates) that were negative for the Fya antigen. Weak anti-D formation was detected after five days. As both cases involved the conscious selection of a blood component that did not entirely meet the normal

requirements for an apporptiate component for the relevant patient, these cases are not included in *Table 18*.

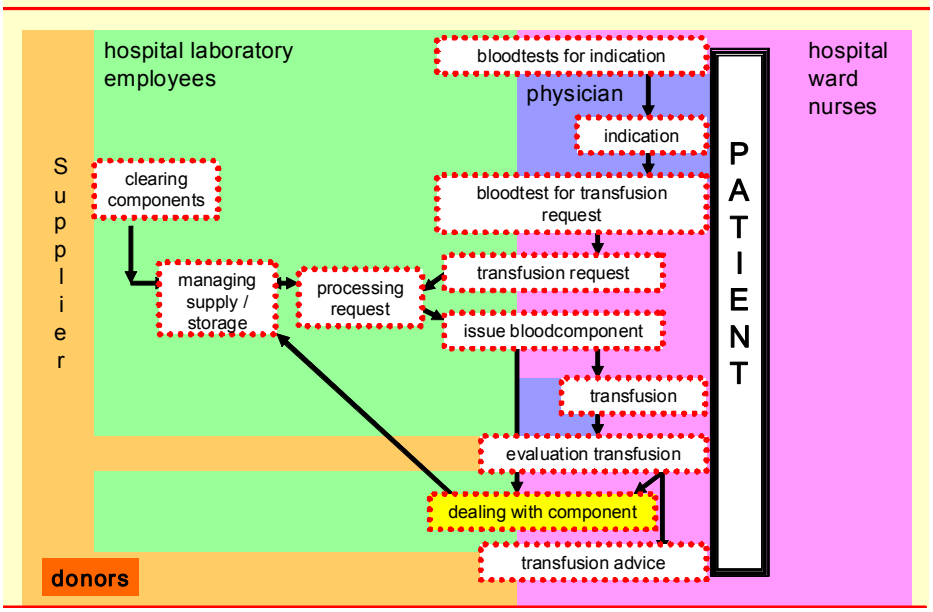

Figure 14 The transfusion chain

Table 18 Nature of risk for the patient and 1st errors for incorrect blood component transfused in 2009

Risk		Step in the chain where 1st error occurred		Type of 1st error	
ABO	30	Tf chain outside hospital	1	Not evaluated	
		Research for indication	1	Identification	
		Request	1	Identification	
		Processing of request	5	Administration	2
				Selection	2
				Other	1
		Release	4	Identification	4
		Transfusion	17	Identification	17
		Unknown	1	Unknown	
Irregular antibody	10	Tf chain outside hospital	1	Not evaluated	
		Request	1	Communication	
		Processing of request	8	Lab procedure	3
				Evaluation	2
				Selection	3
TA-GvHD in risk group	4	Request	3	Communication	3
		Processing of request	1	Communication	
Prevention policy Irras: 7 B19: 3 After Tx: 1	11	Research for Tf request	1	Communication	
		Processing of request	10	Evaluation	1
				Lab procedure	1
				Selection	8
Contamination	1	Stock management/storage	1	Other	
Coagulation	2	Request	1	Administration	
		Unknown	1	Administration	

For the reports of incorrect blood component transfused, 30 (50 %) were evaluated as ABO risk, the components that were administered for the incidents with ABO risk were RBCs 25x, platelets twice and plasma three times.

For the 30 incorrect blood components administered with ABO incompatibility risk, it happened that the unit was actually ABO compatible in 16 transfusions. This involved an RBC concentrate 13 times, a platelet concentrate twice (once when a blood group identical platelet concentrate was erroneously selected and administered to a patient whose blood group had only been determined once and in the other case a platelet concentrate with blood group A negative was given to a patient with blood group A positive) and plasma once (A pos plasma administered to an O pos patient). Despite the ABO compatibility, AHTR occurred in one case in a patient with several irregular antibodies.

In one case, in which O plasma was administered instead of AB plasma in an emergency situation, it was not stated whether the plasma was ABO compatible by coincidence. Seven reactions were reported for 13 ABO incompatible transfusions: six AHTR and one other reaction. The patient was given an RBC concentrate in all these cases. On five occasions this was a patient with blood group O (4x Rh D pos and 1 Rh D neg), with donor blood with blood group A pos being administered five times. Twice a patient with blood group A pos received donor blood with blood group B pos. No reactions were observed in the other six ABO incompatible transfusions. As was the case last year, there were special circumstances in the incompatible transfusions where no transfusion reaction was observed. There was one case of incompatible plasma (O neg) given to a patient (A pos) with acute major blood loss from an abdominal aortic aneurysm. In another case of acute major blood loss, a small amount of A pos RBC concentrate was given to an O pos patient. In a third case of acute major blood loss due to aneurysm, six A pos RBC concentrates were transfused to an O pos patient and no symptoms of hemolysis were observed. In the other three cases the transfusion did not actually take place, twice because the incorrect blood transfusion was detected and stopped almost immediately after starting transfusion (1x A neg and 1x A pos RBC concentrate to O pos patients) and in the other case because the person administering the blood forgot to open the tap (B pos RBC concentrate to A pos patient). These last incidents were registered as incorrect blood component transfused, because the blood component was hung on the drip stand and spiked, so it cannot be excluded that some donor RBCs did enter the recipient's blood.

Two reactions were reported in 10 reports with irregular antibody incompatibility risk (17 %). A DHTR was reported after administration of two E pos RBC concentrates to a patient with weakly positive irregular antibody screening which had been erroneously attributed to non-specific cold antibodies without anti-E being ruled out. On another occasion, 2 RBC concentrates with negative crossmatch were administered to a patient who had a positive irregular antibody screening, but for whom the cell panel did not show a clear pattern. The anti-Fya was only typed afterwards; one of the administered RBC concentrates happened to be Fya neg and the Fya typing of the other unit was not known.

On two occasions, failure to follow the preventive component selection policy for a recipient group formed the reason for reporting an additional category. New allo-antibody formation occurred after failure to follow preventive transfusion advice in a poly-transfused patient and anti-K was detected after administration of a ccee and K pos RBC concentrate to a woman of childbearing age.

For the 30 reports of incorrect blood component transfused with ABO risk, there were 23 cases of identification error as a first error, with this identification error taking place in the last check (bedside check) before administration of the blood component 17 times. In two cases a selection error resulted in a potential ABO risk. The other reports of incorrect blood component transfused (28) this year were mainly selection (11) and communication (6) errors. An overview of the type of risk per first error is provided in *Figure 15*.

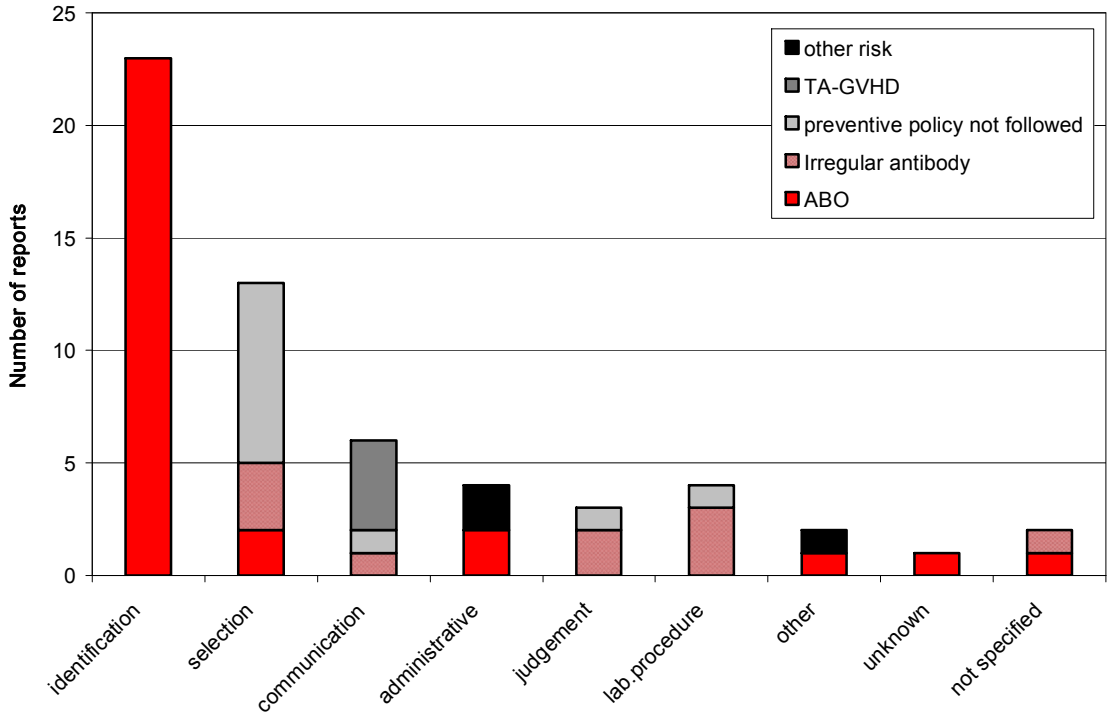

Figure 15 The type of risk per 1st error

Case histories 4 Incorrect blood component transfused

IBCT-1 (preventive policy after transplantation, processing of request, component selection)
Patient X (O neg) received an ABO incompatible donor kidney. Plasma was administered during the transplantation. The transfusion advice is AB plasma due to the ABO incompatible transplantation. However, O neg plasma was selected for patient X and duly administered. The nephrologist discovered afterwards that the transfusion advice had not been not followed.

IBCT-2 (Infection risk, stock management/storage, other)
The blood transfusion laboratory received a recall from Sanquin for RBCs due to a positive bacteriological screening of the associated platelet pool. However, no action was taken until six days later. By that time the RBC concentrate had been administered to a patient. Fortunately, the patient did not suffer any harmful clinical consequences.

IBCT-3 (ABO risk, transfusion, identification)
Patient X and patient Y, both on ward A, require transfusion. Nurse 1 cares for patient X and nurse 2 cares for patient Y. The nurses are not aware that there are two patients on the ward scheduled to receive RBC transfusion that afternoon. The

RBCs for patient X are delivered to ward A by a biomedical scientist and someone signs for receipt. Approximately 1 hour later, the same biomedical scientist delivers the RBCs for patient Y to ward A. Upon delivery, the comment is made that patient Y has already received blood. The technician becomes suspicious and confirms that the blood for patient X has been given to patient Y.

IBCT-4 (ABO risk, issue, identification)
Both the nursing ward and the laboratory are extremely busy when blood for patient X needs to be delivered to the ward by a biomedical scientist. Only the patient's name is used for issue of the blood to the nurse, the date of birth and patient number are not checked. Upon returning to the lab, the technician realises that he has forgotten to perform complete identification. It turns out that the RBC concentrate for patient X2 instead of patient X1 was taken to the ward.

IBCT-5 (ABO risk, request, identification)
Patient Q (blood group O pos) and patient R (blood group A pos) are in the same room and blood has been requested for both. The blood for patient Q has to be collected early in the evening. This is done by the night manager, who is given a patient label with patient data by the nurse. Half an hour after starting the transfusion, patient Q develops AHTR with chills, stomach pain and diarrhoea. The transfusion is stopped and checks reveal that the unit was intended for patient R instead of patient Q. The nurse gave the wrong patient label to the night manager, resulting in blood for patient R being requested from and released by the laboratory.

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.

There is a marked increase in the number of reports of other incidents in 2009 (110) compared to 2008 (83). Symptoms were observed in the patient in seven of these reports. There were also three reports of transfusion reactions (NHTR, new antibody formation and other reaction once each) for which the additional category of other incident was reported. An overview is provided in *Table 19* and some examples are described in *Case histories 5*. A short description is given for a number of other incidents in which patients' symptoms also played a role. 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 19 Clinical symptoms during or after other incident

Nature of reaction	Total	Product	Severity grade				
			0	1	2	3	4
Circulatory overload	1	RBCs			1		
Non-hemolytic transfusion reaction	3	2x RBCs		2			
		1x platelets		1			
Mild non-hemolytic febrile reaction	3	3x RBCs		3			
Other reaction	2	1x RBCs		1			
		1x platelets		1			
New antibody formation	1	RBCs	1				

The products involved in these other incidents were RBCs (78x), platelets (6x), plasma (11x), combination of RBCs and plasma (1x) and autologous drain blood (12x). In two reports, the type of product involved in the incident was not listed. It is noteworthy that the ratio between the reported types of allogeneic products corresponds reasonably well to the ratio between total numbers of administered allogeneic blood components, but that there was a disproportionate number of other incidents for autologous blood. The 12 other incidents with autologous blood are discussed in the section on blood management techniques. A short summary is provided below of the important groups of other incidents that can be distinguished.

A particularly large number of reports (51) of other incidents involved cases in which the product became unsuitable for administration and where this was discovered before the start of the transfusion. *Figure 16* shows the nature of the first error for these reports and the step in the chain where the error was made. In a number of these events, it was unavoidable that the blood component became unusable, e.g. puncturing of the bag when attaching to the infusion. However, more than 70 % of these reports concern incidents in which allogeneic blood components were needlessly lost. Often this relates to the blood component not being returned to the laboratory in a timely manner after a transfusion is cancelled or postponed. Remarkably, there are also several reports of forgetting to administer a blood component present on the ward for the patient. On one occasion, a power cut due to lightning resulted in the loss of 30 RBC concentrates, because the blood storage cupboard did not sound an alarm. Comparison of the blood use in the eight hospitals that submitted reports of events of avoidable loss of blood component to the number of products in the reports, shows that it involves 0.14 % of the RBC concentrates and 0.16 % of the plasma units.

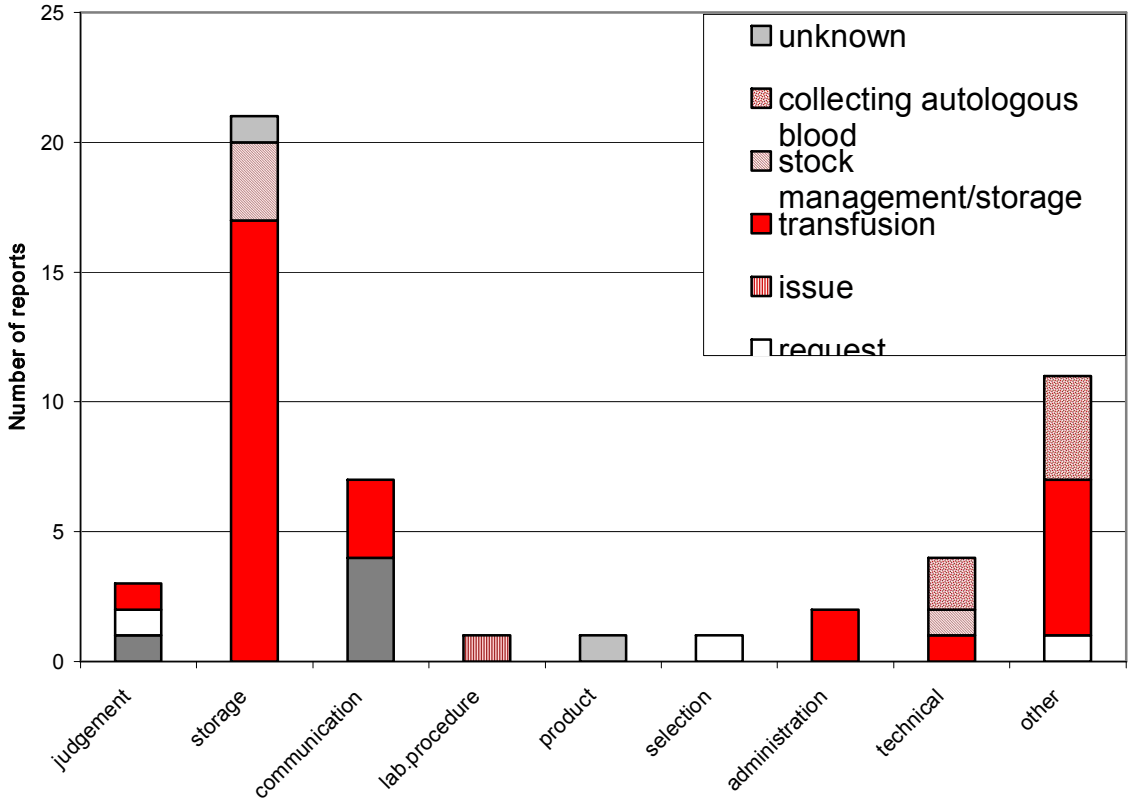

Figure 16 Type of 1st error in blood components that became unsuitable for administration

Donor and product errors resulted in a total of seven reports. This included three reports of donors who developed flu, fever or shingles shortly after donation. Recall of products by Sanquin is not considered here, but is discussed in the chapter on infectious transfusion complications under positive bacterial screening or bacterial contamination of a blood component. Usually hospitals only report donor and product errors in the category other incident if the relevant product has been issued, with or without subsequent transfusion. A number of reports pertain to plasma where the bag was discovered to have a leak after issue and thawing on the ward, or in which the plasma contained particulate matter.

There were three other incidents reported in which someone forgot to order blood for a scheduled procedure or where an urgent request for blood components was not processed as urgent, resulting in a delay in patient treatment. Leakage of the bag that was only discovered after starting the transfusion was also reported three times. There were 16 reports of problems with the infusion resulting in the blood not transfusing properly, wrong setting of the infusion speed or removal of the infusion system by the patient during transfusion.

There were only four reports of request of a blood component based on incorrect Hb result, three where blood was collected from the arm where infusion fluids were also being administered and one where the blood for Hb determination was collected from another patient. This resulted in three cases of the patient being given an unnecessary blood transfusion, with a mild NHFR being observed in one case. On one occasion it remained unknown why blood was administered to a patient who had no indication for transfusion and this patient also suffered a mild NHFR. A blood component was also administered in error to a patient for whom blood was ordered according to protocol due to surgery and who received a transfusion without the doctor having ordered it. There were two reports of a request for blood for someone other than the intended patient that was discovered in time.

Case histories 5 Other incidents

OI-1 Other reaction with additional category Other incident
A 42-year-old woman received a platelet concentrate due to pancytopenia. The patient felt unwell a few minutes after the start of the transfusion, she felt warm and developed palpitations. An increase in blood pressure was observed, but her heart rate and temperature remained unchanged. Despite pre-medication having been ordered, clemastine had not been administered.

OI-2 New allo-antibody formation with additional category Other incident
A female patient aged 81 has a positive screening for irregular antibodies. Anti-Jk(a) is detected. The unit that was administered 16 days previously is found to be Jk(a) positive. However, it is not certain that the unit was actually administered because the transfusion report from the ward was not received by the laboratory.

OI-3 NHTR with sub-category Other incident
Patient X, male, aged 75, received RBCs because of to chronic symptomatic anemia resulting from metastasised bladder cancer. Whilst the 2nd unit was running, patient X developed chills and a temperature increase from 37.5 ºC to 38.3 ºC was observed. It was also noted that part of the RBC concentrate (approx. 100 ml) has tissued, resulting in a large hematoma. A new infusion was started and a further 2 RBC concentrates were administered without further increase in temperature.

OI-4 (Transfusion, communication)

The blood for patient A was collected by nurse 1, but not connected immediately for infusion. Nurse 1 neglects to inform nurse 2 that the transfusion for patient A still needs to be started. It is discovered several hours later that the blood is still on the ward. The blood was needlessly lost as a result.

OI-5 (Request, selection)
Platelets were requested (platelet count 157) for patient Y, a 63-year-old man with liver function abnormalities and rectal blood loss. The platelet concentrate is ordered from the blood service by the laboratory without further inquiry and will be delivered a few hours later. Over 2 hours after the request, the nursing ward contacts the laboratory to ask whether the plasma has thawed yet. It is then discovered that the incorrect blood component has been entered on the request form, as the patient needs plasma to correct abnormalities in the clotting factors. Unfortunately, the platelet concentrate remained unused and reached its expiry date after 4 days.

OI-6 (Transfusion, administration)
Patient Z, male, aged 47, has chronic pancreatitis and nutritional deficiencies. Transfusion is required due to hematemesis. The RBC concentrate is collected from the blood transfusion laboratory at 20:30 and then attached to the infusion standard on the nursing ward. The RBC concentrate is returned to the laboratory at 00:30, but the bag has not been sealed. The unit is not administered, even though this was permitted according to hospital rules (permitted administration period of max. 6 hours after release). The blood component was needlessly lost.

OI-7 (Issue, lab procedure)
The blood transfusion laboratory issues 2 RBC concentrates for patient B at 16:00. It is not an urgent situation. A febrile reaction occurs during administration of the 1st RBC concentrate. The temperature before the start of the transfusion at 18:00 was 37.9 ºC and a temperature of 39.6 ºC was measured at 20:30. The transfusion was stopped at 21:00 because the temperature continued to increase (40.9 ºC). By 22:00 the transfusion of the second RBC concentrate had not started and the 2nd RBC concentrate became unusable because the maximum time after issue had been exceeded.

OI-8 (Transfusion, administration) additional category Circulatory overload
A male patient aged 81, with a history of cardiac problems, received 2 RBC concentrates in rapid succession. A mild NHFR was observed after administration of the 1st RBC concentrate at 18:45. The 2nd RBC concentrate was started at 20:45. Following administration of the 2nd RBC concentrate, the patient became increasingly short of breath, blood pressure increased from 133/77 to 150/90 and heart rate increased from 75 to 95. Crepitations were noted over the lungs. Furosemide was administered intravenously. The infusion time for the RBC concentrates was incorrectly set at 1 hour, because staff failed to take the man’s cardiac history into consideration.

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.
Please indicate where the error arose, any further errors or failed checks, and how the error was discovered.

In comparison to the previous reporting year, there were over 30 % more miss incidents (72) reported in 2009 by 16 hospitals, varying from one to 10 reports, a marked difference from 2008 when nearly half of the reports (24 out of 53) in this category were received from one hospital. The first error in over 75 % of the cases was made in the steps of transfusion request (12) or pretransfusion testing (42) and 41 of these 54 errors involved an error in identification of the patient, blood sample and/or request form. In 19 cases, blood group discrepancy was the reason that an identification error was discovered in a timely manner.

Checks and vigilance by employees of the blood transfusion laboratory were responsible for preventing more serious incidents in the majority of these near accidents. However, there appears to be an increase in the number of reported near misses (19 %) in which an error was discovered by nurses or other staff from clinical areas by checking at issue or checking prior to transfusion on the ward or in the operating room. This could be related to the arising of an improved reporting culture in hospital departments. Two of these 14 reports also indicated that training about blood transfusion had taken place recently.

An overview of the type of errors in near accidents is provided in *Table 20*. In the table, the reports are categorised according to the type of error that was made first with respect to 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 employees from the TRIP Office based on the description of the incident. The majority of the errors were discovered due to a safety procedure (66 %), but as was the case in 2008, a significant number of the near misses involved an error that was not detected by the planned safety measures (20 = 28 %). Only four reports did not describe how the errors were discovered.

As was the case for reports of incorrect blood component transfused, there was a case of calculated risk which was reported as a near accident. This was an emergency situation during a caesarean section in which O neg RBC concentrates were issued for an O neg patient with a positive irregular antibody screening, with a pattern consistent with anti-D. However, anti-Le(a) was found on specificity determination. The RBC concentrates were returned and replaced by Le(a) negative units. As an error did not actually occur, this event was not included in *Table 20*.

There were two cases where the blood component was placed on the infusion stand, but no blood entered the blood stream according to visual observations. The TRIP Office takes the point of view that puncturing of the blood component forms the start of transfusion and that these reports should have been categorised as incorrect blood component transfused. Both reports have been described in *Case histories 6*. Several similar cases have been included in the category incorrect blood component transfused. In future, the TRIP Office will consult with the reporters to obtain as uniform as possible classification of the incidents and avoid having similar incidents registered in different categories.

Table 20 Near miss 2009: type of error that was made initially and way in which the error was discovered

Type of error	Total	Planned safety measures	Discovered through personal vigilance	Coincidence	Not reported
Identification	45	31	5	7	2
Administration	7	3	3		1
Performing test	5	4		1	
Laboratory procedure	4	4			
Communication	3	2	1		
Selection of product	2	1	1		
Storage	1			1	
Product	1	1			
Other	3	1		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 (65 %), whilst communication and selection errors account for less than 10 % of the near miss reports. If we compare this to the first errors in reports of an incorrect blood component being transfused, this reveals a greater percentage of identification errors in 2009 than in 2008 (41 % vs. 23 %). The percentage of reported communication errors for incorrect blood component transfused (10 %) is significantly lower than in 2008 (23 %), whilst the percentage of selection errors (22 %) has increased since 2008 (16 %). An overview of the types of errors in near accidents in *Figure 17* can be compared to *Figure 18*, type of errors for incorrect blood component transfused.

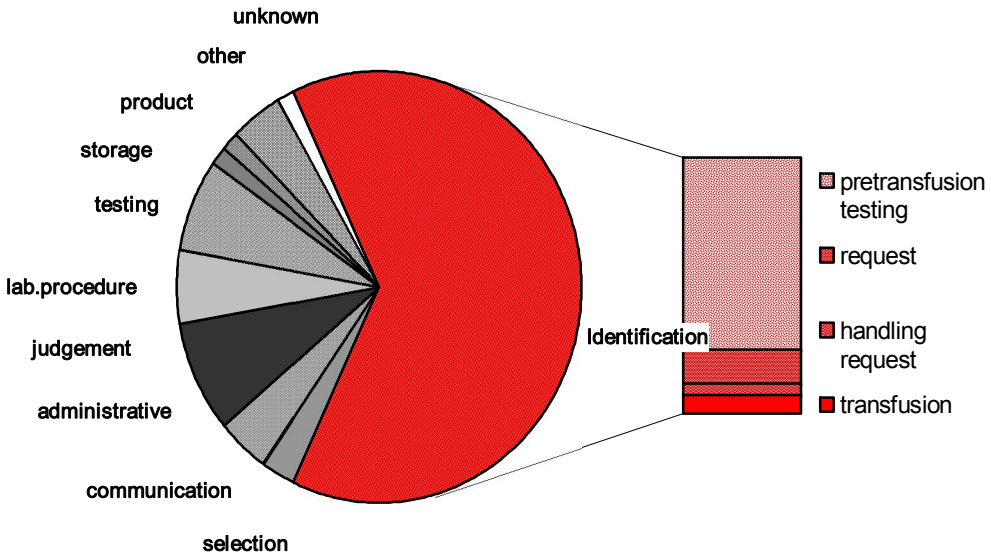

Figure 17 – Near miss 2009
Type of error, identification error split according to step in the chain

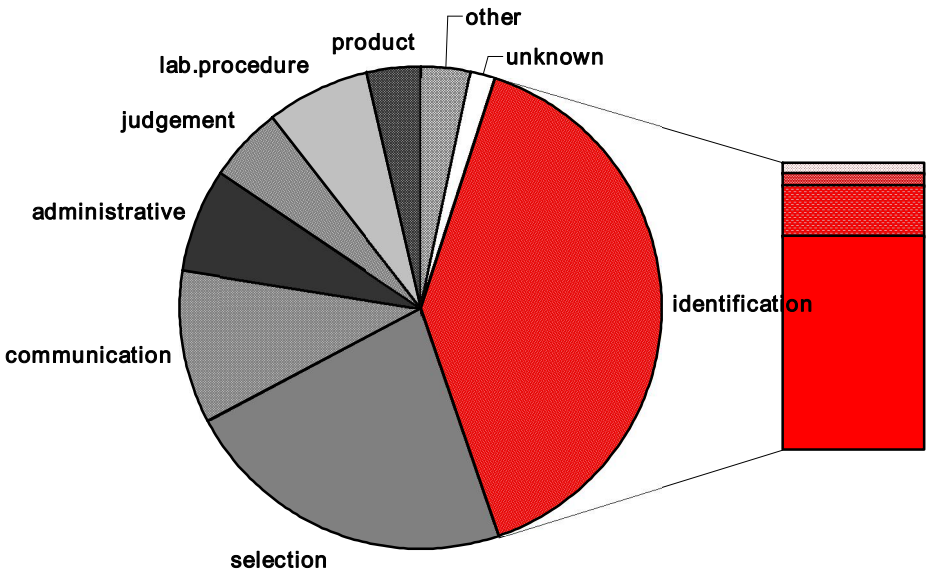

Figure 18 Incorrect blood component transfused 2009
Type of error, identification error split according to step in the chain

Case histories 6 Summary of some reports of near miss

NM-1 (identification, request, alertness of patient)
The OR requested blood for Ms X-Y, without stating date of birth or patient number. The lab has blood ready for Mrs X-Z (also in the OR). The blood is issued without further enquiry and set up in the OR. The patient sees that the maiden name on the label of the blood component is not her name and raises the alarm. The blood is immediately taken down.

NM-2 (identification, processing of request, planned check on ward)
RBC concentrate O pos with unit identification number ..56961 was selected in the computer database for patient A, but RBC concentrate O pos numbered ..21861 was taken from the blood storage cupboard and a cross match test was performed on this. The result was written on the form with number ..56961 and this form was attached to bag ..21861. Not discovered at issue.

NM-3 (storage, secondary storage, coincidence)
Nurse A collected two RBC concentrates simultaneously for patient X, this is permitted because the ward has its own blood storage fridge. The 1st RBC concentrate is set up immediately (10:30), the other unit is placed in the refrigerator. At 14:00, nurse B wants to remove the 2nd RBC concentrate for patient X from the blood storage refrigerator, but it is not present. After asking nurse A, the RBC concentrate is found to have been placed in the ward's household refrigerator.

NM-4 (identification, testing. before TF request, blood group discrepancy)
The impending arrival of a trauma patient is announced in the A&E department. The information on patient Y.Zz is looked up. Blood is collected from patient Y.Zz upon arrival, also for blood group determination, but the patient is not asked to confirm date of birth. The blood group determination produces a discrepancy with the historical blood group of patient Y.Zz born in 1977. The patient in the A&E department turns out to be patient Y.Zz born in 1988. The information on both patients was present in the hospital database.

NM-5 (identification, request, check at issue)
Plasma is requested for patient Ww. The nurse who goes to collect the plasma for patient Ww notes at issue release that the patient information on the label on the blood component does not completely match the information for patient Ww. Investigation reveals that a sticker of another patient with the same surname has been used.

NM-6 (performing test, exam. before TF request, coincidence)
The reagent was not pipetted correctly during the blood group determination of a newborn using the tube method. Rh D neg was determined and the result was passed on. The lab is testing a new method for blood group determination and as a result the baby's blood group is determined again. This test reveals that the blood group is Rh D pos. Fortunately the mother can still be given anti-D in time.

NM-7 (identification, exam. before TF request, staff alertness)
When performing a 12th week pregnancy screening, the biomedical scientist in the blood transfusion lab notes that the request is for a male patient. It transpires that the midwife did not enter any patient information on the request form. At the blood collection clinic the pregnant woman – who barely speaks Dutch – used her husband's hospital card.

NM-8 (identification, transfusion, staff alertness)
Patient B, O pos, needs to receive platelets and the checks were performed by nurses 1 and 2. Immediately after setting up the transfusion, nurse 3 discovers that the checks have not been performed in the right place or the right manner. An A pos platelet concentrate had been set up. The blood component was immediately disconnected.

Look-back by the supplier

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

A total of five reports from hospitals in the category of look-back in 2009. Three reports concerned donors who were confirmed to have the bacterial infection Q fever (pathogen: Coxiella Burnetii) after donation. Sanquin closely monitored the increase in human cases of Q-fever in the South East region of the Netherlands in 2008 and 2009, as transmission by transfusion is conceivable. Some infected individuals remain asymptomatic and a few bacteria in the remaining leukocytes in a labile blood component could be sufficient for transmission.

In two of the Q fever look-backs reported to TRIP by hospitals, the donor only developed symptoms some time (two months) after donation. The recipients had no relevant symptoms and no further investigation was performed. In the third case, the donor developed symptoms of an acute Q fever infection within a few days after donation. The relevant patient underwent serology testing three times and remained negative. In 2008 – 2009 Sanquin worked on the development of a PCR test, which has not yet been validated and made suitable for large-scale use. A recent infection (not reported to TRIP) was found in a recipient who also lives in a highly contaminated area. In this case transmission cannot be confirmed or ruled out.

Two remaining reports in the category look-back would be more appropriate placed in the category other incident: no infection was diagnosed in the donor. One donor's partner was found to be a hepatitis B carrier. Additional tests on the stored sample from the relevant donation gave no indication of infection and the hospital deemed that tests on the patient were not necessary. The second donor later was found not to have met the selection criteria (due to time spent in the United Kingdom). Further examination of the recipients was not necessary.

3.4 Blood Management Techniques (BMT)

When making its annual inventory of the blood use in Dutch hospitals, TRIP for the first time asked for figures on the use of blood management techniques for the reporting year of 2009. These data are necessary in order to relate the number of reactions and incidents to the figures for use. *Table 21* summarises the information received. The numbers provided by the participating hospitals show that these techniques are used regularly. However, the figures for use are not complete (enough) yet. Seventeen hospitals indicated that the hemovigilance officer or assistant does not know the figures for any of the techniques listed in *Table 21*. A pilot on Blood Management Techniques was run from 1 July 2008 till 31 December 2009, aimed at making an inventory of transfusion reactions and incidents for these techniques. Six of the ten hospitals that participated in the pilot on Blood Management Techniques provided figures about use in 2009.

Table 21 Use of blood management techniques

Technique	Number of times 2009	Number of hospitals	Technique not used (hospitals)	Figures not known (hospitals)
Non-mechanical auto-transfusion (administration of drain blood)	7514	18[1]	20	57
Mechanical auto-transfusion (administration of cell-saver blood)	3033	202	25	50
Pre-operative autologous donation			58	20
- patients referred	109	8[3]		
- units collected	208	8[3]		
- units transfused	187	8[3]		
Normovolemic hemodilution	122	6[4]	28	60
Hypervolemic hemodilution	2	2[3]	30	58
Extracorporeal circulation	2177	2	39	52
Fibrin glue	798	12[5]	21	59
Platelet gel	846	5[3]	33	51

[1] 1 hospital reported several hundred times, 1 hospital reported use but gave no figures
[2] 1 hospital reported approx. 2 procedures per month, 1 hospital reported use but gave no figures
[3] 1 hospital reported use but gave no figures; 1 hospital reported in-house PAD
[4] 1 hospital reported use as a rule for every patient (no figures), 1 hospital reported daily use (no figures)
[5] 3 hospitals reported use but gave no figures

In 2009, 33 reports were received of transfusion reactions and incidents with the use of blood management techniques. These reports were made by six hospitals, with a stiking variation in the number of reports per hospital (1 to 22 per facility). The majority (30) of the reports were made by three hospitals that participated in the Pilot for Blood Management Techniques. An overview is provided in *Table 22* of the reactions and incidents that were reported with administration of drain blood, administration of cell-saver blood and pre-operative autologous donation (PAD). No reports were received for the other techniques listed in *Table 21* above. There were three reports of grade 2 severity, 16 reports of grade 1 severity and two reports of grade 0. The imputability was evaluated as possible in 13 cases and probable in 7 cases. There were no clinical consequences in any of the other incidents and as a result the imputability and severity grade are not applicable.

Table 22 – Reports with use of BMT

TRIP category	Drain blood	Cell-saver	PAD
Anaphylactic reaction	2		
Other allergic reaction		2	
Non-hemolytic transfusion reaction	9	1	1
New antibody formation		1	
Other reaction	3		
Circulatory overload			1[#]
Hemolysis product	1[##]		
Other incident	12		
Total	**27**	**4**	**2**

[#] combination of administration of drain blood and PAD
[##] peri-operative administration of intra-operatively suctioned, unwashed drain blood

There were 12 reports in the category of other incident. These incidents were reported by one hospital, all for non-mechanical post-operative auto-transfusion (in combination with pre-operative administration of erythropoietin) for orthopaedic surgery. The most remarkable report involved the detection of air in the entire auto-transfusion system up to the site of infusion in the forearm, shortly after the nurse had checked the patient and seen that the drain blood was almost completely

transfused. The patient did not suffer any harmful effects. Five reports concerned the failure of the infusion line due to a blocked filter, possibly as a result of coagulation. Four of these reports involved a total knee replacement operation, where surgery is performed under bloodless conditions. According to the manufacturer of the drain, the blocked filter was caused by restoring blood flow (too) soon after opening the drain, causing an excess of activated clotting factors to enter the drain blood. According to the manufacturer, the problem can be prevented by opening the line from the drain to the collection bag for auto-transfusion at a later stage. In all cases the drain blood had to be discarded. Remarkably, none of these patients required allogeneic transfusion, because Hb levels were high enough, possibly due in part to the pre-operative administration of erythropoietin.

Two reports concerned the collection bag falling off the drain, possibly due to incorrect connections. There were two reports of the sterile part of the collection bag falling on the ground, either during priming or disconnection. The collected drain blood was lost in all these cases. None of these patients required allogeneic transfusion. There is one report of the collection bag bulging with air. The collected drain blood was discarded and allogeneic transfusion was again not required. In one case it was not possible to empty the bellows into the auto-transfusion bag, resulting in an unknown quantity of drain blood being lost.

There were two reports in the category anaphylactic reaction associated with the administration of drain blood to orthopaedic patients. One report with the of additional category bacterial contamination of blood component (severity grade 1 and imputability possible) reports severe itching and a red rash over the entire body following the administration of 400 ml drain blood. After the administration of the drain blood the patient experienced a decrease in oxygen saturation levels, decreased blood pressure, rigors and confusion, which was treated with clemastine, prednisone, voluven and the administration of oxygen. This resulted in rapid recovery. A Staphylococcus warneri was cultured from the drain blood, which was not deemed virulent enough to explain all the symptoms. The second report of anaphylactic reaction (severity grade 2 and imputability possible) describes a severe reaction following administration of 550 ml drain blood. The reaction was associated with a decrease in saturation levels, severe hypotension, rigors, itching and raised red marks (blisters) on the body, resulting in admission to ICU for observation. The patient had a history of allergic problems (plasters, strawberries, adhesives), but no allergies were reported for the medication administered during surgery (morphine, diclofenac, paracetamol, metoclopramide, esomeprazole). Differential diagnosis includes an allergy to softening agents in the auto-transfusion set in addition to an allergy to medication.

Ten reports of non-hemolytic transfusion reaction were received, all reported chills / rigors and a fever was also reported for seven patients. Three reports listed a negative culture in the drain blood. The blood culture from the patient was also negative for one of these reports, whilst no culture results were reported to TRIP in the other cases.

There were two cases of other allergic reaction with the administration of cell-saver blood, associated with redness of the skin; in one case the redness returned after the administration of cell-saver blood was temporarily halted and then restarted.

There was one report of hemolysis of the product followed by an other reaction (severity grade 2 and imputability probable). The report lists peripheral cyanosis during a hypertensive crisis with intra-operatively suctioned blood that was re-infused peri-operatively in unwashed state to an orthopaedic patient. The Hb concentration in

the plasma was 113 μmol/l (normal < 4 μmol/l). The concentration of free Hb in the administered product was not determined. This is a possible case of hemolysis of the drain blood. In that case, the reaction can be explained by a decreased NO concentration due to Hb-NO binding, which can lead to vasoconstriction and hypertensive crisis. The administration of activated interleukins and/or complement may also play a role.

There were three reports in the category other reaction: one of vomiting, one with chills and a decrease in blood pressure and nausea and the third of rigors with wheezing.

There was one report in the category of transfusion-associated circulatory overload following administration of drain blood in combination with transfusion of PAD blood in a 15-year-old patient. A total of 450 ml drain blood and two units of 150 ml PAD blood were administered at a Hb level of < 8.0 mmol/l, according to the protocol followed in that facility. The chest X-ray confirmed circulatory overload.

There was one remarkable report of new antibody formation following re-infusion of cell-saver blood. A 67-year-old female patient was given a re-infusion of 250 ml blood during a multiple HNP surgery. At that point she irregular antibody screening was negative. Two years later she was found to have anti-D antibodies. She had never previously had a transfusion. All procedures relating to the use of the cell-saver were checked. All tubes and bowls are removed after each surgery, making contamination unlikely. No explanation was found for the anti-D.

The reports show that in practice the transfusion triggers are applied in a different manner for blood management techniques than for allogenic transfusion. Also some (potentially) serious reactions and incidents were reported, which reiterate the importance of hemovigilance with these techniques. Unfortunately, the TRIP data do not allow any conclusions (yet) to be made about the safety of blood management techniques.

3.5 Deceased patients and transfusion reactions (grade 4)

There were three grade 4 reports in 2009 (2008: four), which are described in *Table 23*. In one case the transfusion reaction may have contributed to the death of the patient: transfusion of an un-crossmatched O negative RBC concentrate in an emergency situation resulted in acute hemolytic transfusion reaction based on a previously unknown antibody (anti-K). The patient, with a history of ischemic cardiac problems, stabilised after the administration was stopped and received supportive treatment, but died of a cardiac problems within 12 hours.

Table 23 Reports of patients who died following a transfusion reaction

Category of reaction	Age, gender	Imputability provided	Nature of underlying pathology
Acute hemolytic TR	78, M	Possible	Cardiac patient with bleeding, received unmatched O neg RBCs in emergency situation, was found to have anti-K
TRALI	66, F	Possible	Disseminated malignancy, chemotherapy started, receiving corticosteroids since 2 months due to respiratory problems. Deterioration during transfusion, infectious cause not ruled out. Died after 8 days
Post-transfusion bacteremia/sepsis	76, F	Unlikely	Patient with malignancy and urinary tract infection; died after 2 days with symptoms of sepsis

A general discussion took place with the Expert Committee about the assignment of severity grade 4. As a rule, the severity grade is assigned irrespective of the imputability with which observed symptoms can be attributed to the transfusion. However, a sick patient can die from the underlying condition following a transfusion. As a guideline, TRIP states that grade 4 is applicable if symptoms that could indicate a transfusion reaction were observed and the patient dies without first recovering to the level he/she was at before the suspected transfusion reaction. According to the (draft) definitions of the ISBT, grade 4 should only be used if a link between the death and the reported transfusion reaction is certain, probable or possible. The third report in *Table 23* would not be registered as grade 4 according to ISBT. *Table 24* shows the grade 4 reports to TRIP with imputability certain, probable or possible: the largest category was TRALI.

Table 24 Reports of Grade 4 (imputability certain, probable or possible) 2003 – 2009

Category	Number		Comments
Acute hemolytic transfusion reaction	1	2003	Probable
	1	2009	Possible
Anaphylactic reaction	1	2005	Possible
	1	2007	Probable
Bacterial contamination	1	2003	Possible
Other reaction	1	2005	Possible
	1	2008	Probable
TRALI	1	2005	Certain
	2	2006	Possible
	3	2007	1 Probable, 2 Possible
	1	2009	Possible
Circulatory overload	1	2005	Possible
	1	2006	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 25* shows the data for 2008 and 2009.

Table 25 Number and imputability of reports of grade 2 or higher in 2008 and 2009

Type of reaction	Number of serious reports		Possible		Probable		Certain	
	2008	2009	2008	2009	2008	2009	2008	2009
Acute hemolytic TR	10	11	1	3	4	1	5	7
Delayed hemolytic TR	4	3	-	-	1	1	3	2
TRALI	18	12	6	5	9	5	3	2
Anaphylactic reaction	29	19	10	7	15	11	4	1
Other allergic reaction	5	-	4	-	-	-	1	-
Circulatory overload	17	15	9	5	6	7	2	3
Post-transfusion bacteremia*	4	1	3	-	-	1	1	-
Post-transfusion purpura	-	-	-	-	-		-	-
Post-transfusion viral infection	2	1	1	-	1	1	-	-
Transfusion-associated GvHD	-	-	-	-	-	-	-	-
Other serious reactions	42	36	18[#]	22	18	13	6	1
Total	**131**	**98**	**52**	**42**	**54**	**40**	**25**	**16**

* In 2008, one grade 2 report of bacterial contamination of a blood component was included.
[#] The grade 4 report following an intra-uterine infusion was not included.

4 General considerations, conclusions and recommendations

4.1 What are the trends in 2009 and what has not changed?

The general trends for the reporting year 2009 are summarised in the box.

There was an overall increase in the number of reports, whilst the number of reporting hospitals and the number of blood components administered remained roughly the same.
Examination of the categories reveals that the increase can be explained by more reports in the (usually) non-serious categories NHTR, mild non-hemolytic febrile reactions, new antibody formation and other incidents.

- More non-serious reports
- Fewer serious reports
- Fewer plasma-associated TRALIs
- Increase in digital reports
- Reports made available electronically to the Healthcare Inspectorate (IGZ) and Sanquin

A reflection on the decrease in the total number of serious reports is appropriate here. A noteworthy difference compared to 2008 was observed in the categories anaphylactic reaction, TRALI and other reaction. The significantly lower number of serious reports compared to 2006 and 2007 can be partly explained by the decrease in plasma-associated TRALI reports. The platelet measure introduced at the end of 2009 has not been effective long enough yet to give a detectable effect. The sections on anaphylactic reaction and other reaction show that there is no apparent effect of the plasma rule.

At the start of 2009 the option was introduced of making relevant reports available electronically to the IGZ and Sanquin. As you are aware, the reporting of serious adverse effects (grade 2 or higher) to the IGZ as competent authority became compulsory under the legislation in the framework of the European Directives 2002/98/EC and 2006/61/EC. TRIP has heard from contacts with various reporters that this new situation caused unrest in the hospitals about reports to the Inspectorate. It cannot be excluded that some reporters opted for the path of least resistance in the case of cases of borderline severity and placed them in a lower category.

- Transmission of Q fever not demonstrated
- New test for Hepatitis B, one prior contamination detected by look-back by Sanquin
- New measure against TRALI with the preparation of pooled platelet products cannot be evaluated yet
- No decrease in reports of incorrect blood component transfused

As in previous years, the findings confirm the low risk of blood-transmissible infections: this despite the outbreaks of Q fever in the south east of the country.

There was also no change in the suspected under-reporting of errors and incidents in the transfusion chain on the one hand and – unfortunately – no increase in the reporting of errors on the other

hand in which a patient was exposed to a potentially ABO incompatible transfusion or otherwise incorrect blood component.

4.2 Actions and developments following recommendations in previous TRIP reports

	Current points of attention from reports 2003 - 2007	Comments
1	*Initiatives to prevent errors in the transfusion chain (2007).* *Electronic techniques that check the identification of the patient and the blood component (2007).*	Several ongoing pilots. The majority of the hospitals do not have projects to monitor the blood transfusion chain electronically.
2	*Digital reports to TRIP and making reports available electronically to IGZ (2007).*	85 % of reports in 2009 were submitted electronically. Electronic availability to IGZ by reporters is functional.
4	*Ongoing vigilance for TRALI in order to determine efficacy of the male-only plasma measure that was implemented (2007).*	The level of investigation and the quality of reports has improved.
6	*A hemovigilance assistant for every hospital: an important task is the training of doctors and nurses (2007).*	
7	*Focus on blood transfusion and hemovigilance in the curriculum for the training of medical specialists (2007).*	General status for various training programmes not known to TRIP. TRIP sends the annual report to training institutes for nurses and to those training specialists in the relevant disciplines.
8	*For women younger than 45 years, in addition to Kell negative, also select Rhesus subtype-compatible erythrocytes in order to prevent hemolytic disease in newborns (2007).*	This point is being considered as part of the revision of the CBO Guidelines on Blood Transfusion.
9	*Over-filling also an important category (2006).*	It is not known to TRIP whether actions were undertaken concerning this category in 2008.
10	*Integration of activity as part of the safety management system in hospital with hemovigilance activity (2006).*	This point of concern remains current.

	Current points of attention from TRIP report 2008	Comments
1	*Further research required on factors that influence the number or reports and their relationship to the safety of blood transfusion (TRIP Report 2008).*	TRIP has included an adjustment according to type of blood component and level of blood use in the annual benchmarking graphs to the hospitals.
2	*Each report in the category other reaction must be accompanied by clinical and investigation data. TRIP requests special focus on hypertensive reactions due to unclear significance of reports of this symptom (TRIP Report 2008).*	This will be included by TRIP in the evaluation and asking of additional questions following reports received. No results yet, due to the timeline of the report.
3	*For all transfusion reactions suspected of having a bacterial cause, a culture must be taken from the remaining blood component and the patient and the findings should be included in the report to TRIP (TRIP Report 2008; 2007).*	There has been a slight increase in the number of culture results included in the reports to TRIP.
4	*Improved monitoring of patients at risk of transfusion-associated hemosiderosis can prevent late damage as a result of transfusion and will result in a more realistic number of reports (TRIP Report 2008; also 2006).*	No actions concerning this are known to TRIP.
5	*In order to avoid incidents, relevant education forms should continually focus on the importance of identification and of careful transfer of information and orders (case discussion, training, audit, incident analysis, etc.; TRIP Report 2008).*	A subtitled copy of the educational film 'The strange case of Penny Allison' was sent to all hemovigilance officers in the autumn of 2008. We still receive requests for this regularly.
6	*In the hospitals, the blood transfusion committee must have insight into the scale of the use of blood management techniques as well as ensure vigilance with these techniques (TRIP Report 2008; 2007).*	TRIP pilot for reports ran till the end of 2009; slight increase in the number of reports. Findings of the TRIP inventory applicable in 2009 are described in this report.
7	*It is useful to perform clinical scientific research on various blood components with transfusion reactions as outcome measure. It is also recommended to include alternative products to the 'male-only' FFP, such as SD plasma, in a prospective study of allergic reactions and TRALI, so that it becomes clear which product will be best to prescribe in future (TRIP Report 2008; also 2005).*	A protocol for this study has been developed by partners from TRIP, Sanquin and Eurocet (distributor of SD plasma in the Netherlands). If possible, a pilot for this study will start in 2010. This will focus, among other things, on anaphylactic and other allergic reactions (recommendation 2005 report).

4.3 Conclusions

1. The total number of reports was higher than in previous years. The increase is based on a greater number of non-serious reports, particularly febrile reactions and reports of newly formed irregular antibodies.

2. There was a decrease in the reports of TRALI associated with transfusion of fresh frozen plasma since the introduction of the male plasma rule.

3. As a result of a decrease in the number of reported TRALIs and anaphylactic reactions, there has been a decrease in the total number of serious (≥ grade 2) reports.

4. Anaphylactic reaction is now the largest category of serious transfusion reaction.

5. There has been no decrease in the number of reports of incidents in which the patient was exposed to a potentially incompatible transfusion. Identification of patients, patient material and blood components remain error-prone processes.

6. Due to the lack of regional differences in allergic reactions following administration of platelet concentrates, any difference in the incidence of reactions between platelets in PAS and platelet concentrates in plasma could not be demonstrated.

7. Reports listing the most important symptom as dyspnoea or hypotension form two important clusters in the category other reaction. Sometimes there is insufficient investigation or clinical information to make an adequate diagnosis of the transfusion reaction. As a result, an increasing number of reactions is labelled ‘other reaction’.

8. For one report there was a plausible relationship between post-transfusion bacteremia/sepsis and a bacterial contamination of a blood component.

9. The type of blood management technique (BMT) and the number of times that this technique is used are usually not well known to the hemovigilance officers and assistants. Transfusion reactions and incidents are also observed with blood management techniques.

4.4 Recommendations

A. Recommendations based on the TRIP 2009 Report

1. 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.

2. Criteria must be set that allow for the inclusion of new TRIP categories transfusion-associated dyspnoea and hypotensive transfusion reaction in the TRIP database. These categories must be clearly distinguished from the existing TRIP categories.

3. 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.

B. General recommendations

4. 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.

5. It is useful to record information about the transfusion chain in a standardised manner, allowing for comparisons of transfusion practice and outcomes. The revised CBO guidelines can form a starting point for this.

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)
Plt	platelet concentrate
Tx	transplantation