



Haemovigilance Report

1997 - 2008

**Assessment of reports of serious adverse
transfusion reactions**

Funk MB¹, Günay S¹, Lohmann A¹, Witzenhausen C¹, Henseler O²

Paul-Ehrlich-Institut

¹Division S: Safety of Medicinal Products and Medical Devices

²Unit 7: Haematology / Transfusion Medicine

Paul-Ehrlich-Strasse 51-59
63225 Langen, Germany

www.pei.de/hv-report
pharmakovigilance2@pei.de

Tel.: +49 (0) 6103 – 77 3116
Fax.: +49 (0) 6103 – 77 1268

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1. Abbreviations

AML	Acute myelocytic leukemia
AK Blut	German Advisory Committee Blood / national advisory board for transfusion
Anti-HBc	Antibodies against Hepatitis B-core antigen
AMG	German Medicinal Products Act / German Drug Law
CML	Chronic myelocytic leukemia
EHN	European Haemovigilance Network
FFP	Fresh frozen plasma
HLA	Human Leucocyte Antigen
HNA	Human Neutrophil Antigen
NAT	Nucleic acid amplification technique
PEI	Paul-Ehrlich-Institut
PC	platelet concentrate
RBC	Red blood cell concentrates

2. Introduction

In the past two decades haemovigilance networks have been established in North America and Europe with different aims and structures [1- 5]. The German Haemovigilance System was introduced in 1994 and primarily covers blood collection, manufacturing of blood components and transfusion related reactions [6 – 8]. In contrast to other European countries (EU member states), since 1976, blood components have been defined as medicinal products obliged to obtain a marketing authorisation pursuant to the German Medicinal Products Act (AMG). Therefore the same obligations to report apply to both pharmaceutical companies and blood establishments. According to German legislation (TFG, Transfusion Act, Section 16 and the AMG, Section 63, mainly serious adverse transfusion reactions shall be reported within 15 days in order to identify serious risks and initiate appropriated risk minimisation activities rapidly [9, 10]. In 2006, the Medicinal Products Act was amended in accordance with EU legislation (Directive 2005/61 EC) and the obligation to report was newly regulated in Section 63c AMG. Now adverse transfusion reactions, serious adverse events and donor reactions shall be reported and evaluated by the haemovigilance system.

The main requirements for an efficient haemovigilance system are a precise documentation of the adverse events/reactions by the reporting physician and the blood establishment involved as well as a standardised and transparent evaluation of these reports by the competent authority (Paul Ehrlich Institut). In this haemovigilance report the assessment of the reported data is presented in a concentrated form. Mainly frequency and severity of transfusion reactions are presented to discuss improvements in safety standards and initiated measures if necessary.

3. Methods

All reports of serious adverse transfusion reactions were registered in the database of the Paul Ehrlich Institut. The physicians documented all relevant recipient data, such as transfused blood components, age, gender, underlying diseases, concomitant diseases, and the course of the adverse reaction by using the standardised questionnaire. The blood establishment involved supplemented this information by adding specific data of the donor(s), results of analyses and look back procedures.

Reported reactions were assessed as transfusion reactions conforming to the criteria of the European Haemovigilance Network (EHN). Non-serious transfusion reactions were reported to the PEI in a summarised form (PSUR). Near-adverse reaction events and incorrect blood

components transfused were reported to the PEI on a voluntary basis. According to the Transfusion Act, it is mandatory to report ABO incompatible transfusions to the transfusion officer of the appropriate hospital. Thus, the management of medication errors is handled at the local level whereas product related issues are managed at a state or national level.

3.1 Categories of adverse transfusion reactions

The definitions of the adverse transfusion reactions are based on the recommendation of the EHN [11]. The adverse reactions were classified and evaluated according to the following criteria:

- Serious allergic transfusion reaction (ATR):
Rash, generalized pruritus, urticaria, allergic dyspnea (stridor, cyanosis, wheezing), angioedema, hypotension (drop in systolic blood pressure by ≥ 30 mm Hg), tachycardia (increase of heart rate > 30 beats/ min.), shock, loss of consciousness, asystolia. Symptoms during or within 24 hours of transfusion, and without any indication of other cause.
- Transfusion-related acute lung injury (TRALI):
Acute respiratory distress and bilateral lung infiltrations in the chest radiograph and occurrence during or within 6 hours of the completion of the transfusion and no evidence of transfusion-associated circulatory overload.
- Haemolytic transfusion reaction (HTR)
Fever and a variety of other symptoms (including dyspnea, hypotension, tachycardia, flank or back pain, etc), gross hematuria, inadequate rise of post-transfusion hemoglobin level, drop in haemoglobin level (≥ 2 g/dl within 24 hours), rise in LDH ($\geq 50\%$ within 24 hours), rise in bilirubin, haemoglobinaemia, decrease in haptoglobin is present in a temporal association with transfusion. HTR is confirmed by a positive direct antiglobulin test and/or a positive erythrocyte cross-match. Acute HTR: occurrence within 24 hours of transfusion. Delayed HTR: occurrence between 1 – 28 days after transfusion).
- Transfusion transmitted bacterial infection (TTBI):
Fever $> 39^{\circ}\text{C}$ or a change of $> 2^{\circ}\text{C}$ from pretransfusion value and chills and tachycardia or drop of 30 mm Hg in systolic blood pressure within 4 hours of transfusion. Possible TTBI: detection of bacteria by approved techniques in the transfused blood component but not in the recipient's blood or detection of bacteria in the recipient's blood following transfusion but not in the transfused blood component. Confirmed TTBI: detection of the same bacterial strain in the recipient's blood and in the transfused blood product by approved techniques.
- Transfusion transmitted viral infection (TTVI: HBV, HCV, HIV):
The recipient has evidence of infection post-transfusion and no clinical or laboratory evidence of infection prior to transfusion. In order to clarify the causality, the recipient related look back procedure has to be performed according to Opinion 34/35 of the German Advisory Committee Blood.
- Incorrect blood component transfused (IBCT)/ ABO-incompatible red cell cases:
All reported episodes where a patient was transfused with a blood component or plasma product that did not meet the appropriate requirements or was intended for another patient.

Primarily, the reporting frequencies of serious adverse transfusion reactions were considered, in order to evaluate the benefit of measures taken to improve the safety standard of blood components. In the past, it was difficult to confirm reliably the suspected diagnosis of TRALI, as the data were frequently incomplete. Therefore, a standardized questionnaire has been used since 2006 to record the defined criteria for TRALI based on the specifications of EHN [10]. The diagnosis of TRALI was confirmed if acute respiratory distress during or within 6 hours of transfusion, radiographic evidence of new bilateral pulmonary infiltrates and absence of signs of circulatory overload were fulfilled. In addition, a requirement was made to analyze the blood products involved for leukocyte antibodies in order to distinguish between immune and non-immune TRALI. Leukocyte antibodies have been determined in a standardized form since 2006 [12, 13].

Since 1998 distribution and expiration of blood components have to be documented and reported by the members of the blood donation units, blood banks and hospitals pursuant to the German Transfusion Act (TFG). From this information the approximate annual application of the blood components can be calculated and is published regularly in the report on notifications pursuant to Section 21 German Transfusion Act ([Table 10](#)). To calculate the reporting frequency of serious transfusion reactions, the number of confirmed reactions and fatalities is correlated with the total number of blood components administered. In Tables 2 – 7 the reporting frequency related to specific blood components (RBC, PC, FFP) were calculated for the period of four years. The frequencies of these three four-year periods were then compared (1997 – 2008).

3.2 Measures to improve the safety standards

Between 1997 and 2008 a number of measures were implemented or recommended in order to improve safety and quality of the blood components.

Announcement: Measures implemented or recommended:

- 1998:** Since April 1999, screening of red blood cell concentrate donors and platelet concentrate donors by HCV NAT- pool- testing (HCV-RNA- limit of detection: 5000 IU/ ml).
- 1999:** Since October 1999, screening of fresh frozen plasma (FFP) donors by HCV NAT- pool- testing (HCV-RNA- limit of detection: 5000 IU/ ml).
- 2000:** Since August 2000, leukocyte-depletion of blood cell components (concentration of leukocytes $< 1 \times 10^6$ per unit).
- 2000:** Since February 2001, exclusion of blood donors who have lived in countries with an increased number of variant Creutzfeldt–Jakob disease (vCJD) patients.
- 2002** Since June 2003, introduction of a pre-donation sampling for platelet concentrates (voluntary measure of blood donation establishments according to a recommendation of the German Advisory Committee Blood (Opinion 27). In order to achieve a reduction in the number of microbially contaminated blood components, the separation of at least 15 ml of initial blood was required.
- 2003:** Since May 2004, screening of blood component donors by HIV NAT- pool- testing (HIV-RNA- limit of detection: 10 000 IU/ ml).
- 2006:** Since October 2006, screening of blood component donors with a Hepatitis B core antigen test (anti- HBc test).
- 2008:** Since June 2008, limitation of the shelf life of platelet concentrates to 4 days (4 x 24h) beginning at midnight on the day when the blood was drawn. Recommendation of the German Advisory Committee Blood (Opinion 38) in order to reduce the danger of a fatal transfusion reaction caused by contaminated PC.

4 Results

4.1 Reported reactions and confirmed transfusion reactions according the EHN criteria (1997 – 2008)

Altogether 5269 suspected serious transfusion reactions were reported to the PEI during the 12-year period ([Table 1](#)). The number of reports varied between 377 and 525 cases per year. The majority of all reported suspected cases were transfusion related virus infections (54%), acute transfusion reactions (22%) and TRALI (11%).

In a third of all reports (1831), the suspected diagnosis could be confirmed. 13% (758) were categorised as serious transfusion reactions according to EHN criteria. The majority were allergic transfusion reactions (256), followed by TRALI (184), haemolytic transfusion reactions (132) and transfusion related bacterial infections (77). Transfusion related virus infections were confirmed in 47 cases which corresponded to 6% of all confirmed serious transfusion reactions. In total, 50 cases of ABO-incompatibility were documented mainly because of incorrectly transfused blood components. These cases were reported to the PEI because of serious haemolytic reactions or in rare cases on a voluntary basis.

During the 12-year period, the PEI received 230 reports of suspected transfusion related fatalities. In 61 cases, the suspicion was confirmed. The most frequent causes of death were TRALI (19 cases) followed by serious allergic transfusion reactions (15 cases), haemolytic transfusion reactions and transfusion related bacterial infections (9 cases each). Additionally 6 cases of fatality were reported because of ABO-incompatibility and 2 cases and 1 case, respectively, because of transfusion related virus infections and transfusion associated graft-versus-host disease.

4.2 Allergic transfusion reactions (ATR)

See also [Table 2](#).

EHN- criteria of non serious allergic reactions: Rash, mild allergic dyspnea, hypotension (drop in systolic blood pressure by < 30 mm Hg)

EHN- criteria of severe allergic reactions: hypotension (drop in systolic blood pressure by ≥ 30 mm Hg), allergic dyspnea (stridor, cyanosis, wheezing), shock, intensive care management.

Period:	1997 – 2008
Number of reports:	1220
EHN- criteria confirmed:	1043
Number of non- serious allergic reactions:	787
Number of serious allergic reactions:	256
Serious allergic reactions due to RBC:	156
Serious allergic reactions due to PC:	38
Serious allergic reactions due to FFP:	29
ATR related fatalities:	15
Reporting frequency after application of RBC: (2005 – 2008):	6.2 per 10^6 units
Measures to reduce ART:	no specific measures

Leukocyte-depletion of blood cell components was mainly implemented to reduce the frequency of febrile non haemolytic transfusion reactions (FNHTR) and HLA-alloimmunization.

4.3 Transfusion-related acute lung injury (TRALI)

See also [Table 3](#).

EHN- criteria: Acute respiratory distress and bilateral lung infiltrations in the chest radiograph and occurrence during or within 6 hours of the completion of the transfusion and no evidence of transfusion-associated circulatory overload.

Period:	1997 – 2008
Number of reports:	509
EHN- criteria confirmed:	184
Number of non- immune TRALI:	33
Number of TRALI without leucocyte Ab (LC-Ab) analysis:	41
Number of immune TRALI:	110
Number of immune TRALI with LC-Ab positive FFP donors:	84
Number of immune TRALI with LC-Ab positive RBC donors:	19
Number of immune TRALI with LC-Ab positive PC donors:	7
Number of immune TRALI with LC-Ab positive female donors:	109
Number of immune TRALI with LC-Ab positive male donors:	1
Non- immune TRALI related fatalities:	0
Immune TRALI related fatalities:	19
Immune TRALI related fatalities due to FFP:	16
Immune TRALI related fatalities due to RBC:	3
Reporting frequency after application of FFP: (2001 – 2004):	5 per 10 ⁶ units
Enhanced Surveillance:	2006 – 2008
Reporting frequency after application of FFP: (2005 – 2008):	11 per 10 ⁶ units
Measures to reduce ART since 09/2009:	too early to assess benefit

The data of involved donors in 35 cases of confirmed immune TRALI (2006 - 2007) and results of analysis of their leucocyte antibodies are presented in [Table 4](#) [14].

4.4 Hämolitic transfusion reaction (HTR)

See also [Table 5](#).

EHN criteria: Fever and a variety of other symptoms (including dyspnea, hypotension, tachycardia, flank or back pain, etc), gross haematuria, drop in haemoglobin level ($\geq 2\text{g/dl}$ within 24 hours), rise in LDH ($\geq 50\%$ within 24 hours), rise in bilirubin, positive direct antiglobulin test and/ or a positive erythrocyte cross-match. Acute HTR: occurrence within 24 hours of transfusion, delayed HTR: occurrence between 1 – 28 days after transfusion.

Period:	1997 – 2008
Number of reports:	219
EHN- criteria confirmed:	132
Acute HTR:	116
Delayed HTR:	16
Delayed HTR:	16
Delayed HTR with detection of alloantibodies:	11
HTR due to RBC:	109
HTR due to PC:	7
HTR due to combined transfusion of blood components:	16
HTR related fatalities:	9
HTR related fatalities due to RBC:	7
Reporting frequency after application of RBC: (2005 – 2008):	2.4 per 10^6 units
Measures to reduce ART:	no specific measures

4.5 Transfusion-transmitted bacterial infections (TTBI)

See [Table 6](#).

EHN criteria: Fever > 39°C or a rise of > 2°C within 4 hours of transfusion, chills and tachycardia or drop of 30 mm Hg in systolic blood pressure, detection of the same bacterial strain in the recipient's blood and in the transfused blood product.

Period:	1997 – 2008
Number of reports:	173
EHN- criteria confirmed:	77
TTBI due to PC:	38
TTBI due to RBC:	34
TTBI due to FFP:	5
TTBI related fatalities:	9
HTR related fatalities due to PC:	5*
HTR related fatalities due to RBC:	4
Reporting frequency after application of RBC: (1997 – 2000):	9.3 per 10 ⁶ units
Reporting frequency after application of RBC: (2005 – 2008):	9.6 per 10 ⁶ units
Benefit of Pre-donation sampling procedure (2003):	no reductions of reports

*All 5 platelet concentrates (2 pooled PC and 3 apheresis PC) had reached the end of their shelf life (4th or 5th day after production) at the time of transfusion.

4.6 Results of microbiological analysis, reports from 1997 to 2008

See [Table 7](#).

Period:	1997 – 2008
EHN- criteria confirmed:	77
Agent with medium to high pathogenicity:	43 cases
Agent with low pathogenicity:	34 cases
Confirmation of <i>Staphylococcus epidermidis</i> :	19 cases
Confirmation of <i>Staphylococcus aureus</i> :	10 cases
TTBI related fatalities:	9
Agent with medium to high pathogenicity:	8 cases
Agent with low pathogenicity:	1 case
Recipients with a relevant immunosuppression:	7 cases*

*Patients with malignant diseases (AML, CML, Aplastic anaemia, etc.).

4.7 Transfusion-transmitted viral infections (HBV, HCV, HIV)

See also [Table 8](#).

Criteria according to the opinion 34/35 of the German Advisory Committee

Period:	1997 – 2008
Number of reports:	3003
Number of reports related with HBV:	1104
Number of reports related with HCV:	1745
Number of reports related with HIV:	154
Opinion 34/35 criteria confirmed:	47
Confirmed cases subdivided in:	HBV: 22, HCV: 20, HIV: 5
Transmission due to RBC:	29
Transmission due to PC:	6
Transmission due to FFP:	12
TTBI related fatalities due to HBV infection:	2
Reporting frequency after application of RBC (1997 – 2000):	1.01 per 10 ⁶ units
Reporting frequency after application of RBC (2005 – 2008):	0.46 per 10 ⁶ units
Benefit of NAT mini pool testing (1999/ 2004):	1 HCV- transmission 1 HIV- transmission

7 of 22 HBC- transmissions (32%) were caused by donors, with positive results from retrospective anti-HBc testing (deferred samples). In 14 cases (64%) retrospective anti-HBc testing revealed negative results. In one case no retrospective anti-HBc testing was performed.

Retrospective HBV- NAT testing of the deferred samples was not performed in three cases during the period 1997 – 1998. NAT testing was positive in 17 of the other 19 HBV transmissions (89%). In two cases no HBC genome was detected at the time of transmission by the single donor testing.

After the implementation of the NAT donor screening one case of HIV- transmission and one case of HCV- transmission was reported ([Table 8](#) and [Table 9](#)). In both cases RBC- donors were tested negative by the NAT mini pool testing [15]. In contrast to this, a frequency of two HBC- transmissions on average per year was reported in the period from 1997 to 2006. After the implementation of anti-HBc- single donor screening two cases of HBV- transmission were confirmed within two years (2007 and 2008).

5. Summary/ Conclusions

With regard to all reports

- On the basis of haemovigilance data the reporting frequency can be identified, but not the incidence of serious adverse transfusion reactions.
- The reporting frequency is also influenced by the awareness of specific transfusion complications (e. g. TRALI).

For the period 2005 – 2008 the following conclusion can be drawn:

- The most frequently reported complication were: ATR > TRALI > HTR > TTBI
- The most frequently reported complications due to PC were:
13 ATR cases per 10⁶ units and 10 TTBI- cases per 10⁶ units
- The most frequently reported complications due to RBC were:
6.2 ATR- cases per 10⁶ units und 2.4 HTR- cases per 10⁶ units
- The most frequently reported complications due to FFP were:
11 TRALI cases per 10⁶ units
- The most frequently reported transfusion related fatalities were:
TRALI > ATR > HTR and TTBI

With regard to allergic transfusion reactions

- A significant increase in ART was registered after the application of PC and RBC, which was confirmed by other haemovigilance systems.
- The reasons are unknown, but an improved reporting compliance and an increasing tendency to allergic reactions could be assumed.

With regard to transfusion-related acute lung injury (TRALI)

- The reporting frequency of TRALI after FFP application increased noticeably with the initiation of an enhanced surveillance.
- The great majority of antibody-mediated TRALI was reported after the application of FFP.
- The plasma was derived from female donors with a history of pregnancy.
- At the moment it is too early to assess the benefit of excluding all female donors with a positive history of pregnancy, who were not tested negative for HLA- or HNA-antibodies (implementation of the safety measure: 09/2009) [16].

With regard to haemolytic transfusion reactions

- The great majority of the reported reactions were acute haemolytic transfusion reactions (< 24 h after the onset of transfusion).
- It has to be assumed that not all cases of delayed HTR were reported to the PEI.
- Because of the small number of reported delayed haemolytic transfusion reactions it is difficult to assess the benefit of extended screening such as a testing of recipient specific blood group antigens [17] or enhanced donor screening.

With regard to transfusion-transmitted bacterial infections

- During the period of 12 years the reporting frequency of transfusion-transmitted bacterial infections after the administration of PC remained at a figure of approximately 10 cases per 10^6 units.
- Related fatalities were mostly triggered by agents with medium to high pathogenicity.
- Fatalities after PC administration were found with concentrates which had reached the end of their shelf life.
- A reduction of the reporting frequency of TTBI after the implementation of the pre-donation sampling (2002) could not be confirmed.
- Reasons for the missing effect could be assumed: Underreporting as well as the absences of febrile reactions in recipients with antibiotic treatment despite the confirmation of agents, etc.
- Effective screening test are not available at present, which have sufficient sensitivity and which are able to detect agents in a timely manner.
- Therefore Opinion 38 of the German Advisory Committee Blood recommends a limitation of the shelf life of platelet concentrates to 4 days (4 x 24h) beginning at midnight on the day when the blood was drawn.

With regard to transfusion-transmitted viral infections

- After the implementation of serologic single donor testing at the end of the 1990s it was possible to prevent viral transmission to a large extent.
- NAT mini pool testing (1999 and 2003) was able prevent HIV- und HCV-transmission almost completely.
- HBsAg single donor screening was able to reduce the reporting frequency to 1 – 3 cases of HBV- transmission per year.
- The implementation of the anti-HBc single donor testing (2006) should lead to a further reduction of the diagnostic window period.
- The follow-up testing of the deferred samples showed positive anti-HBc results in a third of all cases of confirmed HBC transmission by the time of transmission.
- In contrast to that, HBV- follow-up testing of the deferred samples showed positive results in 90% of all cases.
- It remains unclear which of these donors would have been detected by NAT mini pool testing.

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7. Tables

Table 1 Frequency of reported serious adverse transfusion reactions according to the EHN criteria and related fatalities (1997 – 2008)

Serious adverse transfusion reactions (SAR)	Reported SAR (suspicious cases) Total number	SAR according to EHN criteria Total number (Percentage)	SAR related fatalities Total number
Allergic transfusion reaction (ATR)	1220	256 (33.8%)	15
Transfusion related acute lung injury (TRALI)	591	184 (24.3%)	19
Haemolytic transfusion reaction (HTR)	219	132 (17.4%)	9
Transfusion transmitted bacterial infection (TTBI)	173	77 (10.1%)	9
AB0 Incompatibility**	50	50 (6.6%)	6
Transfusion transmitted viral infection (TTVI)	3003	47 (6.2%)	2
Post Transfusion Purpura (PTP)	10	10 (1.3%)	0
Transfusion associated GVHD (TA-GVHD)	3	2 (0.3%)	1
Total	5269	758 (100%)	61 (8.05%)*

* Related to 758 (100%) serious transfusion reactions according the EHN- criteria

** Voluntary reporting, not requested by legislation

Funk MB, et al. Bundesgesundheitsblatt 2010; 53 (4): 347 - 56 [18].

Table 2 Reporting frequency of confirmed severe allergic transfusion reactions (ART) and associated fatalities related to blood components (period: 1997 – 2007)

	1997	1998	1999	2000 [#]	2001	2002	2003	2004	2005	2006	2007	2008	97 – 08
Severe allergic transfusion reactions after the administration of:													
RBC	2	2	3	6	5	7	9	14	18	35	32	23	156
PC	0	0	2	2	1	1	8	2	7	4	7	4	38
FFP	1	0	0	3	2	3	1	6	1	2	7	3	29
Combination	2	1	1	1	4	1	2	5	3	4	3	6	33
Total	5	3	6	12	12	12	20	27	29	45	49	36	256
Fatalities after the administration of:													
RBC	0	0	0	1	2	0	1	0	2	0	0	1	7
PC	0	0	0	0	0	0	1	0	0	0	1	0	2
FFP	0	0	0	0	0	1	0	0	0	1	0	0	2
Combination	1	0	1	0	1	1	0	0	0	0	0	0	4
Total	1	0	1	1	3	2	2	0	2	1	1	1	15
Reporting frequency of severe allergic transfusion reactions for the period:													
	1997 - 2000		2001 - 2004		2005 - 2008								
	Transfused Concentrates* x 10 ⁶	ATR (total no.) per 10 ⁶	Transfused Concentrates* x 10 ⁶	ATR (total no.) per 10 ⁶	Transfused Concentrates* x 10 ⁶	ATR (total no.) per 10 ⁶							
RBC	15.837	(13) 0.82	16.340	(35) 2.14	17.417	(108) 6.20							
PC	1.294	(4) 3.09	1.311	(12) 9.15	1.671	(22) 13.17							
FFP	6.346	(3) 0.47	4.781	(12) 2.51	4.474	(13) 2.91							

[#] Implementation of Leukocyte-depletion of blood cell components

* Estimated consumption

Table 3 Reporting frequency of immune and non-immune mediated TRALI, and associated fatalities related to blood components (period: 1997 – 2007)

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	97 – 08
TRALI cases according to EHN- criteria with HLA-/HNA-antibody donor testing:													
negative	0	0	1	1	2	3	3	4	5	4	5	5	33
positive	4	6	2	4	3	3	14	13	12	17	18	14	110
Not done	3	5	6	7	7	5	2	3	3	0	0	0	41
Total	7	11	9	12	12	11	19	20	20	21	23	19	184
TRALI, HLA-/HNA-antibody test results positive in:													
RBC donors	3	1	1	1	2	0	2	1	5	2	1	0	19
PC donors	0	1	0	0	0	0	2	1	0	1	1	1	7
FFP donors	1	4	1	3	1	3	10	11	7	14	16	13	84
Total	4	6	2	4	3	3	14	13	12	17	18	14	110
TRALI related fatalities, HLA-/HNA-antibody test results positive in:													
RBC donors	0	0	0	0	0	0	1	1	0	1	0	0	3
PC donors	0	0	0	0	0	0	0	0	0	0	0	0	0
FFP donors	0	0	0	0	0	0	1	1	2	2	5	5	16
Total	0	0	0	0	0	0	2	2	2	3	5	5	19
Reporting frequency of immune mediated TRALI for the period:													
	1997 - 2000		2001 - 2004		2005 - 2008								
	Transfused concentrates* x 10 ⁶	TRALI (total no.) per 10 ⁶	Transfused concentrates* x 10 ⁶	TRALI (total no.) per 10 ⁶	Transfused concentrates* x 10 ⁶	TRALI (total no.) per 10 ⁶							
RBC	15.837	(6) 0.38	16.340	(5) 0.31	17.417	(8) 0.46							
PC	1.294	(1) 0.77	1.311	(3) 2.28	1.671	(3) 1.80							
FFP	6.346	(9) 1.42	4.781	(25) 5.23	4.474	(50) 11.18							

Columns highlighted grey mark the implementation of leukocyte-depletion (2000) and the implementation of the enhanced TRALI- surveillance (2006).

* Estimated consumption

Table 4 Data of HLA- and HNA- antibody positive donors involved in 35 cases of antibody-mediated TRALI in the period from 2006 to 2007

	TRALI without fatalities	TRALI- related fatalities	Total
Number of recipients	27	8	35
Donors with WBC antibodies	30	10	40*
FFP- donors	26	8	34**
PC- donors	2	0	2
RBC- donors	2	2	4***
Median age of donors [years] (range)	46 (30 – 68)	42 (35 – 56)	43 (30 – 68)
Male donor	1	0	1
Female donors	29	10	39
History of known pregnancies	25	9	34
Median number of pregnancies per donor	2.5	2.0	2.5
Median period [months] between last pregnancy and donation (range)	114 (19 – 480)	138 (72 – 192)	120 (19 – 480)
Results of WBC-Ab testing			
HLA I – Ab positive	4	0	4
HLA II – Ab positive	12	3	15
HLA I- and HLA II- Ab positive	8	5	13
HNA-2a- Ab positive	1	0	1
HNA-3a- Ab positive	5	2	7

* 5 recipients received two different WBC- antibodies from 2 different donors

** 4 recipients received FFP each from two WBC- Ab positive donors

*** 1 recipient received RCP from two WBC- Ab positive donors

Keller-Stanislawski B, et al. Vox Sanguinis 2010; 98 (1): 70 - 7. [14].

Table 5 Haemolytic transfusion reactions (HTR), associated fatalities and reporting frequency related to blood components (period: 1997 – 2007)

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	97 – 08
Hämolytic transfusion reactions after the administration of:													
RBC	22	11	7	2	4	3	2	16	14	14	6	8	109
PC	0	0	0	0	1	1	0	2	0	1	1	1	7
Combination	1	0	2	1	1	2	2	1	2	2	2	0	16
Total	23	11	9	3	6	6	4	19	16	17	9	9	132
Acute and delayed haemolytic transfusion reaction and allo-antibody detection													
Acute HTR	22	10	5	2	6	4	4	18	14	16	7	8	116
Delayed HTR	1	1	4	1	0	2	0	1	2	1	2	1	16
Allo-antibodies	1	1	2	1	0	1	0	1	1	1	1	1	11
Total	23	11	9	3	6	6	4	19	16	17	9	9	132
Haemolytic transfusion reaction and fatalities after administration of:													
RBC	0	2	2	0	0	0	0	1	0	2	0	0	7
Combination	0	0	1	0	0	0	0	1	0	0	0	0	2
Total	0	2	3	0	0	0	0	2	0	2	0	0	9
Reporting frequency of haemolytic transfusion reaction for the period from:													
	1997 - 2000		2001 - 2004		2005 - 2008								
	Transfused Concentrates* x 10 ⁶	HTR (total no.) per 10 ⁶	Transfused Concentrates* x 10 ⁶	HTR (total no.) per 10 ⁶	Transfused Concentrates* x 10 ⁶	HTR (total no.) per 10 ⁶							
RBC	15.837	(42) 2.65	16.340	(25) 1.53	17.417	(42) 2.41							
PC	1.294	(0) 0.00	1.311	(4) 3.05	1.671	(3) 1.80							

* Estimated consumption

Table 6 Transfusion- transmitted bacterial infections (TTBI), associated fatalities and reporting frequency related to blood components (period: 1997 – 2007)

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	97 – 08
Transfusion- transmitted bacterial infections after administration of:													
RBC	4	5	1	0	4	3	2	2	3	2	6	2	34
PC	0	2	4	2	4	3	4	3	6	4	2	4	38
FFP	0	4	0	0	0	0	0	0	1	0	0	0	5
Total	4	11	5	2	8	6	6	5	10	6	8	6	77
Transfusion- transmitted bacterial infections related fatalities after administration of:													
RBC	2	2	0	0	0	0	0	0	0	0	0	0	4
PC	0	0	0	1	0	1	1	1	1	0	0	0	5
FFP	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	2	2	0	1	0	1	1	1	1	0	0	0	9
Reporting frequency of transfusion-transmitted bacterial infections for the period from:													
	1997 - 2000			2001 - 2004			2005 - 2008						
	Transfused concentrates* x 10 ⁶	TTBI (total no.) per 10 ⁶		Transfused concentrates* x 10 ⁶	TTBI (total no.) per 10 ⁶		Transfused concentrates* x 10 ⁶	TTBI (total no.) per 10 ⁶					
RBC	15.837	(10) 0.63		16.340	(11) 0.67		17.417	(13) 0.75					
PC	1.294	(12) 9.27		1.311	(14) 10.68		1.671	(16) 9.57					
FFP	6.346	(4) 0.63		4.781	(0) 0.00		4.474	(1) 0.22					

Small box highlighted grey marks the implementation of the Pre-donation sampling (2002)

Small box highlighted grey marks the limitation of the shelf life of platelet concentrates to 4 days (Opinion 38 of the German Advisory Committee Blood)

* Estimated consumption

Table 7: Results of microbiological analyses in 77 cases of transfusion-transmitted bacterial infections (1997 to 2008)

Agent	Number of blood components with recipient related microbiological analysis				Clinical course of recipients		Fatalities caused by	
	RBC	PC	FFP	Sum	not fatal	fatal	RBC	PC
Agents with low pathogenicity	15	17	2	34	33	1	0	1
Staphylococcus capitis, epidermidis, hominis, saprophyticus und spp.								
Micrococcus luteus								
Corynebacterium spp.								
Propionibacterium acnes								
Agent with medium / high pathogenicity	19	21	3	43	35	8	4	4
Staphylococcus aureus, pyogenes und spp.								
Bacillus cereus								
Escherichia coli								
Enterobacter erogenes, amnigenus								
Klebsiella oxytoca, pneumonia								
Pantoea agglomerans								
Serratia marcescens								
Yersinia enterocolitica								
Enterococcus spp.								
Acinetobacter Iwoffii								
Pseudomonas aeruginosa								
Stenotrophomonas maltophilia								
Total	34	38	5	77	68	9	4	5

* Administration of platelet concentrates at day 4 or day 5 after production

Keller-Stanislawski B, et al. Transfusion Medicine 2009; 19 (6): 340 - 9. [8]

Table 8 Transfusion- transmitted viral infections (HBV, HIV, HCV) and reporting frequency related to blood components (period: 1997 – 2007)

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	97 – 08
HBV infection after administration of:													
RBC	1	1	2	1	0	1	1	2	2	3	1	1	16
PC	0	1	0	0	0	0	2	0	0	0	0	0	3
FFP	0	0	0	0	2	0	0	1	0	0	0	0	3
Total	1	2	2	1	2	1	3	3	2	3	1	1	22
HIV infection after administration of:													
RBC	0	1	0	3	0	0	0	0	0	0	1	0	5
PC	0	0	0	0	0	0	0	0	0	0	0	0	0
FFP	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	0	1	0	3	0	0	0	0	0	0	1	0	5
HCV infection after administration of:													
RBC	4	3	0	0	0	0	0	1	0	0	0	0	8
PC	2	1	0	0	0	0	0	0	0	0	0	0	3
FFP	0	9	0	0	0	0	0	0	0	0	0	0	9
Total	6	13	0	0	0	0	0	1	0	0	0	0	20
Reporting frequency of transfusion- transmitted viral infections for the period of:													
	1997 - 2000			2001 - 2004			2005 - 2008						
	Transfused concentrates* x 10 ⁶	TTVI (total no.) per 10 ⁶		Transfused concentrates* x 10 ⁶	TTVI (total no.) per 10 ⁶		Transfused concentrates* x 10 ⁶	TTVI (total no.) per 10 ⁶					
RBC	15.837	(16) 1.01		16.340	(5) 0.31		17.417	(8) 0.46					
PC	1.294	(4) 3.10		1.311	(2) 1.53		1.671	0.00					
FFP	6.346	(9) 1.42		4.781	(3) 0.63		4.474	0.00					

Column highlighted grey marks the implementation of HCV- NAT mini pool testing (1999)

Column highlighted grey marks the implementation of HIV- NAT mini pool testing (2004)

Column highlighted grey marks the implementation of anti- HBc single donor testing

* Estimated consumption

Table 9 Registered HCV NAT only- and HIV1 NAT only- donations after the implementation of the NAT- pool testing (1999 – 2007)

	NAT testing period (mandatory)	Donations tested	Confirmed NAT only donations Yield Cases*	Yield cases / donations tested	Yield Cases / million donations	Break-through transmissions**
HCV	1999 - 2007	40.837.537	92	1 / 444.000	2.25	1
HIV-1	2004 - 2007	17.112.872	11	1 / 1.556.000	0.64	1

* First time donors and regular donors with positive results of NAT pool-testing and negative results in antibody screening tests leading to donor-exclusion

** In both cases negative test results were found with serological single donor testing and NAT- pool-testing

Nübling CM, et al. Transfusion 2009; 49 (9): 1850 - 8. [15]

Table 10 Manufacturing and estimated usage of blood components during the period 1999 – 2008, reports to the PEI according to TFG Section 21

Year	RBC		PC		PFP	
	Manufacturing units x 10 ⁶	Consumption* units x 10 ⁶	Manufact. units x 10 ⁶	Consumpt.* units x 10 ⁶	Manufact. units x 10 ⁶	Consumpt.* units x 10 ⁶
1999	4.28	3.99	0.41	0.32	1.81	1.74
2000	4.26	3.93	0.42	0.33	1.53	1.43
2001	4.32	4.03	0.39	0.32	1.45	1.38
2002	4.45	4.12	0.38	0.33	1.28	1.23
2003	4.24	3.93	0.37	0.30	1.11	1.05
2004	4.54	4.26	0.41	0.36	1.18	1.11
2005	4.56	4.29	0.43	0.38	1.09	1.03
2006	4.52	4.29	0.45	0.41	1.10	1.05
2007	4.57	4.35	0.48	0.43	1.27	1.22
2008	4.71	4.49	0.51	0.45	1.23	1.17

* The figures were calculated based on the data of expiry reported by the manufacturer and the user