TRIP Annual Report 2008

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Foreword

This is the sixth TRIP report regarding the reporting year 2008. It deals exclusively with hemovigilance, in contrast to reports for 2006 and 2007. A separate report on tissue vigilance in the Netherlands has been published for 2008.

Although the general report set-up will be familiar, there are a number of new tables and text boxes containing case histories. The progressive improvement in the level of information the reports contain means that it is now possible and appropriate to provide you, the professionals, with more detailed information. This report also presents the first results of registrations using the revised definitions which were introduced in 2006 for bacterial problems associated with blood transfusion.

It can be stated that the annual number of reports, including those of severe reactions, has become more or less stable. The question is: where is the improvement, where is the decrease in numbers of registrations of severe reactions and errors?

Firstly, TRIP and I are convinced that activities surrounding hemovigilance in the hospitals have improved the safety and quality of the practice of transfusing blood: one only has to consider improved education and training and the fact that hemovigilance employees are monitoring transfusion triggers. Secondly, a frequency of less than one report of a serious adverse reaction for every 5000 administered blood components means blood transfusion is relatively safe in the Netherlands.

Nevertheless, the practice can become safer. TRIP annually provides data and background information in its reports, but it can only make recommendations that will improve the safety of blood transfusion. The onus is on the concerned institutions and professionals, also taking into account the recommendations of the national CBO Guidelines for Blood Transfusion, currently under revision, to evaluate their own results and, where necessary and feasible, to design and implement well aimed and achievable plans of improvement.

I sincerely recommend this report to you and wish you every success in your work of monitoring and, if possible, improving transfusion safety.

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

Executive summary

TRIP (Transfusion Reactions in Patients)

Dutch National Hemovigilance Office

The objective of TRIP (Transfusion Reactions In Patients) Dutch Foundation for Hemovigilance and its National Hemovigilance Office is to receive reports on side effects and incidents associated with transfusion of labile blood products and to report publicly on transfusion safety. Reports of both serious and non-serious events are captured. They are submitted by the contact persons (hemovigilance officers) in the Dutch hospitals. Reporting is anonymous as to patient and physician; participation is theoretically voluntary but is regarded as the professional standard both in the national transfusion guideline and by the Health Care Inspectorate (Inspectie voor de Gezondheidszorg, IGZ). TRIP also receives information from the blood establishment Sanquin when an incident involves blood components, which have been distributed to the hospitals.

By arrangement with the Health Care Inspectorate and the Ministry of Health, TRIP provides the scientific analysis and annual overview of serious adverse reactions and adverse events as required by the European Union Directives (2002/98/EC and 2005/61/EC).

Reports are initially examined by the TRIP office medical staff and if necessary further information or clarification is requested. An “Expert Committee” appointed by the TRIP steering group reviews the reports before the data are accepted and included in the annual report.

Participation in 2008

Ninety-eight (94%) of the 104 Dutch hospitals participated in the TRIP 2008 data collection. Eighty-nine hospitals submitted reports on transfusion reactions and nine indicated that they had nil to report in the TRIP categories. The closing date for inclusion in this report was 1st April 2009.

The 2008 reports

A total of 1950 reports about transfusion side effects and incidents in 2008 were received, in comparison to 1910 reports concerning 2007 at the closing date last year. 1725 reports were of clinical transfusion side effects and 225 concerned incidents in the transfusion chain. 1306 of the reports (67.6%) were submitted using the online reporting system which has been progressively rolled out.

Severity of the events

In accordance with international practices the reports are graded as to severity. 1750 (89.7%) of the 2008 reports were rated for severity by the reporter. Of these reactions 1612 (92.1%) were rated as grade 0-1 (no or only minor morbidity), 116 (6.6%) as grade 2 (serious), 18 (1.0%) as grade 3 (life-threatening) and 4 (0.2%) as grade 4 (death following a transfusion reaction). The total number of serious reactions (grades 2-4) is 138 which is comparable to 2006 and 2007.

Rating of the imputability

Symptoms or signs in a transfused patient may be related to numerous factors other than the actual transfusion. The reporting form requests an assessment of the imputability, i.e. whether the observed effects can be ascribed to the transfusion. In 2008, 1705 (87.4%) of the reports were rated for imputability. Out of these 1705, 295 (17.3%) were judged to be “certainly” related to the transfusion, 535 (31.4%) “probably”, 726 (42.6%) “possibly” and 149 (8.7%) “unlikely” or “certainly not”.

Types of reactions and incidents

The following types of reports were received: febrile non-hemolytic transfusion reaction 447, mild febrile reaction (>1<2˚C) 255, acute hemolytic transfusion reaction 18, delayed hemolytic transfusion reaction 18, transfusion-related acute lung injury (TRALI) 19, anaphylactic reaction 59, other allergic reaction 167, circulatory overload 38, viral infection 7, post-transfusion bacteraemia / septicaemia 35, hemosiderosis 3, post-transfusion purpura 1, other reaction 97 and new alloantibody 560. Among the incidents there were 57 reports of transfusion of an incorrect blood component (product intended for another patient or not meeting appropriate requirements for that patient) with clinical reactions in nine cases (four rated as grade 2 or higher). TRIP received 80 reports of other incidents, 53 reports of near

misses and 20 reports from hospitals on cases where a blood component had been transfused and the bacteriological screening at the Sanquin blood bank later gave a positive result (optional reporting from hospitals). Sanquin also supplied a total figure for blood components (102) with positive bacteriological screening after transfusion; this figure is more complete than that of the information from hospitals but the latter provides information on the patients involved.

Number of reports in relation to the number of blood components

In 2008 the blood supply organisation Sanquin delivered a total of 706,868 labile blood products to the hospitals. The total number of reports was 1950. This gives an average of 2.8 reports per 1000 blood components distributed nationally, compared to 2.7 per 1000 in 2007 (3.0 including reports which were received after the closing date for the 2007 report). The number of reports per 1000 units transfused in a hospital varies from 0 to 11.14 (the maximum in 2007 was 9.45).

Discussion and conclusions

TRALI

Eighteen of the 19 TRALI reports received met the criteria of the definition, comparable to 23 in 2007. In the autumn of 2006 the blood service implemented a measure (exclusive use of plasma from never-transfused male donors for quarantine plasma for transfusion) in order to reduce the risk of TRALI associated with plasma transfusion therapy. The measure gradually became effective in the course of 2007 and it is still too early to demonstrate an effect.

Blood management techniques

A total of 13 reports of transfusion reactions and 12 incidents associated with the use of autologous blood management techniques were received from nine hospitals. They concern preoperatively donated blood, cell saver use and re-infusion drains. The number of times the techniques were used is not known in all the reporting hospitals. TRIP is conducting a pilot of data collection on adverse reactions and incidents occurring when these techniques are used.

Reflection on transfusion safety

The number of reported errors in the transfusion chain has not shown any reduction since the TRIP registry commenced. In a total of 26 reports in 2008 the patient could have received an ABO incompatible transfusion: fortunately the blood group was compatible in some of these cases. One of the six reactions following an ABO incompatible unit was contributory to the death of the patient. The 57 reports show that not only errors in identification, but also poor communication and record keeping underlie the mistransfusions. Participation in the national database of irregular antibodies, Hematopoietic stem cell recipients and transfusion crossmatch problems (TRIX; currently being rolled out) can reduce the risk of errors.

As in previous years the number of confirmed or highly likely transmissions of infections is very low.

1. | Introduction |

TRIP working method

A thorough knowledge of the types and rates of side effects of blood transfusion is necessary for the timely recognition of known as well as hitherto unknown adverse reactions associated with transfusion of currently available or new types of blood components. Centralised (national) reporting of transfusion reactions (TR) makes it possible to monitor safety in the transfusion chain, discover weak links and pinpoint areas for improvement.

TRIP (Transfusion Reactions In Patients) Foundation was created in 2001 by representatives of the various societies of professionals active in the domain of blood transfusion. Since 2003 it has run a national hemovigilance reporting system in collaboration with regular contact persons in the hospitals and in Sanquin, the national blood supply foundation. Reporting to TRIP is anonymous and in principle voluntary. However the 2004 National Transfusion Guideline and the Health Care Inspectorate (Inspectie voor de Gezondheidszorg, IGZ) regard participation as the norm.

Currently, almost three-quarters of hospitals use the digital reporting system which was launched in 2006, originally as a pilot project.

TRIP asks participants to add all relevant research findings and the grade of severity of clinical symptoms to their reports. In addition, an assessment of imputability is requested, i.e. the likelihood of a reaction being attributable to transfusion. If necessary, TRIP asks the reporter for further explanation or supplementary data. This enables TRIP doctors to judge the reports' coherence and verify the categories of serious or potentially serious reports.

Reporting to TRIP is separate from providing care and separate from other non-voluntary reporting routes: to the IGZ for calamities, to Sanquin for possible consequences for safety of blood components or related components and within the hospital to the committee for Reporting Incidents in Patient Care. The provisions of European Guideline 2002/98/EEC include the obligation to report serious adverse events and incidents possibly related to the quality and/or safety of blood components. TRIP provides the analysis and reports on these events (grade 2 or higher) on behalf of the competent authority IGZ. At the end of 2008, hospitals received a joint circular from IGZ and TRIP informing them of the facility to report serious events and incidents to the IGZ via the TRIP online reporting system and, where relevant, to the Sanquin Blood Bank.

An "expert committee" (EC), appointed from the TRIP governing board, assesses all submitted reports. Definitive inclusion in the TRIP report is subsequent to EC approval.

Since August 2006, TRIP has been involved in a pilot project to develop a national reporting system for serious adverse reactions and/or incidents associated with the use of human tissues and cells. The TRIP tissue vigilance report 2008 describes this system and the findings.

2. | Hemovigilance reports in 2008 |

2.1 Participation

Numbers of actively participating hospitals and the quality of information they submit determine the value of registering and evaluating transfusion reactions nationally. In 2008, 98 of the 104 (94%) of hospitals participated in the registration. Of these, 89 hospitals reported transfusion reactions and nine hospitals indicated that they had nil to report. TRIP received information about blood use as well from all 98 hospitals. As in the past, it was the responsibility of the contact persons in the hospitals 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 the report for 2008 was 1 April 2009.

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

After the closing date for the 2007 report a number of late submissions for 2007 were received: 169 or 8,1% of the final number, of which 13 were grade of severity 2 or higher. The serious reports were three other reactions, one anaphylactic reaction, one circulatory overload and one TRALI, one other allergic reaction and the rest non-hemolytic transfusion reactions. The EC now has 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 from 2002 (the baseline measurement) up to and including 2008, as of 1 April 2009.

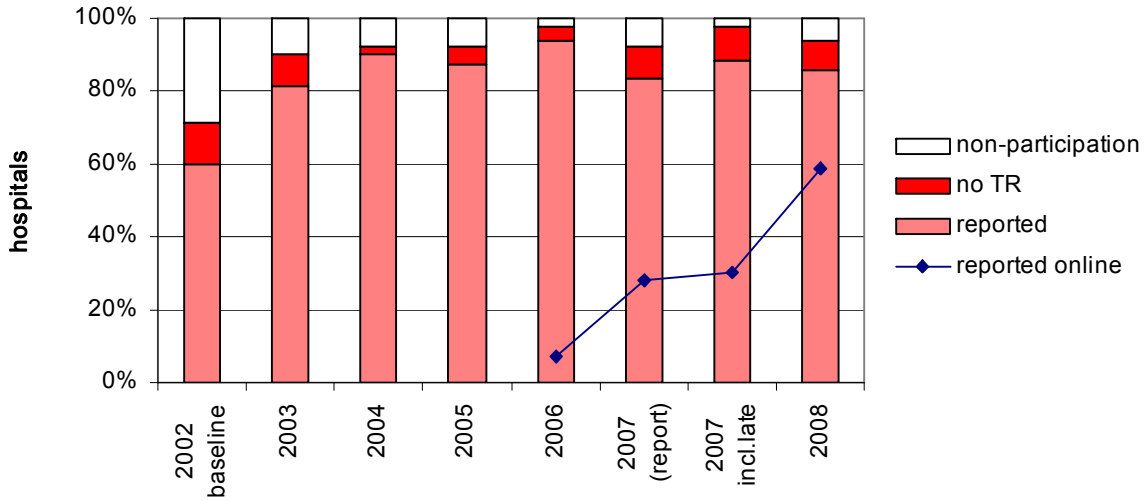


Figure 1 Participation per year

2.2 Summary of data regarding the reports for 2008

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

Reports received

In total 1950 reports of transfusion reactions in 2008 were received; these arose from 89 hospitals. In 2007, the number was 1910 and ultimately, including late reports, 2082 from 92 hospitals. There are some non-serious categories that, until now, have been regarded as optional for reporting: mild febrile reactions, near misses and information from hospitals about positive bacterial screen and other product incidents. TRIP sees it as useful to register these, but does not necessarily need all hospitals to co-operate. Of the total, 401 were for optional reporting categories, arising from 69 hospitals (in 2007: 535 optional reports from 75 hospitals). Annual numbers of reports have been stable since 2005.

Of all reports, 1306 were submitted digitally (67.6%, 59 hospitals).

After EC assessment, reporters received supplementary questions in a number of instances (a total of 25 times). Discussions with the reporter led to nine instances of amending the reporting category. In other cases relevant, supplementary information was forthcoming and in some instances or consensus was reached to adjust the severity or imputability level.

Table 1 (transfusion reactions - TR) shows the number of reports per category for the years 2003 up to and including 2008 and Table 2 shows numbers of incidents for the same period. See 2.3 for separate discussion of transfusion reactions following incidents. These are not included in Table 1.

Table 1 TR* reported to TRIP, 2003 - 2008

Reaction	2003	2004	2005	2006	2007	2008	Grade 2 or higher[#]	No. of hospitals with reports in 2008
NHTR	318	345	435	490	452	447	20	81
Mild febrile reaction	326	341	375	363	327	255	3	63
AHTR	8	14	9	17	11	18	7	14
DHTR	19	14	12	14	11	18	4	11
TRALI	7	9	17	25	31	19	17	15
Anaphylactic reaction	8	21	26	19	54	59	27	23
Other allergic reaction	132	171	219	222	202	167	5	38
Circulatory overload	7	6	27	34	31	38	16	22
Post-transfusion purpura	0	0	0	0	0	1	0	1
TA-GvHD	0	0	0	0	0	1	0	1
Hemosiderosis	0	0	3	5	3	3	1	1
New alloantibody	244	428	571	607	600	560	3	51
Other reaction	54	64	67	61	55	97	11	44
Post-transfusion bacteraemia / sepsis[$]	9	5	10	7	19	35	3	19
Viral infection	5	7	8	7	7	7	1	6
Total TR	1137	1425	1779	1873	1813	1725	118	89
Total reports*	1268	1547	1984	2130	2079	1950	125	89

[#] Imputability certain, probable or possible.
* Total transfusion reactions and incidents.
[$] See 3.2 for changed definitions.

Table 2 Incidents per year, 2003 - 2008

Incident	2003	2004	2005	2006	2007	2008	No. of hospitals with reports in 2008
Incorrect blood component	34	36	60	64	64	57	31
Near miss	31	62	79	77	74	53	12
Other incident	5	12	51	86	100	80	27
Look-back (optional report from hospital to TRIP)		2	2	1	4	9	7
Virally infected component					2	2	1
Positive bacterial screen [$]	61	10	13	27	29	1	1
Bacterial contamination[$]					5	23	15
Total	**131**	**122**	**205**	**257**	**266**	**225**	**47**

[$] See 3.2 for changed definitions.

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, long term morbidity or disability
3	serious morbidity, directly life threatening
4	death as outcome after a transfusion reaction

International usage is to categorise transfusion reactions as to their grade of severity. Reporters rated severity for 1750 reports in 2008 (89.7%). Of these, 570 were grade 0 (32.6%), 1042 grade 1 (59.5%), 116 grade 2 (6.6%), 18 (1.0%) grade 3 and 4 grade 4 (0.2%).

The definition of severity relates to clinical symptoms observed in the patient; it is only meaningful for transfusion reactions. In the following, “clinical transfusion reaction” means all reports in the transfusion-reaction categories, plus reactions arising after reports in the incident categories. Of the 1747 reports of clinical transfusion reactions, 1686 (96.5%) were submitted with a severity grade assigned. *Figure 2* shows the severity grades of clinical transfusion reactions from 2002 up to and including 2008.

Figures reveal a decline in the unnecessary assignment of grade of severity for incidents lacking clinical consequences. Additionally, for clinical transfusion reactions – there is a continuance of two desired trends visible since 2005. Firstly, TRIP has maintained its standpoint that the report must assign a minimum grade of severity 1 if clinical symptoms are present. Secondly, for incidents, reporting should include a subcategory if a reaction occurs. Reporting should include both the reaction's grade of severity and its imputability. Severity and imputability are irrelevant if events do not give rise to clinical features.

There were 138 (7.1% of total) serious reports (grade of severity 2, 3 or 4) and this is thus comparable to 2006 and 2007.

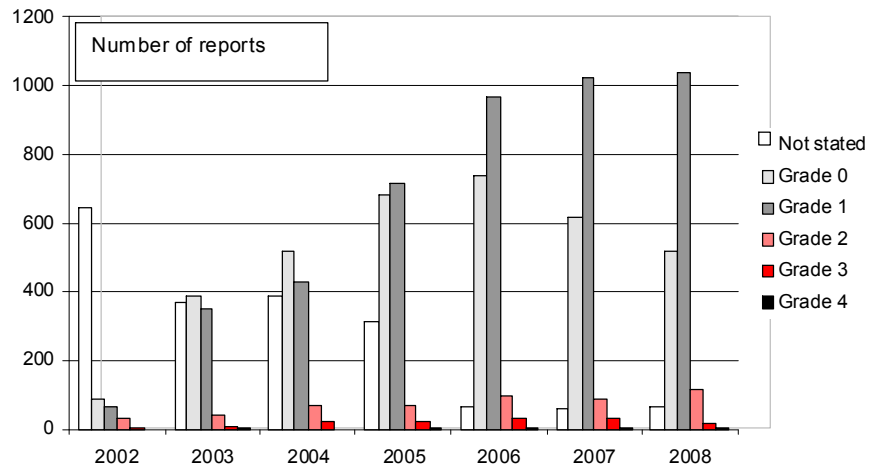


Figure 2 Severity of clinical transfusion reactions, 2002 - 2008

Relationship to the blood transfusion (imputability)

Imputability	*Definition* (imputability is solely 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*	

Reporters assign transfusion reactions imputability: a measure of probability that the reaction resulted from the transfusion.

In 2008, 1705 (87.4%) reported transfusion reactions and included their imputability. Of these, 295 reports (17.3%) show a reaction with a “certain” relationship to the transfusion, 535 (31.4%) “probable”, 726 (42.6%) “possible”, 131 (7.7%) “unlikely” and 18 (1.1%) “excluded”. Numbers of reports submitted as “certain” have slightly declined again – the fact that reporters assigned imputability for fewer of the incident reports lacking clinical consequences explains this.

Figure 3 shows imputability of 1747 clinical transfusion reactions in 2008, compared to previous years; reporters assigned imputability to 1678 of these (95%). Reporters are assigning a “possible” more often than in the past. Reports of clinical transfusion reactions without imputability in 2008 are found particularly in the category of new alloantibodies. This is discussed in the section on this category.

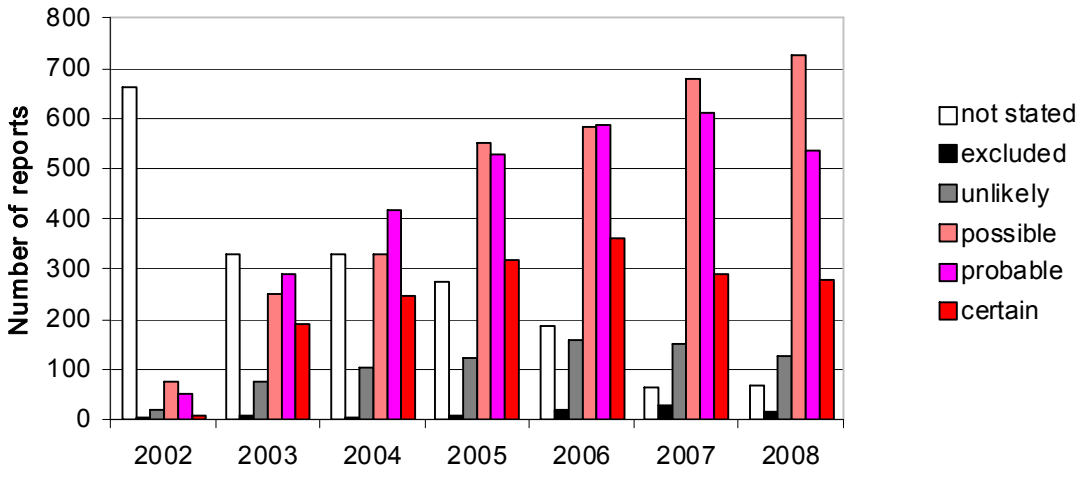


Figure 3 Imputability of clinical transfusion reactions, 2002 - 2008

Numbers of transfusion reactions in relationship to numbers of supplied blood components

In 2008, Sanquin supplied hospitals with a total of 706,868 blood components; this number does not include special components like lymphocytes and granulocytes. The total number of reports for 2008 is 1950. On average, that is 2.8 reports per 1000 components (in 2007: 2.7 included in the annual report, 3.0 including late reports). Table 3 shows the relationship between supplied blood components and numbers of reports.

Table 3 Reports in 2007 and 2008, per type of blood component

Blood component type	Reports 2007	Number delivered 2007	Reports / 1000 2007	Reports 2008	Number delivered 2008	Reports / 1000 2008
RBC concentrate	1522	554,633	2.75	1442	559,372	2.58
platelet concentrate	276	53,701	5.14	249	50,784	4.89
fresh frozen plasma	86	92,568	0.93	74	96,622	0.77
autologous (RBCs, predeposit)	1	78 donations		0	110 donations	
autologous, perioperative (PAD)	2			5		
other components*	1			4		
combinations	91			94		
not indicated	100			82		
TOTAL	**2079**	**700,980**		**1950**	**706,868**	**2.76**

*"Other blood components" in 2008 were epoetin, cryosupernatant plasma, a number of millilitres of RBC to dilute an infusion of bone marrow and a unit for intra-uterine transfusion.

Numbers of reports per 1000 units are approximately stable around 2.9. *Figure 4* shows the course from 2002 up to and including 2008. *Table 4,* in *parts A and B*, shows the distribution of the administered blood components per type of adverse reaction or incident.

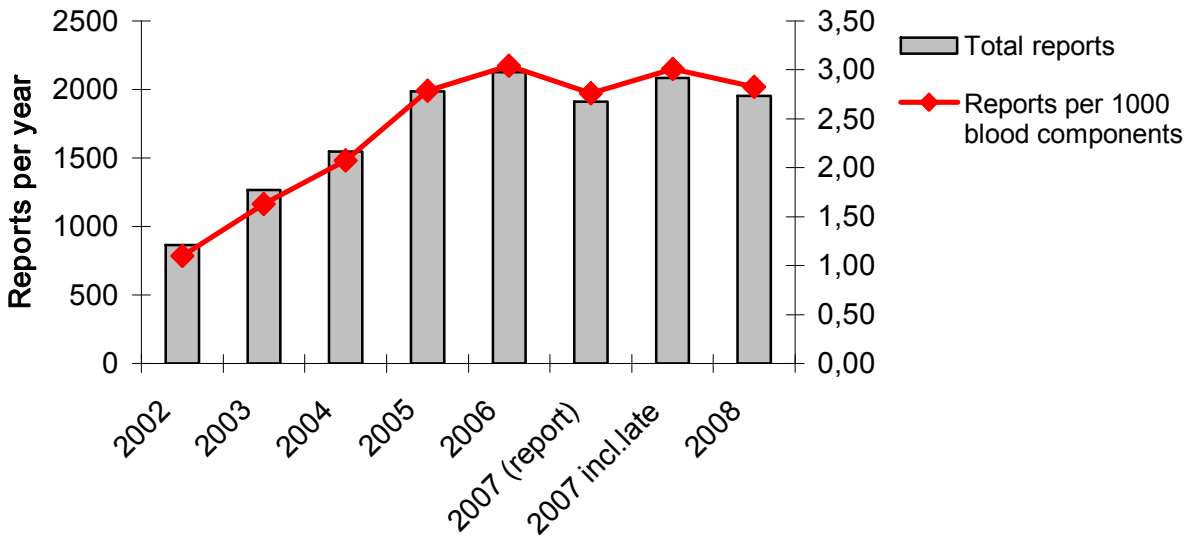


Figure 4 Number of reports per year, 2002 - 2008

Table 4 Distribution of reported blood-component type per category report in 2008

A. Reaction	RBCs	Platelets	Plasma	Combi	Other	Not stated
Non-hemolytic transfusion reaction	376 (84.1%)	44 (9.8%)	6 (1.3%)	15 (3.4%)	3 (0.7%)	3 (0.7%)
Mild febrile reaction	232 (91.0%)	12 (4.7%)	2 (0.8%)	8 (3.1%)	-	1 0.4%)
Acute hemolytic transfusion reaction	15 (83.3%)	2 (11.1%)	-	-	-	1 (5.6%)
Delayed hemolytic transfusion reaction	16 (88.9%)	-	-	2 (11.1%)	-	-
TRALI	9 (47.4%)	4 (21.1%)	1 (5.3%)	5 (26.3%)	-	-
Anaphylactic reaction	13 (22.0%)	28 (47.5%)	12 (20.3%)	6 (10.2%)	-	-
Other allergic reaction	31 (18.6%)	84 (50.3%)	40 (24.0%)	11 (6.6%)	-	1 (0.6%)
Circulatory overload	32 (84.2%)	3 (7.9%)	1 (2.6%)	2 (5.3%)	- -	- -
Post-transfusion purpura	-	-	-	1 (100%)	-	-
TA-GvHD	-	-	-	1 (100%)	-	-
Hemosiderosis	1 (33.3%)	1 (33.3%)	-	1 (33.3%)	-	-
New alloantibody	519 (92.7%)	11 (2.0%)		24 (4.3%)	-	6 (1.1%)
Other reaction	64 66.0%)	18 (18.6%)	6 (6.2%)	5 (5.2%)	1 (1.0%)	3 (3.1%)
Post-transfusion bacteraemia	30 (85.7%)	2 (5.7%)	-	3 (8.6%)	-	-
Post-transfusion viral infection	5 (71.4%)	1 (14.3%)	-	1 (14.3%)	-	-
B. Incident						
Incorrect blood component transfused	40 (70.2%)	8 (14.0%)	1 (1.8%)	5 (8.8%)	2 (3.5%)	1 (1.8%)
Other incident	45 (56.3%)	10 (12.5%)	2 (2.5%)	2 (2.5%)	3 (3.8%)	18 (22.5%)
Near miss	2 (3.8%)	-	1 (1.9%)	1 (1.9%)	-	49 (92.5%)
Bacterially contaminated blood component	6 (26.1%)	17 (73.9%)	-	-	-	-
Positive bacterial screen (optional)	-	1 (100%)	-	-	-	-

Variation among hospitals

The number of transfusion reactions per 1000 blood components per hospital varied from 0 to 11.14 (the maximum in 2007 was 9.45); the median is 2.59. The number of reports per 1000 administered blood components in the 98 institutions that submitted data on time for this report is 3.04. *Figure 5* shows the distribution of number of reports related to the hospitals' blood use.

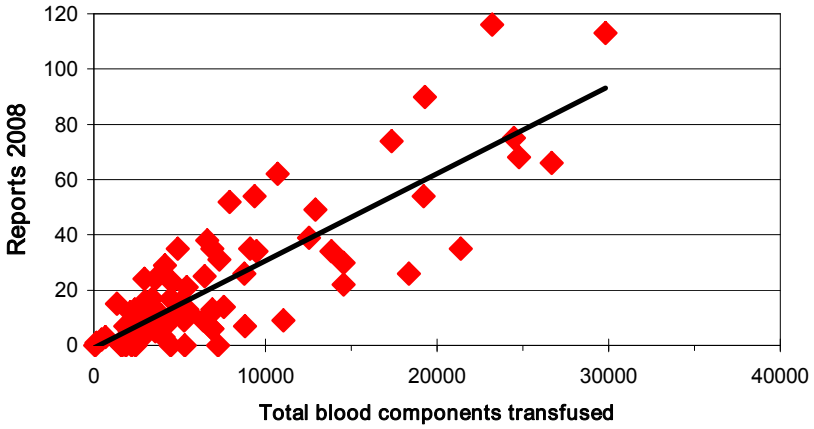
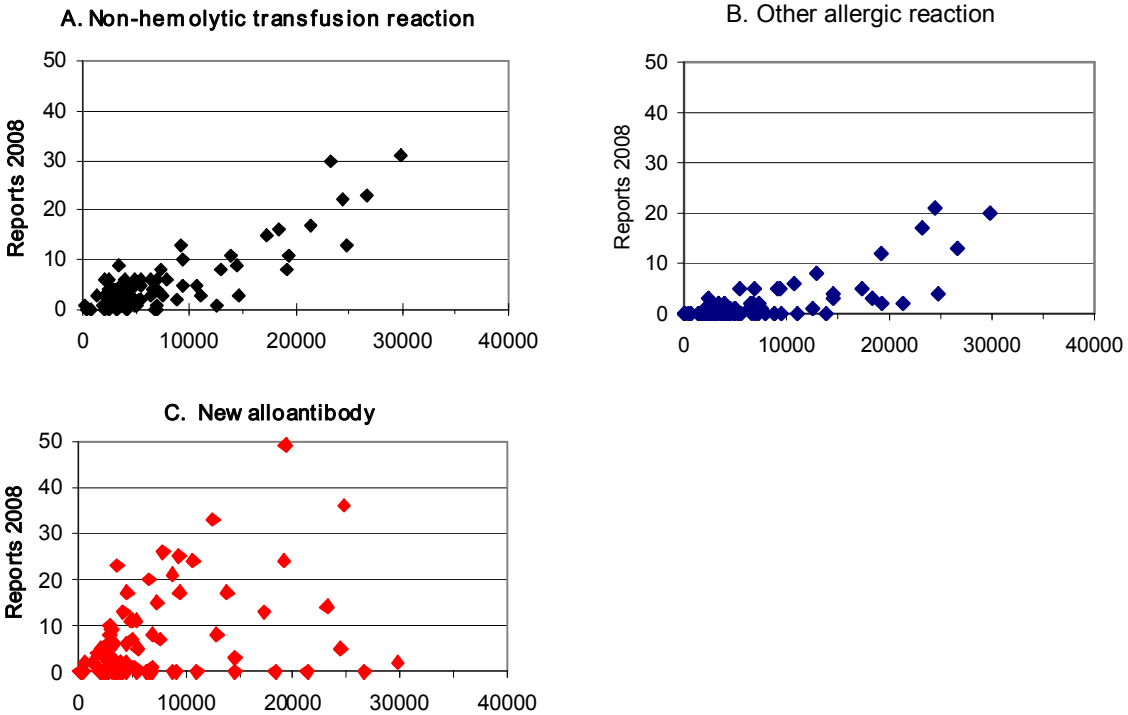


Figure 5 Number of 2008 reports per hospital related to number of administered blood components

Every year TRIP sees a large variation among hospitals in number of reports per 1000 blood components. In 2008, this was no different from previous years. *Figures 6A, B and C* show the largest categories: those of non-hemolytic transfusion reaction (NHTR), other allergic reaction and new alloantibody, and numbers of reports in relationship to numbers of transfused units in each hospital. It can be seen that reports of new alloantibody and other allergic reactions vary more strongly among institutions than reports of NHTR.



Figures 6A, B and C - Reports per hospital in relationship to numbers of administered blood components. A Non-hemolytic transfusion reactions, B Other allergic reactions, C New alloantibody

A variety of factors may explain variations between institutions:

1. Differences due to factors outside the transfusion chain, for instance differences in patient population, differences in the proportions of platelet components.
2. Differences arising from working methods in the blood transfusion chain, which can indicate differences in quality of blood transfusion practice or safety.
3. Differences in reporting cultures among the hospitals.

Factors within an institution, like the providing education and training and the reporting culture probably have a large effect on numbers of reports. TRIP's ultimate goal in registering reports is to acquire more insight into the occurrence of transfusion reactions and incidents and to recommend ways of improving the safety of blood transfusion. TRIP uses the registered data, both individual reports and derived indicators, to do this. Further research is needed into the factors influencing numbers of reports and into how numbers of reports reflect the level of safety of an institution's blood-transfusion practices.

2.3 Data on transfused patients

TRIP requests that reports submitted include the patient's gender and date of birth. Besides the administrative goal of making it possible to detect double reports, information about the patients is essential in understanding the reports submitted and in discovering risk groups with a view to prevention. In the six years during which TRIP has been registering reports, it has observed gradual improvement in the level of detail of the submitted reports.

Figure 7 shows distribution of age and gender for the reports for 2008 (a patient who had a number of reactions is included once for each reaction). *Figure 8* shows the age distribution per reaction category.

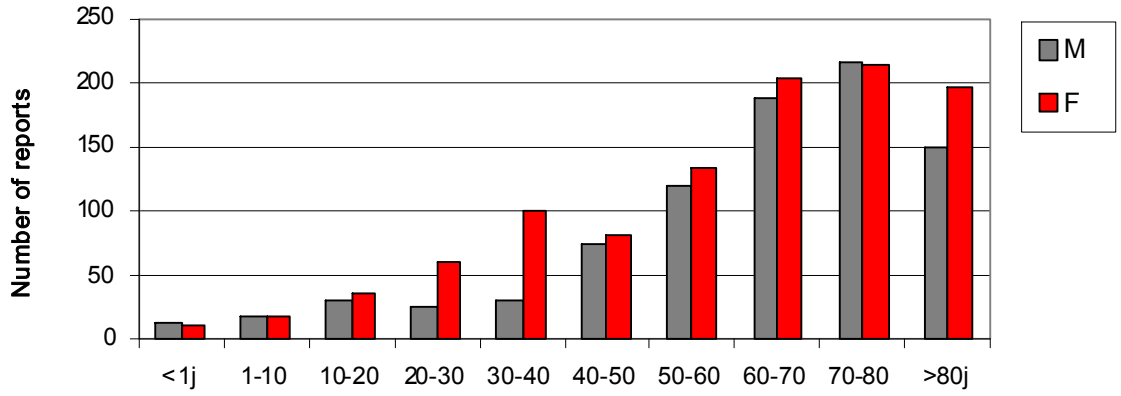


Figure 7 Age and gender of transfused patients

Not all reports record a diagnosis of the transfused patient. Often this information is unavailable in the blood-transfusion laboratory where most work is done surrounding the reports. Since 2008, reporters are asked indicate the requesting specialist; 1593 reports stated this in 2008 (1192 or 91% of digital reports and 401 or 62% of reports on paper).

Information about the diagnosis of all recipients of blood components with or without transfusion reactions is necessary to do a risk analysis. This is information which TRIP does not have; possibilities of cooperation with research groups in this area need exploring.

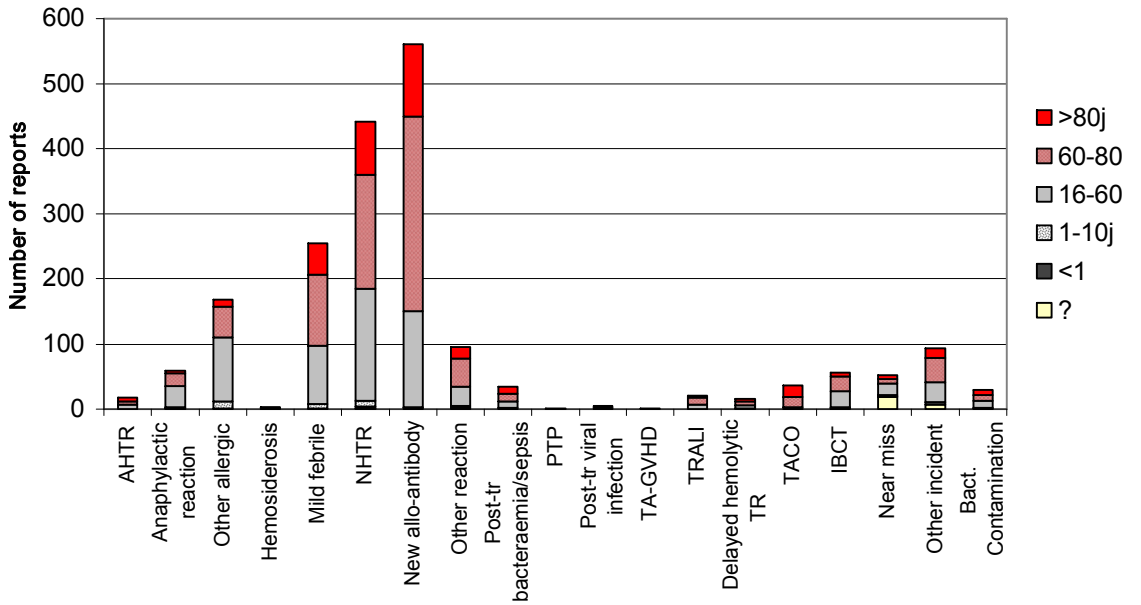


Figure 8 Age distribution of patients per reporting category

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 ≥ 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, bacteriology negative, and no alternative explanation.

Mild 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 2008 is 447 compared to 452 in 2007 and 490 in 2006; numbers of mild febrile reactions are 255 in comparison to 326 in 2007 and 363 in 2006, respectively. Together, these make up a generous third (36%) of the total. Although TRIP saw lower numbers of NHTR and mild febrile reactions for the 2007 report, there were many late submissions in this category in 2007. This 2008 report shows NHTR at familiar levels, but fewer mild febrile reactions. Both categories together showed 24 (20 NHTR and 4 mild febrile reactions) of grade 2 of severity, as was the case in 2007. Generally, grade 2 arises when a hospital admits a patient for observation after receiving a transfusion in day care or there is prolongation of illness.

A good 10% of reported NHTR is associated with using platelet concentrates, while platelets make up 7.6% of distributed labile blood components. The chance of this reaction occurring is somewhat larger for platelets than for RBC concentrates (and lower for plasma).

A number of points are of interest when examining the reports of NHTR. Firstly, numbers of reports that include results of blood work on the patient have improved: 42% in 2006, 46% in 2007 and 58% in 2008 (15 of the 20 reports of grade 2 NHTR). It is possible that digital reporting has encouraged better sharing of information; bacteriological results in the event of febrile reactions are described in the section on bacterial problems accompanying blood transfusion. This year a lower percentage of reports include blood group serological findings. Serology should be investigated in accordance with the Dutch CBO Guidelines for Blood Transfusion (2004). In order not to overburden reporters TRIP restricts itself in asking supplementary questions in the event of non-serious reports. However, if a report is unclear, for instance lacking supporting information for an “unlikely” imputability, TRIP requests supplementary information about investigations in order to validate the report’s coherence.

As in previous years, a significant number of patients in 2008 suffered one or more repeated non-hemolytic transfusion reactions and/or mild febrile reactions (n=33) and there were 14 who, in addition to suffering a febrile reaction, also had an allergic reaction. It is a known fact that some patients have reactions rather often; for these patients it is logical to administering prophylactic antipyretic medication. Outside this group, no good evidence exists for the use of preventive medication (Heddle, 2007).

Compared to previous years, numbers of mild febrile reactions have decreased. TRIP observes that hospitals reporting both NHTR and mild febrile reactions have, in fact, sent in more NHTR than mild febrile reactions, while it would be logical for numbers of mild febrile reactions to be higher. TRIP assumes that hospital nursing wards less consistently reported mild febrile reactions than NHTR.

For some cases of NHTR, the reporting hospital found a positive culture result for the administered unit but judged this to be either irrelevant or possibly resulting from contamination while sampling for the culture. Where the result is not regarded as doubtful, under the 2008 definitions the reporting category should be “bacterial contamination of blood component”.

Acute hemolytic transfusion reaction (AHTR)

Symptoms of hemolysis occurring within a few minutes of commencement of until 24 hours subsequent to a transfusion: one or more of the following: fever/chills, nausea/vomiting, back pain, dark or red urine,

decreasing blood pressure or laboratory results indicating hemolysis within the same period. Biochemical hemolysis testing positive; blood group serological testing possibly positive; bacteriology negative.

In 2008, 18 acute hemolytic transfusion reactions were submitted, eight which were grade 2 in severity 2 and ten of grade 1. Imputability was certain in 6 cases, probable in 7 and possible in 4. In addition there were 4 cases of incorrect blood component transfused leading to an acute hemolytic transfusion reaction. These are discussed in the relevant section.

The acute hemolytic transfusion reaction is a relatively rare transfusion-reaction category: 0.9% (18/1950) of the reports or 2.5 of the 100,000 administered blood components. The number of AHTR fluctuates in the TRIP registration between 8 and 18 cases annually (0.5-1.3%). In 2008, 2 cases of AHTR were reported after administering platelets and 16 after administering RBCs. The male/female ratio is 1:3.5 (overall approximately 1:2 in the TRIP database).

The clinical picture is variable: the most often reported symptoms were fever, chills and dyspnoea. It is sometimes difficult to distinguish the clinical picture from the patient's primary illness. In 15 cases, hemolysis parameters were quoted in support of the diagnosis of acute hemolysis. One patient, with a history of an ABO-in compatible stem cell transplantation, showed hyperhemolysis with an auto-immune hemolytic anemia, which was registered as AHTR, based on the clinical picture and increasing biochemical abnormalities after transfusion while hemoglobin did not rise.. For another patient the diagnosis was made retrospectively based on clinical symptoms after finding an anti-K; hemolysis parameters were not determined. After administration of O-positive platelets, an AHTR was registered; the reporter did not include clinical symptoms or hemolysis parameters, anti-A was found in the eluate.

Serology was not researched thoroughly in every case, making it impossible to pinpoint a cause for the AHTR in all cases. Reporters attributed two cases of AHTR following platelet transfusion to administering O-positive platelets to A-positive donors, with anti-A in the eluate. One patient experienced AHTR twice: reporters attributed this the first time to an anti-Cw and found no serological clarification for the second event. Twice new alloantibody production, anti-E and anti-K, was recorded as an additional category following transfusion where the unit was positive for the relevant antigen. In two further cases, an anti-Fy(a) and an anti-Wr(a) were marked as causal. In the other reported AHTR no causative antibodies were specified.

Delayed hemolytic transfusion reaction (DHTR)

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

In 2008 there were 18 reports mentioned of delayed hemolytic transfusion reactions, in six male and 12 female patients. This number is similar to that in previous years and accounts for 0.9% of the reports (18/1950). In addition, there are two reports of incorrect blood component transfused leading to a delayed hemolytic transfusion reaction; see the relevant section. In 11 cases a new alloantibody was mentioned as an additional category.

The severity of the 18 DHTR was grade 2 four times, grade 1 nine times and grade 0 five times 0 (hemolysis only detectable by biochemical abnormalities). The imputability was judged to be certain 10 times, probable three times, possible twice, unlikely once and twice excluded. The identity of the antibodies responsible is: 3 times anti-Jk(a), once each anti-Wr(a), anti-C, anti-c, anti-Jk(b), anti-K, anti-Fy(b), anti-Lu(a), and once each for the combinations anti-E + anti-K, anti-C + anti-e, anti-Fy(a) + anti-Jk(a) + anti-Kp(a) and anti-E + anti-K + anti-Le(a). In one case, there was no clear identification of antibody for a patient with MDS and a combination of antibodies.

This year as well, numbers of reports of delayed hemolytic transfusion reactions approximate numbers of acute hemolytic transfusion reactions, where the literature indicates factors of 5 to 10 times higher for DHTR. Finding a clinically important new alloantibody should always prompt a check of the patient's hemolysis parameters or the patient's laboratory history for changes in hemolysis parameters LD, indirect bilirubin, haptoglobin and unexplained Hb drop, all of which can point to a DHTR. The importance of doing this is underscored by the fact that in 2008, new alloantibody production led to

discovery of a DHTR 11 times; it is worth noting that 10 reports came from a single hospital. Discovery of a new alloantibody formation, reported as the main category, led to a check for hemolytic transfusion reaction. In 2007, TRIP received only one similar report. In these cases, new allo-antibodies were: three times anti-K, twice anti-E, once anti-Jka, once anti-C, once anti-M, and combinations: anti-E + anti-Jka, anti-c + anti-E + anti-K and anti-c + anti-E + anti-Fya. This increase in reports of new alloantibody formation, with the additional category DHTR, moreover largely coming from one reporter, clearly indicates that the delayed hemolytic transfusion reaction is being missed in Dutch hospitals.

Transfusion-associated acute lung injury (TRALI)

> *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.

In 2008, 19 reports of TRALI came in, a number slightly lower than in 2006 (25) and 2007 (31). TRALI numbers rose from 2003 to 2007, probably due to increased national and international attention for this reaction.

As in previous years, TRIP assessed whether reports fulfilled the national definition of TRALI and judged imputability independent of leucocyte-serology findings. This year, 18 fulfilled the criteria (2007:23) – clinical picture, X-thorax, interval, absence of a more probable explanation – for TRALI. For the report that did not, another possible cause for hypoxia was present – circulatory overload. The number of accepted TRALI reports is comparable to that in 2007. TRIP discusses these below.

Eight (44%) of the reactions arose upon administering RBC concentrates, one for plasma and four for platelets; five patients had received a combination of blood components.

Of the patients, one third was female (average age 53.3; 33.7 – 81.2) and two thirds male (average age 65.4; 30.8 – 80.7). Ten reports are of severity grade 3 and seven grade 2.

At the end of 2006 Sanquin introduced the measure of using exclusively plasma from male, never-transfused donors to prepare quarantined plasma (standard name: freshly frozen plasma) for transfusion. Female plasma more often contains HLA-antibodies and it has been found that some TRALIs occur subsequent to transfusion of plasma-containing blood components in which antibodies are present targeting HLA (Class I or II) or other antigens on the recipient's leucocytes.

Figure 9 shows per reporting year the number of TRALIs with certain, probable or possible imputability in relation to administered blood components. Numbers suggest that 2008 might be revealing a decrease in TRALI with plasma, but numbers are too small to be conclusive.

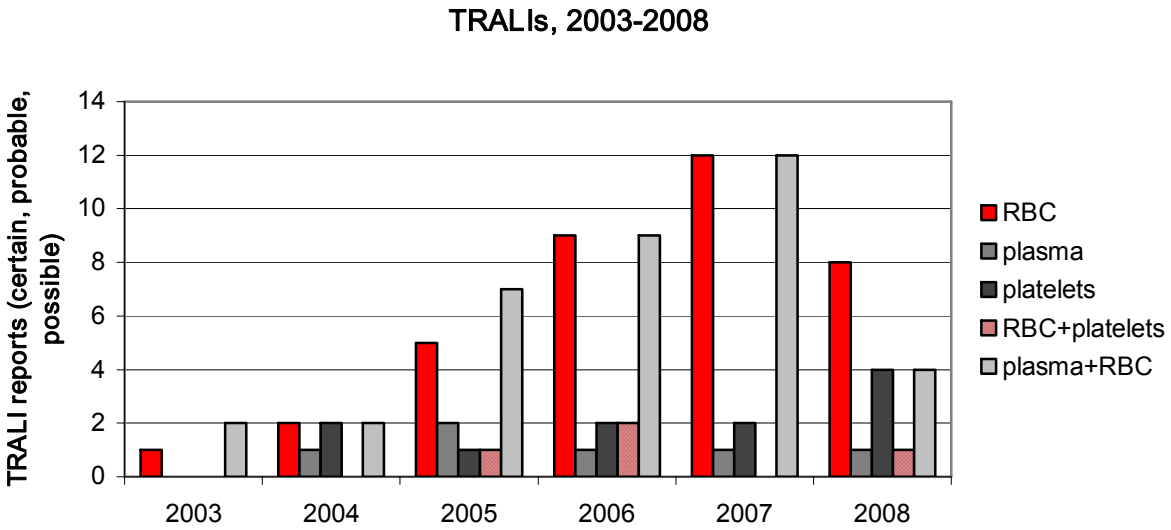


Figure 9 Type of blood component with TRALI reports

Sanquin investigates leucocyte incompatibility for TRALI reports that fulfil the clinical definition. In 2008 16 of the 19 reactions registered as TRALI were investigated by Sanquin, including a crossmatch with fresh leucocytes, or, if antibodies had been found in the donor, establishing whether these were incompatible with the patients' leucocyte markers. Incompatibility was found in nine TRALI cases: the accompanying blood components were RBC concentrate four times, platelet concentrate four times and once plasma from a male donor. In 2007 one TRALI was associated with incompatible leucocyte antibodies in female plasma from the time before implementation of the male-only plasma measure.

The level of investigation seems improved: in the 2007 report there were four cases of donor antibodies being found, but lack of patient material made it impossible to know whether they were incompatible. TRIP does not know how many cases were originally reported to Sanquin as TRALI, but later ended up in another category after being refused for serological investigation or after exclusion of an immune cause following TRALI investigation.

Anaphylactic transfusion reaction

Serious 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 59 reports of anaphylaxis in 2008 (2007: 50, 54 including late reports) in comparison with 19 in 2006 and 26 in 2005. As indicated last year, the increase is due partially to TRIP having made known its standpoint that this category includes combinations of skin rash with signs of airway obstruction and breathing or gastrointestinal symptoms (even without hypotension). Of these reports, 28 are grade 2 or higher in severity 2, compared to 22 in 2005, 13 in 2006 and 22 in 2007. Table 1 shows that, numerically, anaphylaxis remains one of the most important categories of serious transfusion reaction categories, along with TRALI and circulatory overload.

Thirteen reports of anaphylactic TR are associated with transfusion of RBCs, 12 with plasma, 28 platelets and 6 with more than one type of blood component. It is not the case that more serious reactions occur with transfusion of a single type of blood component. The interval between starting transfusion and appearance of symptoms, where indicated (n= 43), varies from 0 minutes to 7 hours and 30 minutes. In *Figure 10* it can be seen that there is a trend towards a shorter interval as the reaction becomes more severe. This underscores the usefulness of intensive monitoring during the first minutes, but it also shows that a serious reaction quite regularly still occurs after a longer interval.

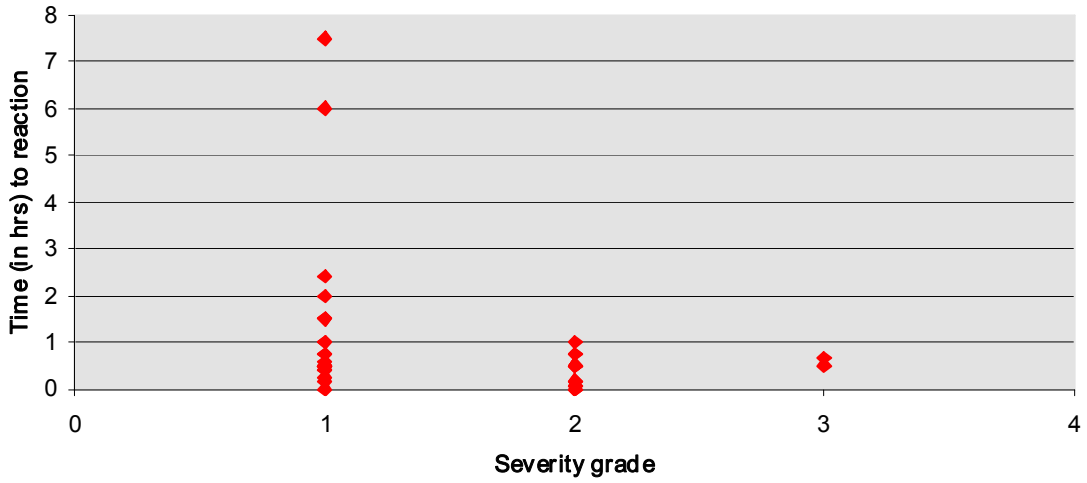


Figure 10 Relationship between grade of severity and time interval for anaphylactic reactions

For 12 reports the hospital indicated that it had found normal IgA levels and/or excluded the presence of anti-IgA. Several others remarked that this investigation would be pointless because previous or later transfusions took place without incident; in fact, only the later transfusions are relevant here, since that an allergy in principle arises from earlier contact with an antigen. International literature quotes anti-IgA as explaining 10-20% of anaphylactic reactions. Notes to 6 reports stated that the patient received other medication that may have induced the reaction.

Five patients also had a transfusion reaction to another administered blood component: anaphylactic reaction (n=1), other allergic reaction (n=20) and febrile reaction (n=2). The median age is 51.5, thus younger that both TRALI and circulatory overload reports; there were approximately equal numbers of male and female patients.

Other allergic reactions

Allergic phenomena such as itching, redness or urticaria (but without anaphylactoid signs) arising from a few minutes of starting transfusion until a few hours after its completion.

The number of reports of “other allergic reaction” has decreased slightly compared to the final count last year: 167 in comparison to 202 in 2007 and 222 in 2006, including late reports. As remarked in 2007, cases that “disappeared” probably were registered in the category anaphylactic reaction, conforming to TRIP's request to place allergic reactions with more than solely skin symptoms in the category anaphylactic reaction.

Among the five reports for which the grade of severity was 2 or higher there are three cases for which reporters considered a different category – the anaphylactic transfusion reaction – but for which they ultimately selected the category “other allergic reaction” as best. One report was of a child admitted for a night for observation due to a skin reaction. In another, the patient complained of feelings of swelling and tightness of the chest, but these could not be objectified.

As for the anaphylactic reactions men and women are equally represented. For “other allergic reactions”, 47% is associated with administering a platelet concentrate and 23% with plasma. Here also, patients are relatively young, probably due to the patient population receiving these types of blood components; the median age is 50.6. Of these patients, 22 (12%) had experienced one or more other allergic, febrile or other transfusion reaction, previously or in 2008.

Circulatory overload

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

There were 38 reports of circulatory overload (also called TACO: transfusion-associated circulatory overload) in 2008, compared to 34 in 2006 and 31 in 2007. One report is of grade 3 severity and 15 grade 2, comparable to previous years. Most reports mention administering RBC concentrates (32.84%) exclusively. Reporters originally considered TRALI in a number of these cases and two cases did reveal incompatible leucocyte antibodies in a donor: this illustrates the fact that leucocyte incompatibility does not have to lead to TRALI. As noted in the report for 2007, the age of patients with circulatory overload is high: median 77.3. Of the three patients younger than 60, two had compromised cardiac function and the third was undergoing plasmapheresis for kidney problems.

It is difficult to distinguish TRALI and circulatory overload clinically, even by chest X-ray. Laboratory determination of brain natriuretic peptide (BNP) or the more stable N-terminal pro-BNP that increase in heart failure and circulatory overload (Transfusion 2009 Jan. 49(1): 13-20) is insufficiently specific in this setting. Clinical symptoms of shortness of breath and sometimes of increased blood pressure were recorded in all reports of circulatory overload in 2008. *Table 5* shows the additional features mentioned in support for diagnosing circulatory overload, to the extent this was communicated to TRIP, based on radiography, cardiac history and the response to diuretics.

Table 5 Findings in reports of circulatory overload

Circulatory overload	Unlikely	Possible	Probable or certain
Total number of reports	3	22	13
Chest X-ray	1	14	6
Response to diuretics		5	6
Diuretics administered (no response information)		1	2
Cardiac pathology (previous or active)	1	7	5

There were nine reports where no chest X-ray was made, for a patient with cardiac pathology or where the patient responded to diuretics.

It remains to be seen to how many TACO cases are preventable. Few reports of circulatory overload came in during the first years of the TRIP registration. One often hears the view that this is a question of fluid balance and therefore not specifically transfusion related. Internationally as well, the problem of circulatory overload has not come to the fore particularly well in hemovigilance registrations. Meanwhile, primarily in France and Canada, it has become clear that TACO is an important cause of death from transfusion-associated complications. Numbers of annual TACO reports do not seem to have stabilised yet in the Netherlands; this may indicate underreporting.

Post-transfusion purpura (PTP)

Serious selflimiting thrombocytopenia possibly with bleeding manifestations (skin, nose, gastrointestinal, urinary tract, other mucous membranes, brain) 124 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

In 2008, one report of PTP came in. Since TRIP began its registration programme there has been only one other report of PTP, in the baseline measurement in 2002. This report concerned a female patient to whom RBCs, plasma and platelet concentrates were administered in connection with a coronary bypass operation. After an interval of six days, she developed acute thrombocytopenia (numbers of platelets fell from 162 to 8 within 48 hours). Lab investigations revealed antibodies against HPA-1a. The severity was judged to be grade 1 with probable imputability.

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

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, with a high mortality. Skin (and liver) biopsies can support diagnosis.

In 2008, one report of TA-GvHD was submitted. Typical skin symptoms were found and the diagnosis of TA-GvHD was seriously, but later excluded. The imputability of this transfusion reaction is therefore “excluded”. Leucodepletion, practised on all blood components since the end of 2001 in the Netherlands, significantly prevents TA-GvHD. Patients at risk receive irradiated blood components as a preventive measure.

Hemosiderosis

Iron overload induced by frequent transfusion with a minimum ferritin levelof of 1000 micrograms/L.

In 2008, three reports of hemosiderosis were received from one institution. Reports have not increased since 2006, although TRIP requested attention to this in its 2006 report. Two patients had MDS and one sickle-cell anemia. In addition, another institution discovered hemosiderosis in a patient analysed for an “other allergic reaction”. Depending on prognosis iron chelation therapy was prescribed.

New allo-antibodies

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).

For 2008, TRIP received 560 reports of new alloantibody production. As in former years, this category is the largest. This year it makes up 28.7% of the total number of reports, comparable to 2007 (564 = 29.6%). Fifty of the 98 participating hospitals sent such reports. Of these 560 reports, a delayed hemolytic transfusion reaction was mentioned as an additional category 11 times. Finding new alloantibodies was the reason to check the patient and hemolysis parameters supported the retrospective DHTR diagnosis. It is remarkable that 10 reports came from the same hospital. See the section on delayed hemolytic transfusion reaction for the discussion. Mention was made twice of a mild febrile reaction as an additional category to new alloantibody production.

Besides the 560 reports of new alloantibody as the main category, there are 23 mentions of new alloantibody production as an additional category to other transfusion reactions or incidents. These were AHTR twice, DHTR 13 times, NHTR three times, mild febrile reaction twice, other incident twice and incorrect blood component transfused once. See the relevant sections for the discussion.

Of the reports of new alloantibody production, 210 were for male and 350 for female patients. In 93 (16.5%) of the reports, there was multiple (two or more) antibody formation. *Table 6* shows the antibodies produced. The administered component was an RBC concentrate in 519 cases, a platelet concentrate in 11 cases, plasma and platelets three times and, in the other cases, RBCs and plasma and/or platelets; in six cases the administered component is unknown. In 490 cases, reporters noted severity of grade 0, in 28 grade 1, 3 times grade 2 and 40 times not stated. One severity grade 2 report is for a patient with sickle-cell anemia, for whom formation of an anti-Fy3 has made finding a compatible donor so difficult that the Expert Committee has decided to place the grade of severity grade higher in this exceptional case. For eight cases of grade of severity 1 and one grade 2, a DHTR was noted as an additional category, clarifying the designation of severity. As well, once formation of HLA/HPA antibodies with grade 2 reported a delay of five weeks in a second course of chemotherapy for AML because sufficient, compatible, platelet donors could not be available earlier.

As in previous years, the largest number of reports is for anti-E: 205 times (36.5%). Second largest is anti-K: 148 times (26.3%). An anti-K was found nine times in a woman of fertile age. For all of these, however, the transfusions took place before 2004 and thus prior to implementing CBO Guidelines. Besides the 148 reports, there is one for incorrect blood component transfused, in which a woman of fertile age (< 45) produced an anti-K. There was also an other incident, in which anti-K appeared subsequent to an unnecessary transfusion based on an incorrect Hb.

In women under 45 years of age, there were 22 cases of an anti-c and/or an anti-E, compared to 26 in 2007. Eight of these patients had their transfusion in 2008; twice the allo-immunisation followed a platelet transfusion. The TRIP 2007 report recommended transfusing Rhesus-subtype compatible units for women under 45. Based on the report of the Dutch research project ”Identification and Prevention of Pregnancy Immunisation”, the new CBO consensus on blood transfusion will recommend solely K-negative and c-compatible transfusions for women of childbearing age.

In the reporting year 2008, 20 reports came in concerning the production of anti-D. These include nine cases of Rhesus-incompatible platelet transfusion, including one woman less than 45 year old. In four cases an anti-G was found, in five an anti-D and an anti-C, but no further research was done for anti-G. For an older man and an older woman, reasons for anti-D production are unknown; Sanquin did gene typing on the donor. TRIP was not informed of the results.

Table 6 New allo-antibodies reported in 2008

Antibody	Number	Antibody	Number
Anti-c	57	Anti-S	12
Anti-C	31	Anti-s	2
Anti-D	20	Anti-Lua	9
Anti-e	4	Anti-Cob	3
Anti-E	205	Anti-Lea	3
Anti-K	148	Anti-A1	1
Anti-Kpa	20	Anti-Bga	1
Anti-Fya	47	Anti-HTLA	1
Anti-Fyb	3	Anti-P1	1
Anti-Jka	49	Anti-f	1
Anti-Jkb	16	Anti-V	1
Anti-Cw	21	Anti-Vel	1
Anti-Wra	13	Anti-Jsa	1
Anti-M	10		

Other transfusion reactions

Transfusion reactions that do not fit into the categories above.

There were 97 reports of other transfusion reactions in 2008, compared to approximately 60 in the years 2004 - 2007. Fifteen are grade 2 or higher in severity. This group includes reports that do not fit the more specific TRIP categories. TRIP examines and discusses clusters with comparable symptoms annually: what is the reason for the increase over previous years?

Firstly there is the cluster of reports in which dyspnoea is the main feature and which fulfil neither the TRALI nor the circulatory overload definition. There were 30 of these in 2008, 5 of them grade 2 or higher in severity, in comparison to 7 (2 serious) in 2007. Therefore part of the increase compared to 2007 lies in this cluster and probably corresponds to the decrease in numbers of TRALI reports which were accepted as conforming to the criteria. Twenty-five of the reports in this cluster also record hypotension (n=10), increased temperature and/or chills (n=5), chills with nausea and vomiting (n=2) or an atypical combination of symptoms that do not fit into a standard category.

Secondly, a cluster of 17 reports (2007: 14) state hypotension as the most important symptom accompanied by increased temperature in nine cases, once associated with a strange feeling in the stomach, once with temperature increases and vomiting and once with pain in the infusion arm. Five of the reports with hypotension are grade 2 or higher. Some foreign hemovigilance systems recognise the hypotensive reaction as a separate category.

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. The transfused blood components were: RBC concentrates six times, once plasma and once a combination of blood components. Reporters do not specify details of blood pressure in all cases. Twice, in reactions assigned grade 1, this was strikingly high, with one case going from 137/68 to 161/138 within 10 minutes, with a half grade of temperature increase and spontaneous recovery within 20 minutes; in another case the blood pressure rose from 117/75 to 147/117 accompanied by swelling of the throat/face and double vision in a patient with HLA antibodies. TRIP is keen to see more detail on the clinical picture in reports of blood pressure increases to be able to discover if this is a relevant phenomenon or nonspecific clinical variation.

In seven reports (2007: 8) there were cardiac symptoms like chest pain, heart palpitations or cardiac arrhythmias. Four showed gastrointestinal symptoms (nausea, vomiting or stomach cramps). Imputability was judged possible or probable in most.

One report describes the observation of swirling and clotting in the umbilical vein during an intrauterine platelet transfusion, after which the foetus, who had congenital malformations, died. The treating physicians judged imputability as probable and named the clinical situation as a determinant – this was a high-risk patient and a high-risk transfusion method.

Four reports mention non-specific clinical deterioration: perspiration, feeling ill, listlessness and once a short period of reduced conscious level (which however was explained neurologically) associated with a RBC transfusion, without decreased blood pressure or respiratory symptoms.

Most remaining reports refer to symptom combinations, of such a nature as not to fit well into TRIP categories. The paragraph about blood management techniques deals with an additional three reports: one with a phlebitis-like picture and one of severe confusion. Table 7 summarises symptoms reported for the category "other reaction" in 2008.

Table 7 Symptoms in the category of "other reaction" in 2008

Symptom	Number of reports	Mentions in the severe category
Other reaction (all reports)	96	15
Temperature increase	39	7
Chills	25	5
Temperature increase and/or chills	52	7
Dyspnoea	32	5
Hypotension	28	5
Chest pain/pressure or arrhythmia	13	3
Skin symptoms	13	2
Nausea/vomiting/diarrhoea	10	2
Hypertension	8	2
Nonspecifically "unwell"	4	1
Bronchospasm	2	0
Phlebitis–like	2	0

Finally, another significant group of registrations of "other reaction", usually as an additional category, is that where platelet transfusion produced insufficient yield. Laboratory investigations into temperature increases, sometimes with dyspnoea or other allergic symptoms revealed this. Thirteen reports in 2008 (2007:9) fell into this cluster; six times HLA antibodies were found, once HLA antibodies were negative and in other cases TRIP had insufficient information.

3.2 Infectious transfusion complications

Post-transfusion viral infection and viral contamination of the blood component

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

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

In 2008 there were seven reports in the category of post-transfusion viral infection. One of these was a cytomegalovirus infection in a two week-old, prematurely born child who had received an RBC transfusion. Imputability was rated as “possible”; barrier nursing had not been applied thus other sources of infection need to be considered.

A second report had to do with post-donation information to Sanquin, where the donor developed flu-like symptoms the day following donation. The recipient, a patient with a hematological maligancy, showed signs suggestive of influenza after transfusion. No virological investigations were performed, however, and possible imputability was assigned for lack of further evidence.

The other five reports concern hepatitis B (in one case combined with hepatitis C), diagnosed after transfusion. In all cases, retesting of pre-transfusion samples and the donors ruled out transfusion as cause of the infection. For one of the reports, staff considered post-transfusion hepatitis and the blood service performed extra donor investigations, but later it was established that the biochemical liver function abnormalities probably were due to a vascular stenosis; the patient’s serological results did not fit acute viral hepatitis.

Two reports were received in in the category viral contamination of blood component. They refer to a donor in whom hepatitis B infection was found on testing a subsequent donation and for whom other tests established retrospectively that the virus was present in an already administered blood component. The recipient of an RBC concentrate with a retrospectively positive PCR, appeared not to be infected. A second patient, who received a platelet concentrate, was infected and showed slight liver function abnormalities – in the absence of viral genotyping, imputability was assessed as probable.

Bacterial problems in relation to blood transfusion

In 2008, TRIP added the reporting categories “bacterial contamination of blood component” and “post-transfusion bacteraemia/sepsis”. This reporting year, there were two reports that fitted the category bacterial contamination according to the old definitions and, according to this system, fell into the category post-transfusion bacteraemia/sepsis. See Case Histories I for their discussion.

Additionally, by adding a particular code to the report in the office database, TRIP kept track as fully as possible of reports where there a transfusion reaction in a patient with a pre-existing bacterial infection. By registering more fully in which reactions bacterial contamination or infection could have played a role, TRIP expects to obtain a better picture of the influence that transfusion and bacterial contamination/infection could have on one another. The first possibility is that the blood component is contaminated with bacteria at the time of its administration and that thus the bacteraemia/sepsis arises in the person receiving this component. The second possibility is that intravascular procedures, like infusion and transfusion, can put a patient at risk for both phlebitis and bacteraemia/sepsis. Thirdly there is the question: could administering a blood component, in particular an iron-containing component like RBC concentrate, activate an existent bacterial infection? This year for the first time, TRIP has attempted to use the more detailed registration to analyse reports where bacterial contamination/infection seems to play a role.

As can be expected when introducing new reporting categories, not all relevant reports were submitted in the correct category or correct additional category. In several cases NHTR, other reaction or other allergic reaction was chosen, sometimes with an additional category of post-transfusion

bacteraemia or bacterial contamination of the blood component. The tables in this section include all suitable reports and not just those actually submitted in the bacterial categories. Other sections of the annual report mention these reports according to the categories in which they were submitted.

Bacterial contamination of blood component and report of positive bacterial screen

Bacterial contamination of the 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.

Table 8 and *Table 9* give an overview of reports in the category or additional category bacterial contamination of blood component. The majority of these (20) concerned units for which Sanquin found a positive result upon culturing the platelet unit, after its administration in hospital. It is striking that, for a variety of reasons, the patient's blood is not always cultured subsequent to Sanquin's notification of a positive bacterial screen (only 5 times was this noted). Logically speaking, it is often not possible to culture an already administered component.

For platelets only three reports came in showing the transfusion-bag culture as positive where patient symptoms alerted the hospital to culture the component. One was submitted in the category bacterial contamination of blood component, the second in other allergic reaction and the third in NHTR, with other reaction as an additional category. In all other cases it was the blood service Sanquin which found the bacterial screen positive for platelets. In 2008, one report was registered in the category positive bacterial screen where the bacteriological confirmation in unknown.

After administering RBCs, four reporters chose the category bacterial contamination of blood component based on positive screen results by Sanquin and nine times reporters chose this category or additional category after finding positive culture results on the remnant of the transfused unit or on segments of tubing on the unit, examined after the patient had shown a reaction. In addition to these 13 reports, seven more fit into this category because of a positive culture result for the component, but these were submissions as NHTR (3), other reaction (1), circulatory overload (1), post-transfusion bacteraemia/sepsis (1) and incorrect blood component transfused (1).

In addition to reports hospitals sent in, Sanquin sent TRIP information about units supplied to hospitals that subsequently proved to be positive on bacterial screen. For 89 initially positive cultures, TRIP learned that one or more associated units had already been administered, amounting to a total of 102 units (18 RBC concentrates and 94 platelet concentrates). Of these, confirmation cultures produced results for 91, 74 of which showed a Propioni Bacterium . In none of these cases did Sanquin receive information of any symptoms of illness. Note that the numbers given by Sanquin for as positively screened/confirmed bacteriogically infected platelets or associated RBC concentrates is much higher than that of the reports from hospitals to TRIP in this category; the fact that this reporting category was introduced later clarifies the disparity. The figure Sanquin gives for the total number is most reliable. TRIP sees it as relevant to receive more detailed information through the hospitals about findings in the patients.

It must be concluded that the number of reports in the category bacterial contamination of blood component is incomplete. Furthermore, in some of these reports, essential information is missing so that it is impossible to say with any certainty whether disadvantageous consequences for the patient ensued.

TRIP would like to emphasise that finding a positive culture of the blood component subsequent to complete or partial administration is not necessarily evidence of pre-existent bacterial contamination of the component. There is a very real chance that the blood component became contaminated during transfusion or after disconnecting the unit. Even when cultures reveal the same bacterium in the

donation and the recipient's blood, it is impossible to say with certainty whether the bacterium infected the patient from the component or the patient transferred it to the component. Only when Sanquin screens the component, revealing bacterial strains identical to those in the patient's blood culture, can there be certainty that the blood component caused the patient's infection. In 2008, four reports came in for which Sanquin had either a positive screen or a positive culture for the blood component and where a positive blood culture for the patient found after transfusion. *Case Histories 1* shows a short summary of three of these. The fourth case is discussed in the section on reports of grade 4 severity.

Table 8 Bacterial contamination of platelets

Culture result Sanquin	Culture result hospital	Blood culture patient	Reporting category (if other than bacterial contamination of blood component) and observed symptoms
Bacillus cereus		not noted	No symptoms observed, patient already taking Tazocin
Propioni bacterium species (12x)		5x not noted	5x no symptoms observed 1x noted patient already taking antibiotics 1x noted patient meanwhile deceased
		1x negative	first platelet concentrate administered fully, contamination established retrospectively, during second platelet concentrate, chills and temperature increase Interval 1 hr and 15 min
		5x not done	5x no symptoms observed: 3x noted that patient already on antibiotics (2 of these deceased in the meanwhile)
		1x positive: Enterococci	no symptoms observed
Gram positive rods		negative	no symptoms observed
Corynebacterium species		negative	no symptoms observed
Anaerobic culture: Gram-positive cocci		not noted	no symptoms observed
	Hemolytic streptococci gr B	negative	temperature increase, chills, tachycardia, hypotension, dyspnoea, nausea and vomiting Interval 15 min
	Staphylococcus epidermidis	negative	NHTR temperature increase and cardiac arrythmias
	Coagulase-negative staphylococci	negative (5 and 7 days after transfusion)	other allergic reaction itching and exanthema Interval 55 min
BactAlert negative	Coagulase-negative staphylococci	Coagulase-negative staphylococci	post-transfusion bacteraemia/sepsis temperature increase, chills, tachycardia, nausea and vomiting Interval 15 min

Table 9 Bacterial contamination of RBCs

Culture result (Sanquin)	Culture result (hospital)	Patient blood culture	Reporting category (if other than bacterial contamination of blood component) and observed symptoms
Micrococcus species		not noted	no symptoms observed
Propioni bacterium species (3x)		1x not noted	not noted
		1x not done	no symptoms observed, by chance both possibly contaminated components administered to the same patient
	Coagulase-negative staphylococci	negative	additional category NHTR: temperature increase and chills
	Bacillus species	not noted	additional category other reaction: skin rash and later temp., patient already on antibiotics
	2x Coagulase-negative staphylococci Sphingomonas paucimobilis Staphylococcus epidermidis Propioni bacterium species Gram+ cocci	6x negative	7x NHTR with additional category bacterial contamination blood component
	Serratia marcescens	1x not noted	
	3x Staphylococcus epidermidis	3x negative	3x NHTR
	3 types of skin flora, not specified further	negative	other reaction
	Staphylococcus epidermidis	not done	circulatory overload
	Coagulase-negative staphylococci	Enterococcus; enterobacter cloaca; coagulase-negative staphylococci	incorrect blood component transfused N.B. patient had been admitted to hospital for recurring sepsis
Not tested	Staphylococcus epidermidis	Staphylococcus epidermidis	post-transfusion bacteraemia/sepsis mild temperature increase, chills N.B. probably different strains antibiogram very different

Post-transfusion bacteraemia/sepsis

Clinical symptoms of bacteraemia/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 2008, 35 reports were submitted in the category or additional category of post-transfusion bacteraemia/sepsis. Administered blood components were RBCs 30 times, platelets twice and three times a combination of RBCs and platelets. These are reactions for which hospital staff collected a blood culture after transfusion or after stopping transfusion because patient symptoms pointed to a possible transfusion reaction and the culture was relevant and positive. The report does not fit the category post-transfusion bacteraemia if the blood culture is already found positive before transfusion.

With two exceptions, patients showed fever, in many cases with chills (13 = 39.4%); other symptoms included hypotension (three times), hypertension (once), dyspnoea (three times) and vomiting (twice). The remaining two cases only mentioned chills/rigors. The interval between commencing transfusion and observing symptoms varied from 15 minutes to 8 hours (average 2 hours and 33 minutes, median 2 hours and 15 minutes), but regrettably it was not documented in three cases. Sanquin found no positive screens for any of these products or derivatives.

In the majority of cases, a culture was performed on the component or a remnant of it (26 = 74.3%) and usually this was negative (24). Twice, more than one component was given sequentially and only some of the administered components could be cultured. There were seven reports of no culture done of the component and twice details were given.

Case Histories 1 summarises three reports where the culture of both the patient's blood and the administered unit was positive. Two cases, registered as post-transfusion bacteraemia, show the same types of bacteria, making transmission by a contaminated unit plausible. Lack of proof of identical genotypes makes it impossible to assign imputability any higher than “possible”.

A positive blood culture in a patient is noted 34 times in other reporting categories as well, but these show that the culture was already positive before transfusion too. Most fall into the category non-hemolytic transfusion reaction (23).

To be able to judge whether numbers of reports in the category post-transfusion bacteraemia/sepsis provide an accurate picture, insight into numbers of reports of NHTR in which blood cultures were taken and their results communicated to TRIP is essential. Table 10 shows the data registered for 2008.

Another area of research interest is whether febrile reactions occur relatively often in patients receiving RBC concentrates, in the presence of a pre-existent bacterial infection. *Table 11* shows an assessment of the presence of pre-existent infection from the available reporting data, which are incomplete on this point. No conclusions can be drawn from *Table 11* because data from which to derive the existence of a pre-existent infection is regularly lacking; the reporting form does not explicitly request this.

Table 10 Summary of cultures per component in the event of NHTR

Component	cultures done	only component culture result	only patient blood culture result	no culture done	not filled in	Total
RBCs	173	48	38	17	100	376
	46.0%	12.8%	10.1%	4.5%	26.6%	100.0%
platelets	19	3	9	1	12	44
	43.2%	6.8%	20.5%	2.3%	27.3%	100.0%
plasma	0	2	3	0	1	6
	0%	33.3%	50.0%	0%	16.7%	100.0%
RBCs+plasma combination	1	0	1	0	0	2
	50.0%	0%	50.0%	0%	0%	100.0%
RBCs+platelets combination	7	0	3	0	3	13
	53.8%	0%	23.1%	0%	23.1%	100.0%
Total	200	53	54	18	116	441
	45.4%	12.0%	12.2%	4.1%	26.3%	100.0%

Table 11 NHTR occurrences with pre-existent infection; blood components involved

Component	RBCs	platelets	plasma	RBCs plasma combined	RBCs platelets combined	Total
Infection present	55	3	1	1	0	60
	91.7%	5.0%	1.7%	1.7%	0%	100.0%
unknown	321	41	5	1	13	381
	84.3%	10.8%	1.3%	0.3%	3.4%	100.0%
Total	376	44	6	2	13	441
	85.3%	10.0%	1.4%	0.5%	2.9%	100.0%

From the above-described findings it can be concluded that, as far as bacteria go, safety of blood components in the Netherlands continues to be at a high level.

Reporters are not applying the amended TRIP definitions unequivocally yet. TRIP expects increased awareness of the amended reporting categories for next year's report. The digital reporting form asks for culture results and full information on these can improve the registrations. TRIP needs better data collection, aimed at clarifying the relationship between the blood components and bacterial infection, to be able to draw reliable conclusions about this in the future.

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

Since 2005, numbers of reports in this category have fluctuated at around 60 per year. The number of cases of incorrect blood component transfused where clinical symptoms are observed shows greater variation: 4 in 2007 and the highest number until now – 16 in 2005. For the 57 instances of incorrect blood component transfused submitted on time for the 2008 report, there are nine cases of clinical symptoms observed in the patient, summarised in *Table 12*. For a more extensive description for a number of reports, see the end of the section on incorrect blood component transfused. One report appears in more detail with transfusion reactions with grade 4 severity.

Table 12 Clinical symptoms after incorrect blood component transfused

Nature of reaction	Total	Component	Grade of Severity				
			0	1	2	3	4
Acute hemolytic transfusion reaction	4	4x RBCs		1	2		1
Delayed hemolytic transfusion reaction	2	2x RBCs		2			
New alloantibody production	1	RBCs	1				
Non-hemolytic transfusion reaction	1	platelets		1			
Other reaction	1	RBCs			1		

In 2008, TRIP assessed the most serious risk that the patient ran for each report in the category incorrect blood component transfused. For example, by confusing patients, where patient X received the component intended for patient Y, the TRIP estimate was that the highest risk would be that of administer an ABO-incompatible blood component, regardless of the blood group of either patient X or Y. As fully as possible, TRIP categorised the reports according to the first error (in terms of time) through which an incorrect blood component was transfused and according to the presence or absence of subsequent safety measures, which failed in this case, meaning the error went unnoticed. TRIP further assessed the first error by its type, for instance identification, communication or selection. TRIP has also registered where the first error occurred in the transfusion chain. See *Figure 11*. If this step lay outside the reporting hospital, TRIP made no further assessment of type of error made there. Usually errors of this type are reported as product errors, for instance, no Parvo-safe RBC's supplied although requested, or donor errors, like retrospectively discovering that a donor did not fulfil all medical requirements, for example because of having been on holiday in an area with malaria. *Table 13* shows a summary of the risk analysis and first error. See www.tripnet.nl.

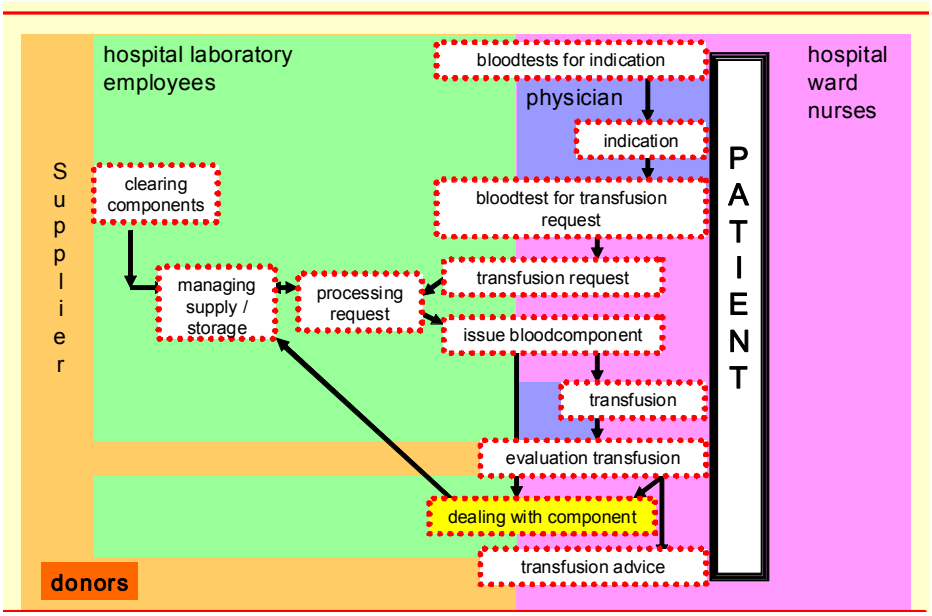


Figure 11 Steps in the transfusion chain

Table 13 Nature of patient's risk and first error in IBCT in 2008

Risk		Step in transfusion chain where first error occurred		Type of first error	
ABO	26	Hospital outside transfusion chain	2	Storage	1
				Identification	1
		Blood tests for indication	1	Laboratory procedure	1
		Request	5	Communication	4
				Identification	1
		Processing request	7	Laboratory procedure	2
				Selection	4
				Identification	1
		Issue	1	Identification	1
		Transfusion	10	Storage	2
				Identification	8
Alloantibody	10	Transfusion chain outside hospital	2	Not assessed	2
		Blood tests for transfusion request	2	Communication	1
				Identification	1
		Request	3	Communication	2
				Assessment	1
		Processing request	2	Laboratory procedure	1
				Selection	1
		Issue	1	Laboratory procedure	1
TA-GvHD in risk group	6	Request		Administration	1
				Communication	5
Preventive policy Irregular antibodies: 9 B19: 2 Irregular antib+B19: 1	12	Transfusion chain outside hospital	2	Not assessed	2
		Request	1	Communication	1
		Processing request	9	Assessment	2
				Laboratory procedure	4
				Selection	3
Thrombosis	1	Processing request		Administration	1
Clotting Hemostasis	2	Request	1	Administration	1
		Processing request	1	Selection	1

Of the 57 reports of incorrect blood component transfused, 26 (45.6%) were assessed as ABO-risk: components administered in these incidents were RBCs 17 times, platelets three times, once plasma, twice combined RBCs and platelets, twice combined RBCs and plasma and once an unnamed component.

Of the 26 reports of incorrect blood component transfused with ABO-risk, by pure chance ABO-compatible RBCs were administered in 12 transfusions. Twice platelets with blood group O were given to patients with blood group A. For 11 ABO-incompatible transfusions, six reactions were reported: further details appear in the next paragraph. For 10 reports of alloantibody risk (17.5%), two reactions were reported: one DHTR after administering several antibody-incompatible RBCs and one NHTR after administering a non-HLA-antibody-compatible platelet component. Failure to follow Kell policy for the target group produced one report of new alloantibody production.

Four cases of AHTR, one DHTR and one other reaction resulted from incorrect blood component transfused with ABO risk. In all of these incidents, a patient with blood group O received RBCs: five times this was donor blood with blood group A and once blood group B. No reactions were observed in other incidences of incorrect blood component transfused with ABO-risk (20). TRIP can clarify this partially because in these cases, by chance, nine times O-positive, once O-negative and twice ABO (not O) identical RBCs were administered. For the remaining 6 incidents, it was twice reported that the administered blood component was ABO-incompatible. The reason that no transfusion reaction occurred for these incompatible transfusions could be the exceptional circumstances. Once, incompatible plasma (A-positive) was given to a B-positive patient, who received large numbers of O-negative RBCs for acute blood loss, and once A-positive RBCs were administered to a patient (O-positive) with very weak anti-A antibodies. Three of the four incidents that do not mention the blood group of either donor or patient occurred in patients who had previously undergone stem-cell transplantation before; no one took this into account for the transfusion. In cases like this, often it is difficult to determine the patient's blood group unequivocally. Case History 2 describes a platelet transfusion with no mention of the ABO blood group either (IBCT-1).

For the 26 reports of incorrect blood component transfused with ABO-risk, TRIP judges that the first error was an identification error in 12 cases: this identification error occurred in the last bedside check before administering the blood component. For the remainder of reports on incorrect blood component transfused (31), identification is the first error only once. Communication (13), laboratory procedure (9) and selection errors (9) constitute an important proportion of these first errors. However, they are distributed more evenly over the different risks. *Table 14* shows a summary of the analysis of ABO-risk reports.

Table 14 Analysis of the ABO-risk for the patient

Step in chain where first error occurred		Type of first error		Subsequent failing safety measures	Total number ofclinical reactions
Hospital outside transfusion chain	2	Storage	1	1 failed next safety measure	4x AHTR 1x DHTR 1x other reaction
		Identification	1	No next safety measure	
Blood tests for indication	1	Laboratory procedure		Several failed next safety measures	
Request	5	Communication	4	Several failed next safety measures	
		Identification	1	No next safety measure	
Processing request	7	Laboratory procedure	2	No next safety measure (1x)	
				Several failed next safety measures (1x)	
		Selection	4	No next safety measure (2x)	
				Several failed next safety measures (2x)	
		Identification	1	1 failed next safety measure	
Issue	1	Identification		Several failed next safety measures	
Transfusion	10	Storage	2	1 failed next safety measure	
		Identification	8	No next safety measure	

Case Histories 2
Short summary of some reports of incorrect blood component transfused – IBCT

IBCT-1 (ABO risk, hospital outside transfusion chain, storage)
Patient X was admitted via A&E and then transferred to the operating theatre with an acute hemorrhage. An HLA-matched platelet concentrate for patient X was ordered urgently through the transfusion laboratory and a platelet concentrate and RBCs were ordered for normal stock. After a period of time, the analyst wondered why the blood had not arrived at the laboratory. Enquiries led to the discovery that the ordered blood had been delivered directly to the operating theatre at the request of a very worried house officer. By this time, following administration of the platelet concentrate bearing the Sanquin label with the name and date of birth of patient X, the non-HLA-matched platelet concentrate meant for laboratory stock had also been administered to patient X.

IBCT-2 (ABO risk, hospital outside transfusion chain, identification)
Patient A had to undergo an urgent operation: the patient file was taken to the operating room in connection with anaesthesia. Based on this file, three RBC concentrates and one FFP (fresh-frozen plasma) were requested. All blood components were administered. After finishing the operation the surgeon, wanting to extract some data from the file, discovered it was not the file of patient A but of patient B. Fortunately both patients had blood group O positive and no irregular alloantibodies.

IBCT-3 (ABO risk, pre-prescription investigation, laboratory procedure)
A Hb of 7.3 mmol/L, determined for a patient V (B positive), was not phoned through to the doctor. A request went in for RBC concentrate for patient V based on a 15-day-old Hb of 5.9 mmol/L. No one noticed the Hb > 6 mmol/L in processing the request. Blood for patient V was issued to the ward. On the ward, someone checked data on the bag of B positive blood against the transfusion form. Concurrently, on the same ward, patient W (O positive) needed blood. Someone checked data for the bag of O positive blood against the accompanying transfusion form. Transfusion of patient V began.
Only after patient W had suffered a transfusion reaction did staff discover that patient V (B positive) had received O positive RBCs. Patient V showed no reaction and a retrospective full crossmatch was negative.

IBCT-4 IBCT + DHTR (ABO risk, request, communication)
Patient A, known to be blood group A positive, received a transfusion of 2 A positive RBC components on day 0, with a Hb of 4.9 mmol/L,. On day 6, the blood transfusion laboratory received a message saying that, a good four months ago, patient A had undergone allogeneic stem-cell transplant with B positive cells. Checks on day 7 showed a Hb of 4.9 mmol/L and patient A received 3 compatible RBC concentrates. Day 27 showed Hb 6.6 mmol/L and LDH 829; day 29 Hb 5.0. Two compatible RBCs were given and the Hb rose to 7.2.

IBCT-5 (ABO risk, processing request, selection)
Definitive determination of patient X's blood group was A positive in 2006. In 2008, after an urgent request for blood, four A positive RBCs and two FFP were issued without crossmatching and administered, instead of the appropriate O negative. The blood group was re-determined, but only retrospectively.

IBCT-6 (ABO risk, processing request, identification)
An HLA-identical platelet concentrate was ordered for patient A. The ward rang the blood-transfusion laboratory a number of times to ask if the platelets were ready. A platelet concentrate arrived at the laboratory, and the analyst ensured its rapid issue for patient A. A little later, another platelet concentrate arrived at the lab, apparently meant for patient A. The earlier platelet concentrate had been meant for patient B, but already had been administered to patient A.

Case Histories 2 (continued)
Short summary of some reports of incorrect blood component transfused – IBCT

IBCT-7 IBCT + AHTR (ABO risk, transfusion, storage)
On a ward, two RBC concentrates meant for two different patients X and Y were temporarily stored in the fridge, contrary to hospital regulations. A little later, an RBC concentrate was taken from the fridge and administered to patient X. When the nurse went to the fridge for patient Y's RBC concentrate, RBCs for patient X were still lying there. The concentrate meant for patient Y meanwhile had been administered in its entirety to patient X.

IBCT-8 IBCT + AHTR (ABO risk, transfusion, identification)
Approximately 2 hours after starting transfusion of an RBC concentrate, patient W (O positive) developed nausea, vomiting and diarrhoea. Additionally, cyanosis was noted. The transfusion was stopped – approximately 200 mL had been administered. Comparison of data for patient W and the RBC took place. The RBC concentrate was B negative and had been issued for patient V (B positive) instead of patient W.

IBCT-9 IBCT + DHTR (alloantibody risk, request, communication)
In hospital 1 diagnosed patient P is known to have irregular antibodies of anti-c specificity. Patient P was admitted to hospital 2 for surgery. Hospital 2 was unaware that patient P had formed allo-antibodies in the past. Screening in hospital 2 did not show any anti-c and patient P received a number of c-positive RBC concentrates. No transfusion reaction was observed and patient P was discharged after some time. A few days later, patient P was admitted to hospital 1 with low Hb. Irregular-antibody screen showed a strongly positive anti-c.

IBCT-10 (alloantibody risk, hospital outside transfusion chain)
Owing to a mix-up of donor identification at the blood bank, a hospital received an RBC concentrate with incorrect information about antigen typing on the label. Happily, the RBC concentrate was administered to a patient without allo-antibodies for those antigens.

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.

In 2008, 80 reports of other incident were received; in nine cases the patient also showed clinical symptoms and signs. Table 15 shows a summary and some examples are described in *Case Histories 3*. A short description accompanies each other incident where the patient displayed symptoms. This underscores how the relationship between incident and symptoms can differ. For some cases, it is reasonable to assume that the incident caused the patient reaction, sometimes the patient reaction leads to discovery of the incident and in some cases the patient's reaction creates a situation in which an incident occurs.

Hospitals reported fewer donor and component incidents to TRIP arising from notifications from Sanquin and this explains the lower number of reports of other incident in 2008 in comparison to previous years (101 reports in 2007). Although this type of report made up 36% of other incidents in 2007, it fell to 15% in 2008. Retrospectively, TRIP can ascribe the decrease in these reports to a fall in numbers of reports from a single hospital where a change of personnel took place. This demonstrates just how much impact the reporting behaviour of a single hospital can have on the national registration. If this hospital had reported numbers equal to the year previous, the total category number would have been 107. TRIP suspects that many hospitals regard the practice of reporting component and donor incidents as optional. If this is the case, the numbers can vary more noticeably from year to year than for other categories not treated as optional.

Table 15 Clinical symptoms with or subsequent to incident

Nature of reaction	Total	Component	Grade of severity					
			0	1	2	3	4	Not noted
New alloantibody production	2	2 RBCs	1					1
Non-Hemolytic transfusion reaction	2	2 RBCs		2				
Mild non-Hemolytic febrile reaction	1	RBCs		1				
Other reaction	4	2x RBCs						
		2x unknown		4				

Thirteen other incidents are discussed in the chapter on blood management techniques. The following sums up briefly other important groups of distinguishable other incidents.

A large number of reports (14 = 17.5%) of other incidents concern storing blood component too long or incorrectly resulting in the component to be unsuitable for transfusion. In three of these cases, sending blood components to another ward or another hospital accompanying the patient played a role. In two other situations, sending along blood components with the patient led to reports of problems tracing the components. Once, faulty registration caused the tracing problems.

Among the other incidents, TRIP again finds a number of reports of transfusing a blood component based on an incorrect, old or incorrectly interpreted result, meaning that the patient received an inappropriate transfusion although the actual component was selected and administered correctly for this patient.

Donor and component errors produced 12 reports. These include a report of a donation where no account was taken of the deferral period of 60 days following a visit to the USA, a donation from a donor later diagnosed with Lyme disease and a donation from a donor who tested positive for hepatitis B at the next donation. Problems with labels on blood components, blood components supplied but not fulfilling requirements the hospitals have agreed or requested and a bag that started to leak during administration all belong to these types of incidents. Two reports mention accidental piercing of the bag when starting administration.

It is remarkable that only two reports in this category concern administering or almost administering a different blood component type from that prescribed. The component in this report fulfils all requirements for a good blood component for the relevant patient. In that sense, there is no question of incorrect blood component transfused. However, there was no indication for the transfusion, a similar situation to transfusing a patient based on an incorrect Hb result or platelet count –categorized under other incident as well. Some reporters placed administering another blood component type than the intended in the reporting category of incorrect blood component transfused or near miss. It would be advisable to have clearer agreements in the future about the most appropriate reporting category.

Case Histories 3
Examples of other incident (OI) reports where a patient showed a transfusion reaction

OI-1 The patient experienced chills and fever, but as no temperature had been taken prior to transfusion, it was impossible to determine the size of the temperature increase. The chills, however, made it possible to assess the reaction as NHTR.

OI-2 The patient being treated with chemotherapy had Hb results > 7.0 mmol/L during checks about 7 and 4 weeks prior to transfusion. Based on subsequent Hb results of 5.9 mmol/L, two RBC components were administered a week later. Hb checks a week after transfusion showed a Hb of 9.1 mmol/L. No evidence was found of patient or blood-sample tube switches. Transfusion was judged to have been unnecessary retrospectively. Approximately a month after this transfusion, the patient was found to have formed anti-K: of the two administered RBC components, one was K-positive.

OI-3 For a patient for whom allo-antibody screening was routinely performed three times a week, during transfusion of RBCs (issued with a valid negative screen) the patient screen was found to be positive. The transfusion was stopped. Anti-Jk(a) was identified, the partially administered component proved to beJk(a)-positive.

OI-4 At the start of transfusion a remnant of 2.5% glucose/NaCl solution was present in the lowest portion of the line. The patient experienced a feeling tingling over the whole body for a period of five to ten minutes. Five minutes after commencing transfusion, administration was interrupted. The system was replaced by a new one with 0.9% NaCl. Once the tingling feeling had disappeared, the transfusion was continued without any further problems.

OI-5 The transfusion was interrupted 20 minutes after commencement because blood was running subcutaneously into the patient's arm; it is unknown how much blood was administered. Checks after disconnecting the RBC concentrate showed a mild temperature increase as well. Approximately 3 weeks later, anti-E formation was established. The partially administered unit and another unit administered the same day proved to be E-positive.

OI-6 The transfusion of RBC concentrate ran subcutaneously for a longer period of time, giving rise to a sizeable hematoma. A surgeon operatively evacuated the hematoma and the wound needed rinsing twice daily. Antibiotics were given preventively.

administration of an incorrect blood component, and which was detected before transfusion.

In 2008, 11 hospitals reported a disappointing total of 53 near misses (varying from one to 24 per hospital). This report describes some of the TRIP analyses of reported near misses and describes a number in more detail.

It is striking that there were very few reports of near misses from the 12 hospitals that participated in 2007 and 2008 in the TRIP incident reporting project (2008: 5, 2007: 9). The PRISMA method used to analyse incidents in the project is, in fact, excellently suited to analysing near misses. TRIP expects to publish a report on the project for incident reporting soon. Mapping near misses on a broad scale should make it possible to discern weak spots in the transfusion chain and assess the effect of safety measures. Numbers at present still are too small to be able to draw reliable conclusions.

In more than two thirds of cases (67.9%), the first error occurred in the steps “request” (11) or “blood test for transfusion request” (25); of these 36 errors, 27 are identification errors (discovered in eight cases by blood-group discrepancies). It not surprising that many near misses occur in these steps of the chain; after all, there are many identification and handover moments, all of them error prone. Nevertheless, within and subsequent to the step “blood test for transfusion request”, large numbers of

safety measures are built into the procedure to promote timely discovery of an error. By comparison: the number of reports of incorrect blood component transfused where the first error occurs in this part of the chain is 19 in 2008 (33.3%), of which 16 in the step “request” and 3 in “blood test for transfusion request”, while 9 (15.8%) first errors were reported in the step “transfusion”. It is striking that the first error for near misses, thus errors discovered on time, are primarily identification errors (64.2%). When we compare that to the first error reporting incorrect blood component transfused, we see that only 22.8% are identification errors, equal to the percentage of communication errors (22.8%) and only slightly higher than numbers of selection errors (15.8%) and laboratory procedure errors (14.0%).

Table 16 shows a summary of the types of errors for near misses. The reports are arranged by appear as the type of error which occurred in time. The right part of the table shows how the error was discovered. Both happenstance and personal alertness played roles in a number of cases. Happenstance was recorded when personal alertness on its own would not have sufficed to notice the error. In some cases the reporters themselves recorded this information on the digital reporting form or noted it in their explanation; in other cases, TRIP specified happenstance on the basis of the description of the incident. Whereas a planned safety measure led to detection in the majority of cases (33 = 62.3%), a planned safety measure failed to discover the error in almost a quarter of the near misses (13 = 24.5%). Unfortunately, there is no mention of how the error was brought to light in a relatively large number of cases (7 = 13.2%).

Table 16 Near misses 2008: type of error made first in time and manner of discovery

Error in	Total	Discovery through			
		planned safety measure	personal alertness	happen stance	not reported
identification	34	26	1	4	3
administration	3			1	2
communication	3	1	1	1	
taking blood sample	2			2	
laboratory procedure	1				1
component	6	4	1	1	
assessment	1		1		
other	3	2			1

Case Histories 4
Summary of a number of reports of near miss (NM)

NM-1 (identification, request, discovered by happenstance)
The transfusion laboratory processed a request for an RBC concentrate. The analyst was feeding patient X1's PIN from the addressograph details on the form into the computer, when he noticed that the requesting physician had hand-written similar name X2 on the request and the same year of birth, but another day and month. Both patients had a low Hb, but only patient X2 needed transfusion.

NM-2 (identification, hospital outside the transfusion chain, discovered through planned safety measure)
A change in surgery schedule meant patient B was to be operated on first instead of patient A. A request came into the laboratory for RBCs for patient B, accompanied by blood tubes with labels for patient A. When the laboratory asked for clarification, it was discovered that labels for patient A were present in patient B's file. Before taking the blood sample, no checks were done of name and date of birth on the blood tube labels.

NM-3 (identification, testing for request, discovered by happenstance)
Laboratory staff stuck a new label for patient Y to a previously collected blood sample for Hb determination, so as to determine antibodies as well from the same tube. By chance, they put the new label on the tube in such a way that one could still see part of the old label. This meant discovering data of patient X on the original label. By accident, the new label had been added to patient X's and not patient Y's Hb tube.

NM-4 (taking blood sample, research for transfusion request, discovered by happenstance)
A house officer arrived at the transfusion laboratory with a request form for blood-group determination and two blood tubes from patient Z. On the spot, a second request form was filled out and the two tubes labelled to indicate 1st and 2nd sampling. Two independent blood samples were signed for. However, the laboratory saw both tubes as resulting from one sampling, and insisted on collection of a third tube from patient Z.

NM-5 (identification, hospital outside the transfusion chain, discovered through planned safety measure)
The gynaecology ward requested 6 RBC concentrates for patient X. In the past, patient X's blood group had been twice determined as A-positive. Short checks of blood group, however, now indicated AB-positive. Personnel then did the full determination twice, establishing the group as AB-positive, and proceeded to select compatible blood components. There had been an error in identifying patient X at admission. This patient was an illegal inhabitant of the Netherlands, using her sister's ID and health insurance cover.

NM-6 (communication, request, discovered through personal alertness)
On a platelet request form for an oncology patient, the box "no special requirements" had been ticked. Nevertheless, the Care Information System noted that the patient must only receive irradiated blood components in connection with a bone-marrow harvesting procedure. In processing the request, the laboratory technician noticed this and checked with the treating physician, resulting in a request for irradiated platelets.

NM-7 (component, transfusion chain outside the hospital, discovered through planned safety measure)
The transfusion laboratory was to issuing platelets with a Unit Identification Number XYZ and did not succeed via GLIMS, the laboratory information system. It appeared there were two platelet units with the number XYZ present in the laboratory, one entered in the system as irradiated and the other as non-irradiated. Sanquin had supplied these units using an emergency procedure because its computer system (Progesa) was down. The hospital's transfusion laboratory had failed to check properly when entering the second platelet unit into stock.

More and better reporting of near misses certainly would improve the quality of analyses TRIP is able to make to further safety in the entire transfusion chain. It appears again and again from reports of incorrect blood component transfused and of near misses how important accuracy is. It is imperative to use simple and reliable identification methods in all steps of the transfusion chain – on forms, blood samples, blood components and when identifying patients. It seems at least as important to promote continuous alertness to risks and constant realisation of the essential nature of good communication and proper administration to all involved in the blood-transfusion chain. Regularly focusing attention on these points by discussing case histories and emphasising continued education and retraining, auditing, incident analysis etc. will help to make blood transfusion safer.

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.

In past TRIP reports, the few reports submitted by hospitals in this category were included under "other incident". It is now relevant to discuss this information separately since publication of this definition in 2008. These are mainly cases where retrospective information shows that a donation could have been infectious; if laboratory investigation proves the unit to have been infectious (e.g. if the archived sample of a previous donation by seroconverted donor proves PCR positive) the category viral or bacterial contamination of the component is applicable.

In 2008, hospitals sent in 9 reports in this category. Syphilis was suspected three times, hepatitis B, HIV and Q-fever once each. Patient infection was excluded in all cases. In one, post-donation information showed that the donor had reported a tick bite retrospectively: the term look-back is dubious here as this would fit more appropriately into the category other incident. Two reports concern recalls not associated with infections: once there were indications of a possible labelling mistake (donor was blood group AB and the label probably noted blood group A; the receiver with blood group A showed no symptoms). Once a plasma unit was recalled in connection with a TRALI report in a different patient; the unit had been already administered and no unexpected symptoms had occurred. These last two reports are look-backs with possible clinical consequences, but not due to the risk of infection. Consideration should be given to extending the definition to cover these reports as well.

3.4 Blood management techniques

In the reporting year 2008, a total of 25 reports in connection with blood salvage techniques came in from 9 hospitals. Table 17 summarises these; they concern transfusion reactions and adverse events upon administering unwashed drain blood (non-mechanical autotransfusion), administering cell-saver blood (mechanical autotransfusion) and pre-operative autologous donation (PAD). Seventeen reports from three hospitals participating in the TRIP pilot reporting project on Blood management techniques are included here as well. This project continues until the end of 2009.

Table 17 Reports for the use of blood salvage techniques

TRIP category	drain blood	cell saver	PAD	total
NHTR	6	0	0	6
Other reaction	5	2	0	7
Other reaction	8	3	1	12
Total	**19**	**5**	**1**	**25**

It is unknown how often Dutch hospitals use blood management techniques. Within the context of its pilot project, TRIP asked those participating to report their use to TRIP. Two hospitals of the seven participating sent in data. One hospital, over the six-month period of the pilot project, had nine reports resulting from 333 (2.7%) procedures of non-mechanical auto-transfusion. Another hospital submitted eight reports: five out of a total of 146 (3.4%) for non-mechanical auto-transfusion and three out of a total of 46 (6.5%) for cell-salvage procedures. A third hospital did not observe any transfusion reactions or incidents during 87 cell-salvage procedures and 72 non-mechanical auto-transfusions. It is striking that two hospitals observed a higher percentage of transfusion reactions or incidents for these procedures than for allogeneic blood transfusion. Naturally, it is impossible to generalise based on data from three hospitals, but the data underscores how important hemovigilance is when using blood management techniques.

Reporters noted six non-hemolytic transfusion reactions in administering unwashed drain blood, all of them were grade 1 in severity; imputability was “possible” four times and “certain” twice. Blood cultures of the patient and the administered component were negative three times. Once only patient blood was cultured and found negative, while in two instances no culturing was done at all.

Reporters registered the category “other reaction” five times for administering unwashed drain blood. Twice they reported a phlebitis-like reaction in the veins of the infusion arm with grade of severity 1 and “probable” imputability. These reactions came in from one hospital and were observed in two different patients on the same day shortly after each other. The charge numbers for the drains were identical. Investigations by the drain manufacturer did not reveal any abnormality. Once, a patient showed severe confusion with chills, nausea/vomiting and redness around the point of entry of the transfusion; severity was graded as 1 and imputability “possible”. The confusion was such that the patient had to be restrained. The patient’s blood culture was negative, but culture of the drain blood was not done. Another patient collapsed and had brief jerks of the arms and legs after administration of 500 ml of drain blood. After administering a second collection bag, the patient became unwell again, pale and nauseous; the reporter assigned grade of severity 2 and possible imputability. There are no data on blood pressure; no cultures were done. The fifth patient in the category “other reaction” had chills, urticaria and hypotension reported as severity grade 1 and certain imputability. The blood culture was negative and drain blood was not cultured.

An “other reaction” occurred in two instances of administering cell-saver blood. One patient exhibited itching and redness around the infusion site with vomiting; when the infusion was started again – rechallenge – the same symptoms appeared anew; reporters assigned severity 1 and probable imputability. The second patient showed hypotension and chills. Reporters assigned neither severity nor imputability.

A striking number of reports came in for the category “other incident” (n=12) in comparison to the number of transfusion reactions (n =13), if one looks at absolute numbers. There was a report of the collection bag falling off the drain, and an unknown amount of drain blood was wasted. Once a blockage between the suction bladder and the drain-collection bag was noted, no further investigation

was done because the system had already been thrown away. The patient received an allogeneic transfusion. Administration of drain blood via the normal infusion line without filters was twice reported; one of these patients showed nausea and vomiting, but this also had been present before transfusion. Another report mentions “something blue” in the drain collection bag – the system and the collected drain blood were thrown away without any further investigation. The patient received two units of allogeneic RBCs. Uncontrollability of the speed of the drip, so that the system had to be replaced and a small amount of drain blood thrown away, was the subject of a further report. Twice, a report mentioned failure to write down the end time on the drain collection bag. This has to be filled in when collection of drain blood commences in order to check on the six-hour term within which drain blood has to have been transfused. One of these reports notes the loss of 160 mL of blood.

Twice, for cell-saver procedures, reports mention clotting of collected blood because the heparin dose, adjusted manually, was too low. In one of these cases 700 ml of blood was wasted. Another report notes ending of the procedure because the suction nozzle was not properly connected to the vacuum system.

An “other incident” involved a pre-operative autologous donation; the autologous component was scanned incorrectly as allogeneic. The transfusion however was assigned and administered to the right patient.

TRIP also received one report of epoetin use, which strictly speaking should be considered a medication incident and it is therefore not counted among the 25 reports of blood management techniques. TRIP is including this “other incident” here because epoetin often is used in combination with blood-saving techniques. An older woman about to undergo a total hip operation pre-operatively received 40,000 E epoetin four times; her hemoglobin rose from 7.7 to 11.3 µmol/L per litre without any interim Hb check. A hemoglobin level this high is undesirable because of increased risk of thrombosis.

3.5 Deceased patients and transfusion reactions (severity grade 4)

There are four reports of severity grade 4 transfusion reactions in 2008. *Table 18* summarises these and the relevant categories discuss them as well. For two grade 4 reports in 2008, the noted transfusion reaction probably played a role in the death of the patient. Two cases registered as grade 4, but were assigned low imputability. These concern patients who received a component for which the blood bank later found a positive bacterial screen result (Propioni bacterium). One patient showed no relevant symptoms; in the second case, there was exacerbation of already severely disturbed hemodynamics.

Table 18 Reports where the patient died after a transfusion reaction

Report category	Age, gender	Imputability assessment	Nature of underlying pathology
Incorrect blood component transfused IBCT	78, F	probable	Severely ill patient on ICU received ABO-incompatible transfusion meant for another patient (unnecessary transfusion), showed clinical deterioration with signs of shock after 10 minutes
Other reaction (umbilical venous occlusion at administration)	0, M	probable	Baby with severe hydrops and congenital deformations received intra-uterine platelet transfusion
Bacterial contamination of blood component	87, M	unlikely	Sanquin recall, bacterial screen: Propioni species; no relevant symptoms
Other reaction	74, M	unlikely	Sanquin recall, bacterial screen: Propioni species; patient with cardiogenic shock and bleeding – showed clinical deterioration after administration

In principle the reporters assess the grade of severity independently rate the imputability In discussing grade 4 reports with the EC, parties acknowledge the important point that one can ascribe high imputability of a reaction to the transfusion, but often the reaction only partially or hardly at all contributes to his/her death. A pragmatic solution to gaining insight into this point is to present individual case histories. Many transfusions are administered to seriously ill patients with a high risk of death.

Table 19 shows the categories of all grade 4 reports since 2003 with certain, probable and possible imputability. TRALI is the largest category with six reports, followed by two reports each for anaphylactic reaction, circulatory overload, other reaction and incorrect blood component transfused. *Table 20* shows a comparison with a number of other hemovigilance systems. This table shows that generally the same categories are implicated in transfusion-related deaths in those systems, but they also mention infections as well (particularly bacterial infections). In the cumulative TRIP data there are no reports of transfusion associated infection with high imputability associated with the death of a patient.

Table 19 Grade 4 reports (certain, probable or possible) imputability, 2003 - 2008

Category	Number	Year	Remarks
Acute hemolytic transfusion reaction	1	2003	Probable
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
Circulatory overload	1	2005	Possible
	1	2006	Possible
Incorrect blood component transfused	1	2007	Possible
	1	2008	Probable

Table 20 Transfusion related mortality in other hemovigilance systems

System	Years	Top five in decreasing order
SHOT	1996 - 2007	TRALI, incorrect blood component transfused, acute transfusion reaction (including acute hemolysis, TACO) TA-GvHD, transfusion-transmitted infection
United States (FDA) – mistakes categorised by clinical result	2005 - 2008	TRALI, non-ABO hemolysis, microbial infection, ABO-hemolysis, TACO, anaphylaxis
France (Afssaps) – imputability certain, probable, possible	2000 -2006	TACO, unknown (mainly NHTR), TRALI, bacterial contamination, ABO-incompatibility (including IBCT)

3.6 Obligatory reports of serious adverse events in the transfusion chain

Conforming to the Common Approach set down by the European Committee in the spring of 2009, this overview includes only reports with possible, probable or certain imputability. Each category includes reactions resulting from other incidents and reactions to incorrect blood component transfused. *Table 21* shows data for 2007 and 2008.

Table 21 Numbers and imputability of reports of grade 2 and higher in 2007 and 2008

Type of reaction	Serious reports		Possible		Probable		Certain	
	2007	2008	2007	2008	2007	2008	2007	2008
Acute hemolytic TR	2	10	1	1	0	4	1	5
Delayed hemolytic TR	4	5	0	0	1	2	3	3
TRALI	25	17	12	4	8	10	5	3
Anaphylactic reaction	21	27	4	10	16	14	1	3
Other allergic reaction	2	5	1	4	1	0	0	1
Circulatory overload	14	16	9	8	5	6	0	2
Post-transfusion bacteraemia*	3	4	0	3	2	1	1	0
Post-transfusion viral infection	2	2	1	1	1	1	0	0
Post-transfusion purpura	0	0	0	0	0	0	0	0
TA-GvHD	0	0	0	0	0	0	0	0
Other severe reactions	28	37	19	17#	6	15	3	5
Total	**101**	**123**	**47**	**48**	**40**	**53**	**14**	**22**

* This category includes “bacterial contamination” under 2007 definitions. 2008 has one report of severity-2 bacterial contamination of blood component.

\# The grade 4 report of an intra-uterine transfusion is not included.

4. | General considerations, conclusions and recommendations |

4.1 Can trends be seen with regard to the safety of blood transfusion?

Six years of registering hemovigilance reports warrant some reflection. Here follow the main findings in the conclusions of the TRIP reports from 2003 to 2007.

Annual Report	Could the reactions have been prevented? What is the situation as to transfusion safety?
2003	Classification: infections –consequences of errors – reactions due to the interaction between patient and blood component. Prevention of errors most likely to lead to safety improvement in the short term.
2004	Increase in near miss reports. Importance of staff alertness and quality awareness in the blood-transfusion chain. For the transfusion reactions – necessity of diagnosis and research into groups at risk.
2005	Increasing number of reports, gradual improvement in the quality of information. Growing insight into TRALI. Importance of non-serious reports as a measure of alertness and a trigger to explore routes to reduce them.
2006	New definition of severity grade 2 connected to EU Guideline 2002/98/EC. Slight increase in reports. Possibility of avoiding, in principle, transfusion reactions for errors and other incidents; focus of attention on implementing Safety Management System in the entire transfusion chain.
2007	Five years: reports stabilised and good knowledge of nature and extent of transfusion reactions. Still unable to evaluate “male-only plasma” in preventing TRALI. Start of TRIX. Importance of the hemovigilance officer and assistant role in education and monitoring levels of blood use.

After the sixth reporting year, we see a more or less stable number of reports, both for serious and non-serious events. We can still state that national reporting has produced “knowledge of the nature and extent of the transfusion reactions”. Thanks in part to the role of hemovigilance personnel; in the Netherlands the use of RBC concentrates is among the lowest in European countries with a well developed blood supply.

TRIP will continue the way it began providing the hospitals with information that mirrors the status of their own reports versus the number of reports received nationally. The availability of this information can be a trigger for the hospitals and research groups to initiate research into clarifications and factors relevant to the safety of blood transfusion in the Netherlands.

At the same time it must be remembered that there are limitations to a system of this type. Firstly, sometimes even after extensive investigation and discussions with experts there may be doubt as to the diagnosis (category) or even the grade of severity of a transfusion reaction. Secondly, spontaneous reports are not a reliable way to measure incidence. For some time, TRIP has been indicating the likelihood that there is underreporting of incorrect blood component transfused. The TRIP registration has made clear that reporting behaviour of the hospitals varies considerably, thus influencing national figures. National hemovigilance registration is not an aim in itself, but an instrument, essential but not perfect.

The variation in reports from year to year needs study and clarification. It is necessary to investigate the relationship between numbers of reports and other indicators and the safety and quality of blood transfusion. In addition to fundamental laboratory work, this demands practice oriented research into the transfusion chain. TRIP trusts that hospitals and other research groups will use TRIP reports to trigger research and to support their own hemovigilance activity.

4.2 Actions and developments resulting from past TRIP recommendations

	Recommendation	Status
1	Initiatives to prevent errors in the transfusion chain and increase the safety of blood transfusion must be rolled out. The present, stable, TRIP reporting system makes it possible to measure the effects. (TRIP report 2007). Numbers of incorrect blood component transfused are impermissibly high. Electronic techniques to check patient and blood-component identification must be implemented as quickly as possible to prevent life-threatening transfusion reactions. (TRIP report 2007).	A questionnaire survey in 2009 reveals that a number of hospitals are planning to use bar-code technology to verify the identity of unit and the patient; other hospitals have taken steps to use bar codes for patient identification, while the majority has not introduced projects involving digital surveillance of the transfusion chain in this way.
2	Use of the digital reporting system must be expanded further. Digital transfer of obligatory reports from hospital to competent authority is a priority (TRIP report 2007).	The majority of hospitals are now reporting digitally; 67% of reports for 2008 were submitted digitally. TRIP hopes this will rise to more than 80% in 2009. At the end of 2008, TRIP and the IGZ sent hospitals a joint letter about reporting serious adverse events and reactions digitally to IGZ from 2009 via the TRIP digital reporting system.
3	In cases where the reporting hospital suspects bacterial contamination (post-transfusion bacteraemia), it is necessary to culture patient blood and the component (TRIP report 2007).	Some progress has been made in the extent to which hospitals are submitting culture results with their reports to TRIP.
4	Hospitals must maintain their present alertness to the transfusion complications TRALI and circulatory overload. In all cases where details of a report fulfil the TRALI definition, both Sanquin and the hospital must investigate immunological mediation by submitting a fresh, patient sample for the crossmatching test. This is needed to establish how effective the implemented “male-only plasma” measure is (TRIP report 2007).	Both the level of research and the quality of reports has improved.
5	TRIP must be given a clear role in drawing up an inventory of adverse reactions to the use of blood management techniques (TRIP report 2007).	TRIP has initiated a pilot project for these reports with a number of hospitals. The number of reports has increased.
6	To increase blood-transfusion safety every hospital must have hemovigilance assistant. An important task is to train doctors and nurses who prescribe and administer blood components (TRIP report 2007).	An important task of hemovigilance is ensuring optimal blood component use. Regrettably, TRIP has been informed of more than one hospital’s failing to appoint a successor for a hemovigilance employee at the end of his/her contract due to cutbacks. This is a reason for concern.
7	The curriculum for medical specialists must devote more attention to blood transfusion and hemovigilance (TRIP report 2007).	Sometimes hemovigilance forms part of blood-transfusion education; TRIP is unaware of its general status in various educational institutes.

	Recommendation	Status
8	It is worth considering selecting RBCs that are Rhesus subtype-compatible as well as Kell-negative for women younger than 45, to prevent Hemolytic illness in newborns (TRIP report 2007).	This point is under consideration within the context of revision of the CBO Guidelines for Blood Transfusion.
9	In addition to TRALI, circulatory overload merits attention, particularly because relatively simple, preventive measures exist, like administering diuretics (TRIP report 2006).	TRIP is unaware of initiatives on this recommendation in 2008.
10	More attention must be paid to reporting transfusion-related iron overload to gain more insight into preventing this adverse reaction in the Netherlands (TRIP report 2006).	TRIP is unaware of any action on this issue.
11	Within the framework of introducing safety management systems*, directors of hospitals and other involved institutions must remain on their guard to ensure the integration of new initiatives into already existing hemovigilance activities and into the general safety system of a given hospital (TRIP report 2006). *Note: in some cases specialised software systems are employed	At the end of 2008, small numbers of hemovigilance personnel were indicating they had received reports via the general safety management system. This was an exception, but did lead to an increase in reports to these people in the hospitals. TRIP has approached a number of software manufacturers as well as representatives of a number of other branch-specific reporting systems. Despite a certain amount of national activity (www.vmszorg.nl), there is no harmonisation at all in many hospitals between hemovigilance personnel and personnel of the safety management systems. This remains a point for attention.
12	Research is needed into the causes of anaphylactic transfusion reactions. Subsequently, one needs to search for blood components that cause fewer anaphylactic reactions and to investigate these components in clinical trials.(TRIP report 2005).	TRIP is working with partners to develop a research protocol to describe more accurately the reported, severe anaphylactic and other allergic reactions and to evaluate a possible role of donor medication.

4.3 Conclusions

1. The number of reports since 2006 has stabilised at approximately 1950, or 2.8 per 1000 distributed blood components. A good correlation exists between the number of NHTR and the number of blood components per hospital, while correlation for other reporting categories is less clear. To understand this, more data are needed about differences in patient populations, transfusion practice and reporting cultures.

2. It is likely that DHTR is being underreported.

3. The number of reports of TRALI fulfilling all the criteria of the definition is comparable to previous years. It is too early to assess the effects of implementing “male-only plasma”.

4. Reports in the category other reaction have increased. Often, sufficient, detailed information is lacking, preventing meaningful analysis. In 2008 a cluster of hypertensive reactions was noted for the first time.

5. The amended TRIP definitions for bacterial problems accompanying blood transfusion are not being applied uniformly yet. Improvement is to be expected from full submission of culture results and clinical information related to the reports.

6. The number of reported errors in the transfusion chain has not improved since the commencement of TRIP registration. Twelve patients received an ABO-incompatible blood component in 2008 and one died partially due to this. In reporting incidents, in addition to errors of identification, faulty communication and lack of proper record keeping are responsible for an important portion (23%) of reports.

7. More better quality reports of near misses would improve the quality of the TRIP analyses related to safety of the transfusion.

8. Increased attention to hemovigilance for Blood Management Techniques has led to increasing numbers of reports. Hospitals experience difficulty in extracting data about the number of times these techniques are employed.

4.4 Recommendations

A. Recommendations based on the TRIP Report 2008

1. Further research is needed into factors influencing the number of reports and into the relationship of the number of reports to the safety of blood transfusion.

2. In the category of “other reaction”, detailed information on clinical and laboratory findings should accompany every report. In particular special attention is requested for reactions featuring hypertension as the significance of reports including this feature is not clear.

3. For all transfusion reactions where one suspects a bacterial cause, consistent culturing should be performed for bacterial identification, with being taken cultures from the remainder of the blood component as well as of the patient's blood. The results should be recorded on the reports to TRIP.

4. Better monitoring of patients at risk of transfusion-associated hemosiderosis could prevent late harm through transfusion and lead to more representative numbers of reports.

5. TRIP stresses the use of relevant forms of education and training to focus attention on the importance of identification and of careful communication of information and assignments. Use can be made of case discussion, group education, audit, incident analysis etc.

6. Hospital blood transfusion committees should be fully aware of the extent of application of blood management techniques and must consider the task of vigilance in relation to their use as part of their remit.

B. General recommendations

7. It is useful to conduct clinical scientific research with different types of blood components using transfusion reactions as outcome measure.. In particular there is a need for prospective investigation of alternative products to “male-only” FFP, such as SD-plasma, to obtain clarity as to which product is best to prescribe.

List of terms and abbreviations

AHTR	acute hemolytic transfusion reaction
CBO	Dutch organisation for healthcare quality
DHTR	delayed hemolytic transfusion reaction
EC	expert committee
FFP	Fresh frozen plasma
IGZ	Netherlands Healthcare Inspectorate
NHTR	non-hemolytic transfusion reaction
PAD	pre-operative autologous donation
Pro-BNP	(N-terminal) pro-Brain Natriuretic Peptide
PTP	post-transfusion purpura
RBC	Red blood cell concentrate
Sanquin	Dutch blood supply foundation
TA-GvHD	Transfusion-associated graft versus host disease
TACO	Transfusion-associated circulatory overload, volume overload after blood transfusion
TR	transfusion reaction
TRALI	Transfusion-related acute lung injury
TRIP	Dutch national hemovigilance office(TRIP = Transfusion Reactions In Patients)
TRIX	Transfusion Register of alloantibody and Crossmatching Problems