TRIP

Annual Report 2007

The TRIP Annual Report 2007 on the transfusion reactions and safety incidents is published under editorial responsibility of, and is guaranteed by TRIP (Transfusion Reactions In Patients) Foundation for Hemovigilance. The board of TRIP Foundation is comprised of representatives of the societies of medical professionals involved in the practice of blood transfusion.

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Foreword

TRIP celebrates its first jubilee this year. I will reflect briefly on the past five years by citing passages from the forewords of the last four reports.

Annual Report 2003: "Blood components are special and that is why special vigilance, hemovigilance, is necessary. Thanks to an initiative from the Healthcare Inspectorate the Netherlands now has an operational national hemovigilance reporting system: TRIP (Transfusion Reactions In Patients). I particularly wish to express thanks Joost de Wolf, Eveline Six – Barones van Voorst tot Voorst and Cees van der Poel (Sanquin) for their pioneering role. The Ministry of Healthcare, Welfare and Sport was extremely cooperative and awarded the necessary start-up subsidy. After two years of activity I can already conclude that the voluntary TRIP system is functional and should be continued. Its functioning is thanks to the enthusiastic cooperation of nurses, doctors, biomedical scientists and technicians in the hospitals and at the national blood service, Sanquin, as well as to the work of the director and staff of the office and the TRIP governing and advisory boards."

Annual Report 2004: "The most important development is that the Ministry of Healthcare, Welfare and Sport has committed to long-term funding for TRIP. Not only did the Ministry take note of TRIP's performance but also the new European legislation requires central reporting of adverse reactions to blood transfusions."

Annual Report 2005: "With careful coaching from the expert and enthusiastic team at the office and often with the assistance of dedicated hemovigilance assistants, the 100-odd hemovigilance officers in the Dutch hospitals submitted considerably more reports to TRIP than in 2004. This year there was also an increase in reports of errors. Importantly, the quality of reports has also improved.
The purpose of central reporting is not only to map out the safety of blood transfusion, but also to indicate where improvements may achieved. A number of recommendations were made in 2004 and in this report we describe how they have been taken up."

Annual Report 2006: "This report demonstrates that the TRIP national hemovigilance reporting system in The Netherlands is now adult. I believe that the calculated incidence of serious reactions, 1 per 5600 transfused labile blood products, approaches the true incidence. With a rate of serious adverse reactions of approximately 1 in 5000, labile blood components and their administration can be said to be safe in comparison to other products and treatments which are applied in the Dutch hospitals."

At its first jubilee TRIP is adult and has earned itself a good name in The Netherlands and abroad. Adulthood means that the number of reports has stabilised and therefore the effect of measures to improve the safety of blood transfusion can be observed and evaluated.

At the same time, TRIP continues to develop and this is seen in the active approach to tissue vigilance. TRIP is applying its experience with hemovigilance to the process of setting up a similar reporting system for tissues and cells of human origin.

Once again, the TRIP staff and governing board have invested their best efforts in producing the report. I will particularly mention three conclusions and recommendations:

- The labile blood components supplied by Sanquin are very safe; the number of confirmed reports of transmitted bacterial and viral infections in 2007 can be counted on the fingers of one hand. Given this quality of labile blood products the expected health benefit of pathogen inactivation would be low.
- There are still too many reports of transfusion of an incorrect blood component. Hospitals should consider implementing electronic systems for the identification of patient, patient blood sample and the unit which is to be transfused to the patient.
- In order to improve the safety of blood transfusion all hospitals should have a hemovigilance assistant in post. An important task of the hemovigilance assistant is that of providing regular training to nurses who perform blood transfusions.

I hope that you will find it both enjoyable and useful to read this Report, the second which we have translated into English.

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

Executive summary

TRIP objective and working methods (hemovigilance)

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 Healthcare 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.

2007 findings (hemovigilance)

Participation

Ninety-six (92%) of the 104 Dutch hospitals participated in the TRIP data collection in 2007. Eighty-seven 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 2008.

The 2007 reports

A total of 1906 reports about transfusion side effects and incidents in 2007 were received, in comparison to 2030 reports concerning 2006 at the closing date last year. 1655 concerned clinical transfusion side effects and 251 were incidents in the transfusion chain. 473 of the reports were in optional reporting categories. TRIP wishes to collect information on a number of types of less serious event but does not need all hospitals to take on the extra work. Hospitals may decide for themselves whether to send in these optional reports. 739 (39%) of the reports were submitted using the online reporting system which has been partially rolled out.

Severity of the events

In accordance with international practices the reports are graded as to severity. 1723 (90.4%) of the 2007 reports were rated for severity by the reporter. Of these reactions 1611 (93.4%) were rated as grade 0-1 (no or only minor morbidity), 78 (4.5%) as grade 2 (serious), 28 (1.6%) as grade 3 (life-threatening) and 6 (0.3%) as grade 4 (death following a transfusion reaction).

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 2007, 1643 (86.2%) of the reports were rated for imputability. Out of these 1643, 308 (18.7%) were judged to be 'certainly' related to the transfusion, 596 (36.3%) 'probably', 578 (35.2%) 'possibly' and 161 (9.8%) 'unlikely' or certainly not'.

Types of reactions and incidents

The following types of reports were received: non-hemolytic transfusion reaction 412, acute hemolytic

transfusion reaction 10, delayed hemolytic transfusion reaction 11, transfusion-related acute lung injury (TRALI) 30, anaphylactic reaction 50, other allergic reaction 185, circulatory overload 27, viral infection 7, bacterial contamination 7, hemosiderosis 3, other reaction 50, new allo-antibody 564 and mild febrile reaction (>1<2°C, optional category) 284. Among the incidents there were 58 reports of transfusion of an incorrect blood component (product intended for another patient or not meeting appropriate requirements for that patient) with clinical consequences in four cases (no reactions rated as grade 2 or higher). TRIP received 102 reports of other incidents, 67 reports of near misses and 24 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 categories). Sanquin also contributed a summary of transfused blood components (98) with positive bacteriological screening; overlap with the hospital information may be presumed although this has not been formally confirmed.

Number of reports in relation to the number of blood components

In 2007 the blood supply organisation Sanquin delivered a total of 700,980 labile blood products to the hospitals. The total number of reports was 1906. This gives an average of 2.7 reports per 1000 blood components nationally, compared to 2.9 per 1000 in 2006 (3.0 including reports which were received after the closing date for the 2006 report). In 2007 the reactions rated as grade 2 or worse totalled 112, or 0.15 per 1000 blood components (1 in 6300). This number is not significantly different from 2006.

Discussion and conclusions

Participation and reports in 2007 compared to 2006

Participation by 92% of the hospitals by the closing date for the report is high, as it has been since 2004. As in previous years there is a considerable variation between hospitals in the ratio of reports to blood use.

Five years of national hemovigilance reporting – what does that mean for transfusion safety in The Netherlands?

The number of reports has stabilized, and that means that the impact of changes in transfusion practice can be detected. The presence of hemovigilance officers and hemovigilance assistants (transfusion safety officers, specialist practitioners of transfusion) in the hospitals holds a major potential for promoting restrictive use of blood components and improving transfusion safety through education on correct transfusion practices. The number of errors however remains unchanged and implementation of available IT methods should undertaken urgently.

Tissue vigilance: method and findings of a pilot reporting system

In 2007 the pilot reporting system for serious adverse reactions and serious adverse events in the production and clinical application of human tissues and cells (launched on 1st August 2006) was continued. TRIP will fulfill the same role for tissues as in hemovigilance, i.e. receiving the reports, providing scientific analysis and reporting publicly on the safety of these transplantations. This will ensure compliance with the European Union tissue directives, which have been implemented in Dutch legislation. As for hemovigilance, TRIP focuses not just on the supply side, but particularly aims to involve the health care professionals. A committee of representatives from the professional bodies involved in transplantation of human tissues and cells has been convened. This group examined the reports and will be responsible for steering the consolidation of tissue vigilance in the Netherlands.

In 2007 a total of 23 reports were received, and nine of these were assessed as ‘serious’. At present it is not possible to determine the percentage of participating hospitals or tissue establishments because the procedures for accreditation of tissue establishments both outside and within hospitals have not been concluded by the ministerial agency. Information on volume of transplantation practice was received from roughly one third of all Dutch hospitals but it is not known how many of the other hospitals use one or more types of tissues and cells.

1. Introduction

TRIP Dutch national hemovigilance system

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. After the granting of an initial subsidy by the Ministry of Health in 2002, TRIP Dutch National Hemovigilance Office was launched early in 2003. It runs 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 participation is regarded as the norm in the 2004 national transfusion guideline as well as by the health care inspectorate.

In the Netherlands the standard blood components are supplied to the transfusion laboratories of the hospitals, which perform the necessary laboratory testing and issue the components according to hospital protocol. Blood components are universally leukodepleted; most platelets are buffy coat-derived pooled products, with either plasma or platelet additive solution. Special products, transfusion advice and reference laboratory services are also provided by Sanquin, which in addition has divisions for diagnostic investigations (including infectious disease testing), research and fractionation of plasma.

Besides reporting to TRIP, provision of care and investigation of TR remain the responsibility of the hospitals. It is also mandatory to refer serious errors and incidents to the hospital's "MIP" committee (Meldingen van Incidenten in de Patiëntenzorg, reports of incidents in patient care). The European blood directive 2002/98/EC lays down a requirement for reporting of serious adverse reactions and incidents which may affect 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, the Health Care Inspectorate (Inspectie voor de Gezondheidszorg, IGZ). Hospitals themselves should submit these reports in parallel to the IGZ, which can thus exercise its supervisory responsibility. In 2007 the Inspectorate and TRIP collaborated in preparing for this to be implemented in practice.

In 2007 the number of participants in the pilot online reporting system progressively increased. The system incorporates a facility for reporters to electronically submit relevant reports to the IGZ. This facility will be activated on a date to be fixed by agreement between TRIP, the IGZ and Sanquin.

In August 2006 TRIP launched a pilot of a national reporting system for serious adverse reactions and events which are associated with the use of human tissues and cells and which may affect the quality or safety of the products, in compliance with the disuse directive 2004/23/EC and its daughter directive. More can be read about this in Chapter 3 of this report. A digital reporting system is under development.

The hemovigilance and tissue definitions can be found on the TRIP website www.tripnet.nl. Reporters are asked to specify the clinical severity of reactions. In addition the imputability is assessed, i.e. the level of certainty with which a reaction can be ascribed to a transfusion or transplantation. Where necessary TRIP requests further details from the reporter. Prior to inclusion in the annual report all reports are reviewed by an 'expert committee' (EC) nominated by the TRIP board.

2. I Hemovigilance I

2.1 Participation

The number of actively participating hospitals and the quality of the information sent in determine the value of national registration and evaluation of transfusion reactions. Ninety-six of the 104 (92%) of the hospitals took part in the registration in 2007. Of the 96, 87 hospitals reported transfusion reactions and nine indicated they had no transfusion reactions to report. In 2007 two new healthcare institutions became (low-volume) blood users, and the number of hospitals was reduced by two because of organisational mergers. In such situations, reporters who cover several sites are advised to report under separate codes until the transfusion and reporting procedures have become uniform. There is a number of hospitals each year that do not send in reports by the closing date: the status of these hospitals in the final summary is 'no information'. The final date for sending in information covering 2006 was 1 April 2007.

Additionally, central Sanquin departments made available to TRIP summaries of serious adverse events and of administered blood components which subsequently showed positive bacteria screening results (for further information see 2.3). TRIP also received a number of reports from contact persons in Sanquin's regional blood bank divisions.

In 2007, after the closing date for the 2006 report, TRIP received a further 96 reports concerning 2006, including 6 reports (febrile reactions) of severity grade 2 or higher. The EC has now assessed these formally. All the figures and tables of this report include the late reports from previous years where relevant.

Figure 1 shows degrees of participation for the years 2002 (the baseline measurement) up to and including 2007, as of the reference date 1 April 2008.

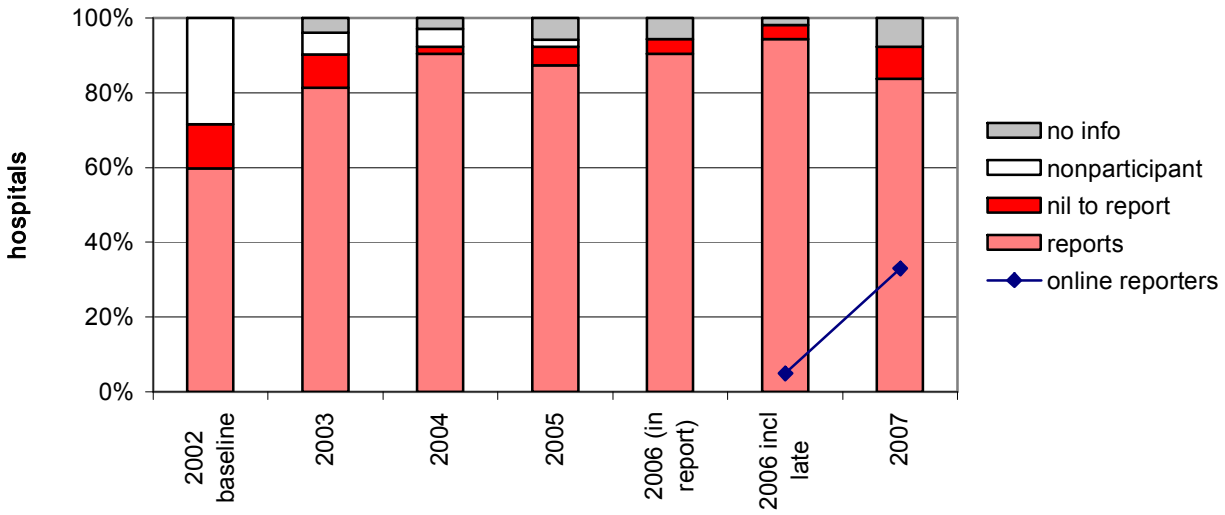

Fig. 1 Participation per year, 2002-7

2.2 Hemovigilance reports 2007

Readers can find all definitions at *www.tripnet.nl*. At the beginning of 2008, TRIP distributed revised definitions, which came into force as of 1 January 2008. TRIP used definitions for 2007 to assess and report on hemovigilance records for 2007.

Reports received

A total of 1910 reports of transfusion reactions in 2007 were received; these arose from 87 hospitals (in

2006: 2030 from 94 hospitals). There are some non-serious categories that are optional for reporting. TRIP sees it as useful to register these happenings, but does not necessarily need all hospitals to co-operate in this. Of the total reports, 475 were for optional reporting categories, arising from 68 hospitals (in 2006: 509 optional reports from 75 hospitals). For 2007, the number of reports is approximately 6% lower than 2006. Some hospitals, including a number of large ones, informed TRIP that they had not submitted all the reports by the cut-off date for inclusion in the annual report.

Of all the reports, 739 were submitted digitally (39%, 28 hospitals).

After the EC assessment, reporters received supplementary questions in a number of instances (30 times). After discussions with the reporter, this led to some instances of amending the category of the transfusion reaction or the relationship of the reaction to the transfusion: 8x category, 8x severity and/or imputability. Reporters were able to give relevant, supplementary information in other cases. Twice, a difference in standpoint between TRIP and the reporter remained about the most appropriate classification of a report, viz. the imputability of a TRALI report which TRIP thought should be lower. In this report the reactions appear according to the final TRIP and EC assessment.

Table 1 shows the number of reports per category for the years 2002 up to and including 2007 and *Table 2* shows numbers of incidents for the same period. See paragraphs on incidents in Chapter 2.3 for a separate discussion of transfusion reactions following incidents.

Table 1 Transfusion reactions (TR) reported to TRIP, 2002 - 2007

Reaction	2002	2003	2004	2005	2006	2007	Number of hospitals (2007)	Number of hospitals (2002-7)
Non-hemolytic transfusion reaction	240	318	344	435	490	412	76	96
Acute hemolytic transfusion reaction	12	8	14	9	17	10	8	34
Delayed hemolytic transfusion reaction	21	19	14	12	14	11	11	39
TRALI	7	6	9	17	25	30	19	37
Anaphylactic reaction	13	8	21	26	19	50	26	47
Other allergic reaction	98	132	171	219	222	185	44	85
Circulatory overload	1	7	6	27	34	27	19	45
Bacterial contamination	12	9	5	10	7	22	13	27
Viral infection	1	5	7	8	7	7	5	11
Post-transfusion purpura	1	0	0	0	0	0	0	1
Transfusion-associated GVHD	0	0	0	0	0	0	0	0
Hemosiderosis	0	0	0	3	5	3	1	2
New allo-antibody	117	244	428	571	607	564	47	66
Other reaction	48	54	64	67	61	50	32	72
Mild febrile reaction (optional)	247	326	341	375	362	284	67	94
Total TR	**818**	**1136**	**1425**	**1779**	**1870**	**1655**	**86**	**100**
Total reports	**862**	**1267**	**1547**	**1984**	**2127**	**1910**	**87**	**100**

*Table 1 does not include reactions to incorrect blood component transfused or other incidents. Relevant paragraphs discuss these.

Table 2 Incidents reported to TRIP, 2002 - 2007

Incident	2002	2003	2004	2005	2006	2007	Number of hospitals (2007)	Number of hospitals (2002-7)
Incorrect blood component trans-	17	34	37	60	64	60	30	71
Other incident (optional)	5	5	14	53	87	102	21	40
Near miss (optional)	12	31	62	79	77	69	16	32
Virally infected blood component					2			
Positive bacterial screening (op-	10	61	10**	13**	27**	24**	11	31
Total	**44**	**131**	**123**	**205**	**257**	**255**	**43**	**78**

** Additional information supplied by Sanquin, see 2.3

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 severity. Reporters rated severity for 1723 reports for 2007 (90.4%; 2006 report: 91.4 %). Of these, 678 were grade 0 (39.3%; 2006 report: 45.7%), 933 grade 1 (54.1%; 2006 report: 47.6%, 78 grade 2 (4.5%; 2006 report: 4.9%), 28 grade 3 (1.6%; 2006 report: 1.6%) and six grade 4 (0.3%; 2006 report: 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 category. Of the 1669 reports of clinical transfusion reactions, 1617 (96.9%; 2006 report: 96.5%) assign severity. *Figure 2* shows severity assigned to clinical transfusion reactions from 2002 up to and including 2007.

The figures reveal a continuing shift of reports of grade 0 to grade 1, a trend that began in 2005 and 2006. The TRIP standpoint is that the severity should be at least grade 1 if clinical symptoms are observably present. If a reaction occurs during or following an incident, TRIP requests reporters to use a subsidiary category, assigning severity and imputability.

There were 112 (5.9%) serious reports (grades 2 up to and including 4) which is comparable to 2006 (124 in the report).

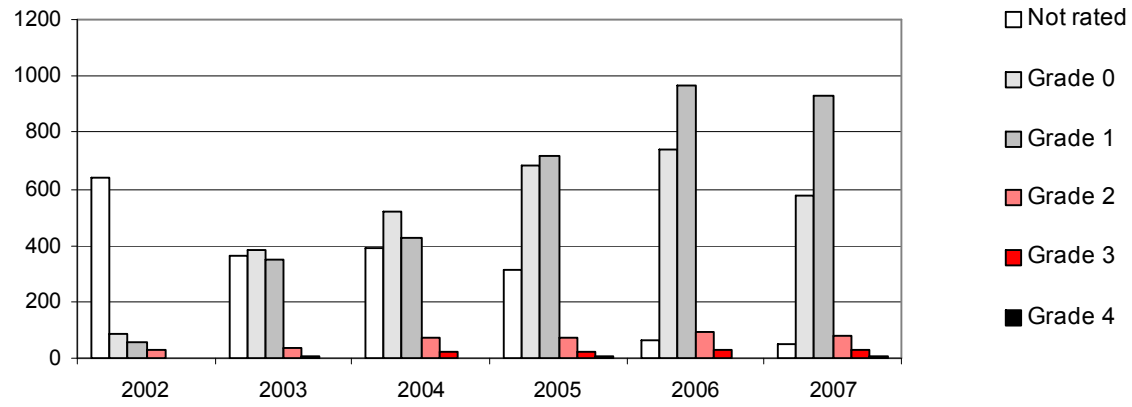

Fig. 2 Severity of the clinical transfusion reactions, 2002 - 2007

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 assess transfusion reactions for imputability: a rating of the probability that the reaction resulted from the transfusion.

In 2007, 1643 (86.0%; 2006 report: 81.1%) reports of transfusion reactions were rated as to their imputability. Of these, 308 reports (18.7%; 2006 report: 23.5%) are deemed to show a ‘certain’ relationship to the transfusion, 596 (36.3%; 2006 report: 34.1%) ‘probable’, 578 (35.2%; 2006 report: 32.7%) ‘possible', 140 (8.5%; 2006 report: 8.9%) ‘unlikely’ and 21 (1.3%; 2006 report: 0.9%) ‘excluded'. Numbers of reports submitted as ‘certain’ have dropped; the fact that reporters assigned imputability for fewer of the incident reports lacking clinical consequences explains this. Figure 3 shows imputability of 1669 clinical transfusion reactions in 2007 compared to previous years; of these, reporters assigned imputability to 1616 (96.8%; 2006 report: 89.3%).

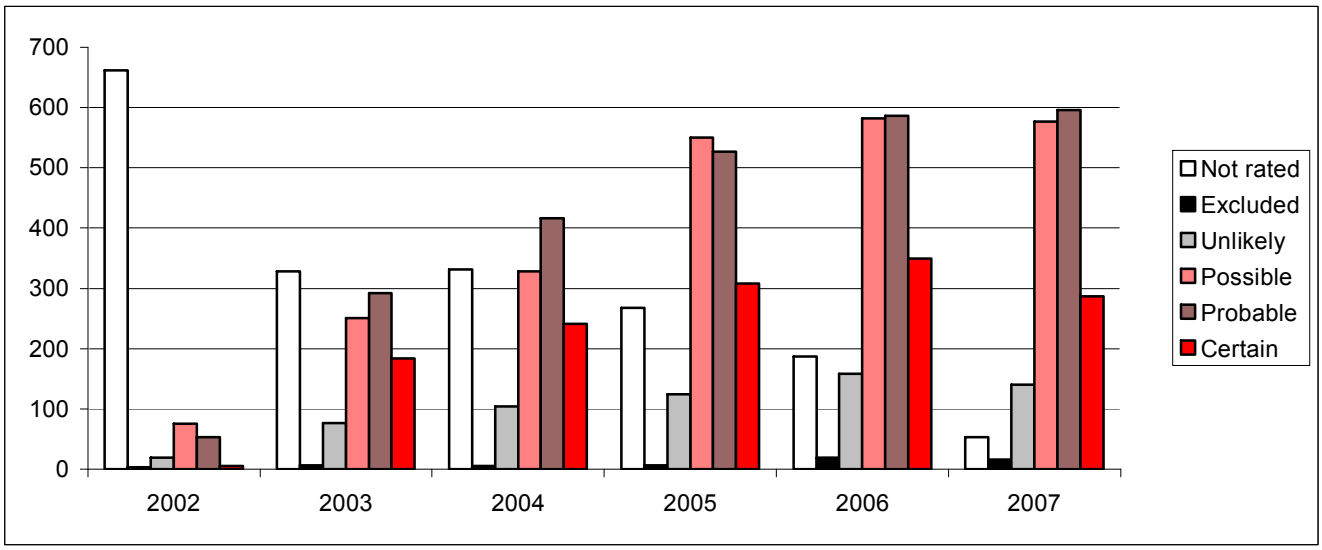

Fig. 3 Imputability of the clinical transfusion reactions 2002 - 2007

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

In 2007 Sanquin supplied the hospitals with a total of 700,980 blood components; this number does not include special components like lymphocytes and granulocytes. This number has dropped slightly for RBC concentrates compared to 2006. The total number of reports for 2007 amounts to 1910. On average that is 2.7 reports per 1000 components (in 2006: 2.9 in the annual report and 3.0 including late reports). *Table 3* shows the relationship between supplied blood components and numbers of reports. When legislation came into force implementing tissue vigilance, peripheral blood stem cells were in-

cluded in that legislation since launching tissue vigilance; accordingly, reports on peripheral blood stem cells are covered in the tissue vigilance chapter.

Table 3 Reports in 2006 and 2007, per type of blood component

Blood component type	Reports 2006	Number delivered 2006	Reports/1000 2006	Reports 2007	Number delivered 2007	Reports/1000 2007
RBC concentrate	1474	556,293	2.65	1404	554,633	2.53
platelet concentrate	252	51,015	4.94	253	53,701	4.71
fresh frozen plasma	91	92,380	0.99	77	92,568	0.84
autologous predeposit (RBCs)	1	216 (donations)		1	78 (donations)	
autologous, perioperative	4			2		
other components*	4			1		
combinations	83			82		
not indicated	222			90		
TOTAL	**2127**	**699,904**		**1910**	**700,980**	

One 2007 report under 'other blood components' concerns an ampoule of anti-D immunoglobulin.

Numbers of reports per 1000 units, per type of blood component too, are somewhat lower than in 2006, but this is not statistically significant. The level of the number of reports per 1000 blood components distributed is comparable to France, which has observed a level of 2.8 to 3.1 reports per 1000 units since its fifth registration year (1998). *Table 4* shows the distribution of type of blood component per adverse reaction or event.

Table 4 Distribution of reported blood-component type per category report in 2007

Reaction	RBCs	Platelets	Plasma	Combined	Other	Not noted
Non-hemolytic transfusion reaction	328 (79.6%)	67 (16.3%)	5 (1.2%)	10 (2.4%)	–	2 (0.5%)
Acute hemolytic transfusion reaction	10 (100%)	–	–	–	–	–
Delayed hemolytic transfusion reaction	10 (90.9%)	–	–	1 (9.1%)	–	–
TRALI	12 (40.0%)	3 (10.0%)	1 (3.3%)	14 (46.7%)	–	–
Anaphylactic reaction	10 (20.0%)	24 (48.0%)	10 (20.0%)	5 (10.0%)	–	1 (22.0%)
Other allergic reaction	40 (21.6%)	87 (47.0%)	43 (23.2%)	15 (8.1%)	–	–
Circulatory overload	19 (70.4%)	3 (11.1%)	1 (3.7%)	4 (14.8%)	–	–
Bacterial contamination	18 (81.8%)	3 (13.6%)	1 (4.5%)			
Viral infection	5 (71.4%)	–	–	2 (28.6%)	–	–
Hemosiderosis	2 (66.6%)	–	–	1 (33.3%)	–	–
New allo-antibody	522 (92.6%)	11 (2.0%)	1 (0.2%)	17 (3.0%)	–	13 (2.3%)
Other reaction	40 (80.0%)	5 (10.0%)	1 (2.0%)	3 (6.0%)	–	1 (2.0%)
Mild febrile reaction	262 (92.3%)	11 (3.9%)	–	8 (2.8%)	–	3 (1.1%)
Incident						
Incorrect blood component transfused	47 (78.3%)	5 (8.3%)	3 (5.0%)	1 (1.7%)	2 (3.3%)	2 (3.3%)
Other incident (optional)	64 (62.7%)	13 (12.7%)	9 (8.6%)	2 (2.0%)	–	14 (13.7%)
Near miss (optional)	12 (17.4%)	1 (1.5%)	2 (2.9%)	–	–	54 (78.3%)
Positive bacterial screening (optional)	4 (16.7%)	20 (83.3%)	–	–	–	–

Variation among hospitals

The number of transfusion reactions per 1000 blood components per hospital varies from zero to 9.45 (the maximum in 2005 was 13.64 and in 2006 28.37). Once again there is a striking variation among hospitals in the number of reports per 1000 blood components. *Figure 4* shows the distribution of number of reports per hospital related to the administered number of blood components, with the same figure for 2006 for comparison. These graphs show only the hospitals whose reports were complete by the closing date for inclusion in the report. As in 2006, two hospitals only sent in reports of serious adverse events or reactions. TRIP can only regret this working method; selective reporting clearly decreases the value of a national reporting system. *Table 5* shows the number of reports per 1000 blood components in relationship to the type of hospital.

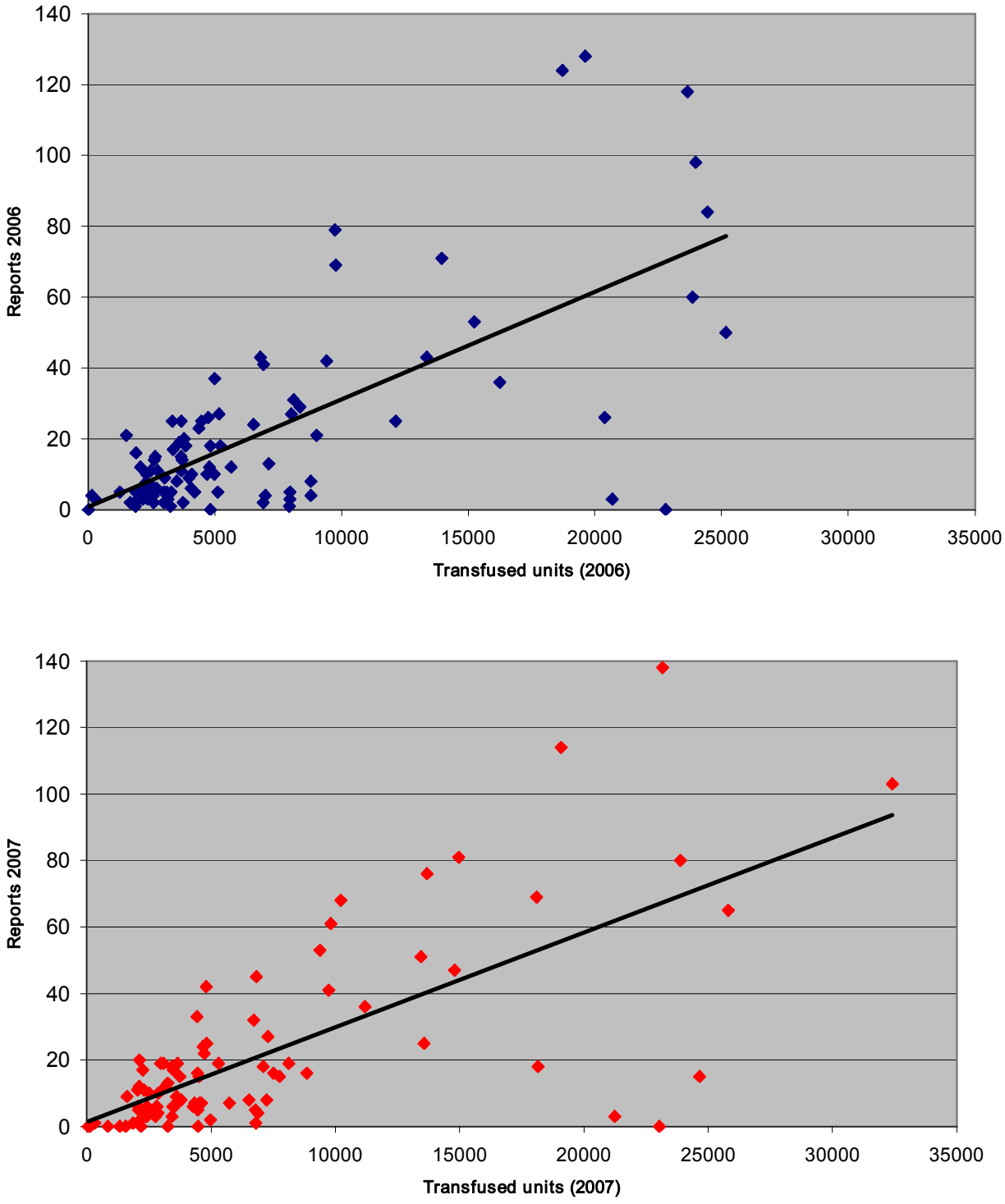

Fig. 4 Number of reports per hospital in 2006 and 2007 related to number of supplied blood components

Table 5 Number of reports of blood use and hospital type in 2007

Hospital type (n* per type)		Number (%) with complete reports and information on blood use		Reports 2007/1000 blood components(range per hospital/median)	2006 final situation (% with complete data)	
Academic	(9)	9	(100%)	2.42 (0.00 – 5.91; 2.52)	2.97	(100%)
Top clinical	(20)	19	(95%)	3.76 (0.15 – 8.75; 3.79)	3.71	(95%)
Other	(75)	67	(89%)	2.78 (0.00 – 9.45; 2.13)	2.96	(96%)
Total	**(104)**	**95**	**(91%)**	**2.92 (0.00 – 9.45; 2.34)**	**3.17**	**(95%)**

* This number can deviate from standard listings of hospitals of each type because in merger situations the contact person may prefer separate reporting until transfusion practice on separate sites is fully comparable.

2.3 Discussion of the reports by category

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

NHTR:
Rise in temperature ≥ 2oC (with or without rigors) during or in the first two hours after a transfusion, with no other relevant symptoms or signs;
or rigors 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. >1oC (<2oC) 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 2007 is 412 compared to 490 in 2006; numbers of mild febrile reactions are 284 and 363, respectively. Together, these make up 36.4% of the total, while that was 40.1% in 2006, including late submissions. Three-quarters of the decrease in the number of reports compared to last year is from this category. Just as last year, a significant number (20 in 2007) is of severity grade 2.

In 2007, 25 patients suffered more than one non-hemolytic transfusion reaction and/or mild febrile reaction and 10 had both a febrile and an allergic reaction on different occasions.

A look at the assignment of imputability shows that reporters generally do not assign a high imputability to transfusion as a cause of febrile reactions. This has to do with the non-specific nature of symptoms and lack of specific laboratory findings to confirm the diagnosis of NHTR. However, it remains important to search for specific causes in patients experiencing chills or elevated temperature during transfusion. *Figure 5* shows the distribution of imputability ratings per type of transfusion reaction.

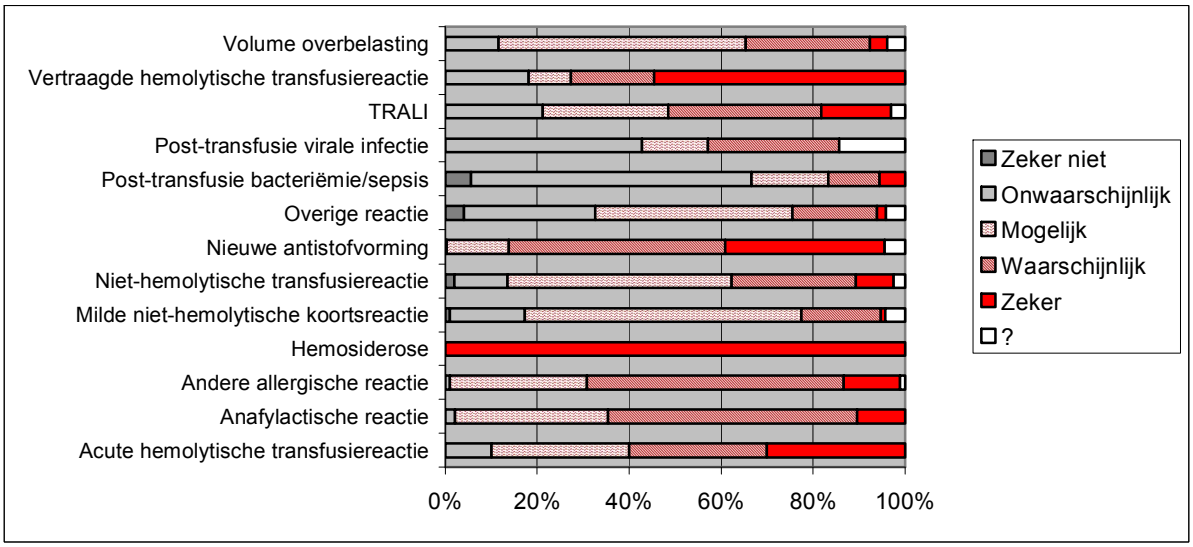

Fig. 5 Imputability levels per type of transfusion reaction

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 2007 ten acute hemolytic transfusion reactions were reported. Three were of severity grade 2 and seven grade 1. Imputability was certain in three cases, probable in three, possible in three and once unlikely. Additionally, an AHTR was reported after administration of an incorrect blood component and one reaction after an 'other incident' (see the relevant sections).

This category is a relatively rare transfusion reaction: 0.5% of the reports in 2007. Compared to previous years, the number of AHTR remains relatively stable (see *Table 2*). In all cases the acute hemolytic transfusion reaction follows an RBC transfusion.

The clinical picture is variable The most frequently reported symptoms were fever and chills: seven times, including two cases where reporters noted more characteristic symptoms of an AHTR. In two cases no clinical symptoms were reported and in one case it was impossible to distinguish a clinical picture resulting from a transfusion reaction in a seriously ill patient and the diagnosis was made based on biochemical values. In one report neither hemolysis parameters nor blood serology could confirm a hemolytic transfusion reaction, which showed a very characteristic clinical picture of fever, lumbar pain, jaundice and dark urine. In two cases reports mentioned appearance of new allo-antibodies: anti-Cw and anti-Wr(a). In one case HTLA antibodies were mentioned as the possible cause of the AHTR. In four cases, with possible (3) and unlikely (1) imputability, immunohematology showed no abnormalities despite presence of an appropriate clinical picture and biochemically demonstrated hemolysis.

Delayed hemolytic transfusion reaction (DHTR)

Symptoms of hemolysis occurring longer than 24 hours after transfusion to a maximum of 28 days subsequent: 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 2007, reports included 11 delayed hemolytic transfusion reactions, comparable to the number in previous years. Additionally, a secondary category of delayed hemolytic transfusion reaction was recorded in three reports where hemolysis was retrospectively detected after discovery of red cell antibodies. However, in 2007 no one reported a DHTR after administration of an incorrect blood component or an

other incident (2006: four). As in previous years, the number of reports of delayed hemolytic transfusion reactions approximates the number of acute hemolytic transfusion reactions, whereas the literature indicates factors of 5 to 10 times higher. It is likely that reactions escape detection if there is no reason to check hemolysis parameters in the absence of clinical features of DHTR or if there are other explanations for raised hemolysis parameters in a sick patient.

All delayed hemolytic transfusion reactions occurred after administering RBCs, while one patient received plasma and platelets in addition to RBCs. Four reactions were grade 2, six grade 1 and four grade 0 (solely laboratory values confirming delayed hemolysis). The imputability is 'certain' in seven cases, 'probable' in four, 'possible' in one and 'unlikely' in two. Antibodies identified as responsible for the delayed hemolytic transfusion reactions were: three times anti-Jk(a), twice anti-Jk(b), three times anti-Fy(a), anti-E and anti-S. In four cases, TRIP has no information about a responsible antibody.

Transfusion-associated acute lung injury (TRALI)

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

In 2007, 30 reports of TRALI were received, of which 29 were severity grade 2 or more (in 2006: 25, of which 20 were serious). As in previous years, TRIP assessed whether reports fulfilled the national definition of TRALI and the imputability was rated independently of findings of leukocyte serology. In total, 23 reports fulfilled TRALI criteria (clinical, chest X-ray, interval, no more probable explanation). Recording hospitals sent insufficient information to judge causes in two cases. TRALI is a serious category: of accepted TRALI reports, three were grade 4, 16 grade 3, two grade 2 and one grade 1. The transfused blood components were RBC concentrates ten times, plasma twice, platelets twice and RBCs with plasma and/or platelets nine times.

An alternative explanation was deemed more probable for the five remaining TRALI reports (imputability unlikely). Sometimes this was the underlying clinical condition of the patient, once circulatory overload seemed more likely and once anaphylaxis. Twice a report of hypoxia apparently related to the transfusion but without changes on the chest X-ray was reclassified in consultation with the reporter under the other reactions, where a cluster of reports of transfusion-associated dyspnoea appears to be emerging.

Table 6 shows a summary of the TRALI reports with accompanying imputability and results of leukocyte-serological testing. Four reports of the 23 TRALIs fulfilling the definition showed an immunological cause with positive crossmatching between donor serum and patient leucocytes (or, if a fresh patient sample was not available, antibodies against a patient HLA antigen); the crossmatch was negative in six cases. Leukocyte-serological testing was incomplete in nine cases and twice no testing took place. It is common knowledge that negative results of leukocyte serology do not exclude TRALI.

Table 6 TRALI reports in 2007

TRALI fulfils definition?	2007	leukocyte serology positive	negative	n.t.	2006	2005
Yes: 23	4 certain	2	1	1	5 certain	6 certain
	10 probable	4	2	4	7 probable	6 probable
	9 possible		3	7	8 possible	3 possible
					1 not reported	
Cannot judge	2		1	1	2	1
Other cause more probable	5	1	1	3	2	3

n.t. = not or incompletely tested

As remarked in TRIP reports 2005-2006, the rigour of investigation (information on X-thorax and underlying patient pathology) are better than in 2003-2004. It is still the case that (after Sanquin has called in the relevant donors) hospitals do not always take a fresh patient blood sample for leukocyte crossmatching tests. In seven cases with incomplete investigation of leukocyte serology, four showed that one or more donors possessed HLA antibodies.

The number of TRALI reports has increased from year to year, probably due to increased national and international attention to this transfusion reaction. Since October 2006 Sanquin has exclusively used the plasma from male untransfused donors to prepare plasma for transfusion. This measure became effective over the course of 2007, because these are quarantine components. One TRALI report in 2007 showed a positive crossmatch with plasma from a female plasma donor. The UK implemented similar measures in 2004, which and these became effective in 2005. No TRALI resulting from administering fresh frozen plasma occurred in the UK in 2005 or 2006. However, it is important to note that SHOT weighs the presence of donor antibodies in defining TRALI.

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, carry out testing for anti-IgA.

There were 50 reports of anaphylaxis in 2007, compared to 19 in 2006 and 26 in 2005. TRIP endorses and has communicated the standpoint that this category includes combinations of skin rash with signs of airway obstruction, breathing and gastrointestinal symptoms (even without hypotension), clarifying some of the increase. Of these reports, 21 are grade 2 or more, compared to 14 in 2006 and 22 in 2005. Numerically anaphylaxis, with TRALI and circulatory overload, remains one of the most important categories of serious transfusion reaction. Of relevant reports, 10 are associated with transfusion of RBCs, 10 plasma, 24 platelets and six with more than one type of blood components. The interval between starting transfusion and appearance of symptoms, where recorded (n=41), varies from 5 minutes to 9 hours and 35 minutes (imputability of this latter report is only ‘possible’), but for 35 reports this was less than two hours. Assigned imputability is certain five times, probable 27 times, possible 17 times and unlikely once (interval 5 hours).

The hospital indicated for 13 reports that it found normal IgA levels and/or lack of anti-IgA. International literature gives anti-IgA as the cause of 10-20% of anaphylactic reactions. Notes to five reports record that the patient taking other medication that may have caused the reaction. For two reactions, the hospital indicated that the patient had had a previous allergic reaction to medication. Five patients also had a transfusion reaction to another administered blood component on a separate occasion: anaphylactic reaction (n=1), other allergic reaction (n=20) and febrile reaction (n=2). The median age of patients is 51.5 years, thus younger than for TRALI and circulatory overload; there are approximately equal numbers of male and female patients. Research must be done to expand understanding of this transfusion reaction and possibly prevent it in the future.

Other allergic reactions

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

The number of reports of 'other allergic reactions' has dropped slightly (185 compared to 222 in 2006); only one records severity grade 2. Probably this is because TRIP requested placing allergic reactions with more than just skin symptoms into the category of anaphylactic reaction.

Men and women are equally represented, as for the anaphylactic reactions. For 'other allergic reactions', 47% is associated with administering a platelet concentrate and 23% with plasma. Here too, patients are relatively young, probably due to the patient population receiving these types of blood components; the median age is 50.6 years. Of these patients, 22 (12%) suffered one or more other allergic, febrile or other transfusion reaction, previously or in 2007.

In twenty reports of 'other allergic reactions', classical, allergic, skin symptoms occurred with elevated temperature. *Transfusion reactions* by M.A. Popovsky (2007) states that elevated temperature is not part of an allergic reaction. It is always necessary to investigate fever; some reports showed possible, alternative causes. However, TRIP's findings are that a rise in body temperature or fever can occur in the 'other allergic reaction' and 'anaphylactic transfusion reaction' categories.

Transfusion-associated 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.

There were 27 reports, compared to 35 in 2006. Once, the patient died (severity grade 4), but imputability was unlikely. Three reports are grade 3 and eleven 2, compared to a total of 24 serious reports of circulatory overload in 2006. Solely RBC concentrates were administered in 19 cases of reports of circulatory overload; plasma, platelets or a combination of components were administered in the remainder. For a number of these TRALI was suspected at first and donor leukocyte antibodies were investigated, though without crossmatching. Patient age for circulatory overload is higher than for TRALI: the median is 72.4 instead of 59.9. Underlying pathology is mixed in both groups and there are no remarkable differences. However, extremely complex clinical situations and septic conditions show up more often in TRALI reports.

It is difficult to distinguish TRALI and circulatory overload clinically, even with chest X-ray. The literature mentions elevation of brain natriuretic peptide (BNP) or the more stable N-terminal pro-BNP in heart failure and circulatory overload (*Transfusion* 48:1143-1150, 2008). For the time being, these laboratory determinations are expensive and evaluation of their usefulness in large groups of patients to support diagnosis and therapy decisions is lacking. Analysis of the reports of TRALI versus circulatory overload shows that a hospital sometimes diagnoses TRALI when there is no response to diuretics, while these are not indicated and can aggravate TRALIs. There is a serious need for better ways of distinguishing between these transfusion complications.

Post-transfusion viral infection

Every viral infection that can be related to a transfused blood component (hepatitis A, B, C, non-ABC, HIV, HTLV, EBV, CMV etc.).

In 2007, just as in 2006, there were seven reports in the category post-transfusion viral infection. None of these reflected a certain, probable or possible transmission of an infection for which the blood bank routinely tests its blood donations.

Just as in previous years, there were reports (n=2) of CMV in (premature) neonates, who, however, were not nursed in isolation and not transfused 'CMV-safe' units. (Special CMV-safe cellular blood components can be ordered for anti-CMV negative patients with reduced immune response, particularly for intrauterine transfusion: these are leukocyte-depleted blood components which additionally come from tested, anti-CMV negative donors.) Given the infection risk from the surroundings, the imputability is only 'possible' or perhaps 'probable' in the case of one of premature twins.

Two reports referred to positive serological results for Epstein-Barr in adults; the time interval after trans-

fusion was a number of years in one case. It makes very little sense for Sanquin to test donors in cases like this. One patient with chronic hemolysis due to sickle cell anaemia did not receive Parvo B19-safe components because hospital protocol did not recommend these. Within four weeks, an aplastic crisis took place; the diagnosis was acute infection with Parvo B19; it was possible to treat the patient without hospital admission. The blood bank did not test further as sources other than the blood transfusion could not be excluded.

Two reports concern hepatitis. In one case, a patient suffered an acute hepatitis B infection approximately 11 months after transfusion of more than 60 blood components. At two weeks after the last transfusions, a single specimen showed the patient to be negative for hepatitis B. At the final date for this report, almost all donors had been tested again and there were no indications for transfer by transfusion. These were not found either in a report of hepatitis C in someone who received three units of RBCs in the US, two of which came from the Netherlands. In that period (the transfusions were in 2002), the Netherlands supplied RBC units from whole blood donations collected for plasma fractionation to the Red Cross blood services in New York.

Bacterial contamination

Bacteraemia following a blood transfusion. Clinical signs may be indistinguishable from a hemolytic transfusion reaction. If the same bacterial species is are found in the patient and in the blood bag (providing this has been stored under appropriate conditions), contamination is certain. It is preferable to investigate whether the strains are identical.

In 2007 TRIP revised the definitions for the category bacterial contamination and the optional reporting category positive bacterial screening. In 2007, the pilot project for the digital reporting system used the new separation into the categories post-transfusion bacteraemia and bacterial contamination of blood component, which were formally came into force from January 2008. In this report TRIP has used the reporting categories of the paper reporting system for 2007. Where necessary TRIP has converted details of reports made within the context of the pilot project, to correspond with the 'old' categories to ensure uniform reporting.

In 2007, reporters named bacterial contamination (post-transfusion bacteraemia) in 22 cases: 18 reports concerned RBCs, 3 platelets and one plasma.

In 16 cases cultures were taken from the component as well as the patient's blood because the patient showed temperature elevation and/or other symptoms. Two reports show a positive component and positive patient culture. Once, the culture showed coagulase-negative staphylococci and the reporter indicated identical strains. In the other, *Staphylococcus epidermis* was found in the component culture, while the patient's blood culture showed *Staphylococcus bovis*. Solely the component culture was positive twice. Solely the patient's blood culture was positive eleven times; two reports showed a positive patient blood culture for the same bacterial type before transfusion, while a further seven cases showed more probable causes for bacteraemia than transfusion.

Four times only the patients' blood was cultured, once finding a more probable cause for bacteraemia than transfusion. In one case, personnel cultured only the component.

One report records a syphilis infection in a mother and her child several months after postpartum transfusion of two RBC concentrates. Although the chance of *Treponema pallidum* surviving in RBCs approximately 2 weeks old is thought to be zero, Sanquin nevertheless tested the donors for syphilis: in both cases the TPHA test was negative which effectively excludes the possibility that the transfusion transmitted the infection to the mother.

Of the 22 reports, ultimately one can conclude for one case that bacterial contamination with coagulase-negative staphylococci from an RBC concentrate is certain. Three reports deem imputability probable and five possible. *Table 7* summarises relevant RBC concentrates, all platelet concentrates and plasma with the reported culture results and observed symptoms.

Table 7 Overview of reports of bacterial contamination

Component	Symptoms (Tf = transfusion)	Screening by Sanquin	Culture result (hospital) on component	Culture result on patient	Imputability
Red blood cell concentrate	chills, temp. elevation >2˚C, dyspnoe, rise in blood pressure, saturation decrease 3 hr after start Tf		*Staphylococcus aureus*	no growth	Possible (had also received nitrofurantoin before Tf with known allergy for this drug)
	Chills within 2 h of start Tf	negative	*Staphylococcus warneri* + vergroenende streptokok	not done	probable
	Temp. elevation >1˚C an <2˚C within few minutes of start Tf		From segment: *Staphylococcus epidermidis*	no growth	possible
	Temp. elevation > 2˚C 8 hr 51 min after start Tf		Not possible	*Streptococcus gallolyticus*	probable
	temp. elevation > 2˚C 2 hr 15 min after start Tf	not applicable	From segments: negative	*Staphylococcus epidermidis*	Possible
	Chills, temp. elevation <2˚C			*Leuconostic species*	possible (3 days earlier blood culture positive for *E.coli*)
	temp. elevation >1˚C and <2˚C within 20 min after start Tf	No report received	Coagulase neg stafylokok	Coagulase neg staphylococcus	certain (identical strains)
	chills, temp. drop 1.1˚C 2 hrs 47 min after start Tf	Not applicable	no growth	*Acetinobacter haemolyticus*	possible (in period before/during/after Tf various other cultures found negative)
Platelet concentrate	temp. elevation > 2˚C, blood pressure drop, dyspnea 15 min after start Tf	no growth	not done	*Bacillus cereus* cultured from peripheral and central line	probable
	temp. elevation > 2˚C 30 min after start Tf	No report received	no growth	coagulase neg staphylococci+ enterococci	unlikely (intravenous line also infected)
	chills, temp. elevation <2˚C, saturation decrease 30 min after start Tf		no growth	Gram neg.staphs + enterococci	unlikely (septic patient, bloo culture 4 days earlier already positive)
Plasma	Chills, temp. elevation >2˚C, fatigue 60 min after start Tf	Not applicable	From segment: negative	centrale line positive	excluded (septic line found)

Information about reports of blood components with positive bacterial screening

Sanquin screens all platelet concentrates for bacteria, performing aerobic and anaerobic cultures. It supplies the components if there are no signs of bacterial growth ('negative to date'). It recalls units showing colour changes indicating bacterial growth (even before establishing and confirming bacterial type).

TRIP received 24 hospital reports indicating that Sanquin had recalled an already-administered blood component due to positive bacteriology. Most cases did not indicate whether a culture could still be taken from the remainder of the component in the hospital; four reports indicated that a culture was performed and one that the hospital laboratory found the culture negative. Reports noted blood-culture results for patients who exhibited a reaction; no blood work had been done on the patient in two reports. *Table 8* shows a summary per component of the reported culture results and any observed reactions or symptoms.

Table 8 Summary of reports of positive bacterial screening

Component	Culture result (Sanquin) on unit	Culture result on unit (hospital)	Blood culture result (patient)	TR with imputability (subsidiary category)	
RBC concentrate (4)	*Propionibacterium* species (2)	not done	*E.coli*	Bacterial contamination	unlikely
				no symptoms observed	
	2x unknown			no symptoms observed (2x)	
Platelet concentrates (19)	*Propionibacterium* species (14)		negative before and after Tf	mild NHFR	certain
			before Tf *E. coli* + *H. parainfluenzae*		
		not done	no growth	mild NHFR	possible
		not done	not done	no symptoms observed	
			not done	no symptoms observed	
			negative	no symptoms observed	
			Initially not done, later several times negative after starting antibiotics		
				no symptoms observed (3x)	
			7 days after Tf *Streptococcus mitis*	first no symptoms observed, later febrile reaction	
	Micrococcus species (3)		*Staph. haemolyticus* from 1 medium(probable contamination)	bacterial contamination	unlikely
				no symptoms observed (2x)	
	anaerobic gram positive rods			no symptoms observed	
	no bacteria cultured in original testing (1)				

In addition, Sanquin informed TRIP that on 91 occasions in 2007 colour change in the test bottle led to recall of one or more blood components which had already been distributed . A total of 98 blood components were transfused (16x RBCs, the rest platelets) which showed positive screening afterwards. For the majority bacterial type was confirmed but it is not known precisely how many of the 98 components had confirmed bacterial growth. Once a reaction was reported to Sanquin: urticaria (TRIP received no information on the type of bacterium). Sanquin's information is more complete this year than previously owing to implementation of central instead of regional registration.

As in earlier TRIP reports, no serious symptoms were seen in 2007 upon administering a unit later found positive in screening. Screening makes it possible to extend the use-by date of platelet concentrates to seven days.

Post-transfusion purpura (PTP)

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

In 2007 no reports of PTP were received. Since TRIP began its registration programme there has been only one report of PTP, in the baseline measurement in 2002.

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 (non-irradiated) blood component, with a high mortality. Skin (and liver) biopsies can support diagnosis.

In 2007, just as in previous registration years, there were no reports of TA-GVHD. Leukodepletion, practised on all blood components since the end of 2001 in the Netherlands, significantly prevents TA-GVHD. Patients at risk receive irradiated blood components too.

In the UK the hemovigilance system SHOT has received over 400 reports of transfusion of non-irradiated blood components to patients with an indication for irradiated components. None of those patients developed TA-GVHD. This shows that the risk is low. That the risk is still present despite leukodepletion emerges from the fact that, since its foundation, SHOT has received one report of TA-GVHD in a patient who had received only leukodepleted blood components (in 2000-2001).

Hemosiderosis

Hemosiderosis in a multiply transfused patient.

In 2007, three reports of hemosiderosis came in from one institution. Reports have not increased from 2006, although TRIP requested attention to this in its 2006 report. A total of 11 reports of hemosiderosis have been received from two hospitals over three years. The patients (10 of the 11 male) are long-term transfusion-dependent. Diagnoses were: 1x beta thalassaemia, 4x myelodysplastic syndrome, 2x aplastic anaemia and 3x acute myeloid leukaemia. Treating physicians prescribed iron-chelation therapy, depending on the prognosis.

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).

As in the past three years, development of new allo-antibodies is the largest category. TRIP received 564 reports (29.6% of the total) from 46 of the 96 participating hospitals. This shows only a slight drop compared to 603 reports from 48 hospitals in 2006, underscoring the readiness of hospitals to report to TRIP parallel with their reports to TRIX, the national Transfusion Register for Irregular Antibodies and X (crossmatching) problems. Analysis of a clinical reaction led to 15 further cases of new antibodies. These were two hemolytic transfusion reactions, an anaphylactic reaction, five non-hemolytic transfusion reactions, two mild non-hemolytic febrile reactions and five delayed hemolytic transfusion reactions, of which severity was grade 2 three times. In incidents, there is one report of new antibody production resulting from transfusion of an incorrect blood component. Conversely, one report in the category of new antibody production records a subsidiary category of a delayed hemolytic transfusion reaction: first a new antibody was detected and subsequently biochemical testing confirmed hemolysis.

In practice only about half the hospitals report this category. If one extrapolates the numbers of reports to all hospitals, one expects 1100 reports for this year in the category. Besides this, development of antibodies is not detected in all cases because screening for irregular antibodies is not routinely repeated after transfusion. *Table 9* shows antibodies identified in 2007 and their numbers. Formation of two or more new antibodies appears in 107 (19.0%) reports.

As in previous years, production of anti-E, with 192 reports (34.0%), is the most important numerically, followed by anti-K with 152 reports (27.0%). These include six reports of anti-K production in women under 45. In three of these, the blood component was administered years before the Dutch Institute for Healthcare Improvement (CBO) blood transfusion guidelines appeared in 2004; one hospital implemented the K-negative policy as of February 2007, but administered the blood component in October 2006. Hospital protocol was followed in this case, meaning not registering this as an incident. Administering a blood component could not explain anti-K production in one patient with thalassemie: all nine transfused units were K-negative when tested. One report came in of an incorrect blood component administered to a woman of fertile age, in whom anti-K and anti-Fy(a) were subsequently found. There are 26 reports of anti-E and/or anti-c production in women of fertile age, compared to 15 in 2006. It only will be possible to evaluate the recommendation in the 2006 report to consider selecting both Kell-negative blood and Rhesus-phenotype compatible RBCs for women under 45 for the reporting year

blood and Rhesus-phenotype compatible RBCs for women under 45 for the reporting year 2008. Four reports indicate anti-Fy(a) production in women in this age group.

In 2007, 18 reports of anti-D production were received. Ten of these (four men and six older women) concerned anti-D production after a Rhesus-incompatible platelet transfusion. In two cases this resulted from an incident: incorrect blood component administered years ago. One report mentions administering O-positive blood to an older woman in an emergency after administering several O-negative units. Reporters assumed non-specific boostering in two older women with no other explanation. A weak donor variant-D seemed responsible for anti-D production in two reports. Finally, in one case reporters presumed anti-G specificity but did not confirm this.

Table 9 Antibodies identified in 2007 and their numbers

Antibody	Number	Antibody	Number
Anti-c	60	Anti-Lea	5
Anti-C	32	Anti-Leb	1
Anti-D	18	Anti-Wra	16
Anti-e	4	Anti-S	14
Anti-E	192	Anti-s	1
Anti-K	152	Anti-M	8
Anti-Kpa	16	Anti-I	1
Anti-Fya	52	Anti-Bga	1
Anti-Fyb	4	Anti-f	1
Anti-Jka	58	Anti-P1	1
Anti-Jkb	22	Anti-Ytb	1
Anti-Cw	20	Anti-Ch	1
Anti-Lua	15	Anti-HTLA	1

Other transfusion reactions

Transfusion reactions that do not fit into the categories above.

There are 50 reports of other transfusion reactions in 2007, compared to 61 from 2006. Six are grade 2 or more. This group includes reports that do not fit the more specific TRIP categories. TRIP searches for specific clusters in this category. Reports of hypotension without allergic symptoms (11 times) are seen in this category once again. One report from this group is grade 4, but in this case there was a clear alternative cause for the hypotension and imputability is ‘excluded’. A further two reports of hypertension record grade 2.

Eight reports mention cardiac symptoms such as chest pain, palpitations or cardiac arrhythmia. Four reports mention gastro-intestinal symptoms (nausea, vomiting or abdominal cramps). Most of these assign possible or probable imputability.

When assessing reports of dyspnoea that do not fulfil the TRALI definition, the EC takes the standpoint that these should be registered as other transfusion reactions since TRIP has no separate category for ‘transfusion-associated dyspnoea’. Seven reports (two of grade 2) fit within this cluster.

Two reports record non-specific clinical deterioration (shortness of breath, dizziness, sweating etc. without blood-pressure drop or bronchial constriction) after a RBC transfusion. One patient recovered when transfusion stopped, whereas symptoms returned when it started again; this happened again with a new unit. Blood-group serological testing did not clarify the reaction.

One remarkable report records hyperkalaemia and hypernatraemia reactions in a foetus following an intra-uterine transfusion.

Another striking group of reports of 'other reaction' (usually recorded as a subsidiary category) is that of cases where platelet transfusion produced insufficient yield. This was established through testing in the context of temperature elevation, with or without dyspnoea. Nine reports belong to this cluster.

Incorrect blood component transfused

All cases in which a patient was transfused with a blood 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.

TRIP received 60 reports in this category, four of which also showed a transfusion reaction. Reports are only slightly fewer than in 2006, making it striking that the number of reports including clinical symptoms in the patient has dropped significantly (2006: 64, including 14 with clinical symptoms, 2005: 58, including 16 with clinical symptoms). Figures of blood use for the hospitals make it reasonable to expect that not every hospital will submit reports in this category every year A look back at the past five years of TRIP registration shows, nevertheless, that there is a number of hospitals that has never submitted a report in the category 'incorrect blood component transfused'. The same obtains for the category 'other incident'.

The category 'new antibody production' discusses a report of antibody production as a consequence of administering an incorrect blood component in the past, but after the reporting hospital implemented the CBO Guidelines. *Table 10* summarises reports of incorrect blood component transfused in 2007 which were accompanied by transfusion reaction in the patient.

Mix-up of patients, blood units and/or crossmatching samples led to administering a blood component meant for another patient 17 times. Transfusion was not indicated for the patient who wholly or partially received the blood component in two of these reports. Two further reports do not clarify whether the recipient required transfusion. RBC concentrates were involved 15 times, platelets once and another component once. In six of these cases, the blood components were ABO-incompatible. In one case, the component was also Rhesus-incompatible. Two other reports said the component was incompatible for the Rhesus blood group. An acute hemolytic transfusion reaction (grade 1) occurred only once, after transfusion of an A-positive component to an O-positive patient. An immunodeficient A-positive patient of 52 received practically all of two units of B-negative RBC concentrate without showing any reaction at all. A 78-year-old A-positive patient received several tens of millilitres of B-negative RBC concentrate without any observable symptoms of hemolysis, while an 87-year-old O-positive patient showed no observable reaction to a comparable amount of A-positive blood component. Of 11 ABO-compatible switches, the report stated the blood group to be O nine times (6x Rh-positive, 2x Rh-negative, once Rh-nonspecified); three times donor blood of group A-positive was given by chance to an A-positive patient and in one incident the blood group was not specified. Neither of the two incidents in which Rh-positive blood was given to Rh-negative patients led to anti-D production; only one report indicated that the patient received anti-D prophylactically. Cases of administering both ABO-incompatible and Rh-incompatible drain blood are described in the chapter on blood-saving techniques.

Transfusion of HLA-matched platelets, where a previously acceptable mismatch proved no longer acceptable, may have contributed to a thrombocytopenic 53-year-old patient with myelodysplasia dying of a cerebral hemorrhage.

A variety of reasons led to failure to take irregular antibodies into account in 15 cases. A transfusion reaction occurred twice. In two cases was not performed despite being indicated. Once personnel failed to type the antibody after positive screening. In the urgent situation that followed it was not possible to

transfuse antibody-compatible blood (anti-Jka). Once, an employee unqualified for the work judged a result incorrectly, meaning no one typed the antibody and a blood component with the cognate antigen was administered. Blood was issued four times on the basis of an invalid (expired) antibody screening result. Problems with individual transfusion advice led twice to administering a blood component containing an antigen for which the patient had antibodies. Four reports describe failure to order or select a typed blood component. In one case, the supplied blood component was not the one the hospital had ordered: it was e-positive instead of the e-negative requested.

During seven transfusion episodes non-irradiated blood components (6 times RBCs, 5 times platelets and 3 times not specified) were administered, whereas radiation was indicated. In some cases, the indication for irradiation did not appear on the request form, once the blood bank supplied a non-irradiated component mistakenly, twice the indication for irradiation was deleted from the laboratory system through miscommunication and two reports mention the mistaken issue of a non-irradiated component.

Hospital policy regarding Kell, Rhesus or Parvo-safe was not followed in 11 cases. Female patients younger than 45 received: Kell-positive RBCs on five occasions, once Rhesus-D-incompatible platelets and twice cE-incompatible RBCs.

In one report transfusion advice for a transplanted patient was not followed, resulting in issuing and administering O-positive instead of AB-positive plasma. One report describes (partial) administration of a blood component that had showed weak positive reactions in the direct antiglobulin test and upon crossmatching. Inaccurate application of the hospital procedure for issuing uncrossmatched RBCs led to issuing B-positive uncrossmatched RBCs instead of O-negative for a B-positive patient. This patient's blood group had been determined twice in the past but not checked on the present admission to exclude patient switches. One report mentioned ignoring hospital policy and failing to crossmatch blood when selecting a blood component for a child younger than one. A number of RBC concentrates was issued and administered in another case to a patient in the evening hours, despite the validity of the antibody screening having expired that morning.

Two reports referred to administering a component different from the one the treating authority requested: once plasma instead of platelets and once plasma instead of albumin.

Table 10 Clinical symptoms after administering an incorrect blood component

Nature of the reaction	Total	Severity grade				
		0	1	2	3	4
Acute hemolytic transfusion reaction	1		1			
Other reaction	3	2				1

Other incidents

Other mistakes/incidents in the transfusion chain, for instance patient transfused whereas the blood was supposed to be kept in reserve, or transfusing unnecessarily on the basis of a wrong hemoglobin result.

There were 102 reports in the category 'other incident'. Six of these led to an observable reaction. *Table 11* summarises these.

One of the most striking reports in this category this year is an instance of the request form being filled in incorrectly on purpose because the person requesting the component did not see the point of the questions; explanation quickly rectified this misunderstanding. This report shows how essential communication and schooling are for hemovigilance. Requests for non-indicated component treatments such as

radiation and washing were the reason for a report in four instances. In one of these cases it transpired afterwards there was actually a radiation indication for a patient who was not yet identified at the time of an urgent request was made (outside responsibility). We did not add this report to the category 'incorrect blood component transfused' because there is question of 'calculated risk' in this case and it is instructive to keep track of how often a risk like this actually arises. One report describes a comparable case in which, in an urgent situation (Hb 1.8 mmol/l), for a patient known to have six irregular antibodies, personnel chose to administer O-negative, uncrossmatched blood in conformity with existing transfusion advice. Afterwards, the blood was found to be positive for the antigen Fya, to which the patient had produced antibodies in the past. No disadvantageous consequences for the patient were observed in any of the above reports. Another case of 'calculated risk' was that of electronic (Type & Screen) issue for a patient in whom an anti-Kp(a) was missed in routine screening because it Kp(a) is not required on the standard panel: the patient showed symptoms of acute hemolysis.

Once, mistakenly, the request was for plasma instead of platelets; the laboratory's alert reaction to the unusual combination of requested components ensured supplying the intended component. Miscommunication in another case caused the issue of only platelets when platelets and plasma were requested. Mistakes in administration or identification of blood components for issue resulted in switched transfusion-report forms or incorrectly transcribed component data, accounting for four reports.

In 14 cases, blood was requested and in 13 cases is was transfused on the basis of an out-of-date or incorrect result. In two cases the Hb had not been determined recently; in two others, no intermediate Hb check took place subsequent to transfusing several units of RBCs; once two units of plasma were ordered but ultimately not administered, based on the previous afternoon's INR result, while a result for that same morning existed. Further situations causing mistakes were: the RBC count was taken for the Hb value; erroneous reporting of the Hb value following determination in a special medium (approximately 1 to 1 dilution); the platelet count (value in EDTA sample with platelet aggregates) communicated by nurse to doctor was incorrect; a blood sample was taken incorrectly (from the arm with the drip) three times.

As in previous reporting years, large numbers of reports arose from failing to pick up / store / move blood components to another ward. A blood component was sent to the wrong ward through the air-tube mail distribution and this unit lay around for 12 hours in a sub laboratory. Seven reports indicated administration of these blood components or a portion thereof: twice this was more than eight hours after issue and one of these cases showed an other allergic reaction. The other RBC units were destroyed.

Forgetting pre-medication is mentioned in the presence of an other allergic reaction. Another administration mistake was failing to check the drip site before starting the RBC transfusion. This mistake prolonged hospital admission by as much as four days because the patient woke up the next day with a swollen, blue arm. A hemovigilance assistant found a patient with an RBC unit on the infusion stand outside in the sun: another remarkable report. A final report related to administering blood components states that the transfusion was stopping temporarily due to increased pulmonary symptoms, meaning the transfusion was took 11 hours.

Approximately a third of the other incidents had to do with blood components which had already been transfused to patients when Sanquin informed the hospital that the donor or component did not fulfil standard donor criteria in retrospect, based on information or donor information received later. This occurred mainly for donors who later stated that they had had a blood transfusion themselves in the past. There was also a striking number of reports there were relating to donors who later (usually the next time they visited) told personnel they had visited an area of risk (7x malaria and 1x Dengue). In two other

cases, the donor showed symptoms of viral infection after donation. Twice a report concerned plasma from a donor who had also donated a component possibly involved in a TRALI somewhere else. To date, TRIP has not received supplementary information in any of these cases to indicate that the recipient had symptoms ascribable to the relevant donation. Components for which Sanquin reported positive bacteriological screening to the hospital are discussed in that section, except for one 'other incident' report: where after receiving the fax warning of bacterial contamination of the component, the biomedical scientist failed to follow protocol, meaning that the doctor in charge only learned of it six days later.

Miscommunication between blood bank and hospital meant a platelet concentrate was left on a mixer for more than 12 hours at a too-high temperature, instead of in the platelet storage cupboard. Hospital protocol states that mixing may take place only for a maximum of four hours. Passive transfer of anti-D was the reason for one report and twice a unit showed a positive direct antiglobulin test. Twice the hospital check on the component blood group showed that it was Rhesus-negative while the component was supplied as Rhesus-positive. An explanation for this could be the presence of a weak D-antigen that only showed up with especially sensitive techniques.

Although the administrative processing of a transfusion is not always flawless, over the years there have been relatively few reports addressing traceability of blood components. In 2007, there were two reports of transfusions for which no one could specify which blood component the patient received.

Failing to request blood for a patient, transfusing a patient after the antibody screening's validity period has lapsed or insufficiently filling in a request form, limiting screening validity to 72 hours, produced four reports. The latter ultimately led to administering two O-negative, uncrossmatched units and unnecessarily rendering useless two O-negative RBC concentrates because they were stored improperly after the urgent request.

A problem involving blood-group determination of a neonate (found twice to be Rhesus D-negative using test tubes and a week later Rhesus D-positive using a cassette) led to failing to give the mother anti-D. A report also came in of a patient with an extremely variable blood group: in 2003 O-positive, 2004 A-positive, 2007 O-positive, in all cases determined twice. It was impossible to trace precise details, unfortunately, but it is likely that a different person was admitted to hospital in 2004 under this patient's name.

Table 11 Clinical symptoms following other incidents

Nature of the reaction	Total	Severity grade				
		0	1	2	3	4
Acute hemolytic transfusion reaction	1		1			
Circulatory overload	1		1			
Non-hemolytic transfusion reaction	1					
Other allergic transfusion reaction	2		2			
New allo-antibody	1	1				

'Near miss' events

Any error that, if undetected, could have led to a wrong blood group result or issuance or administration of an wrong blood component, and which was detected before transfusion.

Logically speaking, the 'near misses' should be much more frequent than the reports of 'incorrect blood component transfused'. The fact that this is not the case has to do with 'near miss' being an optional reporting category; only some hospitals submit reports of near misses. Sixty-nine near misses were recorded throughout 2007. The largest group here remains unchanged: identification faults in various steps of the transfusion chain. It is important to remember here that TRIP only registers the 'first error', whereas often a series of mistakes go together to cause an accident. Analysing incidents often brings

mistakes to light that occurred beforehand in a series, but were not recognised as such in the first instance. This is why it remains difficult to estimate whether near misses reported to TRIP actually reflect accidents that could be anticipated. The value of reporting near misses lies mainly in being able to identify weak spots: where something repeatedly threatens to go wrong, one justifiably could expect an accident at some point. Another possible reason for continuing to report these is being able to judge the effectiveness of safety measures. To do this, though, it is necessary that hospital staff become aware of the usefulness of reporting not only on a national basis but also throughout the entire transfusion chain, otherwise it will remain difficult to compare effects of different safety measures.

A short summary of the reported of errors of identification: only four reports record component identification faults, for instance, exchanging labels on blood bags. Two such mix-ups came to light as late as checking before transfusion on the ward. One instance recorded the blood group typing of a supplied component not matching that ordered from the blood service. Other cases were of faulty patient data being used and/or taking blood from the wrong patient. Half of these mistakes were discovered before or directly upon receipt in the laboratory. The lack of pre-labelled blood-sampling tubes for a patient led to the discovery that incorrect tubes had been used for that patient in the past. In 14 reports laboratory staff discovered that data on the request form differed from data on the blood sample. A telephone request differed from the request form and/or blood sample in two reports, and once the request forms for two different patients came in with blood samples labelled with one patient's name (tubes contained blood of different blood groups). In one case an anonymous blood sample was submitted for blood-group determination. For different reasons and often because of special alertness (for instance noticing an outpatient hospital number for a patient on the ward, or lack of valid screening or the most recent Hb being higher than the transfusion threshold (6 mmol/l) the laboratory contacted the ward, discovering five cases of a request intended for a different patient. The mistake showed up nine times through a discrepancy between the historically established blood group and a newly determined blood group. Lacking results caused the ward to contact the laboratory, bringing to light an identification mistake. In seven cases it remains unclear how the mistake was discovered; for five of these, a nurse reported to the laboratory that blood had been taken from the wrong person or that a patient's tubes had the wrong labels. Checks before administration on the ward revealed twice that requests for blood-group determination and RBC units were labelled with someone else's very similar surname.

Three reports concern components; one supplied as Rhesus-D negative was found in the hospital to be Rhesus-D positive, once antibody typing during hospital checks deviated from the type on the label, and once an order of blood components for two different patients was delivered by the blood service with the card attached to one of the components showing the name of the patient with the other's hospital number.

Failing to take into account irregular antibodies, forgetting to request irradiated blood, wrongly selecting a component (O-positive plasma for an A-positive child; e-negative blood component for a patient known to have anti-E), issuing components in spite of lapsed screening validity or issuing blood-group-identical blood after only one determination of the blood group caused seven reports. A blood-group discrepancy brought to light a case of failing to determine blood group properly and two cases of interpreting blood group test results wrongly. A hematology biomedical scientist discovered another case of wrongly interpreting a manual blood-group determination. A remarkable report was the near miss where the IT department of a hospital unintentionally tested the combining of data from two hospital locations in the production environment: good information was replaced by mistaken information and correction left the mistaken information in place for one patient in Logistics Information Systems.

Reports relating to autologous blood components (blood management techniques

Three reports from three different hospitals deal with transfusion reactions using blood management techniques in 2007. As recommended in the memorandum on Blood Management Techniques, these should also be covered by hemovigilance. In 2008, in fact, TRIP will commence a pilot project targeting reports of transfusion reactions and incidents. It is not known how often Dutch hospitals use blood-saving techniques.

Two reports mention non-mechanical auto-transfusion: one records a non-hemolytic transfusion reaction of grade 1 and 'possible' imputability when re-infusing non-washed, filtered drain blood. The other records an incident of administering an 'incorrect blood component', in which a student on work experience connected the receiving bag for the drain to the patient in the next bed. The mistake was discovered quickly, so only a small amount of ABO-incompatible drain blood was administered. No transfusion reaction occurred and the hemolysis parameters showed no hemolysis.

The third report records administration of an autologous, pre-operative donation. An 'other reaction' (hypotension) occurred, grade 1, with 'unlikely' imputability. A second autologous unit was transfused without problems.

Deceased patients and transfusion reactions (grade 4)

Six reports in 2007 are of grade 4. *Table 12* below summarises these and they are further discussed in the relevant sections.

In discussing grade-4 reports with the EC, parties acknowledged the important point that a reaction with high imputability can be ascribed to the transfusion, but often the reaction only partially or hardly at all contributes to the patient's death. The comments about underlying clinical conditions of relevant patients in Table 12 illustrate this. Those working with the British hemovigilance system SHOT are used to judging all cases of patients deceased separately in one of three ways: ascribable to transfusion problems, partially ascribable to transfusion problems or the consequence of underlying patient pathology. In all the grade 4 reports in 2007, patient death is either only partially related to the transfusion reaction or unlikely to be a consequence of it.

Table 12 Reports recording decease of the patient (grade 4)

Reaction category	Age, gender	Indicated imputability	Nature of underlying pathology
TRALI	66 M	probable	palliative care for metastasised malignancy
TRALI	76 M	probable	re-operation due to bleeding complication in sigmoid resection connected to diverticulitis
TRALI	9 M	possible	serious abdominal trauma and intestinal perforation, diffuse intravascular coagulation
circulatory overload	53 M	unlikely	chronic liver failure, bleeding from oesophageal varices
other reaction	61 M	unlikely	hypotensive reaction with detachment of artificial heart valve
incorrect blood comp	52 M	possible	serious thrombocytopenia, no transfusion reaction, death from cerebral hemorrhage

Five years of TRIP: what has that meant for transfusion safety in the Netherlands?

This is the fifth annual report TRIP is publishing on recorded transfusion reactions and incidents. Numbers of reports have stabilised and participation is high. How far has TRIP succeeded in achieving its aim of improving transfusion safety?

A first point is that the registration has produced 'good knowledge of the nature and extent of serious

adverse reactions and events connected to transfusions' in the Netherlands. If one compares numbers of reports to numbers of supplied components, the level is the same as in France, which uses a comparable set of reporting categories. Changes to transfusion policies or practice will most likely reflect in numbers of reports.

TRIP's second aim is to make focused recommendations to increase transfusion safety. *Figure 6* shows types of reports from 2002 - 2007. Where can parties profit from information? Where can parties prevent transfusion reactions?

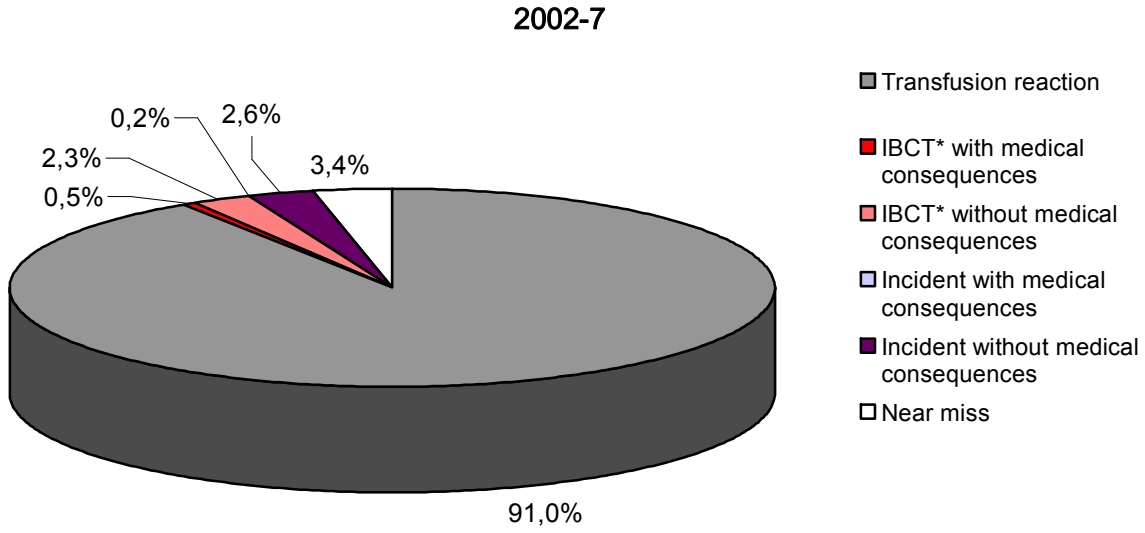

Fig. 6 The distribution of types of reports from 2002 up to and including 2007

The blood components are extremely safe as far as infection risks go. Since TRIP began, the measure ‘male-only plasma’ has come into force to prevent TRALI. It is too early to judge the effects. Meanwhile, research within and outside the Netherlands is making the role of different production techniques for blood components in transfusion reactions clearer. Solely by continuing to record and register all transfusion reactions at the national level, can we monitor effects of variations in component preparation and draw comparisons with what happens in other countries.

For the laboratory part of the chain, there are limited numbers of reports which concern different laboratory methods. More reports concern mistakes, which fortunately are often detected on time. TRIX is an tool for reducing transfusions of incorrect blood components in the presence of antibodies, a previous stem cell transplantation or other transfusion problems.

The last five years have seen no changes in the transfusion chain that could reduce numbers of reports of incorrect blood component or near miss. For the time being, the Netherlands is in a phase where a high number of reports indicates better alertness and not lack of safety. Both the British hemovigilance system SHOT and the French registration system show decreases in numbers of reports of incompatible blood transfusions. They ascribe this result primarily to education. It is crucial that hospital hemovigilance professionals have sufficient time and support to develop their tasks in this area further. It is also important to invest in developing and implementing IT methods targeting the prevention of identification faults.

On the clinical side, two items need attention: good prescription of blood components and respecting recommended transfusion triggers. TRIP has not mapped this out at the national level yet, but hemovigilance assistants in many hospitals are doing good work under the responsibility of the blood transfusion

committee and the hemovigilance officer. Several organisations institutes has discovered that training and audit activities reduce blood use. This earns back the hemovigilance assistant's salary, makes available more money for other activities and reduces numbers of patients exposed to transfusion. Effects of 'hemovigilance' are much broader than simply ensuring reporting. In hospitals that already observed triggers before hemovigilance was implemented, making any financial benefit from hemovigilance less visible, a the hemovigilance assistant monitors and improves quality in the transfusion chain.

2.4 Overview of mandatory reports of serious adverse reactions and events in the transfusion chain (in conformity with European Union legislation)

Table 13 Numbers and imputability in reports of grade 2 and higher in 2006 and 2007

Type of reaction	Number of serious reports		Cannot judge (not rated)		Excluded, unlikely, possible		Probable		Certain	
	06	07	06	07	06	07	06	07	06	07
Acute hemolytic TR	5	3	0	0	1	2	2	0	2	1
Delayed hemolytic TR	8	4	0	0	1	0	1	1	6	3
TRALI	22	29	3	0	6	16	8	8	5	5
Anaphylactic reaction	13	21	0	0	3	5	5	15	5	1
Other allergic reaction	10	1	0	0	3	1	3	0	4	0
Transfusion-associated circulatory overload	24	15	0	0	9	10	10	5	5	0
Bacterial contamination	3	6	0	0	3	3	0	2	0	1
Post-transfusion viral infection	2	4	0	0	1	3	0	1	1	0
Post-transfusion purpura	0	0	0	0	0	0	0	0	0	0
Transfusion-ass. GVHD	0	0	0	0	0	0	0	0	0	0
Other serious reactions	42	28	0	0	28	19	9	5	5	4
Total	**129**	**111***	**3**	**0**	**55**	**59**	**38**	**37**	**33**	**15**

* One report of grade 4 is not included because there no transfusion reaction occurred (see Table 12).

2.5 Conclusions

1 Hospital participation remains high. It is important that all hospitals submit their reports before the closing date.

2 The number of reports has stabilised. The number of mistakes is not increasing, but not decreasing either. This means that the TRIP reporting system can function well to monitor measures still to be taken to reduce mistakes in the transfusion chain. In 2007, there were 60 reports of administering an incorrect blood component. This is impermissibly high, indicating that transfusion-chain safety must improve further.

3 The online reporting system is functioning well. In 2007, 28 hospitals actively participated in digital reporting. In general, the digital reports contain more information on laboratory findings, enabling TRIP to analyse and compile these reports more rapidly and more effectively.

4 Numbers of non-hemolytic transfusion reactions and mild febrile reactions in this report have dropped in comparison to 2006. TRIP sees it as important to continue to report these. Registration can bring to light unexpected causes; these relatively frequent, non-serious reactions gauge how effective the reporting system is for the entire chain.

5 in 2007, more reports came in indicating bacterial contamination. However, cultures were not performed in all cases to make and confirm a definitive diagnosis.

6 There are not many reports of viral or bacterial infection through a blood component (with high imputability): in 2007, there were three serious reports of suspected bacterial contamination (imputability certain or probable) and one of viral infection. There were no reports of transmitting sicknesses for which donations are screened. Consequently, in the present situation pathogen inactivation will contribute very little to increased safety of blood components.

7 The number of reports of suspected TRALI has increased; however, the level of diagnostic investigation lags behind. Even in cases of thorough testing of leukocyte serology, there are few positives. Against the background of increasing numbers of reports, it is too early to say whether introducing the policy of 'male-only plasma' will prevent TRALIs.

8 As in 2006, there are reports of (serious) adverse reactions associated with the use of blood management (autologous) techniques. There are too few reports to make clear the magnitude of this problem.

9 It is useful to report 'near misses' in the transfusion chain. Until now, received reports chiefly are generated in parts of the chain that blood transfusion laboratories and blood transfusion committees easily oversee.

2.6 Initiatives and developments in response to recommendations of the TRIP Annual Report 2006

1 *Recommendation 1 from the TRIP report 2005 remains in force:*
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 through comparative research in clinical science.

2 *In addition to TRALI, circulatory overload is an important category for attention, particularly because relatively simple, preventive measures exist, like administering diuretics.*
As far as TRIP knows, no action was taken on the first two recommendations in 2007.

3 *Vigilance is needed as well in areas of adverse reactions and events related to using blood-saving techniques.*
The TRIP website contains a draft guideline from the TRIP governing board on procedures and vigilance in blood management techniques. A number of hospitals has registered to participate in a pilot project reporting adverse reactions and events while applying blood management techniques.

4 *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.*
Registered TRIP reports can underpin the re-evaluation process within the context of revising the CBO Guidelines for Blood Transfusion.

5 *More attention must be paid to reporting transfusion-related iron overload to gain more insight into preventing this adverse reaction in the Netherlands.*
TRIP is unaware of any action yet in this direction.

6 *Online reporting should be further stimulated to facilitate more rapid reporting and thus promote optimal analysis. Together with this a means should be developed to enable the reporter to electronically send relevant reports of serious adverse reactions or serious adverse events to the competent authority, The Netherlands Health Care Inspectorate (IGZ).*
The functionality to send on reports has been developed and tested and the IGZ agrees with it. When TRIP was drawing up this 2007 report, the IGZ was still experiencing delays in activating this function.

7 *Within the framework of introducing safety- management systems, directors of hospitals and other involved institutions must remain on guard to ensure the integration of new initiatives into already existing hemovigilance activities and into the general safety system of a given hospital.*
TRIP has contacts with representatives of a number of other branch-specific, reporting systems. Despite a certain amount of national activity (see for instance 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.

2.7 Recommendations

A. Recommendations based on the TRIP Report 2007

1 Initiatives to prevent mistakes in the transfusion chain and improve the safety of blood transfusion must now be opened out. The present, stable, TRIP reporting system makes it possible to measure the effects of these developed initiatives.

2 More recorders of events must start reporting digitally reporting system. Digital transfer of obligatory reports from hospital to competent authority is a priority.

3 In cases where the reporting hospital considers bacterial contamination (post-transfusion bacteraemia), it is essential to culture the patient blood and the blood component to identify bacteria.

4 Present alertness to the transfusion complications TRALI and circulatory overload must be maintained. In all cases where details of a report fulfil the TRALI definition, both Sanquin and the hospital (by submitting a fresh patient sample for the crossmatching test) must investigate a cause mediated by the immune system. This is important to establish the effectiveness of the implemented 'male-only plasma' measure.

5 TRIP must have a clear role in drawing up an inventory of adverse reactions to the use of blood-saving techniques.

B. General recommendations

6 Numbers of incorrect blood components administered 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.

7 To increase blood-transfusion safety actually, every hospital must have a hemovigilance employee. One important task of this employee is to school doctors and nurses involved in prescribing and administering blood components.

8 The educational curriculum for medical specialists must devote more attention to blood transfusion and hemovigilance.

3. Tissue vigilance

3.1 Introduction

Tissue vigilance means: ‘systematically monitoring serious adverse reactions and events in the entire chain of body material of human origin, with the aim of arriving at a safer and more effective use of tissues and cells’.

Governed by Article 11 of Directive 2004/23/EC of the European Parliament and of the Council, all Member States must implement a system for reporting, investigating, registering and passing on data on serious adverse reactions and events associated with the medical use of human tissues and cells. In 2005 the Dutch Ministry of Health, Welfare, and Sport (VWS), acknowledging the similarities with the existing hemovigilance system as regards quality systems and legislation, asked TRIP to draw up an inventory and set up a reporting system for tissue vigilance. Importantly, TRIP is independent of healthcare institutions as well as of suppliers of human bodily material for transplantation.

In April 2006 the Directive came into force. In August 2006 TRIP launched a pilot reporting system, which it extended by two years at the end of 2006, thus until the end of 2008. The system for reporting and registering serious adverse reactions and events associated with the use of human tissue and cells, functions on a voluntary basis. TRIP registers and uses its expertise to analyse these reports. As for the hemovigilance reports, TRIP provides the obligatory summary of reports to the competent authority. These activities, launched in the second half of 2006, continued into 2007. As in 2006, TRIP requested figures for distributed tissues and cells at the end of 2007. A new feature is that TRIP is actively approaching the hospitals. The programme includes stimulating these hospitals to appoint a tissue vigilance officer and to keep track of and report numbers of tissues and/or cells used in 2007.

3.2 The reporting system

Whenever severe adverse reactions and events are observed that could be related to the quality and safety of tissues and cells, the hospital reports this to the tissue establishment. The hospital may also report directly to TRIP. The tissue establishment transmits to TRIP the reports of adverse reactions and/or events from the hospitals. The tissue establishment also reports any adverse reactions or events involving a donor or a procedure within the tissue establishment. *Figure 7* represents the system in a flow chart. At the time of compiling this report, hospitals and tissue institutes report all calamities (very serious adverse events) to the IGZ, but not (yet) all other serious adverse reactions and events in the tissue and cell chains.

Fig. 7 Flow chart of tissue vigilance reporting

In principle a preliminary report of serious adverse reactions and events should be submitted within a set number of working days. When the investigations have been concluded the type of reaction or adverse event can be modified if necessary. The reporter indicates imputability too. Here imputability means the likelihood that an observed event or a reaction is related to the transplantation. The TRIP office provides advice and assistance to those assessing these events.

TRIP has made some improvements to the reporting forms for tissue vigilance. See the TRIP website for the reporting guide, definitions and other materials (www.tripnet.nl). TRIP has begun developing an online reporting procedure.

3.3 Advisory committee for tissue vigilance

During 2007, an advisory committee was formed to advise the office and TRIP's governing board on the set-up of the tissue vigilance system and on registering and assessing tissue reports. Committee members are experts in the field of human tissues and cells and come from a variety of professional associations and tissue establishments. The advisory committee met twice in 2007.

3.4 Tissue vigilance officer

The law requires the designation of a responsible person within tissue establishments. This person is responsible in law for reporting. In 2006 TRIP recommended that governing boards of hospitals using human tissues and cells likewise appoint a responsible person, even if they do not have activities requiring accreditation as a tissue establishment. This person, in addition to his/her accountability for reporting, also oversees information, presence of protocols and traceability of components within the tissue/cell chain. The tissue vigilance officer may be assisted by a tissue vigilance assistant.

In 2007, 21 of the 109 hospitals already had or proceeded to appoint a tissue vigilance officer (19%; for the time being the denominator includes hospitals TRIP knows do not transplant or apply and human tissues or cells). The professional background of tissue-vigilance functionaries is rather varied (see *Table 14*). The proportion of tissue banks that have appointed a responsible person is much higher: 79%.

Table 14 Professional background of tissue vigilance officers

Background of tissue vigilance officer in hospitals:

11	Clinical chemists (3 also hemovigilance officer)
3	Orthopedic surgeons
2	Donation functionaries
1	Chairman of tissue and donation committee
1	Director of patient care
1	Head of operating theatre
2	Unknown

3.5 Tissue vigilance reports 2007

For the year 2007, TRIP received 23 reports of adverse reactions and events related to transplanting cells and tissues. Reports came from three tissue banks working outside the hospitals and from four hospitals. *Table 15* shows numbers of reports per type of tissue/cell.

Table 15 Number of reports in 2007 per type of tissue/cell

Number	Type of tissue/ cell
11	Peripheral blood stem cells, autologous
1	Peripheral blood stem cells, allogeneic
6	Corneas
1	Sclera
2	Reproductive cells
1	Cartilaginous cells
1	Cardiovascular tissue

The advisory committee reviewed the reports. Nine of them (39%) fall into the category of 'serious adverse reactions or serious adverse events'. *Table 16* summarises information on the nature of these serious adverse reactions and/or events.

Table 16 Summary of the reported serious adverse reactions and events in 2007

Number	Nature of the report
3	Bacterial contamination: 2 corneas (not transplanted, serious adverse events) and 1 sclera, imputability unlikely.
2	Neurological symptoms accompanying an autologous, peripheral blood stem cell transplant. Imputability is not certain yet. Nevertheless, there are several references in the literature to epileptic seizures in stem cell transplants. Symptoms seem related to using dimethyl sulphoxide (DSMO) to freeze the material.
1	Genetic abnormality accompanying the use of donor sperm; the child has a balanced translocation. Imputability is certain.
1	Other reaction; the clinical picture revealed circulatory overload accompanying an autologous peripheral blood stem cell transplant. Imputability is certain.
2	Two other incidents, one featuring a mistake with a donor, whose material was cleared for donation in spite of prophylaxis for malaria. The other records patient demise after a heart-valve transplant; testing showed a different cause of death.

3.6 Distributed and used tissues and cells

TRIP requested tissue banks and hospitals to indicate how many tissues and/or cells they supplied or used. In approaching institutions, TRIP proceeded from available information about accredited tissue banks and establishments (n=18; www.farmatec.nl). The majority of tissue banks (79%) supplied the data requested, while a much lower number of hospitals (34%) did so. *Table 17* summarises information received. Different hospitals indicated that information was not centralised within the hospital; they still hoped to answer.

Table 17 Data on numbers of distributed and used units of tissues and cells

* 76% of approached tissue banks reported supplied tissues and cells

** 34% of hospitals supplied information on tissues and cells used

Type	Distributed*	Applied**
Skin	1912355 cm^2	184 cm^2
Bone	795 Bone chips	570 Bone chips
	1104 Femoral heads	379 Femoral heads
	858 Bone	
Cartilage	185	4
Ocular tissue	822 Corneas	75 Corneas
	365 Sclerae	37 Sclerae
	64 Amnion membranes	27 Amnion membranes
Auditory ossicles	42	2
Cardiovascular tissue	169 Heart valves	32 Heart valves
	45 Vessels and patches	20 Vessels and patches
Hematopoietic stem cells	27 Bone marrow (unrelated)	
	718 PBSC (unrelated and autologous)	122 PBSC (autologous)
		42 PBSC (related)
	38 Umbilical cord blood	
Reproductive cells	850 Sperm (donor)	
Other tissues: Islets of Langerhans, ligaments, fascia, tendons, foetal tissues		

3.7 Conclusions

1 More reports came in for 2007, the first full reporting year of the pilot project. Nine of the 23 reports (39%) show serious adverse reactions or events.

2 Information came in from a third of the hospitals on the extent of their use of tissues/cells in treating patients. Many hospitals still lack a central point of contact for matters concerning tissue vigilance involves.

3.8 Recommendations

1 Hospitals should receive more information and support while implementing tissue vigilance in order to further promote the appointment of tissue vigilance officers.

2 Priority should be given to setting up an online reporting system, facilitating reporting adverse reactions and events and thus increasing numbers of reports.