TRIP annual report 2013

# Hemovigilance

## Extended version



TRIP
Hemo-en biovigilantie

TRIP Annual Report 2013

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## Extended version

The TRIP annual report 2013, extended version, concerning hemovigilance reports in The Netherlands in 2013 is published under editorial responsibility of the TRIP Foundation (Transfusion and Transplantation Reactions In Patients). The TRIP board and the TRIP Office are advised by representatives of the various professional bodies and stakeholder organisations involved in blood transfusion and in the transplantation or application of human tissues.

TRIP
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# Contents

# Foreword

TRIP has pleasure in presenting you with this, its 11th hemovigilance report. The chapter structure has been changed in line with the ongoing process of redesigning the capture of transfusion reactions and incidents. TRIP's policy, determined in consultation with the hemovigilance advisory board, is to strengthen the focus on the main trends which emerge from the submitted reports of the past year. These are presented first, with recommendations for improving transfusion practice and safety. Next you will find the account of working methods and participation by the reporting hospitals, the main tables of data and further discussion of the results. It is TRIP's express intention to simplify the reporting system, so that the necessary hemovigilance data can be collected as simply as possible. A clearer focus on the relevant information will make it easier to analyse the transfusion reactions and incidents and make recommendations for practice.

A striking and encouraging observation in 2013 is the falling trend of reports of incorrect blood component transfused in comparison to past years, and notably in those reports where the patient was, or could have been, exposed to an ABO incompatible blood component. This can be partly attributed to the well-functioning Dutch hemovigilance system and by the active hemovigilance officers, transfusion safety officers and other hemovigilance professionals in the hospitals.

TRIP thanks all the hemovigilance contact persons for their contribution and wishes you every success in your own activities in the transfusion chain. I particularly wish to acknowledge the members of the Hemovigilance Advisory Board and the staff of the TRIP office for their enthusiasm and commitment which are reflected in the quality of this report. Finally, I hope that you will find satisfaction and inspiration in reading it.

Dr. Martin R. Schipperus
*President, TRIP Foundation*

# 1. Results in 2013

## 1.1 Trends in 2013 with regard to the safety of blood transfusion

### General

The data collected by TRIP about 2013 confirm that the risks of receiving blood in The Netherlands are very low. Overall a total of 4 reactions per 1000 distributed units were reported: 0.2/1000 were serious reactions. In 2013 there were two reports of post-transfusion bacteremia/sepsis which the assessing experts accepted as meeting criteria for transfusion-transmitted bacterial infection (TTBI) which possibly or probably were caused by a contaminated blood component. There were three reports of post-transfusion viral infection, but in one case the transfusion could be excluded as a potential source of the infection; in the other two transmission by transfusion was not demonstrated but could not be excluded either. Among the errors and incidents there was a declining trend in comparison to preceding years in the numbers of incorrect blood component transfused (IBCT) and notably of those IBCT reports where the patient could have been (and in some cases was) exposed to an ABO incompatible unit.

The decline in use of blood components continued (Figure 1), with better compliance with recommended triggers a likely cause along with other possible contributory factors. The number of distributed red blood cell concentrates per 1000 in the population (26) is among the lowest in Western Europe.

### Serious reactions

In 2013 98 serious reactions were reported where the relation to transfusion was assessed as definite, probable or possible. In this group the 21 reports of 'other reaction', i.e. without a specific diagnosis (classification), top the list. Four of these were classified as serious because of hospital admission from a day care setting, whereas the reaction was not serious in itself. The assessment of the reported signs and symptoms was hindered by lack of information about the patient's diagnosis, the clinical situation and the course of the reaction. The reporting category of other reaction is intended for registration of previously unknown types of reaction but should not be used as an easy way out if a reaction has not been investigated sufficiently (or documented in the report). TRIP hopes that in future, improved instructions as well as steering by the reporting software will make it clearer which information should be given in the reports.

Transfusion-associated circulatory overload (TACO) occupies the second position with 20 reports. TACO is regarded as a largely preventable transfusion reaction. Together with the members of the hemovigilance advisory board, TRIP is developing a tool to assist clinicians in assessing TACO risk factors at the time of prescribing a transfusion and in taking appropriate precautions such as prescribing a slower speed of infusion and/or preventive diuretics.

### Other reactions

The large number of other reactions of all levels of severity reported in 2013 was also striking: 206 reports in total. As in previous years two specific clusters can be discerned, which are recognised as separate categories in other hemovigilance systems: transfusion-associated dyspnea (TAD) and hypotensive reaction. TRIP has decided to adopt the subgroup of transfusion-associated dyspnea as a new reporting category. It is important to note that in 2013, as in previous years, the absence of additional clinical information impeded the assessment of reports of other reaction and of their imputability. TRIP hopes to obtain some improvement when it implements a new digital reporting system, through better guidance for reporting hospitals on the necessary supporting information.

### New allo-antibodies

In 2011 the revised national blood transfusion guideline was published. This includes new recommendations to prevent allo-antibody formation in women of child-bearing age as well as other at-risk groups such as patients who already have an irregular antibody or patients with MDS (provide Rhesus phenotype and Kell compatible units). Possibly as a result of the implementation of the guideline, a declining trend is seen in the reports

of new allo-antibody formation relevant for hemolytic disease of the fetus and newborn among women of child-bearing age (Figure 16). There is a decline in the numbers of delayed hemolytic transfusion reactions (even taking the reduced use of red blood cells into consideration), which can also be a result of implementation of the recommendations (Figure 11). The steady increase in use of the TRIX national Transfusion Register of irregular antibodies and Xmatch problems may also have contributed to this decline.

### Remarkable incidents

Several reports (from 2013 and earlier years) about problems associated with (re)installation of computer programmes, use of computerised support tools or information technology highlight the potential risks in the transfusion chain. This type of error or incident can remain undetected for a prolonged period and carry risk for a patient on more than one occasion, or to more than one patient. Staff alertness was often key in detecting these failures.

### Improvements to reporting system necessary

In 2013 TRIP consulted the hospital users about possible ways of improving the efficiency and user-friendliness of the hemovigilance reporting system. The results of this consultation will provide input to the necessary rebuilding of the reporting system. The key points leading to the decision to upgrade, as well as the unchanged objectives of hemovigilance reporting (box), were presented in relevant meetings from the end of 2013 onwards.

***Considerations:***

- Optimal efficiency and effectiveness of reporting system
- Clear guidance about desired information and why

***Guiding principles:***

- Learn from errors and incidents and prevent the occurrence of similar events in future
- Safety of blood transfusion
- Continue data collection so that trends can be seen

## 1.2 Recommendations

**Recommendations based on the 2013 TRIP Report**

| | |
|---|---|
| 1. Conclude reports of transfusion reactions quickly, preferably within three months, in conjunction with the treating physician so that the relevant information can be retrieved relatively easily. | Hemovigilance officers and transfusion safety officers |
| 2. Assess reactions with dyspnea consistently for the possibility of circulatory overload by actively asking the treating physician or contact person about investigations, treatment and clinical course | Hemovigilance officers and transfusion safety officers, TRIP |
| 3. Increase the learning effect of incident reports by web publishing of anonymised case descriptions describing causes and consequences | TRIP in collaboration with hemovigilance officers and transfusion safety officers |

# 2. Overview of 2013 hemovigilance results

## 2.1 Method and participation

By means of a central registry of transfusion reactions (TR) and incidents the transfusion chain can be monitored and weak links can be detected. The incidence of recognised transfusion reactions is tracked and hitherto undescribed reactions to existing or new blood component types can be detected in timely fashion.

TRIP Foundation (originally: Transfusion Reactions In Patients) was created in 2001 by representatives of the professional societies involved with blood transfusion. Since 2003 the TRIP Hemovigilance Office has managed a national reporting system for transfusion reactions in collaboration with contact persons in the hospitals and within Sanquin Blood Supply, the national blood service. Since August 2006 TRIP has also managed a national reporting system for serious adverse reactions and events associated with the clinical use of human tissues and cells (biovigilance). When this role for TRIP became permanent in 2012, the Foundation's statutes were changed so now TRIP formally stands for Transfusion and Transplantation Reactions in Patients. TRIP produces a separate annual biovigilance report, which can also be found on www.tripnet.nl under Publications, TRIP reports.

Reporting to TRIP is anonymous and is voluntary in principle; each hospital reports using a code known to the regular contact persons the hemovigilance officer and hemovigilance employee (transfusion safety officer). The Healthcare Inspectorate however regards participation as a professional standard, as does the national "CBO" blood transfusion guideline (2004 and 2011 revisions). TRIP reporting is separate from a hospital's responsibility to provide care.

Nearly all reports are sent in using the online reporting system. When a reaction or incident is reported, results of relevant investigations are also requested together with an assessment of severity and imputability, i.e. the likelihood with which a reaction can be ascribed to a blood transfusion. If necessary TRIP asks the reporter for additional information or comment. By this means the TRIP physicians check all reports for coherence and verify the type of reaction for all reported serious reactions. Each year TRIP checks for duplicate reports and merges them in consultation with the reporters.

The European directive 2002/98/EC requires reporting of all serious adverse reactions and serious adverse events which could have a link with safety and/or quality of blood components. TRIP provides the analysis of these serious (grade 2 or higher) reports and prepares the annual overview for the competent authority, the Ministry of Health and the Healthcare Inspectorate (Inspectie voor de Gezondheidszorg, IGZ). Hospitals can use the TRIP reporting system to forward serious reports to the IGZ and – if necessary – to Sanquin.

The TRIP board has instated an Expert Committee which assesses all serious reports; a random selection of non-serious reports is also checked. Only after the expert assessment are the reports included in the reported data. The Expert Committee is composed of representatives of professional societies as well as a number of professionals approached because of their specific expertise; they are also members of TRIP's hemovigilance advisory board.

The effectiveness of national reporting of transfusion reactions and incidents depends on the participation of all the relevant organisations. In 2013 the number of hemovigilance contact addresses was unchanged: there were 98 hospitals and four "designated" independent treatment centres which have been licensed by the Ministry to receive and administer blood components to patients.

In 2013, 91 of the 98 hospitals reported transfusion reactions and/or events and six indicated that they had no reports in the TRIP categories. Among the four designated clinics one informed TRIP that there had been nothing to report. One indicated that any reactions would be reported by the supplying hospital transfusion laboratory with which they had established their contract; the third informed TRIP that no blood transfusions had been administered in 2013. This brings the total participation to 98%. The closing date for inclusion of

submitted reports was 1 February 2014. Hospitals which had not submitted their information before the closing date have the status of non-participant in this annual report.

Additionally, the Sanquin central quality department provided information to TRIP: overviews of serious reports and figures concerning blood components which had been transfused but later were found to be positive on bacteriological screening (see section 3.2).

A total of 95 hospitals and one independent treatment centre supplied figures about blood use. For the first time TRIP also asked about numbers of patients transfused because this information is also requested in the annual data submission to the European Commission. Alongside the transfused units, the number of transfused patients can also be used as a denominator for the reported transfusion reactions and events. In total, 74 facilities provided this information for each type of blood component; another two hospitals provided a total number of patients transfused but were not able to provide a breakdown by type of blood component.

Late information about previous years has been incorporated in all the relevant tables and figures in this report. After the closing date for the 2012 report a further 76 reports were received (3% of the final total). The late 2012 reports were formally assessed by the experts along with the 2013 submissions.

## 2.2 Reported reactions and incidents

All definitions can be found on www.tripnet.nl.

### Reports received

The total number of reported transfusion reactions and incidents in the transfusion chain in 2013 is 2452, which is 5% less than the number of reports in 2012, in line with the reduced use of blood components. The reports were submitted by 91 hospitals. Out of the total, 2430 reports were submitted electronically (99%, 90 hospitals).

After assessment of all the reports by TRIP physicians, a number of striking or complex reports (approximately 25) were discussed in detail in a meeting of TRIP staff, Expert Committee and reporters. All serious reports - those of grade 2 or higher, as well as all reports in serious categories - were reviewed by the experts, as was a sample of the non-serious reports.

Table 1 and Table 2 show the numbers of reports of each type in the years 2006-2013. The incidents are presented first in this report because they are potentially preventable. Transfusion reactions which followed incidents (24 in total) are discussed separately in the section about incidents in chapter 3.1 and have not been included in Table 2.

**Tabel 1. Incidents per reporting category, 2006 - 2013**

| Incident | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | No. of hosp. with reports in 2013 | No. of hosp. with reports, cumulative* |
|---|---|---|---|---|---|---|---|---|---|---|
| Incorrect blood component transfused | 64 | 64 | 59 | 61 | 59 | 47 | 52 | 37 | 22 | 89 |
| Near miss | 77 | 74 | 55 | 72 | 70 | 45 | 46 | 32 | 14 | 53 |
| Other incident | 86 | 100 | 83 | 111 | 118 | 138 | 138 | 105 | 30 | 74 |
| Look-back (info provided to TRIP by hospitals)# | 3 | 4 | 11 | 8 | 56 | 30 | 7 | 24 | 12 | 37 |
| Bacterial contamination of blood component$ | 27 | 34 | 25 | 26 | 45 | 43 | 42 | 23 | 13 | 59 |
| Hemolysis of product | - | - | - | - | - | 2 | - | - | - | 2 |
| **Incidents, total** | **257** | **276** | **233** | **278** | **349** | **305** | **285** | **221** | **42** | **88** |

* *Hospitals counted according to status in 2013 following mergers etc.*

# *Combined with virally infected blood component, see comment in chapter 3.2*

$ *Combined with positive bacteriological screening of blood component, see comment in chapter 3.2*

***Abbreviation:*** *Hosp. = hospital*

**Table 2. Reported transfusion reactions, 2006 - 2013**

| Reaction | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | Reports of grade 2 or higher# | No. of hosp. with reports in 2013 |
|---|---|---|---|---|---|---|---|---|---|---|
| AHTR | 19 | 11 | 18 | 18 | 21 | 17 | 7 | 10 | 6 | 7 |
| DHTR | 14 | 11 | 18 | 8 | 7 | 9 | 8 | 4 | 2 | 4 |
| New allo-antibody formation | 607 | 602 | 610 | 757 | 814 | 831 | 850 | 848 | 0 | 72 |
| TACO | 34 | 31 | 39 | 42 | 47 | 39 | 56 | 67 | 20 | 39 |
| TA-GVHD | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Hemosiderosis | 5 | 3 | 5 | 2 | 4 | 2 | 0 | 4 | 1 | 3 |
| NHTR | 490 | 452 | 453 | 488 | 506 | 504 | 456 | 438 | 14 | 76 |
| Mild non-hemolytic febrile reaction | 363 | 328 | 275 | 360 | 363 | 366 | 382 | 332 | 1 | 69 |
| TRALI | 25 | 31 | 21 | 13 | 17 | 12 | 9 | 6 | 5 | 5 |
| Anaphylactic reaction | 19 | 54 | 65 | 71 | 73 | 67 | 59 | 66 | 17 | 30 |
| Other allergic reaction | 222 | 202 | 171 | 181 | 184 | 191 | 180 | 190 | 3 | 48 |
| Post-transfusion purpura | 0 | 0 | 1 | 0 | 0 | 2 | 1 | 0 | 0 | 0 |
| Other tf reaction | 61 | 55 | 101 | 136 | 164 | 217 | 225 | 216 | 21 | 59 |
| Post-tf bacteremia/sepsis§ | 7 | 19 | 37 | 55 | 41 | 61 | 50 | 47 | 6 | 29 |
| Post-tf viral infection | 7 | 7 | 7 | 3 | 1 | 5 | 2 | 3 | 2 | 1 |
| Post-tf malaria | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| **Total transfusion reactions** | **1873** | **1806** | **1822** | **2134** | **2242** | **2324** | **2285** | **2231** | **98** | **93** |
| Total grade 2 or higher#* | 108 | 103 | 131 | 102 | 96 | 102 | 101 | 98 | | |
| **Total reports** | **2130** | **2082** | **2055** | **2412** | **2591** | **2629$** | **2570** | **2452** | | |

# *Imputability definite, probable, possible*

§ *Up to and including 2007: bacterial contamination; see explanation of modified definitions in chapter 3.2*

* *Total number including reactions following incidents*

$ *5 submitted reports provided insufficient information and were excluded*

***Abbreviations:*** *AHTR = acute hemolytic transfusion reaction; DHTR = delayed hemolytic transfusion reaction; TACO = transfusion-associated circulatory overload; TA-GVHD = transfusion-associated graft versus host disease; NHTR = non-hemolytic transfusion reaction; TRALI = transfusion-related acute lung injury; tf = transfusion*

## Severity and imputability of the transfusion reactions

| Severity grade | Definition |
|---|---|
| 0 | No morbidity |
| 1 | Minor morbidity, not life-threatening |
| 2 | Moderate to serious morbidity, may or may not be life-threatening; or leading to hospitalisation or prolongation of illness; or associated with chronic disability or incapacity |
| 3 | Serious morbidity, directly life-threatening |
| 4 | Mortality following a transfusion reaction |

Acoording to international practice, the transfusion reactions were rated for their severity. The definition of severity refers to the clinical features observed in the patient and is only relevant for transfusion reactions. These totalled 2238, i.e. 2231 reports in the categories of reactions and seven following incidents. The grade 4 reports are reviewed in section 3.5.

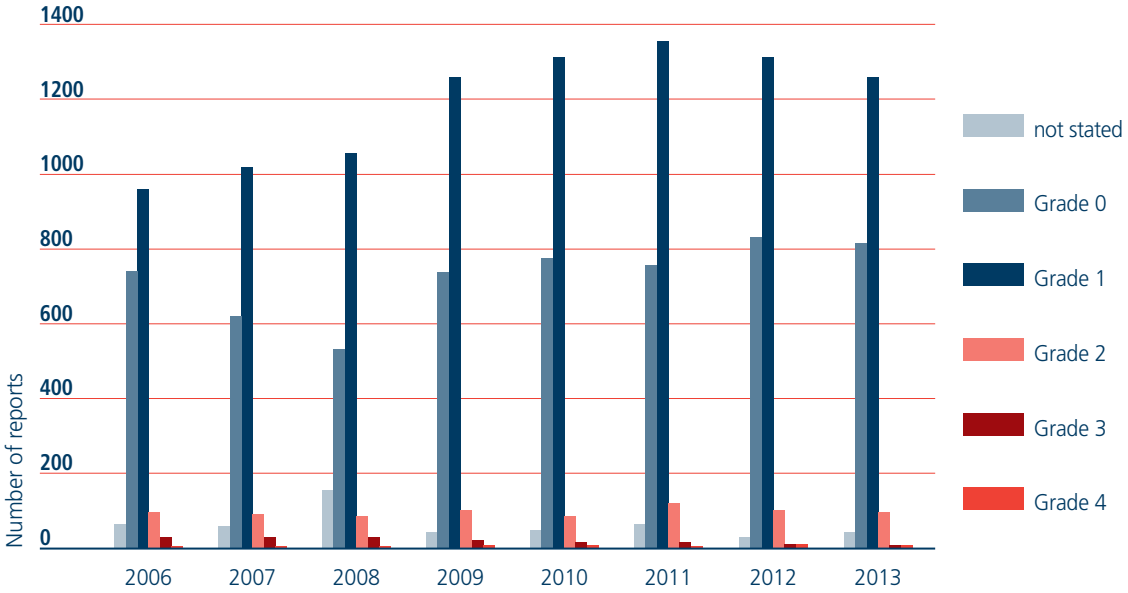



**Figure 1. Severity of the transfusion reactions, 2006 - 2013**

Figure1 shows the severity of the transfusion reactions from 2006 up to and including 2013. The total number of serious reactions in 2013 (grade 2 or higher) was 115; this figure has varied between 115 and 145 since 2006.

## Relationship to the blood transfusion (imputability)

The reports were assessed for their level of imputability, i.e. the likelihood with which the reaction can be attributed to the transfusion. The imputability rating, as that of the severity, is only relevant for reports where the patient showed a reaction. Figure 3 shows the imputability of the 2238 transfusion reactions in 2013 compared to previous years. Out of 115 reports which were grade 2 or higher, 98 were assessed as having being possibly, probably or definitely related to the transfusion; this number is similar to previous years.

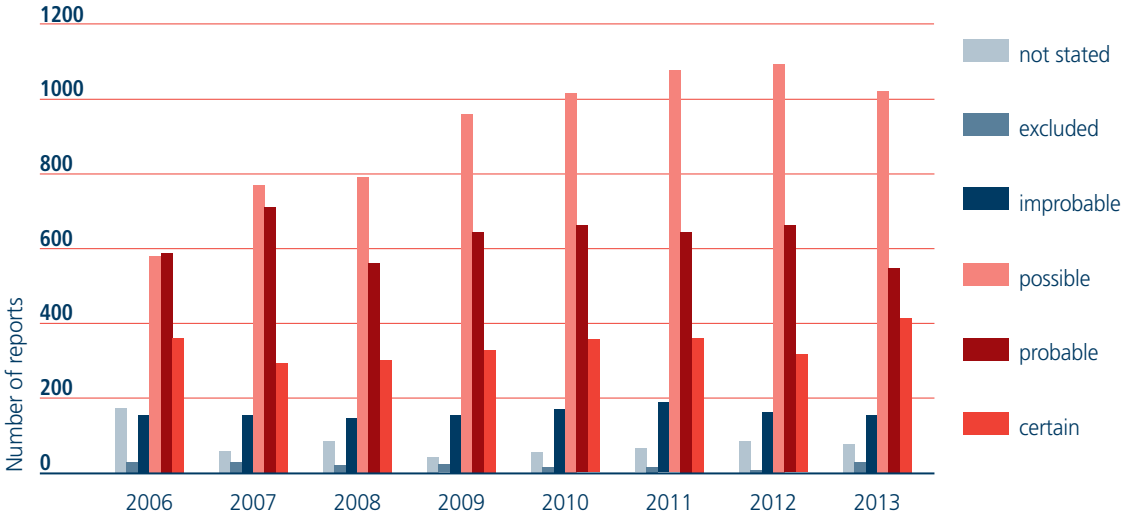



**Figure 2. Imputability of the transfusion reactions, 2006 - 2013**

## Reports in relation to the number and type of distributed blood components

In 2013 Sanquin distributed a total of 565.136 blood components to the Dutch hospitals: this number does not include special components like lymphocytes and granulocytes.

The total number of reports for 2013 was 2452. Using the total number of distributed blood components as a denominator, that makes 4.34 reports per 1000 blood components distributed nationally, or 4.28 after exclusion of the reports relating to autologous blood management techniques (see paragraph 3.4) or SD-plasma. The decline in blood use continued in 2013 (Figure 3). The numbers of reports in relation to the numbers of distributed blood components are shown in Table 3. Table 4 shows the distribution of the types of blood components for each of the reporting categories of incidents and reactions.

**Table 3. Number of reports per type of blood component in comparison to 2011 and 2012**

| Type of blood component (bc) | 2013 | | | | | 2012 | | 2011` | |
|---|---|---|---|---|---|---|---|---|---|
| | Number of bc supplied | Number of reports | | Reports per 1000 bp | | Reports per 1000 bp | | Reports per 1000 bp | |
| | | All | Serious# | All | Serious# | All | Serious# | All | Serious# |
| Red blood cell concentrate | 443.936 | 1966 | 68 | 4,43 | 0,15 | 4,20 | 0,14 | 3,78 | 0,12 |
| Platelet concentrate | 54.129 | 292 | 18 | 5,39 | 0,33 | 4,42 | 0,21 | 5,77 | 0,29 |
| Fresh frozen plasma | 67.071 | 59 | 3 | 0,88 | 0,04 | 1,28 | 0,08 | 0,94 | 0,13 |
| Blood management techniques[2] | - | 24 | 0 | | | | | | |
| SD-plasma | - | 7[1] | 1 | | | | | | |
| Other blood product | - | 0 | 0 | | | | | | |
| Combinations | - | 62 | 8 | | | | | | |
| Not stated | - | 42 | 0 | | | | | | |
| **Total** | **565.136** | **2452** | **98** | **4,34** | **0,17** | **4,13** | **0,16** | **3,88** | **0,15** |

# *Imputability certain, probable, possible*

[1] *In addition one of the combinations was a serious report where the recipient received both RBC and SD-plasma*

[2] *2013: drain blood only; see section 3.4*

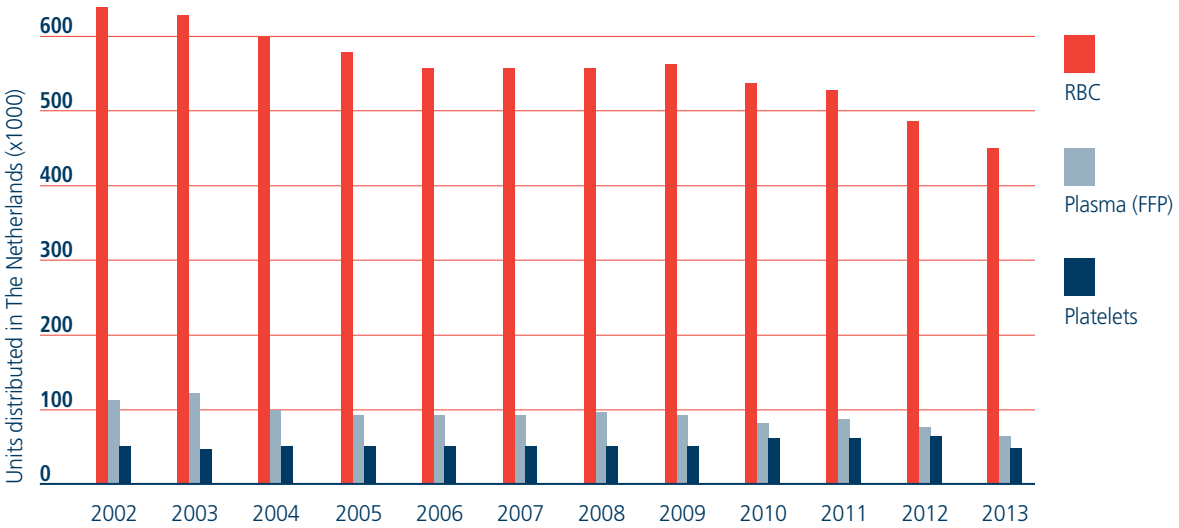



**Figure 3. Distributed units of blood components per year**

*(Information from Sanquin for the TRIP report)*

**Table 4. Distribution of types of blood components per category of report* in 2013**

| A. Incidents | RBCs | Platelets | Plasma | Combi-nation | Other# | SD-plasma | Not stated |
|---|---|---|---|---|---|---|---|
| Incorrect blood component transfused | 32 | 5 | - | - | - | - | - |
| | 86% | 14% | | | | | |
| Other incident | 83 | 8 | 4 | 4 | 3 | - | 3 |
| | 79% | 8% | 4% | 4% | 3% | | 3% |
| Near miss | 4 | 2 | 1 | 1 | - | - | 24 |
| | 13% | 6% | 3% | 3% | | | 75% |
| Bacterially contaminated blood component | 5 | 18 | - | - | - | - | - |
| | 22% | 78% | | | | | |
| Look-back | 16 | 8 | - | - | - | - | - |
| | 67% | 33% | | | | | |
| **B. Reactions** | | | | | | | |
| Non-hemolytic transfusion reaction | 345 | 66 | 2 | 12 | 13 | - | - |
| | 79% | 15% | 0% | 3% | 3% | - | - |
| Mild non-hemolytic febrile reaction | 315 | 12 | 3 | - | 2 | - | - |
| | 95% | 4% | 1% | - | 1% | - | - |
| Acute hemolytic transfusion reaction | 9 | - | - | 1 | - | - | - |
| | 90% | - | - | 10% | - | - | - |
| Delayed hemolytic transfusion reaction | 4 | - | - | - | - | - | - |
| | 100% | - | - | - | - | - | - |
| TRALI | 4 | 1 | - | 1 | - | - | - |
| | 67% | 17% | - | 17% | - | - | - |
| Anaphylactic reaction | 17 | 33 | 9 | 5 | - | 2 | - |
| | 26% | 50% | 14% | 8% | - | 3% | - |
| Other allergic reaction | 47 | 95 | 37 | 6 | 1 | 4 | - |
| | 25% | 50% | 19% | 3% | 1% | 2% | - |
| New allo-antibody formation | 802 | 14 | - | 19 | - | - | 13 |
| | 95% | 2% | - | 2% | - | - | 2% |
| Other reaction | 177 | 21 | 3 | 9 | 5 | 1 | - |
| | 82% | 10% | 1% | 4% | 2% | 1% | - |
| Post-transfusion bacteremia/sepsis | 40 | 6 | - | 1 | - | - | - |
| | 85% | 13% | - | 2% | - | - | - |
| Transfusion-associated circulatory overload | 59 | 4 | - | 4 | - | - | - |
| | 88% | 6% | - | 6% | - | | - |

* *Smallest categories not shown*

\# *Drain blood*

*% Percentage of the total reported incidents/reactions in that category*

## 2.3 Information about the patients

Table 5 gives an overview of the distribution of age and sex of patients per type of reaction or incident.

**Table 5. Distribution of age groups of patients per category of report* in 2013**

| A. Incident | <1y | | 1-20 | | 20-60 | | 60-80 | | >80y | | Not stated or N/A[1] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | M | F | M | F | M | F | M | F | M | F | |
| Incorrect blood component transfused | - | - | 2 | 3 | 4 | 9 | 9 | 3 | 3 | 4 | - |
| Other incident | - | - | - | 1 | 2 | 20 | 19 | 20 | 22 | 16 | 3 |
| Near miss | - | - | - | - | 2 | 6 | 3 | 6 | - | 1 | 14 |
| Bacterially contaminated blood component | 3 | 1 | 1 | 1 | 4 | 3 | 4 | 5 | 1 | - | - |
| Look-back | - | - | - | - | 5 | 1 | 6 | 3 | 4 | 2 | 3 |
| **Total (incidents)*** | **3** | **1** | **3** | **5** | **19** | **39** | **41** | **37** | **30** | **23** | **20** |
| % of incidents per age group | 2% | | 4% | | 29% | | 39% | | 26% | | |
| **B. Reactions** | | | | | | | | | | | |
| Non-hemolytic transfusion reaction | - | - | 16 | 9 | 59 | 75 | 126 | 95 | 37 | 24 | - |
| Mild non-hemolytic febrile reaction | 1 | 1 | 11 | 8 | 36 | 41 | 74 | 77 | 41 | 40 | 2 |
| Acute hemolytic transfusion reaction | - | - | - | - | - | 3 | 3 | 2 | 2 | - | - |
| Delayed hemolytic transfusion reaction | - | - | - | - | 1 | 2 | 1 | - | - | - | - |
| TRALI | - | - | - | - | 0 | 2 | 1 | 3 | - | - | - |
| Anaphylactic reaction | - | - | 10 | 5 | 9 | 13 | 14 | 8 | 4 | 3 | - |
| Other allergic reaction | - | 1 | 26 | 23 | 39 | 39 | 33 | 20 | 1 | 4 | 1 |
| Transfusion-associated circulatory overload | - | - | - | - | 4 | 7 | 18 | 9 | 18 | 11 | - |
| New allo-antibody formation | - | - | 1 | 2 | 74 | 125 | 200 | 269 | 54 | 122 | 1 |
| Other reaction | - | 1 | 7 | 5 | 16 | 26 | 58 | 48 | 28 | 27 | - |
| Post-transfusion bacteremia / sepsis | - | - | 3 | 2 | 3 | 8 | 10 | 12 | 4 | 5 | - |
| **Total (transfusion reactions)*** | **1** | **3** | **71** | **54** | **241** | **343** | **540** | **544** | **191** | **238** | **4** |
| % of reactions per age group | 0,2% | | 6% | | 26% | | 49% | | 19% | | |

* *Smallest categories not shown; they were included in the totals*

[1] *Age and/or gender not stated or not relevant*

# 3. Discussion of reports per category

## 3.1 Incidents in the transfusion chain

Various reports, including some from previous years, received by TRIP involve incidents when (re)installing software, using IT support technologies and/or automation. These incidents carry a risk that they may remain undetected for some time and cause problems on more than one occasion or for several patients. Staff alertness was often pivotal in detecting these errors.

Reports of incidents generally provide limited information. A better understanding of problems can be obtained by compiling a case description in collaboration with the reporter. This also enables the reporter to check whether the information provides enough clarity for analyses and for arriving at conclusions or corrective actions. Selected reports can be used by TRIP for such a descriptive account and made suitable for publication, for instance via the TRIP website. This would provide informal information to hospitals about reported problems which could be a hazard for other organisations.

### Incorrect blood component transfused (IBCT)

*All cases in which a patient was transfused with a component that did not fulfil all the requirements of a suitable component for that patient, or that was intended for a different patient.*

- 35 IBCT reports submitted by 22 hospitals, 1-4 reports per hospital
- 6 reports with additional category IBCT submitted by 5 hospitals
- 2 reports of a calculated risk situation
- 4 late 2013 reports IBCT will be included in the 2014 report

The number of IBCT reports where the patient was at risk for an ABO incompatible transfusion amounted to 10 and was considerably lower compared to 2012 (n=19) and previous years since 2008 (n=16-31). The number of IBCT reports concerning the risk of an incompatible transfusion in patients with an irregular antibody was seven. This number is comparable to the yearly level of approximately 10 per year, which showed an exceptional peak of 17 in 2012. The description of risks as used in this risk classification can be found on www.tripnet.nl. The number of identification errors, n=8, in reports of IBCT with ABO risk dropped compared to previous years. In four cases the mix-up of blood components or patients occurred at the bedside on administration of transfusion (Figure 4).

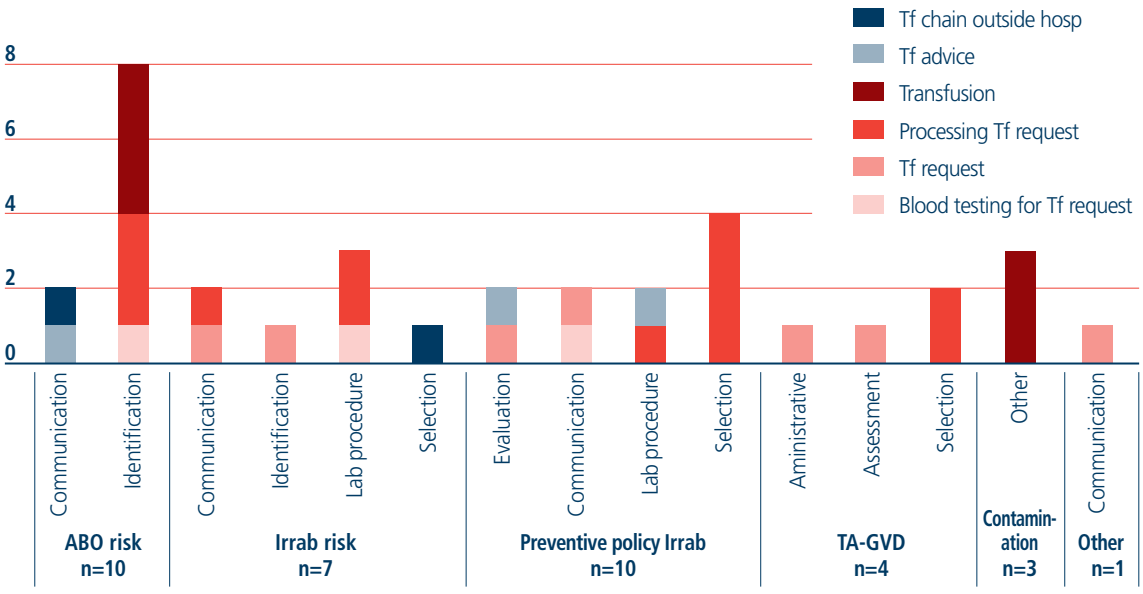



**Figure 4. IBCT 2013 Step in the transfusion chain where 1st error was made and type of error according to risk**

***Abbreviations:*** *Tf = transfusion; hosp = hospital ; Irrab = irregular antibody; TA-GVHD = transfusion-associated graft versus host disease*

In 50% of reports relating to ABO risk or irregular antibody risk the administered blood component by chance happened to be compatible (Figure 5).

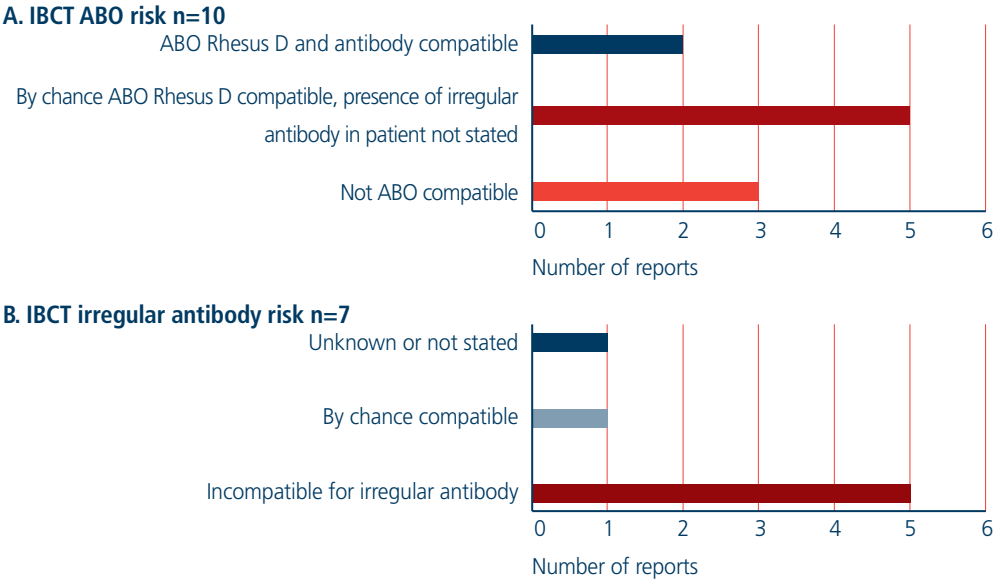



**Figure 5 A and B. Compatibility of administerd blood components in ABO risk (A) and irregular antibody risk (B)**
***Abbreviations:*** *IBCT = incorrect blood component transfused; Irrab = irregular antibodies*

It is remarkable that none of the IBCTs with ABO risk and only one IBCT with irregular antibody risk led to a transfusion reaction in the patient. Sequelae of IBCT were mainly the formation of a new irregular antibody in patients in an at-risk patient group who were transfused with a blood component that did not meet the requirements for preventive component matching to avoid potential antibody formation (Table 6 and 7).

**Table 6. Reaction or findings after administration of an IBCT in 2013**

| Type of risk IBCT | Bp | Reaction | Imputability * | Grade* |
|---|---|---|---|---|
| Irrab | Plt | Other reaction[$] | certain | 1 |
| Preventive policy | | New antibody | | |
| Irrab formation | RBC | Anti-K | certain | 0 |
| | RBC | Anti-K | probable | 0 |
| | RBC | Anti-E | probable | Not stated |
| | RBC | Other allergic reaction | possible | 1 |
| Calculated risk | RBC | New antibody formation[#] | certain | 1 |

* *Imputability and severity grade regarding the transfusion reaction*

[$] *Rigors, insufficient platelet count rise and increased HLA antibodies*

[#] *Rigors after administration of 'type and screen' RBC (Kpa positive). Analysis of TR revealed a positive crossmatch and an anti-Kpa in the patient*

In six reports IBCT was registered as additional category to mark a transfusion reaction or other incident where further analysis revealed that (in the past) a blood component had been transfused that did not meet all requirements for that particular patient (Table 7).

**Table 7. Reports with additional category IBCT 2013**

| Reporting category | Type of risk IBCT | Description | Number IBCT |
|---|---|---|---|
| New allo-antibody formation | Preventive policy irregular antibody | 1x lab procedure error and 1x selection error => special requirements not met | 2 |
| New allo-antibody formation | Preventive policy irregular antibody | Lab procedure error => transfusion of Rhesus phenotype compatible RBC based on flawed Rhesus phenotyping. | 1 |
| NHTR | Irregular antibody | Administrative error => rigors with transfusion of platelet concentrate that was subsequently found to be not completely HLA-compatible. | 1 |
| TACO | Irregular antibody | Storage error => contrary to hospital protocol RBC stored on hospital ward and transfused after expiry of screening results | 1 |
| Other incident | ABO | 1x Technical error => after moving transfusion lab and recommissioning of software, spontaneous generation of lab results without lab investigations having been done. This led to IBCT for several patients. | 3 |

***Abbreviations:*** *IBCT = incorrect blood component transfused, RBC = red blood cell concentrate, NHTR = non-hemolytic transfusion reaction, TACO = transfusion-associated circulatory overload*

## Near Miss

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

- 32 near miss reports, 14 reporting hospitals, 1 – 11 reports per hospital
- 18 cases (56%) involved mix-up of patients, labels, blood samples or reagents
- 5 late reports 2013 will be included in the 2014 report

Figure 6 shows how errors in near miss reports were detected.

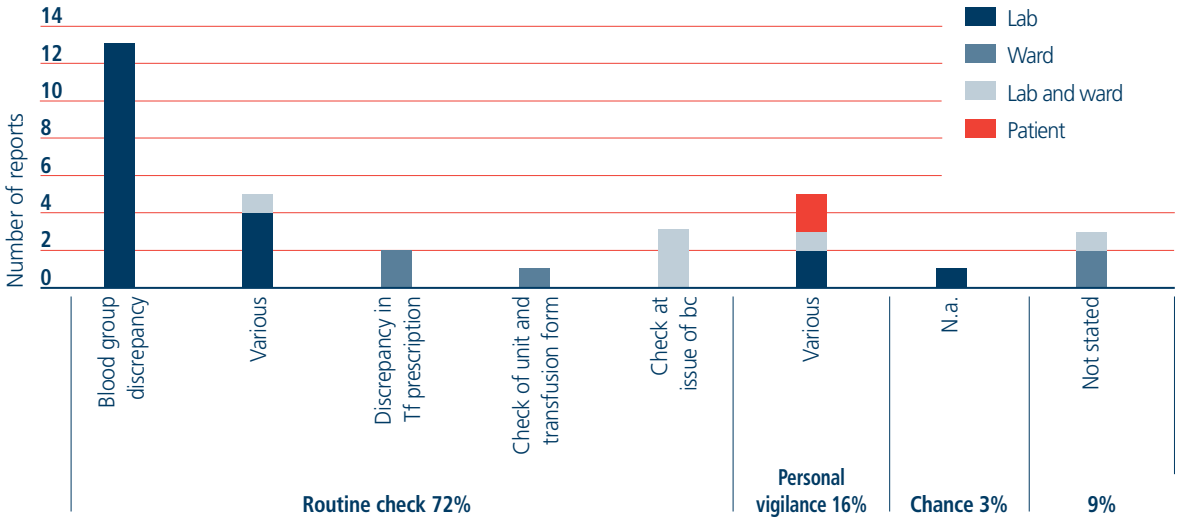


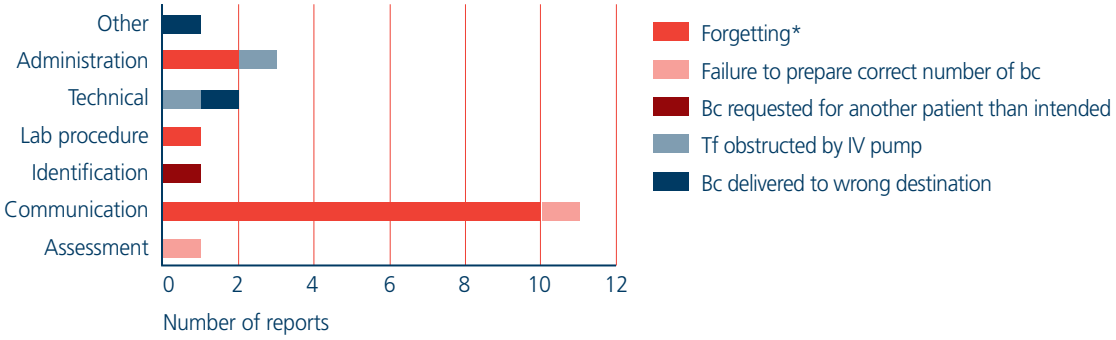

**Figure 6. Detection of error in near miss reports in 2013**

### Other incident (OI)

*Error or incident in the transfusion chain that does not fit into any of the above categories, for instance patient transfused whereas the intention was to keep the blood component in reserve, or transfusing unnecessarily on the basis of an incorrect Hb result or avoidable wastage of a blood component*

- 105 reports OI, 30 reporting hospitals, 1-15 reports per hospital
- 3x OI with additional category: other reaction (2x) and IBCT (see explanation in chapter IBCT)
- 6x mix-up of patients/labels with blood component data, mix-up of lab results or type of blood component
- 35 reports had additional category of OI

The largest subgroups in 2013 in the category of other incident (figure 7, 8, 9) were delayed start of transfusion (n=20), which in seven cases also led to wastage of a blood component, unnecessary transfusion (n=12) and the wastage of (a large part) of a blood component (n=51). In 34 cases wastage was deemed avoidable. Nine reports mentioned difficulties that occurred with transfusion like the infusion running into tissues or incorrect transfusion time. Incidents regarding traceability or post-donation information were reported in three cases.




* *Forgetting of: transfusion request/ordering of bc/dispatch or receipt of bc/starting of transfusion*

**Figure 7. Delayed transfusion: type of first error and short description of incident**

***Abbreviations:*** *Tf=transfusion*

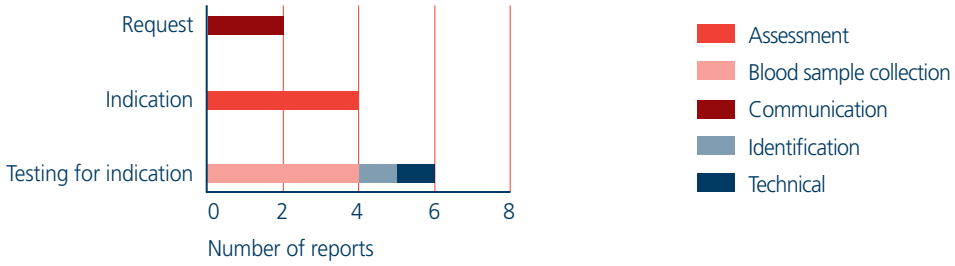



**Figure 8. Other incident 2013 involving unnecessary transfusion*: type of first error and step in transfusion chain**

* *Unnecessary transfusion concerns patients for whom it should have been clear before transfusion that transfusion was not (or no longer) needed, e.g. due to incorrect blood sampling from arm with IV drip*

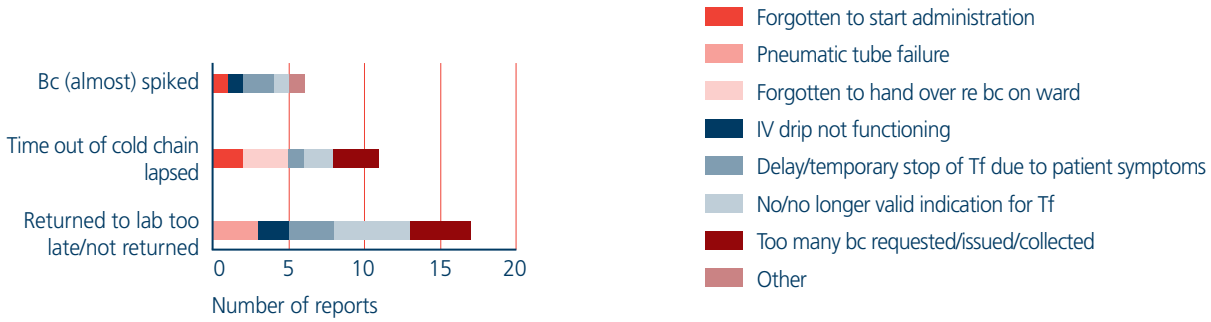



**Figure 9 Avoidable wastage of blood component (n=34): cause and reason for wastage**

***Abbreviations:*** *Tf=transfusion*

**Table 8. Additional category OI**

| Blood component | Reporting category | Description | Type of OI | Aantal |
|---|---|---|---|---|
| 2x RBCs | TACO | No indication for 2nd RBC | Unnecessary Tf | 2 |
| | Other reaction | No indication for Tf (Hb 6.1 mmol/L) | | |
| 5x RBCs | Mild NHFR (n=4) | Patient had fever before Tf. According to hospital protocol Tf should have been continued slowly | Unnecessary stopping of Tf | 5 |
| | NHTR | | | |
| 17x RBCs | Mild NHFR (n=10) | No/incomlete analysis of Tf | TR reported to transfusion lab too late or not reported | 21 |
| 2x plts | NHTR (n=4) | | | |
| 2x drain blood | Anaphylactic reaction | | | |
| | Other allergic reaction | | | |
| | Other reaction (n=5) | | | |
| 2x RBCs | Anaphylactic reaction | No form accompanying Tf | TR incorrectly analysed | 3 |
| 1x plts | Other reaction (n=2) | Doctor not informed regarding TR | | |
| | | Remainder of bc not saved contrary to hospital protocol | | |
| 4x RBCs | NHTR | Not all investigations for type of TR carried out | TR insufficiently analysed | 4 |

***Abbreviations:*** *RBC = red blood cell concentrate, TACO = transfusion-associated circulatory overload, Tf = transfusion, TR = transfusion reaction, NHTR = non-hemolytic transfusion reaction, plt = platelet concentrate.*

## 3.2 Infectious transfusion complications

### Post-transfusion viral infection

***Post-transfusion viral infection***

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

In 2013 three reports of post-transfusion viral infection were submitted. One hepatitis B infection was diagnosed by a hospital after a look-back communication from Sanquin Blood Supply (unit transfused in 2011). The patient's blood results were consistent with the patient having had hepatitis, however the infection had resolved so it was not possible to investigate whether the strains were identical. Therefore it was impossible to confirm or exclude transmission by transfusion, and the imputability was recorded as possible.

The other two reports of post-transfusion viral infection were of hepatitis C and these were also reported to Sanquin. In these cases a so-called reverse look-back (also known as trace-back) investigation was performed to see whether the donor(s) could be the source of the infection. In one case all donors but one were traced and found to be negative for hepatitis C; the remaining donor could not be contacted, so the imputability remains possible. In the other report of post-transfusion hepatitis C, the patient was transfused in 1999; the hospital was not able to provide details of identification numbers of units so it was not possible to exclude transfusion as the source of the infection.

Table 9 gives an overview of all reports of post-transfusion viral infections (possibly transmitted by transfusion) in 2002-2013. In the majority of reports the further investigation demonstrated that transmission was unlikely or excluded (difference between the total and the numbers of certain/probable and of possible imputability in Table 9).

**Table 9. Viral reports to TRIP, 2002 - 2013**

| Virus | Post-transfusion viral infection* total | Number probable or certain | Number possible | Comment |
|---|---|---|---|---|
| Hepatitis B | 16 | 7[#] | 4[#] | [#] Donations in 1991, 1993, 2006-2008, 2011; infections detected (also or only) through look-back investigations by Sanquin |
| Hepatitis C | 13 | 0 | 5[$] | [$] Donations before 2000 with the exception of the first case described above |
| Hepatitis A | 1 | 0 | 0 | 2006 report, tf in 2003, no further investigation by Sanquin |
| Hepatitis E | 1 | 0 | 0 | |
| B19 | 2 | 1[1] | 1 | [1] Components not B19-safe; no investigation |
| CMV | 12 | 2[2] | 5 | [2] Not confirmed; components not requested as CMV-safe and/or other source of infection likely |
| EBV | 6 | 0 | 1[3] | [3] Report in 2003, other source possible, long interval |
| HIV | 2 | 0 | 1[4] | [4] Report from 2003, unconfirmed |
| HTLV | 0 | 0 | 0 | |

* *Prior to 2008 : Viral infection*

[#] *Look-back performed after diagnosis of occult hepatitis B in the donor; see discussion in TRIP hemovigilance report 2011, extended version*

## Look-back

***Look-back by the supplier***

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

***Viral contamination of blood component***

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

### Definitions

In 2013 discussions took place with the hemovigilance advisory board about reporting categories. It was remarked that a 'look-back' communication (these are generally but not exclusively to do with donations which later are found to have possibly been infectious) makes no distinction between units which were, and units which were not later proven to have contained the infectious agent. For this reason the two categories will be merged in this report and the definition will be adjusted when the reporting system is rebuilt. There were no reports of virally contaminated blood component in 2013.

### Information from hospitals

A total of 24 reports were sent to TRIP by hospitals after they had received a look-back communication from Sanquin. The reports concerned hepatitis B (13x), malaria risk (some reports concerned a donor who might have had asymptomatic malaria parasitemia and the others were of inappropriate donations by donors during the deferral period following travel to an endemic area), 1x hepatitis C, 1x syphilis, 1x tuberculosis contact and once a recall because of post-donation information (febrile illness within 48 hours after donation). In no case were there clinical consequences for the patient.

### Information from Sanquin

In 2013 13 seroconversions were detected in the standard infectious disease testing in donors who had previously donated with a negative (normal) test result for that infection (5x hepatitis B, 2x HIV, 1x hepatitis C and 5x syphilis). Three of the five hepatitis B seroconversions represented positive results in the hepatitis B core antibody test which was introduced in 2011, indicating a previous infection. In 11 cases a look-back investigation was initiated according to the national guideline, whereas in two cases only plasma for fractionation had been donated. The look-backs were all completed and revealed no evidence of transmission. In the testing on plasma pools, one pool was found to have a positive PCR (polymerase chain reaction) for hepatitis A. The donor was traced and found to have recently had hepatitis A; the standard deferral period had been taken into consideration. A platelet concentrate had been manufactured using the hepatitis A PCR-positive donation; it was found that the recipient had expired from their underlying illness.

Since TRIP started collecting data a number of transmitted infections have been detected through look-back investigations (Table 9). Not all hospitals send reports to TRIP about look-back communications and the recipients. As discussed in the 2012 TRIP report, firstly all hospitals should report back to Sanquin what the findings are (or why it has been decided not to investigate the patient further). In cases where there is no evidence of infection or this has been excluded, it is not necessary to report to TRIP. A report should always be sent to TRIP if there is a possibility that the patient has been infected (reporting category: post-transfusion viral infection).

## Bacterial problems associated with blood transfusion

Table 10 shows the numbers of reported bacterial problems associated with blood transfusion in 2008-2013. Figure 10 on page 23 clarifies the way they are assigned to the different categories and how the possibility of a transfusion-transmitted bacterial infection is assessed based on the results of investigations. This is followed by discussion of the reports in the categories relating to bacterial problems.

**Tabel 10. Reported bacterial problems associated with blood transfusion, 2008-2013**

| | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 |
|---|---|---|---|---|---|---|
| Bacterial contamination of a blood component or positive bacterial screen | 25 | 26 | 44 | 43 | 42 | 23 |
| Bacterial contamination of a blood component or positive bacterial screen as additional category* | 7 | 22 | 17 | 19 | 16 | 10 |
| Post-transfusion bacteremia/sepsis | 37 | 55 | 41 | 61 | 50 | 47 |
| Post-transfusion bacteremia/sepsis as additional category* | 1 | 8 | 17 | 13 | 14 | 6 |

* *Subsidiary (additional) category of bacterial contamination of blood component applies if bacteriological culture by the hospital is positive following a reported transfusion reaction or incident; correct technique for sampling of the unit is essential, however the reports do not always include information about the method used.*

## Bacterial contamination of blood component and report of positive bacterial screen

***Bacterial contamination of a blood component***

*Relevant numbers of bacteria in a (remnant of) blood component or in the bacterial screen bottle of a platelet component, or in material from the same donation, demonstrated in the approved way with laboratory techniques, preferably including typing of the bacterial strain or strains.*

***Positive bacterial screen***

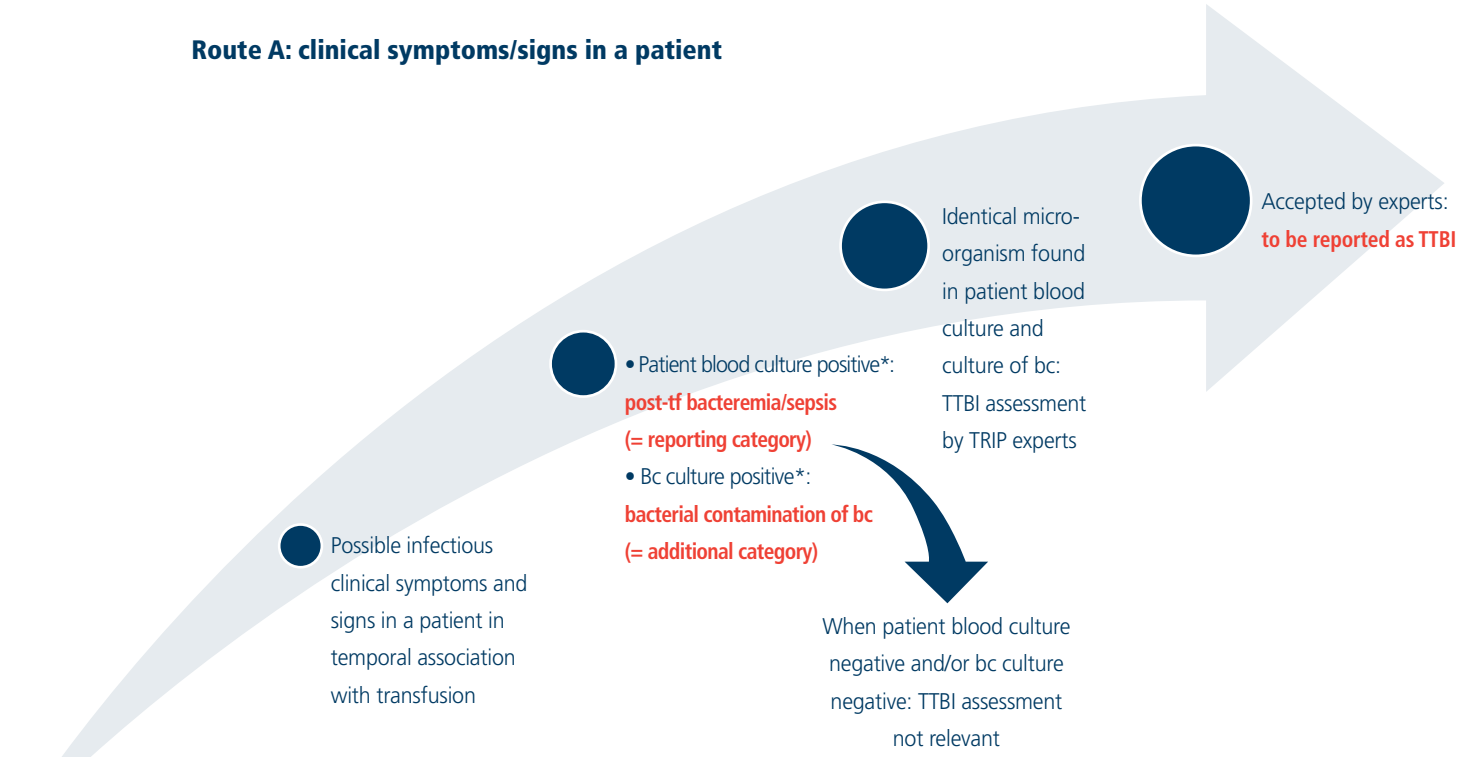
*The blood service reports a positive bacteriological screen, but bacterial contamination of the rele vant material is not confirmed by a positive culture result on the same material or other products made from the same donation.*

These two categories capture cases where a hospital has been informed by Sanquin that a distributed blood component has subsequently shown a positive result in the routine bacterial screening which is performed on all platelet concentrates. The distinction between bacterial contamination, where onward culturing of the screening bottle demonstrates a bacterial species, and positive bacterial screen without confirmation of bacterial growth, was introduced in 2008 when TRIP adjusted the definitions. The reason for this was that the initially positive screening result (a colour reaction in the culture bottle) may have been caused by a pathogen even if it did not grow in the confirmatory culture. In 2013 the hemovigilance advisory board decided that there is no benefit in maintaining two separate categories. The hospitals are informed of the culture result but this is not till later. Sanquin follows the same procedure for all cases with an initially positive screening result. In this report the two groups have been merged.

Reports from hospitals

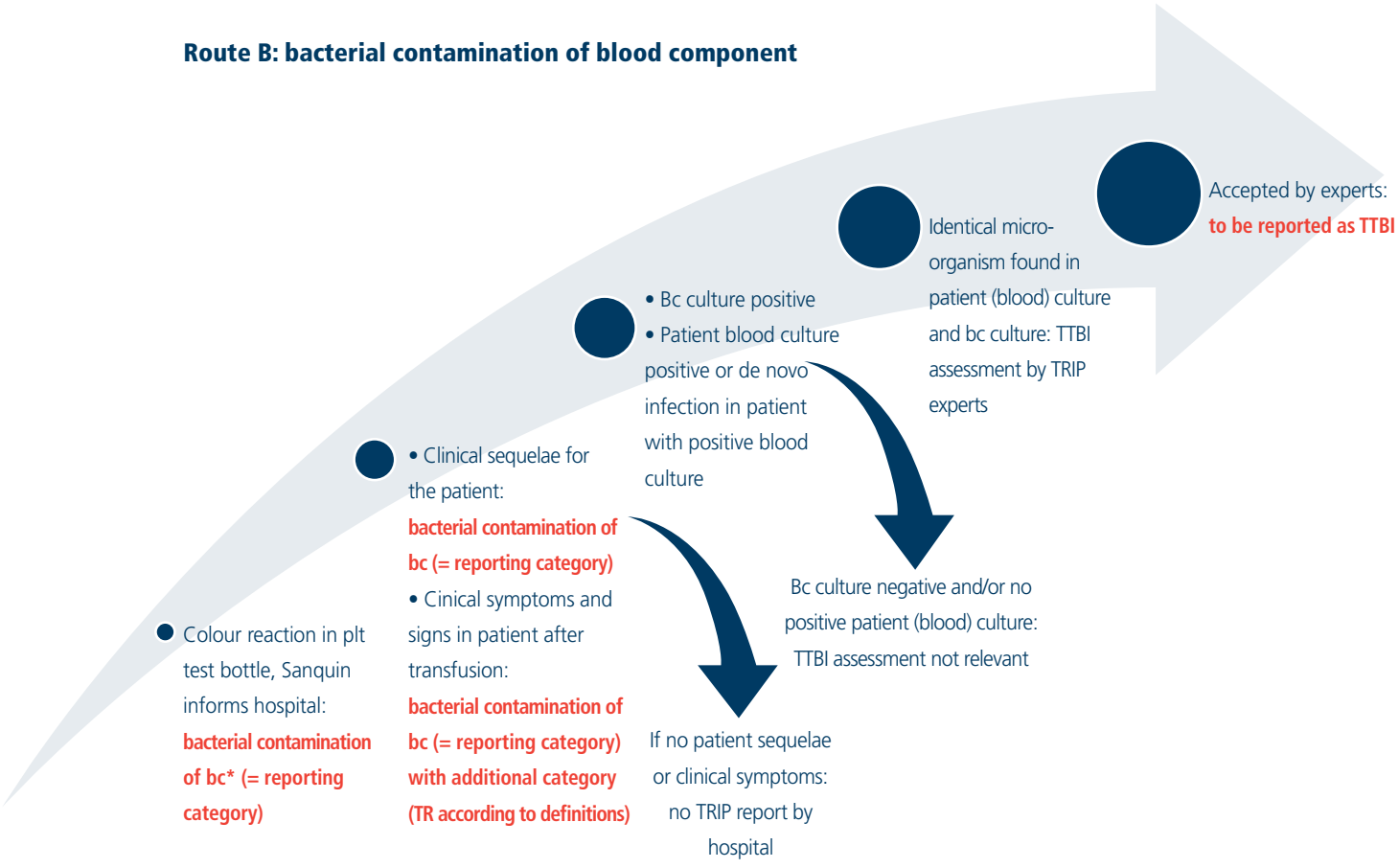
- In 2013 TRIP received 23 reports of bacterial contamination of a blood component (including reports of positive bacterial screen) from 12 hospitals; these were reports of patients who had received a blood component (a platelet concentrate or a RBC unit from a donation included in a pooled platelet unit) which later produced a positive result in the bacterial screen by Sanquin.
- In none of these cases was a reaction reported to TRIP
- Bacterial contamination of a blood component was reported 17x as a subsidiary category, in cases where a hospital recorded a positive bacterial culture result on a unit analysed following a transfusion reaction (9x post-transfusion bacteremia/sepsis, 6x a febrile reaction, 2x an other reaction).
- In two patients with post-transfusion bacteremia/sepsis (and subsidiary category of bacterial contamination of a blood component) the same agent was determined in the patient's blood culture as in the result obtained by Sanquin, see under post-transfusion bacteremia/sepsis.

## Route A: clinical symptoms/signs in a patient




** Culture result should be deemed relevant*

## Route B: bacterial contamination of blood component




** Total figure provided annually by Sanquin*

**Figure 10: Bacterial problems associated with blood transfusion: reporting categories and assessment of TTBI**
***Abbreviations:*** *bc = blood component, tf = transfusion, plt = platelet concentrate, TR = transfusion reaction*

## Information from Sanquin

In 2013, 165 positive results were obtained in the bacterial screening of platelet units (202 associated components had been distributed). In 69 cases, one or more components had already been transfused: out of the total of 83 units there were 14 RBC and 69 platelet concentrates (61 pools and 8 apheresis units). In all, 4 reactions were reported to Sanquin. One of these (non-serious) involved a neonate, and a relation between the reported signs and the transfusion was judged to be unlikely.

**Table 11. Summary of bacterial screening of platelet concentrates by Sanquin 2008-2013**

| Total figures | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 |
|---|---|---|---|---|---|---|
| Plts with initial positive result | Not requested | 325 | 332 | 321 | 238 | 165 |
| Units already transfused (TCs and associated RBC units) | 102 | 108 | 106 | 125 | 90 | 83 |

***Abbreviations:*** *Plt = platelet concentrate; RBC = red blood cell concentrate*

TRIP comment

- Were some reactions reported to Sanquin and not to TRIP?
  Each year TRIP receives information from Sanquin (without hospital identifiers) about reported serious transfusion reactions, in order to ensure that the database of reported reactions is as complete as possible. The reaction in a neonate mentioned above was also reported to TRIP but the reporting hospital indicated there had been no signs or symptoms attributable to the transfusion.
- Strikingly, the total number of cases where the unit showed an initial reaction in the bacterial screening was the lowest in 2013 since TRIP started asking Sanquin for this information. The reduction can be explained because the manufacturer, at Sanquin's request, adjusted the culturing cupboards to reduce the number of false positives. The number of associated units which had already been transfused was not significantly different from former years.
- A report should always be sent to TRIP if there is a suspicion of an infection or other possible medical consequence for the patient. If there were no consequences it is not necessary to report to TRIP.
- The TRIP advisory board recommends that the arrangements for annual exchange of information between Sanquin and TRIP should be updated so that the a complete and accurate picture is obtained.

## Post-transfusion bacteremia/sepsis

*Clinical symptoms of bacteremia/sepsis arising during, directly after or some time subsequent to a blood transfusion, for which there is a relevant, positive blood culture of the patient with or without a causal relation to the administered blood component.*

- 47 reports of post-transfusion bacteremia/sepsis from 29 hospitals
- 2x with an additional category of bacterial contamination of a blood component (unit cultured by the hospital; see case histories) with the same species: in these cases transmission of the bacteria by the unit was judged possible or likely.
- 6x post-transfusion bacteremia/sepsis was reported as additional category. In these cases investigations following symptoms associated with a blood transfusion revealed a positive blood culture which probably had a different source, other than the transfused blood component. In most of these cases the reporter indicated that the course of the patient's signs and symptoms was typical of a non-hemolytic transfusion reaction.

### Case histories, transfusion-transmitted bacterial infection (TTBI)

***Case 1***

The patient, aged 61, became generally unwell during administration of a platelet concentrate in the day care unit; the transfusion was stopped. This led to recovery and she was allowed to go home (the doctor presumed that the symptoms had an allergic origin) but a few hours later she returned with nausea, a high temperature and syncopal tendency. Staphylococcus hominis was cultured from the platelet concentrate and the patient's blood. Bacterial screening by Sanquin remained negative. With antibiotic treatment the patient improved within 24 hours. Reported as post-transfusion bacteremia/sepsis grade 2, imputability possible.

***Case 2***

A patient aged 93 showed a rise in temperature and became red in the face after post-operative transfusion of a RBC after a hip operation (no information given about antibiotic treatment). Staphylococcus hominis was found in the RBC unit and patient's blood culture; bacterial screening of the related platelet unit was negative. Reported as post-transfusion post-transfusion bacteremia/sepsis grade 1, imputability probable.

Table 12 summarises the reports since 2002 in which the same species was demonstrated in the remnant of the unit or material from the donor and in the patient's blood culture (with identical species if further investigated). Since 2011 such cases have been formally reviewed by the panel of transfusion experts before they are formally endorsed as possible cases of TTBI.

**Table 12. Reports of post-transfusion bacteremia/sepsis[1] where the same bacterial species was found in the patient's blood culture as in the transfused unit or the donor: 2002 - 2013**

| Bacterial species | Blood component | Severity | Number | Year |
|---|---|---|---|---|
| Coagulase negative staphylococci | RBC | Not stated | 1 | 2002 |
| | RBC | 1 | 4 | 2009, 2011, 2012, 2013 |
| | Platelets | 2 | 2 | 2008, 2013 |
| | Platelets | 1 | 2 | 2006, 2010 |
| Bacillus cereus | Platelets | 2 | 3 | 2003, 2004, 2005 |
| | | Not stated | 1 | 2003 |
| Salmonella group B | Platelets | 2 | 1 | 2011 |
| Yersinia Enterocolitica | RBC | 4 | 1 | 2009 |
| Hemolytic streptococci group C | Platelets | 2 | 1 | 2012 |
| Hemolytic streptococci group G | Platelets | 2 | 1 | 2005 |
| Staphylococcus aureus | Platelets | 3 | 1 | 2005 |
| Streptococcus dysgalactiae | Platelets | 2 | 1 | 2010 |
| Streptococcus salivarius and coagulase negative staphylococcus | Plasma | 2 | 1 | 2005 |
| **Total** | | | **20** | |

[1] *Before 2008: bacterial contamination*

## Post-transfusion other infection

***Post-transfusion other infection***

*Any case of infection other than with a virus or bacteria, e.g. a parasitic infection or variant Creutzfeldt Jakob Disease) which has been demonstrated within a relevant time interval following a blood transfusion.*

There has been no report in this category since the confirmed report of post-transfusion malaria in 2011.

## 3.3 Non-infectious transfusion reactions

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

***Non-hemolytic transfusion reaction (NHTR)***

*Rise in temperature of ≥ 2°C (with or without rigors/chills) during or in the first two hours after a transfusion, with no other relevant symptoms or signs; OR rigors/chills with or without a rise in temperature within the same time limits. No evidence (biochemical or blood group serological) for hemolysis, and no alternative explanation.*

***Mild (non-hemolytic) febrile reaction (mild NHFR)***

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

In 2013, 438 reports of non-hemolytic transfusion reactions (NHTR) and 332 reports of mild non-hemolytic febrile reactions were received by TRIP: figures which are comparable to last year. Eighteen reports (15 NHTR and 3 mild NHFR) were of severity grade 2, usually because the reaction led to the patient being admitted to hospital.

Table 4 shows which blood components were associated with the reported reactions. As noted in earlier years, transfusions of platelets as well as of shed blood collected in drains were more often associated with NHTR than with mild NHFR. These cases relatively often reported chills/rigors without a rise in temperature (see the 2010 and 2011 TRIP reports).

Sometimes dyspnea or shortness of breath was among the listed symptoms. The information did not always make it clear whether dyspnea was a prominent feature, so that led to TRIP asking questions for clarification. In cases where dyspnea was prominent, the reaction was registered as an other reaction. When the reporting instructions are updated for the new online reporting system which is under construction, it is the intention to provide clearer guidance on the information which is needed, so that fewer questions will be needed and time to acceptance will be shorter. A rise in temperature can cause faster breathing and this may be associated with an (increase of) shortness of breath in some patients.

### 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.*

**Table 13. Acute hemolytic transfusion reactions, 2006 - 2013**

| | AHTR total | Gender | | Number of AHTR (imputability possible, probable, certain) | Severity | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | F | M | | 0 | 1 | 2 | 3 | 4 |
| 2006 | 19 | 10 | 9 | 18 | 1 | 11 | 5 | 1 | |
| 2007 | 11 | 7 | 4 | 10 | | 8 | 2 | | |
| 2008 | 18 | 14 | 4 | 17 | | 10 | 7 | | |
| 2009 | 18 | *13 | *4 | 17 | | 11 | 4 | 1 | 1 |
| 2010 | 21 | 8 | 13 | 20 | | 14 | 5 | 1 | |
| 2011 | 16 | 10 | 6 | 14 | | 6 | 7 | | 1 |
| 2012 | 7 | 5 | 2 | 7 | | 4 | 2 | | 1 |
| 2013 | 10 | 7 | 3 | 10 | | 4 | 6 | | |
| **Total** | **120** | ***74** | ***45** | **113** | **1** | **68** | **38** | **3** | **3** |

* *1x patient sex not stated*

In 2013, 10 acute hemolytic transfusion reactions were reported. This number suggests there could be a declining trend but because of the small number of reports there is no statistically significant change. In four reports the causal antibodies are mentioned: anti-Wra (2), anti-Jkb and a low-frequency antibody (probably anti-Miltenberg). In one case anti-M was demonstrated after the reaction. However anti-M is rarely associated with an acute hemolytic reaction, so it cannot be assumed that it caused the reaction.

## Delayed hemolytic transfusion reaction (DHTR)

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

*If new antibodies are found without biochemical confirmation of hemolysis, report as new alloantibody.*

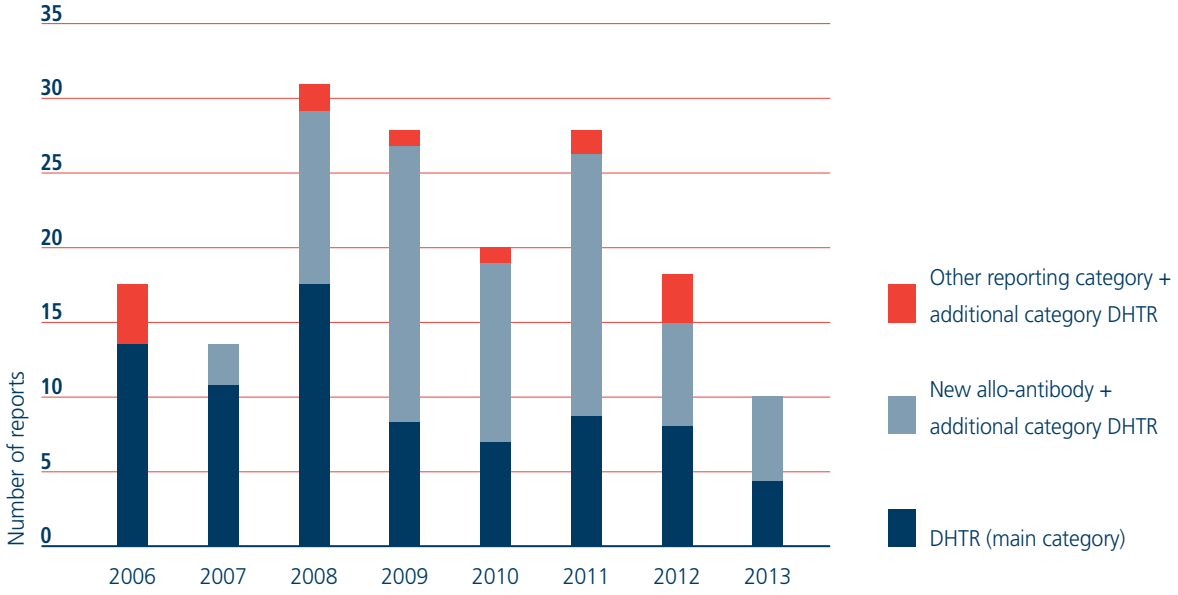



**Figure 11. Delayed hemolytic transfusion reaction as main category or as additional category, 2006 - 2013**

**Table 14. Delayed hemolytic transfusion reactions by imputability and severity, 2006 - 2013**

| | Category DHTR | DHTR, imputability definite, probable or possible | Severity 2 | 1 | 0 |
|---|---|---|---|---|---|
| 2006 | 14 | 13 | 8 | 5 | - |
| 2007 | 11 | 9 | 4 | 4 | 1 |
| 2008 | 18 | 15 | 4 | 6 | 5 |
| 2009 | 8 | 8 | 3 | 5 | - |
| 2010 | 7 | 7 | 5 | 2 | - |
| 2011 | 9 | 9 | 1 | 8 | - |
| 2012 | 8 | 7 | 1 | 5 | 1 |
| 2013 | 4 | 3 | 2 | - | 1 |
| **Total** | **79** | **71** | **28** | **35** | **8** |

**Table 15. New allo-antibody formation with additional category DHTR by severity, 2006 - 2013**

| | New allo-antibody and additional category DHTR | Severity 2 | 1 | 0 |
|---|---|---|---|---|
| 2006 | - | - | - | - |
| 2007 | 3 | - | 1 | 2 |
| 2008 | 11 | 1 | 8 | 2 |
| 2009 | 19 | 1 | 7 | 11 |
| 2010 | 12 | 1 | 6 | 5 |
| 2011 | 17 | - | 12 | 5 |
| 2012 | 7 | 1 | 5 | 1 |
| 2013 | 6 | - | 4 | 2 |
| **Total** | **75** | **4** | **43** | **28** |

In 2013 there were four reports of DHTR and a further six reports where DHTR was recorded as an additional category in patients with new allo-antibody formation. In contrast to previous years, no incidents were reported which had led to a DHTR. There is an apparent declining trend of DHTR reports, but owing to the small numbers it is not statistically significant.

A decline can be seen in the number of cases of DHTR which have been reported since 2008, even after taking account of the reduced numbers of blood transfusions ($p<0.05$). The declining trend could partly be the result of progressive implementation of the TRIX national database of irregular antibodies. At the time of writing this report 78 of the 98 reporting laboratories of hospitals have their connection to TRIX (Transfusion database of irregular antibodies and cross(X)match problems) up and running. One 2013 DHTR report came from a hospital which was not yet connected to TRIX at the time of the component selection and reaction. However not all cases of DHTR can be prevented. Patients are not systematically tested for new allo-antibody formation after a blood transfusion, so there will always be a small risk of missing a newly formed allo-antibody at later pre-transfusion screening if its concentration has gone below the detection threshold.

In 2008 TRIP started systematically reporting reactions according to the sequence of events, with the main reporting category corresponding to the reaction which was noted first. From then on, roughly half of the DHTR have been reported as an additional category in cases where detection of a new allo-antibody and subsequent checking of biochemical hemolysis parameters or an unexpected drop in hemoglobin led to the diagnosis of a DHTR (Fig. 11).

In 2009 and 2010, TRIP consistently asked reporters of clinically significant allo-antibodies whether there had been signs or test results suggestive of hemolysis. This only elicited a small number of extra cases of DHTR which was then reported as an additional category. The tactic failed to increase detection of DHTR to the published 5 - 10x higher incidence than that of AHTR.

## Transfusion-related acute lung injury (TRALI)

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

Six cases of TRALI were submitted and accepted following expert review. All gave serious morbidity: four were rated as grade 2 and two of grade 3. The reports were sent in by five hospitals; one report, where chest X-ray changes were largely unilateral, was judged to be of unlikely imputability.

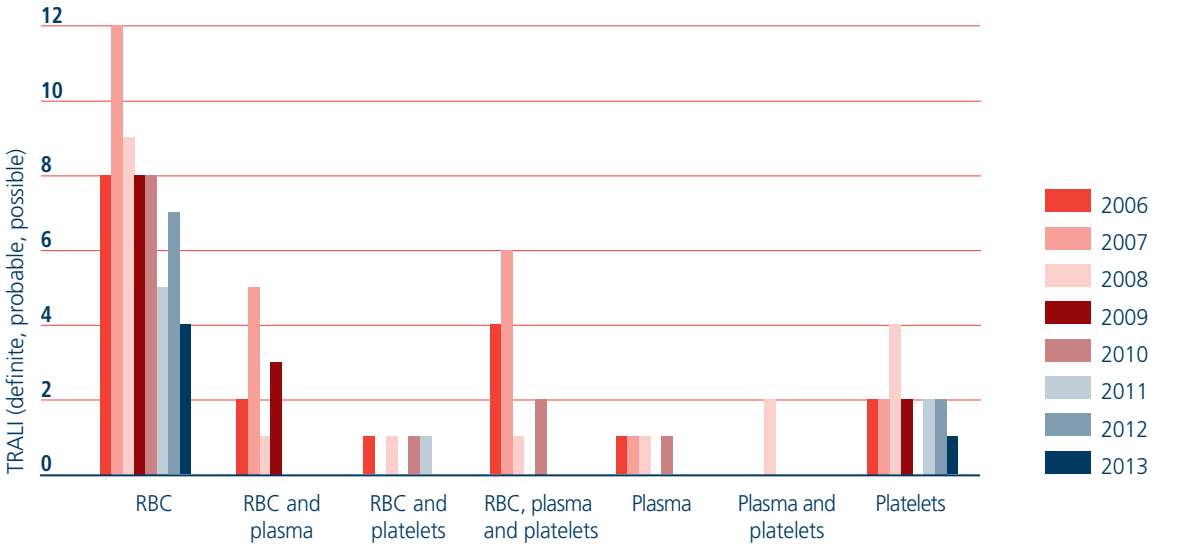



**Figure 12. Type of blood component associated with TRALI, 2006 - 2013**

Figure 12 shows the blood component types which were associated with the reported TRALIs in 2006 - 2013. The annual number of reported cases has gone down since 2008, after the introduction of the male-only plasma, i.e. the exclusive use of plasma donated by male donors who have never received a blood transfusion - this applied to all units distributed from 1st July 2007. TRALI can be caused by incompatibility between the patient's HLA/HNA type and antibodies present in transfused plasma. The plasma measure reduces the likelihood of a plasma unit containing HLA antibodies. Since November 2009 only male plasma has been used as added conservation fluid for pooled platelet concentrates. One of the TRALIs in 2013 arose following transfusion of a pooled platelet unit with plasma as conservation fluid. The incidence of TRALIs associated with platelet transfusion was always low and does not appear to have changed since the platelet measure.

TRALI has not been reported with the use of SD-plasma. When the Dutch SD-plasma, Omniplasma, became the standard product supplied by Sanquin it was agreed that reports of adverse reactions should be channelled through TRIP (the arrangements are summarised and explained on www.tripnet.nl). This ensures that information about TRALI or other reactions to Omniplasma will be brought to the attention of transfusion professionals as well as to the pharmacovigilance agencies.

On reviewing the data reported to TRIP it was noted that there were several cases where the hospital initially considered the possibility of a TRALI but subsequently decided that circulatory overload was more probable. It is essential to be alert to both possibilities, and to properly investigate suspected cases, including a chest X-ray, so that patients are diagnosed and managed correctly.

## Anaphylactic transfusion reaction

*Rapidly developing reaction occurring within a few seconds to minutes after the start of transfusion, with features such as airway obstruction, in and expiratory stridor, fall in blood pressure ≥ 20 mmHg systolic and/or diastolic, nausea or vomiting or diarrhoea, possibly with skin rash.*
*Hemolysis testing and bacteriology negative, test for IgA and anti-IgA.*

In 2013 66 cases were reported as anaphylactic reactions, 17 of them of grade 2 or higher and definite, probable or possible imputability. These figures are comparable to previous years. Anaphylactic reactions represent one of the most important causes of serious transfusion-associated morbidity.

During the hemovigilance advisory board's discussions it was remarked that many clinicians think of anaphylactic shock when an anaphylactic reaction is referred to. The definition of anaphylactic reaction (above) also

encompasses non-serious anaphylactic reactions. The reaction must be allergic in nature and there must be systemic features such as gastro-intestinal symptoms or bronchospasm. Hypotension is not necessarily present. Over a third (29) of the cases were initially reported in a different category (nearly all as other allergic reaction) and were reclassified as anaphylactic reaction at TRIP's request because an other allergic reaction should be characterised by exclusively skin manifestations.

Table 20 shows the numbers of anaphylactic reactions in 2008-2013 and the blood components which were transfused to the patients. In the literature it is reported that allergic reactions are more common with single-donor (apheresis) platelets than with pools (ANSM hemovigilance report, France: Ansm rapport d'activité hémovigilance 2011) and are reduced by the use of platelet additive solution (PAS). The incidence is also lower with SD-plasma than with FFP. In 2013 the proportions of types of components distributed countrywide were similar to 2012, i.e. approximately 10% of apheresis platelet units, over 70% 5-donor pooled buffy coat platelets with plasma from one male out of the five donors, and approximately 20% pooled units made with platelet additive solution. On the basis of the cases reported to TRIP to date no clear conclusion can be drawn about the risk of anaphylactic reactions with different types of platelet units. Sometimes the prescriber may select a particular type of platelet concentrate because of the patient's history; moreover not all the reports to TRIP specify the type of platelet unit.

**Table 16. Anaphylactic reactions and associated blood components, 2008 – 2013**

| Anaphylactic reaction | 2008 | | 2009 | | 2010 | | 2011 | | 2012 | | 2013 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Serious | All | Serious | All | Serious | All | Serious | All | Serious | All | Serious | All |
| RBC | 7 | 14 | 4 | 12 | 4 | 18 | 3 | 15 | 2 | 11 | 3 | 16 |
| Platelets | 14 | 30 | 7 | 31 | 10 | 38 | 7 | 27 | 7 | 23 | 9 | 33 |
| *Pool, plasma* | *2* | *11* | *4* | *16* | *6* | *18* | *4* | *14* | *5* | *13* | *6* | *24* |
| *Pool, PAS* | *2* | *4* | *2* | *4* | *1* | *5* | *1* | *3* | *0* | *0* | *0* | *3* |
| *Apheresis* | *3* | *5* | *0* | *4* | *0* | *4* | *0* | *3* | *0* | *2* | *2* | *4* |
| *Not specified* | *7* | *10* | *1* | *7* | *3* | *11* | *2* | *7* | *2* | *8* | *1* | *2* |
| Plasma | 5 | 15 | 8 | 23 | 3 | 13 | 8 | 18 | 5 | 20 | 2 | 9 |
| Platelets and RBC and/or plasma | 4 | 4 | 0 | 3 | 1 | 2 | 1 | 4 | 0 | 2 | 2 | 5 |
| RBC and plasma | 0 | 2 | 0 | 0 | 0 | 1 | 1 | 2 | 1 | 3 | 0 | 0 |
| SD-plasma | | | | | | | | | | | 1 | 2 |
| Other[1] | 0 | 0 | 1 | 2 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| **Total** | **30** | **65** | **20** | **71** | **19** | **72** | **21** | **65** | **15** | **59** | **17** | **65** |

[1] *Unwashed drain blood*

Following an anaphylactic reaction, guidelines recommend determining the patient's IgA level and testing for the presence of anti-IgA in an IgA-deficient patient as this is a proven cause of transfusion-associated anaphylactic reactions. In the years 2003 up to and including 2013 anti-IgA was four times found to be the cause of an anaphylactic reaction reported to TRIP. Out of the serious anaphylactic reactions reported in 2013, three mention that IgA deficiency and/or anti-IgA had been ruled out by laboratory investigation.

## Other allergic reaction

*Allergic phenomena such as itching, redness or urticaria but without respiratory, cardiovascular or gastro-intestinal features, arising from a few minutes of starting transfusion until a few hours after its completion. Hemolysis testing and bacteriology negative if performed..*

**Tabel 17. Other allergic reactions and associated blood components, 2008 - 2013**

| Other allergic reaction | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 |
|---|---|---|---|---|---|---|
| RBC | 31 | 41 | 39 | 37 | 36 | 47 |
| Platelets | 85 | 86 | 88 | 105 | 82 | 95 |
| *Pool, plasma* | *35* | *52* | *60* | *60* | *47* | *60* |
| *Pool, PAS* | *22* | *10* | *6* | *15* | *2* | *2* |
| *Apheresis* | *8* | *7* | *7* | *7* | *7* | *11* |
| *Not specified* | *20* | *17* | *15* | *11* | *26* | *22* |
| Plasma | 44 | 44 | 41 | 40 | 51 | 37 |
| Platelets and RBC and/or plasma | 7 | 8 | 7 | 7 | 5 | 4 |
| RBC and plasma | 4 | 0 | 5 | 2 | 5 | 2 |
| SD-plasma | | | | | 1 | 4 |
| Other[1] | 0 | 2[1] | 4[1] | 0 | 0 | 1 |
| **Total** | **171** | **181** | **184** | **191** | **180** | **190** |

[1] *Unwashed drain blood*

The number of other allergic reactions, 190, and the proportions of different types of transfused components are similar to past years. Most of the reactions were not further investigated; in a total of ten reports in 2013 it was stated that the patient's IgA level was normal.

As in the past, a number of patients had more than one allergic and/or anaphylactic reaction. Often the hospital states that the patient has had previous reactions or TRIP checks this with the hospital after noting that a date of birth matches up. Approximately 30 patients in 2013 were reported with a second allergic and/or anaphylactic transfusion reaction (or more). The majority were hemato-oncological patients or were receiving treatment by plasmapheresis. Half of these patients were younger than 21 years of age.

## Transfusion-associated circulatory overload (TACO)

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

- 67 reports from 39 hospitals, 1 - 6 reports per hospital with reports
- 12 reports (6 NHTR, 2 post-transfusion bacteremia/sepsis, 2 other reactions, 1 TRALI and 1 anaphylactic TR) also had TACO as an additional category

Transfusion-associated circulatory overload can potentially be prevented by adjusting (slowing) the speed of transfusion, reducing the volume administered or administering diuretics. For this to be effective, it is necessary to determine which patients are at increased risk of developing TACO. A number of possible risk factors were evaluated in the TACO cases reported to TRIP in 2013. We assessed whether one or more of these risk factors were noted as present in the 2013 TACO reports (Figure 13).

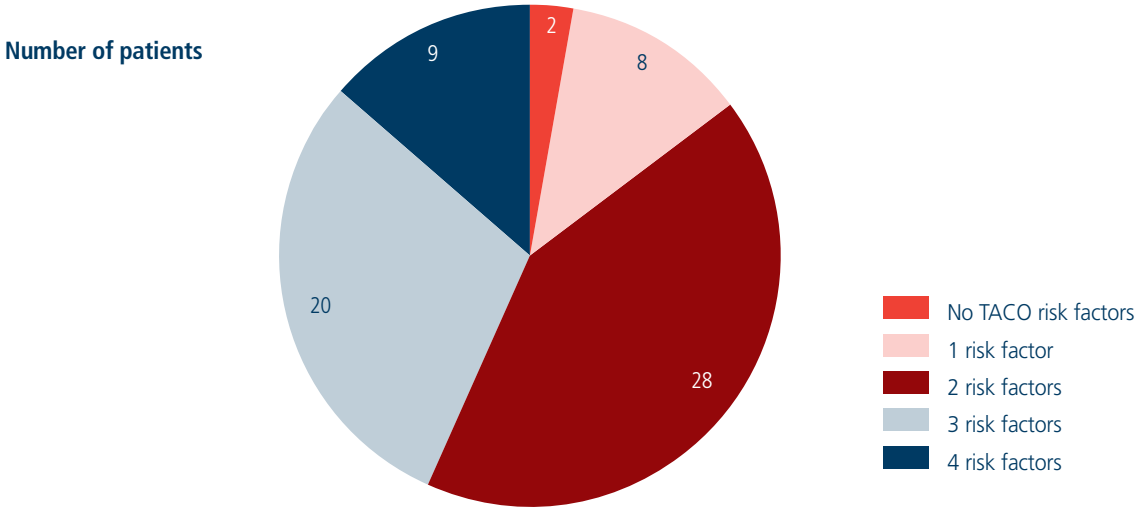



**Figure 13. Number of risk factors recorded per TACO case in 2013***

* *Regarded as factors increasing TACO risk: cardiac history, renal impairment, chronic anemia, positive fluid balance before transfusion, administration of more than one unit and/or IV fluids, previous TACO, age > 60 years, small patient, pregnancy/post-partum.*

The proportion of TACO cases where a rise in temperature is noted with or without chills amounted to approximately 30% in the last two years (Figure 14). According to Mark Popovsky increased body temperature may be seen in 65% of TACO cases (presentation at NVB-TRIP symposium, 2014). It is not clear whether the temperature increases the risk of developing TACO or is one of the manifestations of this complication of blood transfusion. Although TRIP has repeatedly noted that TACO can be associated with a rise in temperature, it cannot be excluded that some cases of TACO were reported as other reaction because the hospital regarded a rise in body temperature as not consistent with TACO. In all reported reactions with significant (increased) dyspnea an assessment should be made of whether there were features suggestive of TACO, by asking the treating physician about findings of physical examination, management and the effect of diuretic treatment (if instituted) on diuresis and dyspnea. The results of imaging (notably chest X-ray) are relevant in diagnosing this type of transfusion reaction. It is important to avoid both over- and underreporting, so that future trends in reports can contribute to determining whether implementation of measures to prevent TACO has led to a reduction of cases.

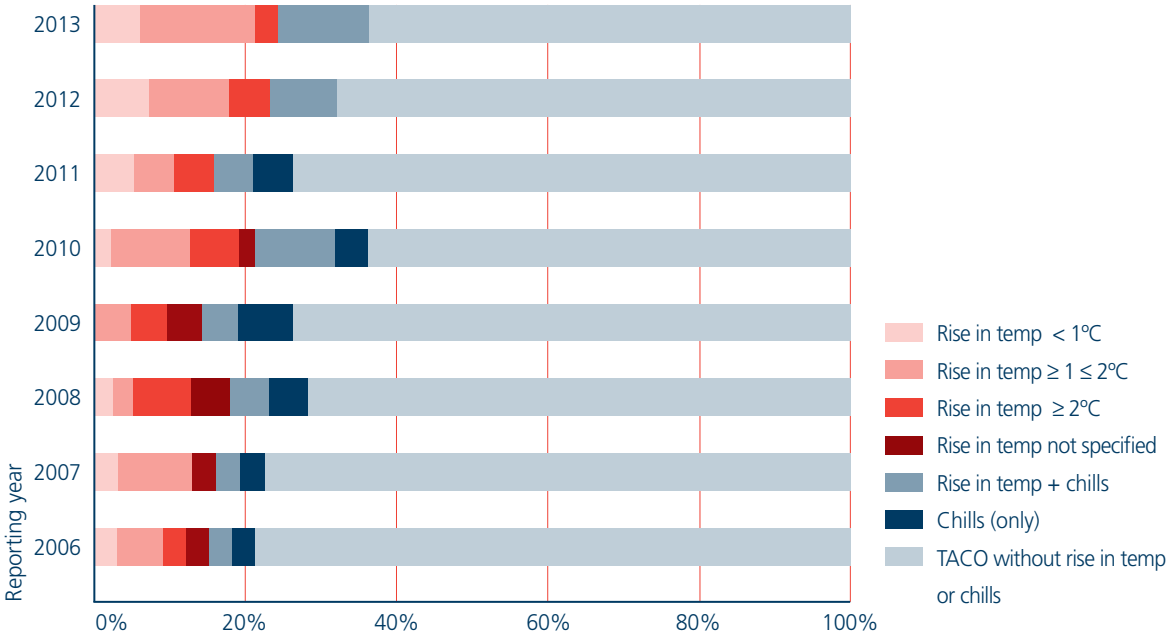



**Figure 14. TACO cases with/without associated rise in temperature/chills, 2006 - 2013**

### Post-transfusion purpura (PTP)

*Serious self-limiting thrombocytopenia possibly with bleeding manifestations 1-24 days after a transfusion of a red cell and/or platelet concentrate.*

In 2013 post-transfusion purpura was not reported. Since the beginning of TRIP reporting a total of five cases of PTP have been reported, all in female patients. The finding of HPA antibodies (most commonly HPA 1A antibodies) supports the diagnosis. In general PTP is very uncommon in association with leukodepleted blood components.

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

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

TA-GVHD was not reported 2013, as in previous years. Leukodepletion, which has been applied to all blood components in The Netherlands since the end of 2001, greatly reduces the occurrence of TA-GVHD.

### Hemosiderosis

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

Four reports of post-transfusion hemosiderosis were received in 2012. This category has been poorly reported since TRIP started collecting data. In 2013 the hemovigilance advisory committee advised TRIP to close the category for routine reporting.

### New allo-antibody formation

*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).*

- 848 reports, 72 reporting hospitals, 1-50 reports per hospital

The reports of new allo-antibody formation were analysed as in 2012 to see if a reduction in reported anti-c, anti-C, anti-e, anti-E en anti-K could be demonstrated among women younger than 45 at the time of transfusion. For this patient group, recommendations were made for preventive Kell compatible RBC transfusion and for Kell and Rhesus phenotype-compatible RBC units in the "CBO" national transfusion guidelines in 2004 and 2011, respectively. A number of aspects should be borne in mind when examining the results:

1. Some hospitals implemented recommendations before the formal recommendation; conversely in a few hospitals there may have been a delay.
2. An overall increase in reports of new allo-antibody formation until about 2008 was observed, in line with an increase in the number of hospitals reporting this category to TRIP.
3. There has been a decline in distributed and transfused red blood cells each year since 2002.
4. In The Netherlands there is no routine post-transfusion screening of transfused patients for possible development of irregular antibodies.
5. Development of irregular antibodies such as anti-K, -c, -C, -e, -E, and -D can also occur following transfusion of platelets or from pregnancy/delivery.
6. Besides the recommendation of preventive matching on Kell and Rhesus phenotype for females of child-bearing potential, similar recommendations have been made for preventive component matching for other at-risk patient groups. The guideline is available in English (link on www.tripnet.nl).

**Re 1** From hospital contacts we know that a number of hospitals implemented targeted preventive Kell-compatible component selection as early as the 90s. From 2005 transfusion of Kell-positive red blood cells to a woman younger than 45 can be regarded as not in compliance with professional standards. With regard to cC and eE antigens approximately half of the respondents indicate that preventive measures were in place well before 2011; from 2012 the policy should have been in place in all hospitals for female patients of child-bearing potential.

**Re 3** Stricter observation of transfusion triggers and reduced use of blood for other reasons will lead to a reduction of cases of new allo-antibody formation.

**Re 4** Women < 45 years of age tend not to be regular transfusion recipients, they are mainly transfused in the perinatal period. They are most likely to be subsequently re-screened for irregular antibodies during their next pregnancy. This means that the interval between transfusion and detection of a new allo-antibody will tend to be longer in women of child-bearing potential than in the total group of patients with new allo-antibody formation. The average interval of all analysable cases of new allo-antibody formation following transfusion in 2002 or later was 275 days. The interval in the subgroup of female patients < 45 years old was approximately double: 557 days. This suggests that an effect of introducing preventive component selection could be seen approximately 2 years afterwards.

**Re 5** Even if the preventive recommendations for females of child-bearing potential are followed, some cases of allo-antibody formation will still arise.

**Re 6** Preventive component matching for other at-risk groups such as the multiply transfused will lead to a reduction of antibody formation against these antigens among these other transfusion recipients.

Figure 15 shows that the overall number of reported new allo-antibodies per year of transfusion rises up to 2010 while the number among female patients less than 45 years old remains fairly steady per transfusion year until 2009 and goes down from 2010. The figure fits with an initial growth of the TRIP reporting system combined with a decline of cases in the target group of females of child-bearing potential. Figure 16 shows the subgroup of women < 45 years of age with a subdivision according to type of allo-antibody and number of patients.

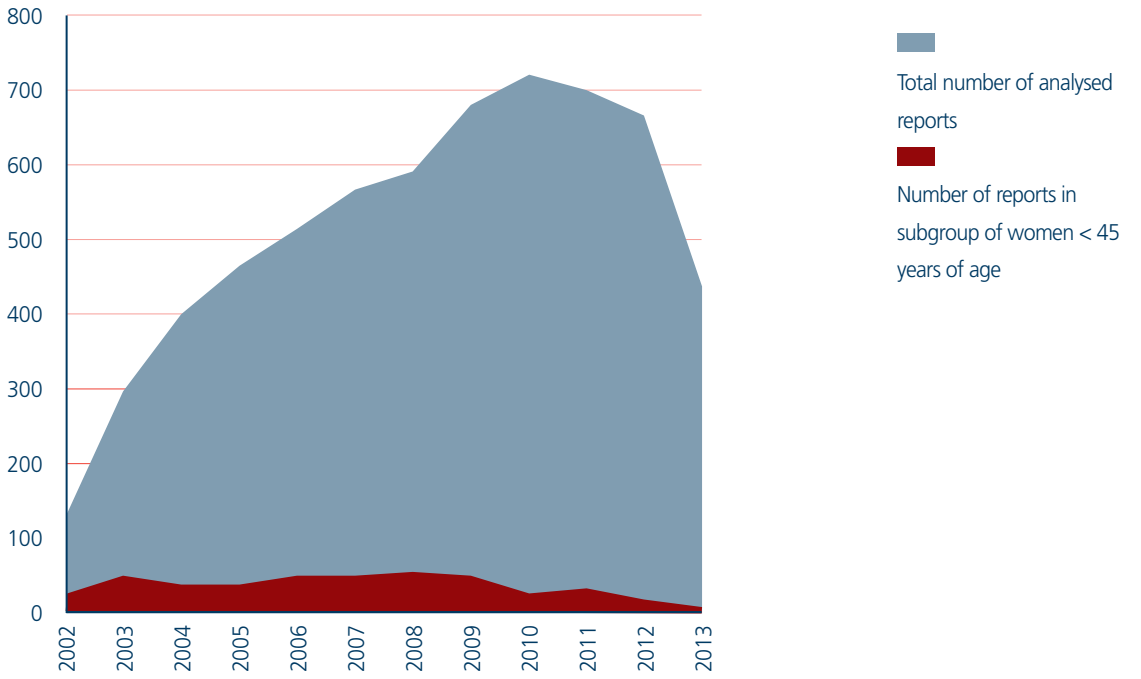



**Figure 15. Total number of analysed reports and number of reports in women < 45 years of age according to year of transfusion**

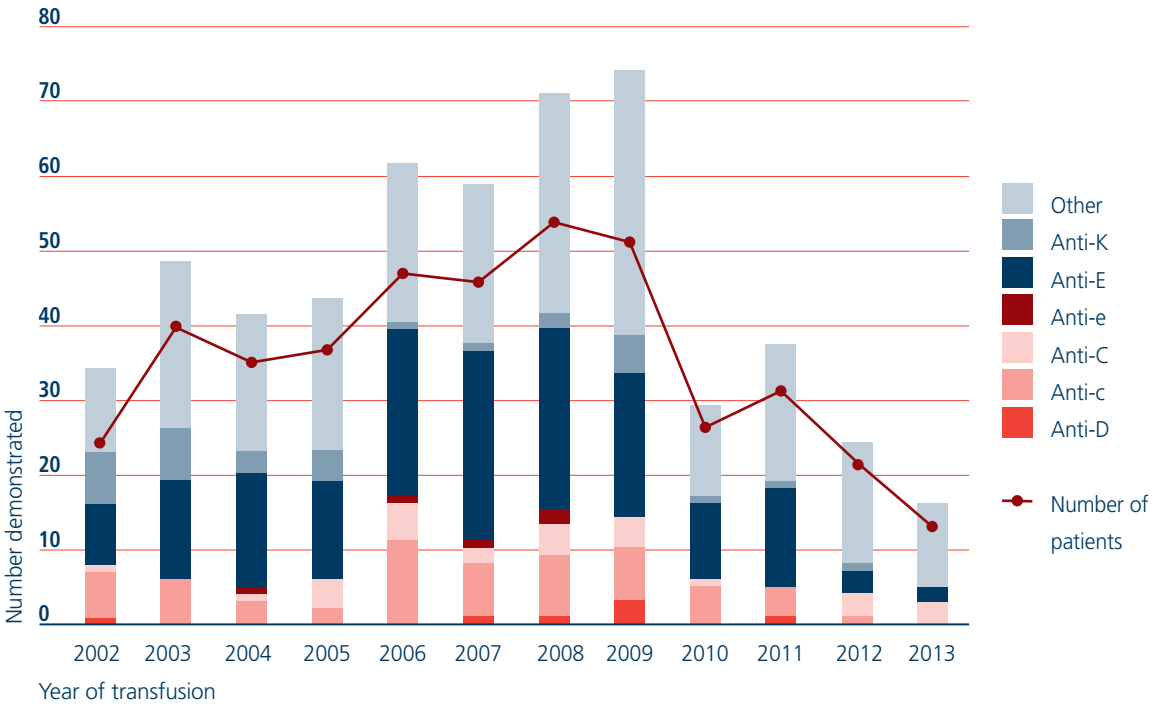



**Figure 16. Allo-antibodies* in women < 45 years of age at the time of transfusion**

** Allo-antibody after platelet transfusion:* *3x anti-D (2x 2009, 2011) 1x anti-c (2005)*
*11x anti-E (2002, 2005, 2007, 2x 2008, 2x 2009, 2010, 2011, 2x 2012)*

*New allo-antibody following IBCT:* *1x anti-D (2007) 2x anti-c (2009, 2012) 1x anti-C (2005)*
*2x anti-E (2010, 2013)*
*12x anti-K (2x 2003, 4x 2005, 2008, 3x 2009, 2010, 2012)*

## Other transfusion reaction

*Transfusion reaction that does not fit into the categories above.*

With 216 reports of other reaction this category is now fourth in total numbers and it accounts for the largest number (29) of reports of severity grade 2 or higher, out of which 21 have certain, probable or possible imputability. In 13 reports the patient had to be hospitalised after transfusion at the day care unit. In four out of these 13 cases the admission to hospital, which by definition leads to registration as severity grade 2, was for precautionary observation for a clinically non-serious reaction.

The category of other reaction was primarily intended so as to be able to register and report on rare or previously undescribed complications that might be related to transfusion. Table 18 shows a breakdown of the other transfusion reactions in 2013.

- As in previous years, in 2013 two clusters are observed which are specifically defined in other hemovigilance systems: hypotensive reaction (in 2013 n=47 reactions with hypotension) and transfusion-associated dyspnea (TAD, n=34 reactions with dyspnea).
- In 2013 there were two remarkable reports with fulminant symptoms consistent with sepsis, however without confirmatory evidence in the form of e.g. positive blood culture. In both cases the patients were chronically transfusion-dependent due to a malignancy. After consultation with experts and reporters it was suggested that TRIP should develop criteria for classification of a report based on the internationally described characteristics of "systemic inflammatory response syndrome" (SIRS).
- In some reports the type of transfusion reaction cannot be determined. As in previous years some reports lack clinical and laboratory information and this hinders classification and assessment of Imputability.

**Table 18. Types of reports classified as other reaction**

| Type of reaction | Total 2013 | Number certain/ probable | Number possible | Number grade 2 or higher* | Remarks | Total 2012 |
|---|---|---|---|---|---|---|
| Hypotensive reaction | 47 | 7 | 33 | 2 | 33 x BP drop quantified; in 20 cases drop of ≥ 30 mm Hg systolic and/or diastolic, including 4x systolic ≤ 80 mm Hg | 42 |
| Reaction with dyspnea | 34 | 2 | 27 | 3 | 12 x dyspnea as solitary or predominant feature | 30 |
| Rise in BP | 6 | 1 | 4 | 0 | 3 x BP rise quantified: median 55 mm Hg systolic | 14 |
| (Possible) cardiac signs/ symptoms | 9 | | 8 | 0 | Including tachycardia as solitary feature | 10 |
| Did not fit standard criteria | 73 | 15 | 36 | 7 | E.g. interval too long after Tf, BP rise or drop combined with fever | 63 |
| Unproven sepsis | 2 | - | 2 | 2 | Clinical signs and symptoms but blood culture neg or not done | Not assessed |
| Solitary sign/symptom or combination of clinical features, possibly in part due to clinical condition | 45 | 3 | 22 | 7 | Without specific transfusion-related cause | 57 |
| **Total** | **216** | **29** | **136** | **21** | | **216** |

* *Imputability certain, probable, possible*

***Abbreviation:*** *BP = blood pressure*

### *TRIP workshop 2013*

In the spring of 2013 TRIP hosted a workshop with reporters concerning the desirability of adding transfusion-associated dyspnea (TAD) and hypotensive reaction as (sub?)categories to the TRIP reporting system. The conclusions of the workshop and subsequent discussion with the Hemovigilance Advisory Board were:

1. Reporting categories should be extended to include the (sub)category: transfusion-associated dyspnea (TAD)

   *ISBT definition for TAD: respiratory distress within 24 hours of transfusion that does not meet the criteria of TRALI, TACO, or allergic reaction. Respiratory distress should be the most prominent clinical feature and should not be explained by the patient's underlying condition or any other known cause.*

2. For the time being not to formalise a (sub)category of hypotensive transfusion reactions.

   *Draft definition based on ISBT definition: Drop in blood pressure during or within 1 hour of completing transfusion with systolic drop in BP of ≥ 30 mm Hg combined with systolic blood pressure ≤ 80 mm Hg. Symptoms should respond rapidly to cessation of transfusion and supportive therapy.*
   *Most hypotensive transfusion reactions occur very rapidly after the start of transfusion (within minutes). Hypotension is usually the sole manifestation but facial flushing and gastrointestinal symptoms may occur. All other types of transfusion reaction presenting with hypotension, especially anaphylactic reaction, should be excluded. The underlying condition of the patient must also have been excluded as a possible explanation for the hypotension.*

3. Provided that the transfusion reaction in other respects meets the standard definition, there is no extra merit in registering additional symptoms and signs as other reaction, especially if these symptoms/signs may be explained by the underlying condition of the patient.

### *Remarks regarding the 2013 reports*

1. **Transfusion-associated dyspnea (TAD)**
   Of the 2013 reports of other reaction it could not always be ascertained that dyspnea was the predominant feature. TRIP is hoping that better classification will be possible through introduction of category TAD as in this category TACO, TRALI and anaphylactic reaction should be excluded. Only one report in 2013 met the definition of TAD, but imputability was assessed to be unlikely due to the serious onderlying condition of the patient. Based on the 2013 data arguments for the introduction of this new reporting subcategory are few.

   ***Case report TAD***
   A male patient (83 yrs) is admitted for rectal blood loss. Due to chronic symptomatic anemia one unit of RBCs is transfused. Two and three quarter hours after the start of transfusion the patient suffers dyspnea and fever >1<2 °C. A chest X-ray did not show specific abnormalities. Blood culture and blood group serology did not reveal abnormalities either. Colitis was diagnosed and antibiotic treatment was started. Report: other reaction, severity grade 1, imputability unlikely.

2. **Hypotensive transfusion reactions**
   From the 47 reports that described a drop in blood pressure or hypotension as the sole or predominant feature, 33 reports specified the blood pressure values. In several reports a potential cause for the drop in blood pressure could be pinpointed. The Hemovigilance Advisory Board advised TRIP to assess which reports do actually meet the international definition. The international (ISBT) definition for this category specifies a drop in blood pressure of ≥ 30 mm Hg combined with a systolic blood pressure as low as ≤ 80 mmHg. Four reports, all of possible imputability and associated with transfusion of RBCs, met this definition. Other transfusion-related causes as well as clinical conditions that could provide a more probable explanation of a drop in blood pressure should be excluded. It was not possible to assess this in all reports.

   ***Case history: hypotensive reaction***
   A 42 year-old female patient suffering from severe metrorrhagia, not previously transfused before, receives a transfusion with one RBC. 15 minutes after the start of transfusion she shows a drop in blood pressure (BP), dizziness and palpitations: BP before transfusion 113/57 mm Hg, 10 mins after starting transfusion 75/45, subsequently 93/54 and after resolution of the reaction 100/57. Blood group serology, biochemical investigations and culture of the unit RBCs did not reveal any abnormality. IV fluids were administered. (Despite a query by TRIP, no information could be obtained on the possible administration of antihistamines.) The patient did not have an IgA deficiency. The reaction was clinically judged not to be an anaphylactic reaction; she is however allergic to adhesive plaster.

Other reaction conclusions:

1. In 2013 there were two reports describing a fulminant course of symptoms and signs suspect for sepsis, however without additional evidence to support the diagnosis, such as a positive blood culture. For reports of other reaction it is essential to have information on underlying illness and clinical condition of the patient to be able to make an assessment of the transfusion reaction.

2. Partly because of insufficient relevant clinical information there were no unequivocal examples of the proposed subgroups of TAD and hypotensive reaction that could illustrate the usefulness of these subgroups.

## 3.4 Blood management techniques (BMT)

**Table 19. Reports regarding blood management techniques 2008 - 2013**

| BMT | M | F | Number of TRIP reports: Drain blood | Number of TRIP reports: Cell saver | Number of TRIP reports: PAD[$] | Total | Reports grade ≥ 2 | Number of reporting hospitals |
|---|---|---|---|---|---|---|---|---|
| 2008 | 14 | 12 | [#]20 | 5 | 1 | 26 | 1 | 9 |
| 2009 | *9 | *23 | 28 | 4 | 1 | 33 | 3 | 6 |
| 2010 | 15 | 22 | 34 | 3 | | 37 | 1 | 5 |
| 2011 | 26 | 38 | 64 | | | 64 | 2 | 8 |
| 2012 | 25 | 25 | 50 | | | 51 | 3 | 8 |
| 2013 | 13 | 13 | 26 | | | 26 | 0 | 6 |
| **Total** | ***102** | ***133** | **[#]222** | **12** | **2** | **237** | **10** | **22** |

* *1x gender not stated*

[#] *1 report concerned preoperative administration of erythropoietin as pretreatment for a drain blood procedure*

[$] *PAD= preoperative autologous donation*

**Table 20. Reported reactions associated with drain blood procedures, 2008 - 2013**

| Trip category | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | Total | Number of reporting hospitals |
|---|---|---|---|---|---|---|---|---|
| Anaphylactic reaction | | 2 | 1 | 1 | | | 4 | 3 |
| Other allergic reaction | | | 1 | | | 2 | 3 | 1 |
| Hemolysis of product | | | | 2 | | | 2 | 2 |
| Mild non-hemolytic febrile reaction | | | | 2 | 4 | 2 | 8 | 3 |
| Non-hemolytic transfusion reaction | 6 | 9 | 18 | 37 | 24 | 14 | 108 | 12 |
| Other incident | 9 | 12 | 6 | 8 | 4 | 3 | 42 | 4 |
| Other reaction | 5 | 4 | 8 | 14 | 17 | 5 | 53 | 10 |
| Post-transfusion bacteremia/sepsis | | | | | 1 | | 1 | 1 |
| Transfusion-associated circulatory overload | | 1 | | | | | 1 | 1 |
| **Total** | | | | | | | **222** | **20** |

- The reports related to blood management techniques in 2013, as in 2011 and 2012, all concerned drain blood procedures.
- The drop in number of reports in 2012 continues in 2013.
- In 2013 there were no reports of severity grade 2 or higher relating to BMT.
- Almost half of the reports in the period 2008-2013 concerned a non-hemolytic transfusion reaction. Second largest is the category other reaction; among these are 21 reports of hypotension (3 reports of severity grade 2). In 2013 there were no reported hypotensive reactions.

**Table 21. Number of hospitals that apply BMT, 2010 - 2013**

| BMT type: Number of hospitals | 2010 yes | 2010 no | 2010 ? | 2011 yes | 2011 no | 2011 ? | 2012 yes | 2012 no | 2012 ? | 2013 yes | 2013 no | 2013 ? |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Drain blood | 21 | 24 | 58 | 23 | 20 | 57 | 23 | 20 | 55 | 24 | 21 | 53 |
| Cell saver | 21 | 23 | 59 | 22 | 21 | 57 | 24 | 21 | 53 | 24 | 18 | 56 |
| PAD# | 9 | 47 | 47 | 10 | 52 | 38 | 11 | 62 | 25 | 5 | 60 | 33 |
| Normovolemic hemodilution | 3 | 32 | 68 | 3 | 33 | 64 | 2 | 28 | 68 | 2 | 37 | 59 |
| Hypervolemic hemodilution | 1 | 31 | 71 | 4 | 32 | 64 | 2 | 26 | 69 | 3 | 36 | 59 |
| Extracorporeal circulation | 4 | 47 | 52 | 4 | 46 | 50 | 4 | 40 | 454 | 4 | 45 | 49 |
| Fibrin glue | 15 | 24 | 64 | 20 | 25 | 55 | 12 | 22 | 64 | 9 | 33 | 56 |
| Platelet gel | 4 | 37 | 62 | 1 | 45 | 54 | 1 | 38 | 59 | 2 | 42 | 54 |

# *Preoperative autologous donation*

**Table 22. Application data of BMT 2009 - 2013**

| BMT technique Total applied | 2009* | 2010* | 2011* | 2012* | 2013* |
|---|---|---|---|---|---|
| Drain blood | 7514 | 8821 | 11464 | 7209 | 5536 |
| Cell saver | 3033 | 5001 | 4282 | 2501 | 5097 |
| PAD# | | | | | |
| - patients referred | 109 | 153 | 59 | 26 | 17 |
| - units donated | 208 | 289 | 113 | 50 | 6 |
| - units administered | 187 | 224 | 38 | 29 | 4 |
| Normovolemic hemodilution | 122 | 1412 | 1250 | ?* | ?* |
| Hypervolemic hemodilution | 2 | 0 | 1172 | ?* | ?* |
| Extracorporeal circulation | 2177 | 4430 | 5606 | 3981 | 3577 |
| Fibrin glue | 798 | 1056 | 1437 | 350 | 1123 |
| Platelet gel | 846 | 1225 | 510 | 30 | 24* |

* *Some hospitals submit approximations for application data or state that they use BMT but do not provide numbers*

# *Preoperative autologous donation*

Hospitals that use BMT and application data:

- There remains a lack of clarity concerning application of BMT in the hospitals. Despite the CBO blood transfusion guideline's recommendation regarding hemovigilance for BMT and five years of inventorying application data by TRIP, Table 21 shows that the hemovigilance professionals in half of the hospitals were unable to state whether BMT were applied in their institution. Presumably this information is known, but is not available to the hemovigilance staff.
- There is further drop of 23% in application of drain blood procedures. Possibly this technique is used less often, one reason being that drain blood procedures are not cost-effective (C. So-Osman: thesis Leiden 2012 Patient Blood Management in Elective Orthopaedic Surgery: Chapter 7).
- The number of reports concerning drain blood procedures has dropped by half in comparison to 2011 and 2012.

## 3.5 Deceased patients and transfusion reactions (grade 4)

In 2013 there were eight reports of transfusion reactions of severity grade 4, including two reports of other reaction that clinically presented as sepsis but could not be substantiated due to fulminant illness, as blood cultures could not be taken in time. The remaining grade 4 reports were of unlikely imputability and/or had a clear cause other than transfusion (imputability excluded). The grade 4 reports are summarised in Table 23.

**Table 23. Reports of patients who died following a transfusion reaction**

| Category of reaction | Age, gender | Blood component | Imputability | Clinical situation |
|---|---|---|---|---|
| Other reaction | 62, M | RBC | Possible | Metastasised prostate carcinoma. Tf at day care unit, deterioration at home, died shortly after arrival at the hospital. Clinical presentation: sepsis, unconfirmed. Unit culture negative. |
| Other reaction | 83, M | RBC+plt | Possible | Progressive MDS, clinical presentation: sepsis. Unconfirmed. |
| Mild non-hemolytic febrile reaction | 35, M | RBC | Unlikely | Pancreatic carcinoma and suspected pulmonary embolism. Fever after administration of 50 ml. After 15 mins circulatory arrest. Resuscitation (35 min) unsuccessful. |
| Other reaction | 75, M | Plt | Unlikely | Chronic hemodialysis patient, cardiac arrhythmia during operation for intestinal ischemia |
| Other reaction | 77, F | RBC | Unlikely | Chronic hemodialysis patient, cardiac failure; tachycardia and chest pain after administration of 20ml; cardiopulmonary arrest. |
| Other reaction | 75, M | SD-plasma + RBC | Excluded | CABG re-operation; hypotension, ECG changes and postop. cardiopulmonary arrest. |
| Other reaction | 56, M | Plasma | Excluded | TTP; hypotension, dyspnea, abdominal pain. Autopsy revealed microangiopathy in heart, pancreas and other organs with TTP. |
| 'Calculated risk' | 80, F | RBC | Unlikely | Bleeding AAA, during operation patient died without symptoms of TR. In retrospect patient had anti-K. 2 out of 4 uncrossmatched 0 neg units were K+. |

***Abbreviations:*** *Tf = transfusion, Plt = platelet concentrate, MDS = myelodysplastic syndrome, CABG = coronary artery bypass graft, TTP = thrombotic thrombocytopenic purpura, AAA = abdominal aortic aneurysm, TR = transfusion reaction*

Table 24 gives an overview of grade 4 reports to TRIP since 2003 that had an imputability assessment of certain, probable or possible. The main categories were TRALI (9), other reaction (8) and TACO (5).

**Table 24. Reports of grade 4 (imputability certain, probable or possible), 2006 - 2013**

| Reaction | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | Total |
|---|---|---|---|---|---|---|---|---|---|
| Acute hemolytic transfusion reaction | | | | 1 | | 1 | 1 | | 3 |
| Anaphylactic reaction | | 1 | | | | | | | 1 |
| Other reaction | | | 1 | | 3 | 1 | 1 | 2 | 8 |
| Post-transfusion bacteremia/sepsis* | | | | 1 | | | 1 | | 2 |
| TRALI | 2 | 3 | | 1 | 2 | | 1 | | 9 |
| Incorrect blood component transfused | | 1 | 1 | | | | | | 2 |
| TACO | 1 | | | | 2 | 1 | 1 | | 5 |
| **Total** | **3** | **5** | **2** | **3** | **7** | **3** | **5** | **2** | **30** |

* *Prior to 2008: bacterial contamination*

## 3.6 Overview of mandatory reports of serious adverse reactions

In accordance with the Common Approach drawn up by the European Commission, only reports with imputability certain, probable or possible have been included. Reactions that occurred after administration of an incorrect blood component or other incident have been included here in the relevant category. Table 25 shows the data for 2012 and 2013.

**Table 25. Number and imputability of reports grade 2 and higher in 2012 and 2013**

| | Total | | Possible | | Probable | | Certain | |
|---|---|---|---|---|---|---|---|---|
| | 2012 | 2013 | 2012 | 2013 | 2012 | 2013 | 2012 | 2013 |
| Hemolytic TR | 7 | 8 | 2 | 2 | 3 | 2 | 2 | 4 |
| Anaphylactic TR | 13 | 17 | 3 | 7 | 7 | 9 | 3 | 1 |
| Other allergic TR | 1 | 3 | - | 1 | - | 2 | 1 | - |
| TRALI | 9 | 5 | 5 | 4 | 4 | - | - | 1 |
| TACO | 26 | 20 | 13 | 10 | 7 | 7 | 6 | 3 |
| Post-transfusion bacteremia/sepsis | 7 | 6 | 4 | 6 | 2 | - | 1 | - |
| Post-transfusion viral infection | - | 2 | - | 2 | - | - | - | - |
| NHTR / mild NHFR | 16 | 15 | 13 | 11 | 3 | 4 | - | - |
| Other reaction | 21 | 22 | 12 | 17 | 6 | 5 | 3 | - |
| **Total** | **100** | **98** | **52** | **60** | **32** | **29** | **16** | **9** |

***Abbreviations:*** *TR = transfusion reaction; NHTR = non-hemolytic transfusion reaction; mild NHFR = mild non-hemolytic febrile reaction*

# List of terms and abbreviations

| | |
|---|---|
| AAA | abdominal aortic aneurysm |
| AHTR | acute hemolytic transfusion reaction |
| a.b. | antibody (formation) |
| Bc | blood component |
| BMT | blood management techniques |
| CBO | CBO quality organisation in healthcare |
| DHTR | Delayed hemolytic transfusion reaction |
| FFP | Fresh frozen plasma |
| Hosp | Hospital |
| IBCT | Incorrect blood component transfused |
| ICU | intensive care unit |
| IGZ | Healthcare Inspectorate (Inspectie voor de Gezondheidszorg) |
| Irrab | Irregular antibody (formation) |
| Mild NHFR | mild non-hemolytic febrile reaction |
| NHTR | non-hemolytic transfusion reaction |
| OI | other incident |
| PAD | preoperative autologous donation |
| PAS | platelet additive solution |
| Pt | patient |
| PCR | polymerase chain reaction |
| Plt | platelet concentrate |
| Post-Tf bact/sepsis | post-transfusion bacteremia/sepsis |
| PTP | post-transfusion purpura |
| RBC | Red blood cell concentrate |
| Sanquin | Sanquin Blood Supply Foundation |
| SD | solvent detergent (virus reducing treatment) |
| TA-GvHD | Transfusion-associated graft versus host disease |
| TACO | Transfusion-associated circulatory overload |
| Tf | transfusion |
| TR | transfusion reaction |
| TRALI | Transfusion-related acute lung injury |
| TRIP | TRIP Foundation (Transfusion and Transplantation Reactions In Patients) |
| TTBI | transfusion-transmitted bacterial infection |

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