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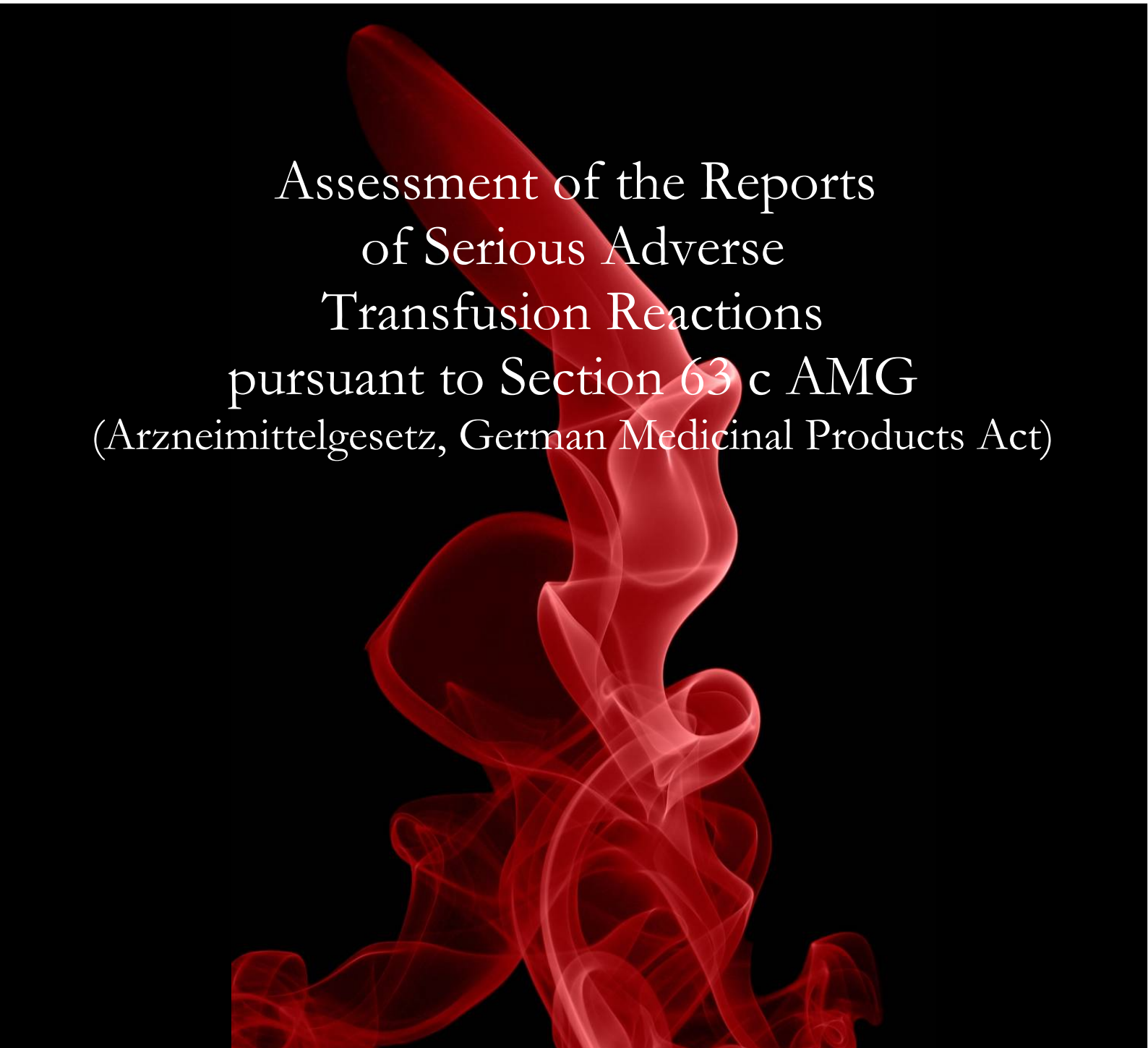

Assessment of the Reports of Serious Adverse Transfusion Reactions pursuant to Section 63 c AMG

(Arzneimittelgesetz, German Medicinal Products Act)

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Paul-Ehrlich-Institut (PEI, Langen)
Bundesinstitut für Impfstoffe und
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Paul-Ehrlich-Straße 51–59
63225 Langen

Editor

PD Dr. Markus Funk
Dr. Serife Günay
Pharmakovigilanz II, PEI
Tel.: +49 (0)6103/77–1060
E-Mail: pharmakovigilanz2@pei.de

Dr. Corinna Volz-Zang,
Pressestelle PEI
Tel.: +49 (0)6103/77–1093
E-Mail: Corinna.Volz-Zang@pei.de

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The Paul-Ehrlich-Institut is an institution of the Federal Republic of Germany.

Following colleagues contributed on this report:

Dr. Annette Lohmann[1], Herr Jochen Halbauer[1], Frau Cornelia Witzenhausen[1], Frau Klaudia Wesp[1], Herr Olaf Henseler[2] und Dr. Brigitte Keller-Stanislawski[1]

[1] Department S: Department Safety of Medicinal Products and Medical Devices
[2] Department 7: Department of Haematology and Transfusion Medicine

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Mrs. Constanze Taylor and Mrs. Dagmar Fecht-Schwarz

Contents

1. Introduction

This current haemovigilance report from the Paul-Ehrlich-Institut summarises the reporting data from 2010 and compares the data from the past thirteen years (1997 – 2009) with the current haemovigilance data. With regard to individual transfusion reactions, the report refers to the data from other haemovigilance systems [1 – 4].

In evaluating the data, a further increase in serious allergic transfusion reactions is observed – a development which has already manifested itself in the past year. This has also been confirmed by other haemovigilance systems. On the other hand, after the decrease in immunogenic TRALI reactions, which could already be seen in the past year due to the introduction of measures to reduce the risk of TRALI in the manufacture of therapeutic fresh plasma in September 2009, confirmed immunogenic TRALI reactions have decreased even further. The Paul-Ehrlich-Institut considers these 15 month data as evidence that this largely discussed measure has been effective.

New items were included into the reporting such as transfusion-associated circulatory overload, donor look-back procedures, and reports on serious events in the manufacture of blood components. In compliance with Directive 2005/61/EC, the Paul-Ehrlich-Institut has reported all confirmed serious transfusion reactions and events to the European Commission. The consolidation of all relevant haemovigilance data shall serve to evaluate the safety standards for blood components throughout Europe in the future.

As has already been emphasised in previous reports, a functioning haemovigilance system is an essential prerequisite for accurate documentation of adverse events on the part of the treating physicians and the blood donations facilities concerned as well as for a standardised and transparent evaluation of the data reported on the part of the Paul-Ehrlich-Institutes. The evaluation of the events reported serve to show the frequency and severity of the transfusion reactions in order to discuss possible improvement in the transfusion system and to establish measures that may possibly be required. The Paul-Ehrlich-Institut would like to express thanks to all individuals and (blood donation) facilities who helped collect the data available.

2. Abbreviations

AML	Acute myeloid leukaemia
AK Blut	German Advisory Committee Blood / national advisory board for transfusion
AMG	Arzneimittelgesetz (German Medicinal Products Act ("The Drug Law")
Anti-HBc	Antibodies against hepatitis B-core antigen
ATR	Acute transfusion reactions
BNP	Brain natriuretic peptide
CML	Chronic myeloid leukaemia
FFP	Fresh frozen plasma
GvHD	Graft versus Host Disease
HLA	Human Leucocyte Antigen
HNA	Human Neutrophil Antigen
HTR	Haemolytic transfusion reaction
IHN	International Haemovigilance Network
LDH	Lactate dehydrogenase
NAT	Nucleic acid amplification technique
PEI	Paul-Ehrlich-Institut
PC	Platelet concentrate
RBC	Red blood cell concentrate
SAR	Serious adverse reaction
TACO	Transfusion-associated circulatory overload/ Transfusion-associated volume overload
TTBI	Transfusion transmitted bacterial infection
TTVI	Transfusion transmitted viral infection
TRALI	Transfusion related acute lung injury

3. Methods

All reports of serious adverse transfusion reactions received by the Paul-Ehrlich-Institut conforming to Section 16 paragraph 2 TFG (Transfusionsgesetz, German Transfusion Act) are registered in the database of the Paul-Ehrlich-Institut. The reporting physician documents all relevant recipient data, such as transfused blood components, age, gender, underlying diseases, concomitant diseases, and the course of the adverse reaction by using a standardised questionnaire. The blood establishment involved supplements this information by providing specific data of the donor(s), results of analyses and look back procedures. Reported reactions are assessed as transfusion reactions conforming to the criteria of the International Haemovigilance Network (IHN). Near miss events and incorrect blood components transfused were reported to the PEI on a voluntary basis. Conforming to the Transfusion Act, it is mandatory to report AB0 incompatible transfusions to the transfusion officer of the appropriate hospital. Measures taken to prevent medication errors should therefore be implemented within the hospital.

3.1 Categories of transfusion reactions

The definitions of the serious adverse transfusion reactions are largely based on the recommendation of the IHN [5]. The adverse reactions were classified and evaluated according to the criteria in Box 1: Definition of serious adverse transfusion reactions (in accordance with the IHN criteria).

Primarily, the reporting frequencies of serious adverse transfusion reactions were considered to evaluate the benefit of measures taken to improve the safety standard of blood components. Cases of an acute (allergic) transfusion reaction reported in 2010 were subdivided into further categories with the aid of the classification of the Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF, Scientific Medical Committees) [6]. Conforming to this classification, a distinction was made between allergic transfusion reactions, Grade I and Grade II and serious allergic or anaphylactoid transfusion reactions, Grade III and Grade IV.

To confirm the suspected diagnosis of TRALI, a reporting questionnaire (see www.pei.de – haemovigilance – reporting questionnaire H2c) as well as a standardised questionnaire are used to record the criteria for TRALI in conformity with the specifications of the IHN.

Febrile non-haemolytic transfusion reactions (FNHTR) were described in this report for the first time for 2010. Since these cases are by definition only low-grade or medium-grade reactions, they were not included in the table of serious transfusion reactions (Table 1).

Conforming to Section 21 TFG, the amount of blood components prepared by the German blood donation facilities and the loss at manufacturers and users are reported to the PEI [7]. The approximate actual annual consumption of the individual blood components can be estimated and is published in the report by the PEI pursuant to Section 21 TFG on a regular basis (Table 9). In Tables 2-7, the reporting frequency of transfusion reactions per each blood component is determined for a period of four years, and a total of three four-year-periods and two single calendar years (2009 and 2010) are compared with each other.

Box 1: Definition of serious transfusion reactions (conforming to the IHN criteria)

Acute transfusion reaction (ATR):

Rash, itching, urticaria, exanthema, allergic dyspnoea, angiooedema, laryngeal oedema, drop in systolic blood pressure by > 30 mmHg, tachycardia (increase in heart rate > 30 beats/ min.) bronchospasm/cyanosis, shock, loss of consciousness. Onset of the symptoms during or within 24 hours of transfusion, and without any indication of other cause.

Transfusion-related acute lung injury (TRALI):

Acute respiratory distress (occurrence during or within 6 hours of the completion of the transfusion), dyspnoea, hypoxemia, new bilateral lung infiltrations in the chest radiograph, and no evidence of hypervolaemia (cardiac, renal, iatrogenic).

Haemolytic transfusions reaction (HTR):

Pyrexia with a variety of other symptoms (including dyspnoea, hypotension, tachycardia, flank or back pain, etc.), gross haematuria, inadequate rise of post-transfusion haemoglobin level, drop in haemoglobin level (>2g/dl within 24 hours), rise in LDH (>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 °C or an increase of > 2 °C from pretransfusion value, chills and tachycardia. TTBI is confirmed by detection of the bacteria in the transfused blood product or in the recipient’s blood and by detection of the same bacterial strain in the recipient's blood and the transfused blood component.

Transfusion transmitted viral infection (TTVI: HBV, HCV, HIV):

A post-transfusion infection of the recipient is strongly suspected when there is a seroconversion. To confirm the causal relationship, the look-back procedure (conforming to Opinion 34/35 of the "AK Blut" (German Advisory Committee Blood) must be performed.

Transfusion associated circulatory overload (TACO):

Respiratory distress, tachycardia, hypertonia, typical signs of cardiogenic lung oedema in the chest radiograph, evidence of a positive liquid balance and/or cardiac injury during or within 12 hours post transfusion.

Febrile non-haemolytic transfusion reaction (FNHTR):

Occurrence of one or more symptoms within 4 hours post transfusion: Fever ≥ 38 °C or increase in temperature by ≥ 1 °C post transfusion, chills, sensations of cold, possible other symptoms causing malaise, no evidence of HTR or TTBI. Most suspected cases of FNHTR are of non-serious course.

Incorrect blood component transfused (IBCT):

Administration of AB0 incompatible blood components.

3.2 Measures to improve the safety standards

Between 1997 and 2010, a number of measures were implemented or recommended by the PEI and the AK Blut (German Advisory Committee Blood) 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 referring to a single donation).
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 red blood cell and platelet concentrates (residual 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 "AK Blut" (German Advisory Committee Blood (Opinion 27)).
2003	Since May 2004, screening of blood component donors and donors of fresh frozen plasma by HIV NAT pool testing (HIV RNA limit of detection: 10,000 IU/ml).
2006	Since October 2006, screening of blood component donors and donors of fresh frozen plasma 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 "AK Blut" German Advisory Committee Blood (Opinion 38) in order to reduce the danger of a fatal transfusion reaction caused by contaminated PC).
2009	Since September 2009, introduction of donor screening to reduce the risk of TRALI. Blood from female donors may only be admitted to the preparation of plasma if the donors do not have a history of pregnancy and/or if the tests for leucocyte antibodies are negative. The detection for leukocyte antibodies is performed in compliance with the methods described in the literature [8, 9].

4. Results

4.1 Serious transfusion reactions according to IHN criteria (1997 - 2010)

Altogether 702 transfusion reactions were reported to the PEI in 2010. For the period from 1997 - 2010, there was a total number of 6469 reported cases suspected of having had a transfusion reaction. The number of reported cases varied during the entire period between 298 and 702 cases per year (mean value: 498 cases).

100 of 702 cases reported in 2010 were febrile non-hemolytic transfusion reactions which are not listed in table 1. 219 of the remaining 602 reported cases were less serious acute (allergic) transfusion reactions (grade I and II). These cases were no longer taken into account in further evaluations. Out of the 383 remaining serious reactions, the IHN (International Haemovigilance Network) criteria were confirmed in 171 cases, thus establishing a causal relationship between transfusions and reactions (cf. Table 1).

Out of those 171 confirmed transfusion reactions, 110 serious allergic reactions, 29 cases of transfusion associated circulatory overload, 18 haemolytic reactions, four TRALI reactions, four incorrectly transfused blood components, three transfusion transmitted bacterial infections, two transfusion transmitted viral infections, and one case of a post transfusional purpura were documented. No cases of transfusion associated GvHD occurred in 2010.

When observing the period from 1997 to 2010 (cf. Table 1, Figure 1), a similar distribution can be seen. 427 of the 1042 confirmed serious transfusion reactions are allergic reactions, followed by TRALI reactions (201), haemolytic reactions (157), transfusion transmitted bacterial infections (82), and AB0 incompatibilities (62). With altogether 49 cases of transmissions, transfusion transmitted viral infections were in the lower range of the frequency scale. Whereas there has been a significant increase in severe allergic transfusion reactions, the number of TRALI reactions declined. The number of transfusion transmitted bacterial and viral infections remained constant (cf. Tables 5 and 7 and Figure 3).

In 2010, altogether five fatal outcomes of transfusion reaction were documented, three fatalities after acute allergic transfusion reactions, and two cases after transfusion associated circulatory overload. In the entire period of 14 years (1997 - 2010), 71 fatalities were due to the administration of blood components. The most frequent fatalities documented were TRALI reactions and severe allergic reactions (20 cases each), followed by transfusion transmitted bacterial infections (ten cases and haemolytic transfusion reactions, three after TACO and two after transfusion transmitted viral infections, and one fatality after a GvHD reaction.

4.2 Acute (allergic) transfusion reactions (ATR)

See also Table **2**

IHN criteria for non-serious allergic reactions: Rash, drop in systolic blood pressure < 30 mm Hg, mild allergic dyspnoea.

IHN criteria for severe cases: Drop in systolic blood pressure > 30 mmHg, pronounced dyspnoea, shock, intensive care management.

Since 2009, the reported cases have been subdivided into allergic transfusion reactions Grades I and II and anaphylactoid transfusion reactions Grades III and IV, to obtain better distinguishing criteria. This subdivision has its basis on the guidelines on the treatment of acute anaphylactic reactions of the Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF, Working Group of Scientific Medical Specialist Associations) [6].

Classification of the severity of allergic (transfusion) reaction in compliance with the AWMF

Grade	Skin	Abdomen	Respiratory tract	Cardiovascular system
I	• Itching • Flush • Urticaria • Angiooedema			
II		•Nausea •Abdominal colic	• Rhinorrhoea • Hoarseness • Dyspnoea • Arrhythmia	• Tachycardia (increase ≥20/min) • Hypotension (decrease ≥20mmHg sys.)
III		• Vomiting • Defecation	•Laryngeal edema •Bronchospasm •Cyanosis	• Shock
IV			•Apnoea	•Cardio-vascular arrest

Of 329 reported allergic transfusion reactions, the IHN criteria were confirmed in 178 cases. 68 of these cases were rated as non-severe reactions (Grades I and II), whereas 110 recipients showed symptoms of a serious reaction (Grades III and IV).

Presentation of cases with ATR (see also table 2)

	1997-2009	2010		2010 total	1997-2010
Number of reports	1490			329	1819
IHN criteria confirmed	1294			178	1472
Number of	787	Grade I cases	4	68	855

non-serious cases		Grade II cases	64		
Number of serious cases	317	Grade III cases	95	110	427
		Grade IV cases	15		
Serious ATR following **RBC** administration	243	Grade I cases	1	36	338
		Grade II cases	35		
		Grade III cases	49	59	
		Grade IV cases	8		
		Deaths	2		
Serious ATR following **PC** administration	65	Grade I cases	0	18	97
		Grade II cases	18		
		Grade III cases	13	14	
		Grade IV cases	1		
Serious ATR following **FFP** administration	59	Grade I cases	1	9	88
		Grade II cases	8		
		Grade III cases	18	20	
		Grade IV cases	2		
Serious ATR following **combination** treatment	12	Grade I cases	2	5	34
		Grade II cases	3		
		Grade III cases	15	17	
		Grade IV cases	1		
		Deaths	1		

ATR reporting frequency per 10^6 transfused units in relation to the appropriate period

Products	2005-2008	2009	2010
RBC	6.2	6.2	13.56
PC	13.2	31.6	29.72
FFP	2.91	13.69	17.36

From 2009, the number of serious allergic transfusion reactions rose from 28 to 59 cases. This is equivalent to an increase in the reporting frequency from 6 per 10^6 units per year in 2009 to 13 cases per 10^6 units in 2010. Of 53 patients with ATR following RBC administration, detailed data were available to the PEI. 27 patients had developed an onco-haematologic disorder, 12 had a cardiologic disorder, 6 had a pulmonary complication (COPD, ARDS, pneumonia) and 8 received RBCs during surgical intervention. No specific measures are currently planned to reduce ATR. If the number of cases, however, increases further, a more intensive collection of data must be considered.

Case report from 2010

A 70 year old male patient following renal failure showed reactions of hypotension, arrhythmia, and pulseless ventricular tachycardia 15 minutes after the beginning of the transfusion. Successful resuscitation was achieved after mechanical chest compressions and defibrillation.

4.3 Transfusion associated acute lung insufficiency (TRALI)

See also Table **3** and references [10, 11]

IHN criteria: Acute respiratory distress (symptoms develop within 6 hours following the beginning of the transfusion), dyspnoea, new bilateral lung oedema (confirmed by chest radiograph), no evidence of hypervolaemia (cardiac, renal, iatrogenic).

Of those 60 TRALI reactions reported in 2010, the IHN criteria were fulfilled in 4 cases. 3 of these cases were rated as non-immune TRALI reactions (without evidence of HLA/ HNA-antibodies in the donor), and one case was rated as immune TRALI reaction following administration of RBCs.

Presentation of TRALI cases (see also table 3 and references [10,11])

Period	1997 – 2009	2010	1997 – 2010
Number of reports	586	60	646
IHN criteria confirmed	197	4	201
Number of non-immune TRALI	36	3	39
Number of TRALI without/with incomplete leucocyte Ab (LC-Ab) analysis	41	0	41
Number of immune TRALI	120	1	121
Number of cases with Ab positive FFP donors	89	0	89
Number of cases with Ab positive RBC donors	21	1	22

Number of cases with Ab positive PC donors	10	0	10
Number of cases with Ab positive female donors	120	0	120
Number of cases with Ab positive male donors	3	1	4
Fatal cases after non-immune TRALI	0	0	0
Fatal cases after immune TRALI	20	0	20
TRALI related fatalities due to FFP	16	0	16
TRALI related fatalities due to RBC	3	0	3
TRALI related fatalities due to PC	1	0	1

TRALI reporting frequency per 10^6 transfused units referred to the appropriate period

Products	2005-2008	2009	2010
RBC	0.46	0.88	0.22
PC	1.8	6.77	0
FFP	11.18	4.56	0

The benefit of the measure taken to reduce TRALI (09/2009) can be confirmed.

Case report of immune TRALI (2010)

A 78 year old male patient developed acute respiratory distress with a decrease in the oxygen saturation, lung oedema, and pulmonary infiltrates confirmed in the radiograph after the administration of two RBCs. Pneumonia was considered as possible other suspected cause of the symptoms. Intubation with intensive respiration (PEEP) was indicated. The next day, the symptoms subsided, so that extubation of the patient was possible. HLA Grade I and II antibodies were detected in one of the RBCs. The donor of the RBC was a 48 year old male donor with negative transfusion history. No antigen detection was performed in the recipient.

4.4 Haemolytic transfusion reaction (HTR)

See also Table **4**

IHN criteria: Pyrexia and a variety of other symptoms (including dyspnoea, hypotension, tachycardia, flank or back pain etc.), gross haematuria, drop in haemoglobin level > 2g/dl within 24 hours, rise in LDH > 50% in 24 hours, rise in bilirubin, positive direct antiglobulin test, positive erythrocyte cross match.

Presentation of cases with haemolytic transfusion reaction (see also table 4)

Period	1997 – 2009	2010	1997 – 2010
Number of reports	237	41	278
IHN criteria confirmed	139	18	157
Acute HTR	121	9	130
Delayed HTR	18	9	27
Delayed HTR, alloantibodies (irregular erythrocytic Ab)	13	9	22
HTR due to RBC	115	16	131
HTR due to PC	7	2	9
HTR due to combined transfusion of blood components	17	0	17
Fatal cases due to HTR	9	0	9
HTR related fatalities due to RBC	7	0	7

HTR reporting frequency per 10^6 transfused units referred to the appropriate period

Products	2005-2008	2009	2010
RBC	2.41	1.32	3.55
PC	1.80	0	4.25

Case report of an acute haemolytic transfusion reaction (2010)

An 80 year old woman with underlying onco-haematologic disorder received two RBCs and developed sweating, chills, dyspnoea, bronchospasm, anxiety, hypertension (syst. RR: >200 mmHg), and exanthema of the extremities. Her LDH level rose from 398 U/l to 986 U/l, and bilirubin rose from 3.68 mg/dl to 9.76 mg/dl. The direct antiglobulin test was positive before and after the transfusion, Ab detection and erythrocyte cross match, however, were negative. The presence of a clinically relevant alloantibody was rated as unlikely.

Case report of delayed haemolytic transfusion reaction (2010)

A 70 year old male patient received multiple transfusions and multiple RBC due to ruptured abdominal arterial aneurysm. 13 days post transfusion, haemolytic serum was detected without further symptoms as an incidental finding. The direct Coombs test was positive and a newly identified anti-Kell antibody could be identified.

4.5 Transfusion transmitted bacterial infections (TTBI)

See also Table **5**, Table **6** and References [12]

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

Presentation of cases with transfusion transmitted bacterial infections (see also tables 5, 6 and References [12])

Period	1997 – 2009	2010	1997 – 2010
Number of reports	189	31	220
IHN criteria confirmed	87	3	90
TTBI due to PC	49	2*	51
TTBI due to RBC	33	1	34
HTR due to FFP	5	0	5
TTBI related fatalities	12	0	12
TTBI related fatalities due to PC	8	0	8**
TTBI related fatalities due to RBC	4	0	4
Fatal course in recipients with relevant immunosuppression	9	0	9***

* Administration of an apheresis platelet concentrate led to TTBI in both cases

**All eight platelet concentrates had reached the end of the shelf life at the time of transfusion (4th day and 5th day respectively, after manufacture).

***Fatal course occurred in patients with malignant underlying disease (CML, AML, aplastic anaemia, etc.).

TTBI reporting frequency per 10^6 transfused units referred to the relevant period

Products	2005-2008	2009	2010
RBC	0.80	0	0.22
PC	10.77	4.51	4.25
FFP	0.22	0	0

Case reports from 2010

Case 1

A 36 year old woman with AML developed a rise in body temperature, chills, sweating, malaise, urticaria, dyspnoea, and tachycardia after administration of an RBC and an A-PC. The patient showed no signs of haemolysis. The microbiological examination of the

recipient's blood revealed Streptococcus agalactiae (B-streptococcus), which, regularly, have haemolytic properties.

The examination of the residue in the RBC bag showed Streptococci agalactia without any haemolytic properties. The microbiologists hold the view that a causal relationship is possible.

Case 2

A 77 year old male patient with chronic renal insufficiency received RBC and developed chills and a rise in the body temperature > 2 °C. Two hours following the reaction, the symptoms subsided. Pantoea agglomerans could be detected both in the RBC and in the patient's blood.

4.6 Transfusion transmitted viral infections (TTVI: HBV, HCV, HIV)

Criteria in accordance with Opinion 34 of the AK Blut (German Advisory Committee Blood).

Presentation of cases with transfusion transmitted viral infections

Period	1997 – 2009	2010	1997 – 2010
Total number of reports	3077	82*	3159
Number of reports related to HBV	1136	33	1169
Number of reports related to HCV	1784	42	1826
Number of reports related to HIV	157	6	163
Number of cases with likely or confirmed viral transmission (Opinion 34 D)	47	2	49
HBV	22	1	
HCV	20	0	
HIV	5	1	
Transmission due to RBC	29	1	
Transmission due to PC	6	1**	
Transmission due to FFP	12	0	
Fatal cases after HBV transmission	2	0	

* One suspected case of combined HBV and HCV transmission was counted only once.

** The HBV transmission was due to an apheresis PC.

HBV transmission (2009)

The HBV transmission relates to a case from 2009 initially reported to the PEI within a donor related look back procedure. The transmission to a woman patient was confirmed in early 2010. This recipient had received a PC transfusion during the time window phase.

Case of HIV (2010)

Donor deferral and follow-up testing of the previously performed donation occurred due to a positive result of an HIV Ab test and at the same time HIV-NAT pool testing. A negative result could be confirmed in the serological follow-up test. The follow-up test of the deferred sample with a second NAT test showed a positive result and confirmed fresh seroconversion at the time of the previous donation. The examination of the RBC recipient of the previous donation showed fresh seroconversion. An HIV sequence homology in the donor and the recipient confirmed an HIV transmission.

Two other transfusion transmitted viral infections were reported to the PEI: Two cases of a CMV and one case of a hepatitis A transmission. These cases could not be confirmed.

Reporting frequency of TTVI per 10^6 transfused units referred to the respective period

Products	2005-2008	2009	2010
RBC	0.46	0	0.22
PC	0	0	2.12
FFP	0	0	0

After HCV / HIV-NAT donor screening was introduced, altogether three cases of viral transmission due to blood components were documented: One case of HCV transmission and two cases of HIV transmission (Table 7, Figure 5). In all cases, the transmission was caused by RBC donors who tested negative in the NAT examination of the pooled plasma [13]. In contrast to this, the mean frequency of HBV transmissions was 2 cases per year in the period from 1997 to 2006. After donor screening with anti-HBc single testing was introduced (10/2006) three cases of transfusion transmitted HBV infection were confirmed in the 4-year period following this period.

4.7 Transfusion associated circulatory overload, TACO [3]

IHN criteria: Dyspnoea, tachycardia, hypertension, typical signs of cardiogenic lung oedema in the radiography of the thorax, confirmed positive fluid balance and/or cardiac damage within 12 hours following transfusion.

Presentation of cases with transfusion associated circulatory overload

Period of time	2010
Total number of all cases reported	33
Confirmed cases (IHN criteria)	29
RBC	18
PC	2
FFP	2
Combination	7
Fatalities	2*
Underlying diseases of the recipient: Pre-existing cardiovascular disorder, DIC, haemorrhagic shock, known liver cirrhosis, renal disorder	15
Age of the recipients (mean) (range)	62 (14 - 94)

*The fatalities are a 94 and a 79 year old patient with known cardiac insufficiency, and thus an increased risk of cardiac volume overload.

4.8 Febrile non-haemolytic transfusion reactions (FNHTR)

FNHTR is defined by the occurrence of one or more of the following symptoms within 4 h post transfusion:

- Fever ≥ 38 °C or a rise in the body temperature by ≥ 1 °C post transfusion
- Shivering
- Chills
- Sensations of cold
- Other signs of malaise
- Exclusion of HTR or TTBI

FNHTRs are non-serious transfusion reactions by definition. Even though some of the cases were initially monitored in intensive care, the initial symptoms rapidly subsided in all patients without exception. The table below summarises 34 cases of medium-grade FNHTR, however, these cases are not included in the evaluation of serious transfusion reactions.

FNHTR	2010
Total number of all cases reported	100
Medium serious FNHTR	34
Transmission due to RBC	28
Transmission due to PC	3
Transmission due to FFP	0
Transmission due to a combination of products	3

With regard to two cases of FNHTR, HLA Class I antibodies were identified in the recipients as a possible cause. The reaction occurred after the administration of a red blood cell concentrate and a platelet concentrate. In another case of FNHTR, HLA Class I/HLA Class II antibodies could be detected in the recipient after administration of a red blood cell concentrate.

4.9 Number of reported donor related look back procedures and cases of confirmed transmission in 2010

Including cases with a confirmed transmission 2010 and 2009.

Reported cases in 2010		Transmission
HCV	122	
HBV	843	(1*)
HBV + HCV	1	
HAV	2	
HIV	50	1
HIV + Treponema pallidum	1	
Treponema pallidum	5	
CJD	2	
Chron. Toxoplasmosis	1	
Total	**1027**	**1**

*Transmission occurred in 2009. The donor related look back procedure was also introduced in that same year. HBV transmission was confirmed in 2010 (cf. 4.6 Transfusion transmitted viral transmissions).

831 look back procedures were initiated by a positive anti-HBc Test result. In around half of these donors, the anti-HBs examination showed a value >100 U/ml. In none of the cases with an isolated anti-HBc positive donor did an HBV transmission occur. Opinion 34/35 is currently revised by a working party of the "AK Blut" (German Advisory Committee Blood) to reduce the number of look-back procedures in the event of non-specific positive anti-HBc results.

4.10 Listing of reports of serious events in 2010

Listing of the serious events reported which by definition occurred during the manufacture, storage, or transport

None of the blood components affected were released for transfusion. Reports to the PEI were summarised in the table below in defined subgroups.

Reports of serious events	2010
Donor exclusion criteria were known in retrospect to had been fulfilled	146
Adverse donor reactions (allergic reactions)	1
Faults in the material/defective bag systems	5
Contamination during the manufacture	2
Incorrect labelling	3
Test problems/test failures	1
Storage problems (interruption of the cooling chain)	1
Incorrect allocation of products (risk of incorrectly transfused blood components)	1
Total	160

Oncological disease in donors was diagnosed in 87 of 146 of the cases. The presence of disease was not known at the time of donation. Fulfilment of donor exclusion criteria was realized only in retrospect. The presence of disease was not known at the time of the donation.

// 5. Summary/Conclusions //

In relation 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 a raised awareness for specific transfusion complications and the reporting obligation in accordance to set legal obligations [14].

For the period of 2010

- The most frequently reported complications due to PC were:
  29.7 ATR and 4.25 TTBI events per 10^6 units
- The most frequent complications due to RBC were:
  13.1 ATR and 3.55 HTR events per 10^6 units
- The most frequent complications due to FFP were:
  17.4 ATR events per 10^6 units

For the period 1997 – 2010

- The most frequently reported suspected diagnoses were:
  TTVI > ATR > TRALI > HTR > TBBI
- The most frequent transfusion associated fatalities were:
  TRALI, ATR > TBBI and HTR

Acute (allergic) transfusion reactions

- A significant increase in ATR was registered after the application of PC and RBC which was confirmed by other haemovigilance systems [1, 2].
- The reasons are unknown, but an improved reporting compliance and an increasing tendency to allergic reactions is observed.

Transfusion-related acute lung injury (TRALI)

- After the measures to reduce immunogenic TRALI had been implemented, as per September 2009 at the latest, the cases of the TRALI reactions reported as well as associated fatalities decreased.

Haemolytic transfusion reactions

- The reporting frequency for HTR has remained constant in the past few years. No risk-reducing measures are currently planned [15].

Transfusion-transmitted bacterial infections

- In 2010, 31 suspected cases were notified of which in three cases non fatal outcome was confirmed
- Fatal cases were in most cases caused by pathogenic agents with high human pathogenicity.
- Fatalities after PC administration were in almost all cases found with concentrates which at the time of transfusion had reached the end of their shelf-lives.
- Opinion 38 of the German Advisory Committee Blood has therefore – since 2008 – recommended 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.
- After limiting the shelf life, the reporting rate of bacterial infections due to PC is 4.5 and 6.2 cases per 10^6 units for 2009 and 2010, respectively.
- Screening tests suitable for use in practice timely after donation which detect bacterial contaminations with high sensitivity are currently tested.
- The use of pathogen inactivation must be further investigated in comparative studies.
- With regard to the frequency of reported and confirmed bacterial transmissions, there is no significant difference between pool PCs and apheresis PCs.

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 pool testing (1999 and 2003), with the exception of a few cases, was able to prevent HIV- und HCV-transmission almost completely.

- A complete record of all infected donors, however, will not be possible due to the diagnostic window phase and the variability of HIV.
- HBsAg single donor screening led to a reduction of the reporting rate for HBV transmission to one to three cases per year.
- The implementation of anti-HBc single donor testing (2006) enables us to record donors with persisting HBV infection in whom HBsAG is not detectable.
- For 2010, one case of HIV and for 2009 one case of HBV transmission were confirmed.
- The implementation of HCV-NAT pool testing enabled us to test around 40 million donations in the period from 1999 to 2009, 92 with a possible NAT and a negative ELISA test result.
- The implementation of HIV-NAT pool testing enabled us to test around 17 million donations between 2004 and 2007, eleven with a positive NAT and negative ELISA test result [13].
- With the implementation of HIV-NAT pool testing since 2004, the HIV transmission rate is 2 cases per 30 million transfused red blood cell concentrates.

Transfusion-associated circulatory overload (TACO)

- The evaluation of the reports from 2010 confirmed an increased risk for volume overload in patients with cardiovascular diseases and kidney insufficiency [16].

Data on the donor look-back procedure

- The great number of look-back procedures in non-specific positive anti-HBc findings shows the need of a revision of the Opinion 34/35 criteria.

Serious adverse events

- The significance of oncological and neurological/neurodegenerative disorders which became known in retrospect for the safety of blood components should be discussed.

// 6. References //

1. SHOT reports. www.shotuk.org/home.htm
2. Annual Hemovigilance Reports. www.swissmedic.ch/haemo.asp
3. Annual Hemovigilance Reports. www.swissmedic.ch/haemo.asp
4. Andreu G, Morel P, Forestier F, Debeir J, Rebibo D, Janvier G, Hervé P: Hemovigilance network in France: organization and analysis of immediate transfusion incident reports from 1994 to 1998. Transfusion. 2002;42(10):1356-1364
5. International Haemovigilance Network (IHN): Definition of adverse transfusion events. www.ihn-org.net
6. www.uni-duesseldorf.de/AWMF/ll/061-025.htm
7. Gesetz zur Regelung des Transfusionswesens – TFG 1998; BGBI. I S. 175
8. ISBT Working Party on Granulocyte Immunobiology, Bierling P, Bux J, Curtis B, Flesch B, Fung L, Lucas G, Macek M, Muniz-Diaz E, Porcelijn L, Reil A, Sachs U, Schuller R, Tsuno N, Uhrynowska M, Urbaniak S, Valentin N, Wikman A, Zupanska B: Recommendations of the ISBT Working Party on Granulocyte Immunobiology for leucocyte antibody screening in the investigation and prevention of antibody-mediated transfusion-related acute lung injury. Vox Sanguinis. 2009;96:266-269
9. Bux J: Transfusion-related acute lung injury (TRALI): a serious adverse event of blood transfusion. Vox Sanguinis. 2005;89(1):1-10
10. Keller-Stanislawski B, Reil A, Günay S, Funk MB: Frequency and severity of transfusion related acute lung injury (TRALI) – German haemovigilance data (2006–2007). Vox Sanguinis. 2010;98(1):70-77
11. Keller-Stanislawski B, Reil A, Günay S, Funk MB: Frequency and severity of transfusion related acute lung injury (TRALI) – German haemovigilance data (2006–2007). Vox Sanguinis. 2010;98(1):70-77
12. Funk MB, Lohmann A, Guenay S, Henseler O, Heiden M, Hanschmann KMO, Keller-Stanislawski B: Transfusion transmitted Bacterial Infections – Haemovigilance Data of German Blood Establishments (1997–2010). Transfus Med Hemother. 2011;38;266-271
13. Nübling CM, Heiden M, Chudy M, Kress J, Seitz R, Keller-Stanislawski B, Funk MB: Experience of mandatory NAT screening across all blood organizations in Germany: NAT yield versus breakthrough transmissions. Transfusion. 2009;49:1850- 1858
14. Keller-Stanislawski B, Lohmann A, Günay S, Heiden M, Funk MB: The German Haemovigilance System – reports of serious adverse transfusion reactions between 1997 and 2007. Transfusion Medicine. 2009;19(6):340-349
15. Funk MB, Günay S, Lohmann A, Henseler O, Keller-Stanislawski B: Bewertung der Maßnahmen zur Reduktion schwerwiegender Transfusionsreaktionen (Hämovigilanzdaten von 1997 bis 2008). Bundesgesundheitsblatt. 2010;53(4): 347-356
16. Li G, Rachmale S, Kojicic M, Shahjehan K, Malinchoc M, Kor DJ, Gajic O: Incidence and transfusion risk factors for transfusion-associated circulatory overload among medical intensive care unit patients. Transfusion. 2011;51(2):338-343

7. Graphics and tables

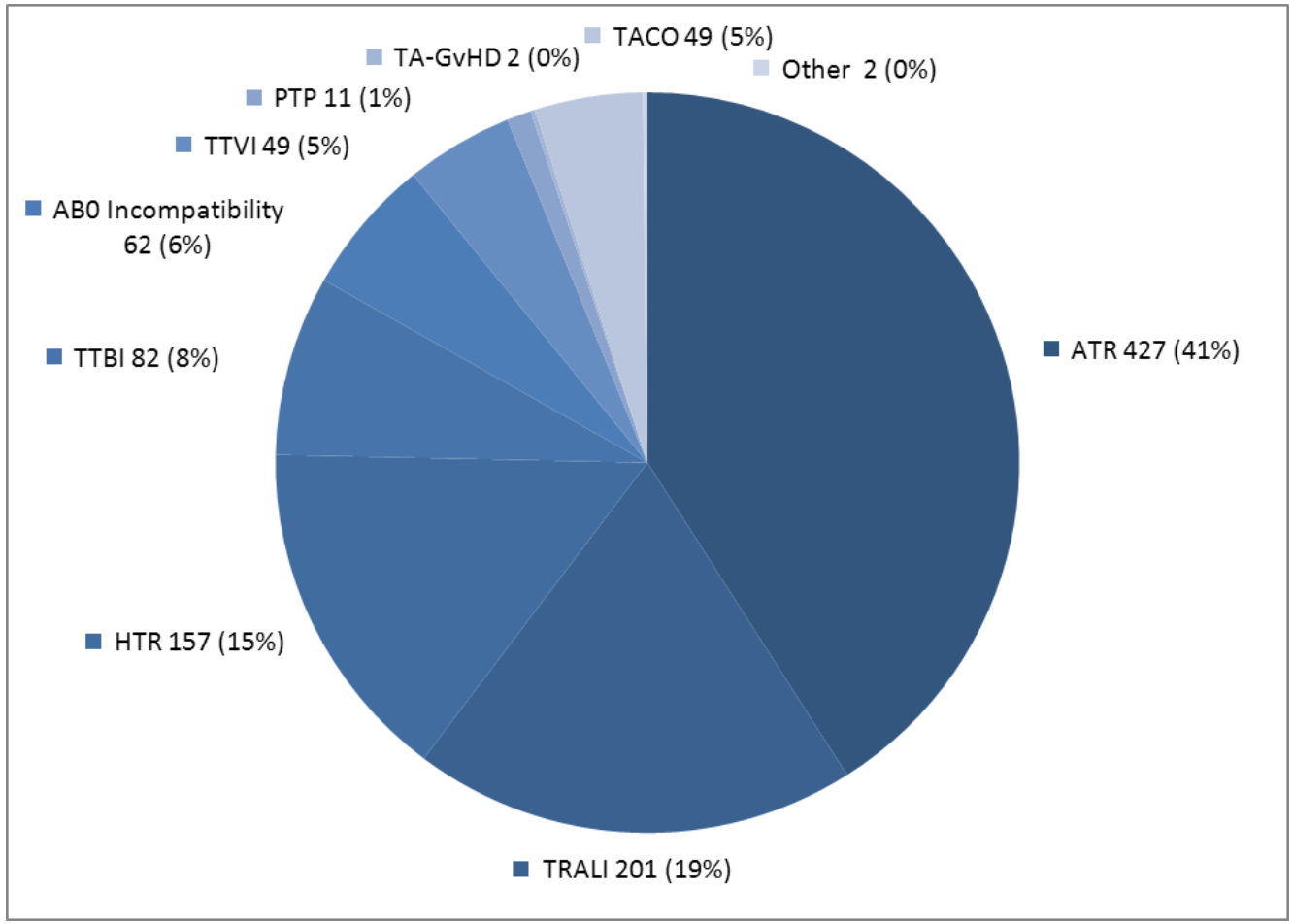

Figure 1:
Number of transfusion reactions (cumulative) (conforming to the IHN criteria) for the period from 1997 – 2010

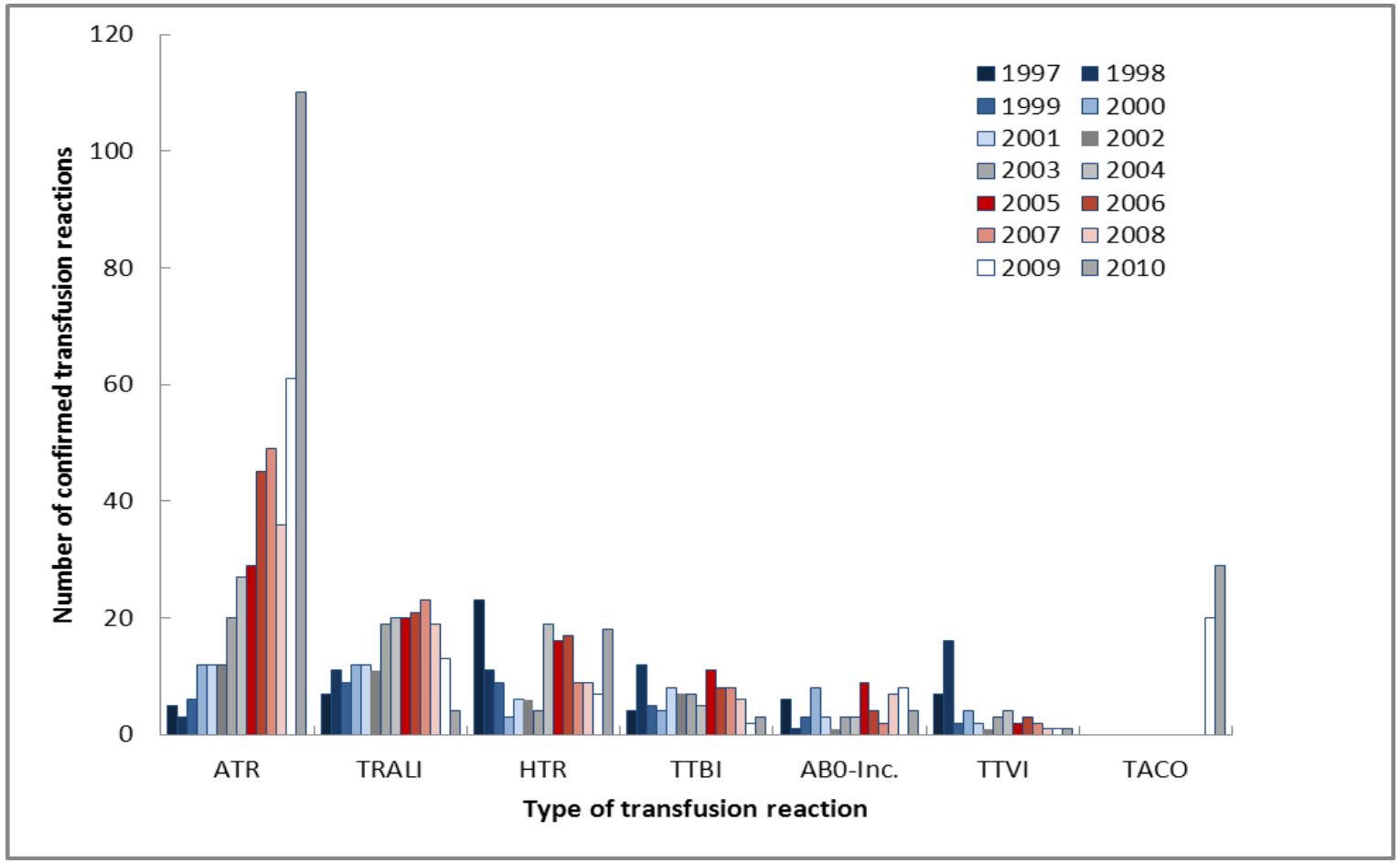

Figure 2:
Comparison of the annual figures for confirmed transfusion reactions (conforming to the IHN criteria) for the period from 1997–2010

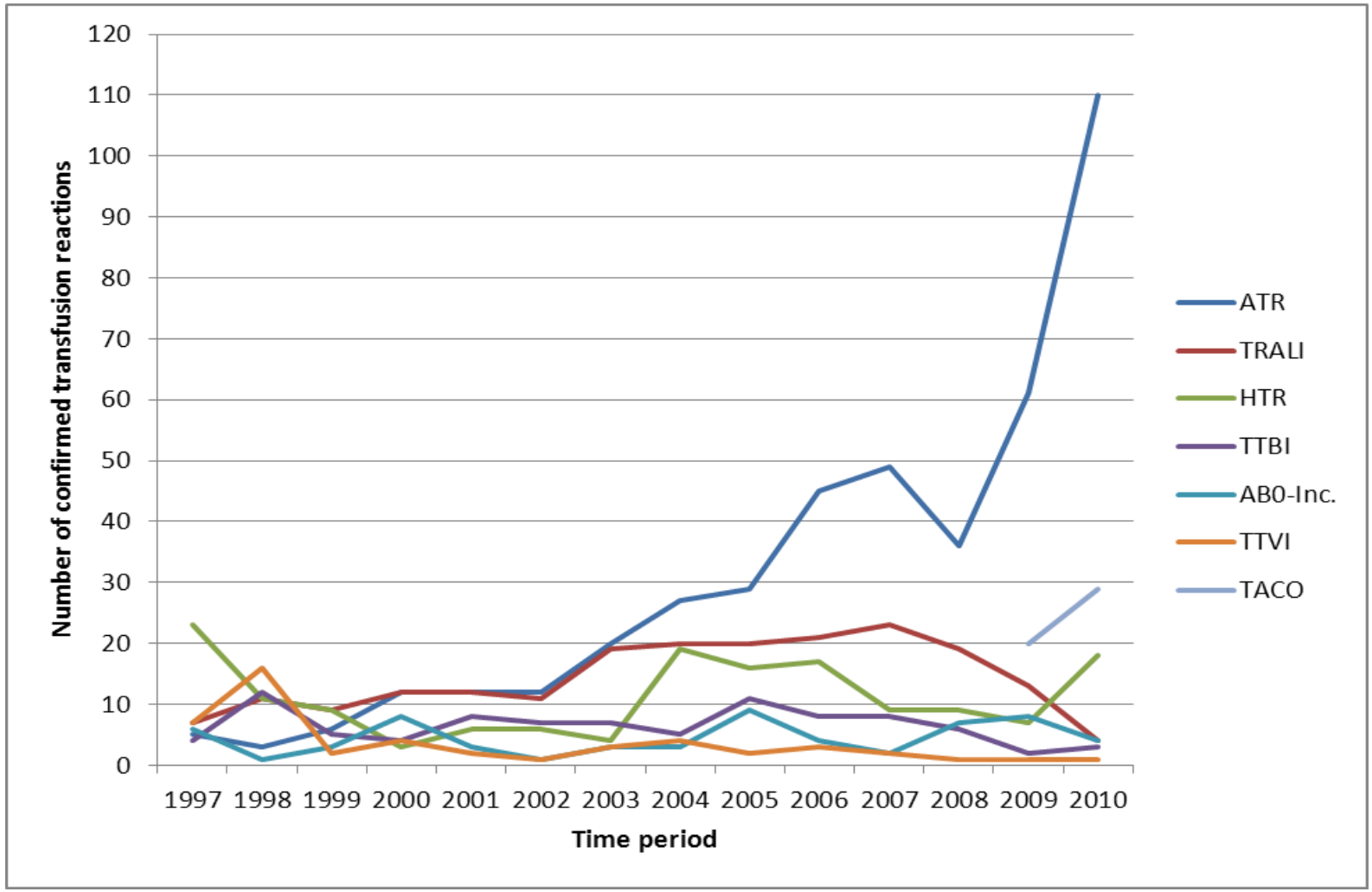

Figure 3:

Frequency of the annual confirmed transfusion reactions for the period from 1997-2010

Table 1 Total number of reported transfusion reactions, serious transfusion reactions (STR) conforming to the IHN criteria and transfusion associated fatalities 1997 – 2009 and 2010

Serious transfusion reactions (STR)	**Reported suspected STR cases**		**STR conforming to the IHN criteria Total (in %)**			**STR with fatal course Total (in %)**		
	1997 – 2009	**2010**	**1997 – 2009**	**2010**	**1997 – 2010**	**1997 – 2009**	**2010**	**1997 – 2010**
Acute (allergic) transfusion reaction (ATR) (Grade I – Grade IV)	1490	329	317 (36.4%)		(36%)			
Serious ATR (Grades III and IV)				110 (64.3%)	427 (41%)	17	3	20
Transfusion-ass. acute lung injury (TRALI)	668	60	197 (22.6 %)	4 (2.3 %)	201 (19.3 %)	20	0	20
Haemolytic transfusion reactions (HTR)	237	41	139 (16 %)	18 (10.5 %)	157 (15.1 %)	9	0	9
Transfusion transmitted bacterial infections (TTBI)	189	31	79 (9.1 %)	3 (1.8 %)	82 (7.9 %)	10	0	10
AB0 incompatibility	58	4	58 (6.7 %)	4 (2.3 %)	62 (6 %)	6	0	6
Transfusion transmitted viral infections (TTVI)	3077	82	47 (5.4%)	2 (1.2%)	49 (4.7 %)	2	0	2
Post transfusional purpura (PTP)	10	1	10 (1.1%)	1 (0.6%)	11 (1.1 %)	0	0	0
Transfusion associated GVHD (TA-GVHD)	3	0	2 (0.2 %)	0	2 (0.2%)	1	0	1
TACO	21	33	20	29 (17 %)	49 (4.7 %)	1	2	3
Other	14	21	2	0	2	0	0	0
Total	**5767**	**602**	**871**	**171**	**1042**	**66 (7.6 %)***	**5 (2.9%)***	**71 (6.8 %)***

* referred to the total number of each confirmed serious transfusion reaction (1997 - 2009: 871, 2010: 171, 1997 - 2010: 1042 is equivalent to 100%)

Table 2 Serious acute (allergic) transfusion reaction (ATR Grades III and IV), associated fatalities and reporting frequencies referred to the blood components transfused

	1997	**1998**	**1999**	**2000***	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**1997 - 2010**
Serious allergic reactions after administration of:															
RBC	2	2	3	6	5	7	9	14	18	35	32	23	28	59	245
PC	0	0	2	2	1	1	8	2	7	4	7	4	14	14	66
FFP	1	0	0	3	2	3	1	6	1	2	7	3	15	20	64
Combined	2	1	1	1	4	1	2	5	3	4	3	6	4	17	55
Total	5	3	6	12	12	12	20	27	29	45	49	36	61	110	430
Fatal cases after administration of:															
RBC	0	0	0	1	2	0	1	0	2	0	0	1	2	2	11
PC	0	0	0	0	0	0	1	0	0	0	1	0	1	0	3
FFP	0	0	0	0	0	1	0	0	0	1	0	0	2	0	4
Combined	1	0	1	0	1	1	0	0	0	0	0	0	0	1	5
Total	1	0	1	1	3	2	2	0	2	1	1	1	5**	3	23
Reporting frequency of serious allergic reactions for the period:															

	1997 – 2000		2001 - 2004		2005 - 2008		2009		2010		
	Transfused. products*** x 10^6	ATR (total no.) per 10^6	Transfused. products*** x 10^6	ATR (total no.) per 10^6	Transfused. products*** x 10^6	ATR (total no.) per 10^6	Transfused. products*** x 10^6	ATR (total no.) per 10^6	Transfused. products*** 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**	4.535	(28) **6.17**	4.500	(59) **13.11**	
PC	1.294	(4) **3.09**	1.311	(12) **9.15**	1.671	(22) **13.17**	0.443	(14) **31.6**	0.471	(14) **29.72**	
FFP	6.346	(3) **0.47**	4.781	(12) **2.51**	4.474	(13) **2.91**	1.096	(15) **13.69**	1.152	(20) **17.36**	

* Implementation of leucocyte depletion
** These cases refer to patients with serious underlying diseases. A relation between the transfusion reaction and the fatal outcome cannot be ruled out.
*** Calculated consumption

Table 3 Reporting frequency of immune and non-immune mediated TRALI and associated fatalities related to the transfused blood components

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	1997 - 2010
TRALI cases conforming to IHN criteria, donor testing for HLA-/HNA antibodies:															
Negative	0	0	1	1	2	3	3	4	5	4	5	5	3	3	39
Positive	4	6	2	4	3	3	14	13	12	17	18	14	10	1	121
Not done	3	5	6	7	7	5	2	3	3	0	0	0	0	0	41
Total	7	11	9	12	12	11	19	20	20	21	23	19	13	4	201
TRALI, HLA-/HNA antibody test results positive in:															
RBC donors	3	1	1	1	2	0	2	1	5	2	1	0	4	1	24
PC donors	0	1	0	0	0	0	2	1	0	1	1	1	3	0	10
FFP donors	1	4	1	3	1	3	10	11	7	14	16	13	5	0	89
Total	4	6	2	4	3	3	14	13	12	17	18	14	12	1	123
TRALI related fatalities, HLA-/HNA antibody test results positive in:															
RBC	0	0	0	0	0	0	1	1	0	1	0	0	0	0	3
PC	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
FFP	0	0	0	0	0	0	1	1	2	2	5	5	0	0	16
Total	0	0	0	0	0	0	2	2	2	3	5	5	1	0	20

Reporting frequency of immune mediated TRALI for the period:

	1997 – 2000		2001 - 2004		2005 - 2008		2009		2010	
	Transfused. products* x 10^6	TRALI (total no.) per 10^6	Transfused. products* x 10^6	TRALI (total no.) per 10^6	Transfused. products* x 10^6	TRALI (total no.) per 10^6	Transfused. products* x 10^6	TRALI (total no.) per 10^6	Transfused. products* 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**	4.535	(4) **0.88**	4.500	(1) **0.22**
PC	1.294	(1) **0.77**	1.311	(3) **2.28**	1.671	(3) **1.80**	0.443	(3) **6.77**	0.471	(0) **0**
FFP	6.346	(9) **1.42**	4.781	(25) **5.23**	4.474	(50) **11.18**	1.096	(5) **4.56**	1.152	(0) **0**

The first column highlighted grey marks the implementation of leucocyte depletion (2000)
The second column highlighted grey marks the beginning of intensive monitoring by the PEI
The third column highlighted grey marks the implementation of risk-minimising measures taken in the manufacture of therapeutic fresh frozen plasma (09/2009)
* Calculated consumption

Table 4 Haemolytic transfusion reaction (HTR), associated fatalities and reporting frequencies related to transfused blood components

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	1997 - 2010
Haemolytic transfusion reactions after the administration of:															
RBC	22	11	7	2	4	3	2	16	14	14	6	8	6	16	131
PC	0	0	0	0	1	1	0	2	0	1	1	1	0	2	9
Combined	1	0	2	1	1	2	2	1	2	2	2	0	1	0	17
Total	23	11	9	3	6	6	4	19	16	17	9	9	7	18	157
Acute and delayed haemolytic transfusion reaction and HTR with positive Ab test result:															
Acute HTR	22	10	5	2	6	4	4	18	14	16	7	8	5	9	127
Delayed HTR	1	1	4	1	0	2	0	1	2	1	2	1	2	9	25
Irregular RB-Ab	1	1	2	1	0	1	0	1	1	1	1	1	2	16	29
Total	23	11	9	3	6	6	4	19	16	17	9	9	7	18	154
Haemolytic transfusion reactions with fatal cases after administration of:															
RBC	0	2	2	0	0	0	0	1	0	2	0	0	0	0	7
Combined	0	0	1	0	0	0	0	1	0	0	0	0	0	0	2
Total	0	2	3	0	0	0	0	2	0	2	0	0	0	0	9

Reporting frequency of haemolytic transfusion reactions for the period:

	1997 – 2000		2001 - 2004		2005 - 2008		2009		2010	
	Transfused. products* x 10^6	HTR (total no.) per 10^6	Transfused. products* x 10^6	HTR (total no.) per 10^6	Transfused. products* x 10^6	HTR (total no.) per 10^6	Transfused. products* x 10^6	HTR (total no.) per 10^6	Transfused. products* 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**	4.535	(6) **1.32**	4.500	(16) **3.55**
PC	1.294	(0) **0.00**	1.311	(4) **3.05**	1.671	(3) **1.80**	0.443	(0) **0.00**	0.471	(2) **4.25**

* Calculated consumption

Table 5 Transfusion transmitted bacterial infections (TTBI), associated fatalities and reporting frequencies related to blood components

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	1997 - 2010
Bacterial infections after administration of:															
RBC	4	5	1	0	4	1	2	2	3	2	6	3	0	1	34
Pool PC	0	3	3	1	1	3	3	1	4	3	1	2	1	0	26
Apheresis PC	0	0	1	3	3	3	2	2	3	3	1	1	1	2	25
FFP	0	4	0	0	0	0	0	0	1	0	0	0	0	0	5
Total	4	12	5	4	8	7	7	5	11	8	8	6	2	3	90
Bacterial infections with fatal cases after administration of:															
RBC	2	2	0	0	0	0	0	0	0	0	0	0	0	0	4
Pool PC	0	1	0	0	0	0	1	0	1	0	0	0	1	0	4
Apheresis PC	0	0	0	1	0	1	0	1	0	1	0	0	0	0	4
FFP	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	2	3	0	1	0	1	1	1	1	1	0	0	1	0	12

Reporting frequency of transfusion-transmitted bacterial infections for the period:

	1997 – 2000		2001 - 2004		2005 - 2008		2009		2010	
	Transfused. products* x 10^6	TTBI (total no.) per 10^6	Transfused. products* x 10^6	TTBI (total no.) per 10^6	Transfused. products* x 10^6	TTBI (total no.) per 10^6	Transfused. products* x 10^6	TTBI (total no.) per 10^6	Transfused. products* x 10^6	TTBI (total no.) per 10^6
RBC	1.294	(10) **0.63**	16.340	(9) **2.14**	17.417	(14) **0.80**	4.535	(0) **0.00**	4.500	(1) **0.22**
PC	6.346	(11) **8.50**	1.311	(18) **13.73**	1.671	(18) **10.77**	0.443	(2) **4.51**	0.471	(14) **4.25**
FFP	15.837	(4) **0.63**	4.781	(0) **0.00**	4.474	(1) **0.22**	1.096	(0) **0.00**	1.152	(0) **0.00**

The column highlighted in grey marks the implementation of pre-donation sampling (2002)
Small boxes highlighted grey mark the limitation of the shelf life of platelet concentrates to 4 days (Opinion 38 of the German Advisory Committee Blood) (2008)
* Calculated consumption

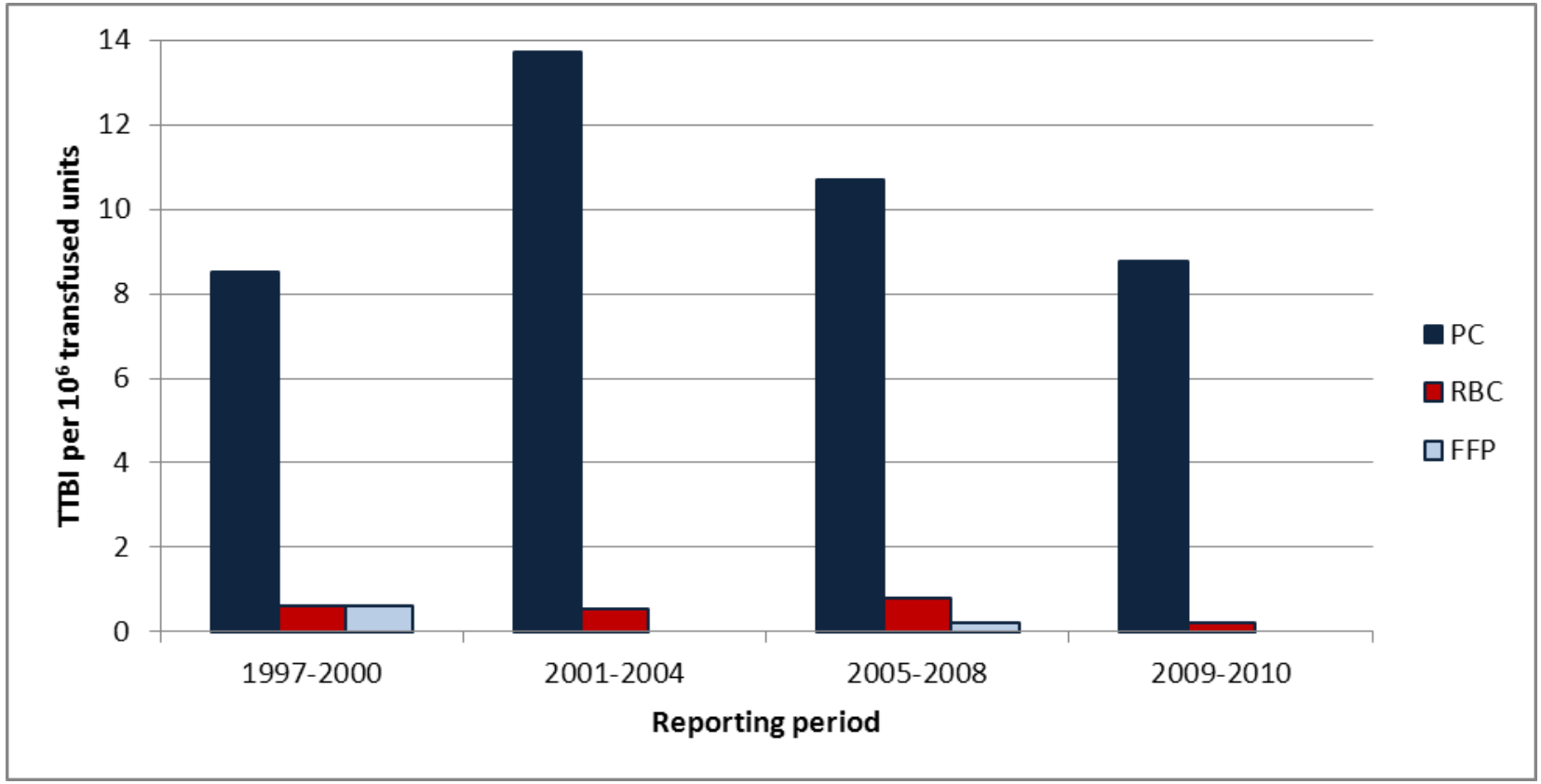

Figure 4

Reporting rate of transfusion transmitted bacterial infections (TTBI) per 10^6 transfused PC, RBC, and FFP units from 1997 to 2010

Table 6 Results of microbiological analyses in confirmed cases of transfusion-transmitted bacterial infections (1997-2010)

Agent	**Number of blood component** with recipient related microbiological analysis				**Clinical outcome** of recipient		**Fatalities** caused by	
Genus/Species	RBC	PC	FFP	Total	not fatal	fatal	RBC	PC
Agents with low (human)-pathogenicity								
Staphylococcus capitis, epidermidis, hominis, saprophyticus and spp. **Micrococcus luteus**, **Corynebacterium** spp. **Propionibacterium acnes**	**14**	**18**	**2**	**37**	**36**	**1**	**0**	**1**
Agent with medium/high pathogenicity								
Staphylococcus aureus **Streptococcus** pyogenes and agalactiae **Bacillus cereus**, **Escherichia coli** **Enterobacter** erogenes, amnigenus **Klebsiella** oxytoca, pneumonia **Panoea** agglomerans, **Serratia** marcescens **Yersinia** enterocolitica, **Enterococcus** spp. **Acinetobacter** lwoffii, **Pseudomonas** aeruginosa **Stenothrophomonas** maltophilia	**20**	**30**	**3**	**53**	**42**	**11**	**4**	**7**
Total	**34**	**48**	**5**	**90**	**78**	**12**	**4**	**8***

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

Table 7 Transfusion-transmitted viral infections (HBV, HIV, HCV) and reporting frequency related to transfused blood components

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	1997 - 2010
HCV infections after the administration of:															
RBC	4	3	0	0	0	0	0	1	0	0	0	0	0	0	8
Pool PC	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Apheresis PC	1	1	0	0	0	0	0	0	0	0	0	0	0	0	2
FFP	0	9	0	0	0	0	0	0	0	0	0	0	0	0	9
Total	6	13	0	0	0	0	0	1	0	0	0	0	0	0	20
HIV infections after the administration of:															
RBC	0	1	0	3	0	0	0	0	0	0	1	0	0	1	6
PC	0	0	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	0	0
Total	0	1	0	3	0	0	0	0	0	0	1	0	0	1	6
HBV infections after the administration of:															
RBC	1	1	2	1	0	1	1	2	2	3	1	1	0	0	16
Pool PC	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Apheresis PC	0	1	0	0	0	0	2	0	0	0	0	0	1	0	4
FFP	0	0	0	0	2	0	0	1	0	0	0	0	0	0	3
Total	1	2	2	1	2	1	3	3	2	3	1	1	1	0	23

Reporting frequency of transfusion transmitted viral infections for the period:

	1997 – 2000		2001 - 2004		2005 - 2008		2009		2010	
	Transfused. products* x 10^6	HTR (total no.) per 10^6	Transfused. products* x 10^6	HTR (total no.) per 10^6	Transfused. products* x 10^6	HTR (total no.) per 10^6	Transfused. products* x 10^6	HTR (total no.) per 10^6	Transfused. products* x 10^6	HTR (total no.) per 10^6
RBC	15.837	(16) **1.01**	16.340	(5) **0.31**	17.417	(8) **0.46**	4.535	(0) **0.00**	4.500	(1) **0.22**
PC	1.294	(4) **3.10**	1.311	(2) **1.53**	1.671	(0) **0.00**	0.443	(1) **2.26**	0.471	(0) **0.00**
FFP	6.346	(9) **1.42**	4.781	(3) **0.63**	4.474	(0) **0.00**	1.096	(0) **0.00**	1.152	(0) **0.00**

The first column highlighted grey marks the implementation of HCV NAT pool testing; the second column highlighted grey marks the implementation of HIV NAT pool testing.
The third column highlighted grey marks the implementation of anti-HBc single donor testing.
* Calculated consumption

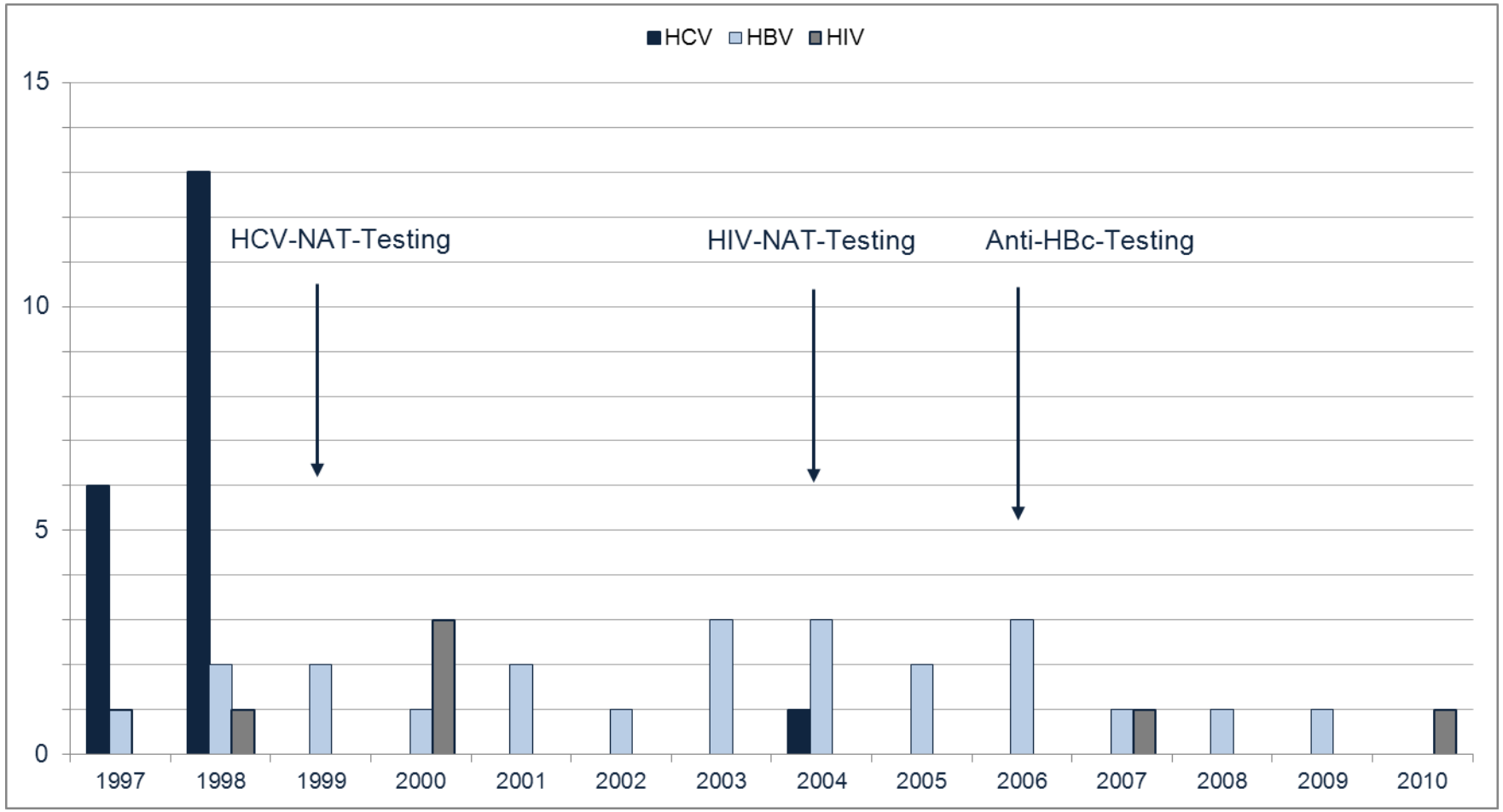

Figure 5 Transfusion transmitted viral infections (in accordance with Opinion 34) after administration of blood components for the period of 1997-2010 marked with the implementation of extended donor screening

Table 8 Reported AB0 incompatibility due to incorrectly transfused blood or blood components and reporting frequencies related to the transfused blood components

	1997	**1998**	**1999**	**2000**	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**1997 - 2010**
AB0 incompatibility:															
RBC	6	1	3	8	3	1	3	3	9	4	2	7	8	4	62
AB0 incompatibility with fatal cases:															
RBC	1	1	1	0	0	0	0	0	1	0	0	2	0	0	6

Reporting frequency of transfusion transmitted viral infections for the period:

	1997 – 2000		2001 - 2004		2005 - 2008		2009		2010		
	Transfused. products* x 10^6	AB0 incomp. (total no.) per 10^6	Transfused. products* x 10^6	AB0 incomp. (total no.) per 10^6	Transfused . products* x 10^6	AB0 incomp. (total no.) per 10^6	Transfused. products* x 10^6	AB0 incomp. (total no.) per 10^6	Transfused. products* x 10^6	AB0 incomp. (total no.) per 10^6	
RBC	15.837	(18) **1.14**	16.340	(10) **0.61**	17.417	(22) **1.26**	4.535	(8) **1.76**	4.500	(4) **0.89**	

Table 9 Manufacture and estimated consumption of blood components from 1999 to 2010
Reports to the PEI conforming to TFG (Transfusionsgesetz, Transfusion Act) Section 21

Year	RBC		PC		FFP		RBC, PC, FFP
	Manufacture Units x 10^6	**Consumption*** Units x 10^6	**Manufacture** Units x 10^6	**Consumpt.*** Units x 10^6	**Manufact.** Units x 10^6	**Consumpt.*** Units x 10^6	**Consumpt.*** Units x 10^6
1999	4.28	3.99	0.41	0.32	1.81	1.74	**6.05**
2000	4.26	3.93	0.42	0.33	1.53	1.43	**5.69**
2001	4.32	4.03	0.39	0.32	1.45	1.38	**5.73**
2002	4.45	4.12	0.38	0.33	1.28	1.23	**5.68**
2003	4.24	3.93	0.37	0.30	1.11	1.05	**5.28**
2004	4.54	4.26	0.41	0.36	1.18	1.11	**5.78**
2005	4.56	4.29	0.43	0.38	1.09	1.03	**5.70**
2006	4.52	4.29	0.45	0.41	1.10	1.05	**5.75**
2007	4.57	4.35	0.48	0.43	1.27	1.22	**6.00**
2008	4.71	4.49	0.51	0.45	1.23	1.17	**6.11**
2009	4.74	4.54	0.52	0.44	1.14	1.10	**6.08**
2010	4.77	4.5	0.55	0.47	1.20	1.15	**6.12**

***Discrepancies between the amounts manufactured and amounts consumed are attributed to material loss due to expiration dates and loss by the consumer.