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Haemovigilance Annual report 2015

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Additional information is available on our website www.swissmedic.ch/haemovigilance

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Abbreviations

°C	degrees Celsius
AB	antibodies
Ag	antigen
ARDS	acute respiratory distress syndrome
BD/BTO	blood donation/blood transfusion organisation
BG	blood group
BMA	biomedical analyst
BP	blood product
BP	blood pressure
CH	Switzerland
CT	compatibility testing
CT	computed tomography
DAT	direct antiglobulin test, also known as direct Coombs test
e.g.	for example
FFP	fresh frozen plasma
FNHTR	febrile non-haemolytic transfusion reaction
FOPH	Federal Office of Public Health
g/l	grams per litre
h	hour(s)
Hb	haemoglobin
HBV	hepatitis B virus
HCV	hepatitis C virus
HEV	hepatitis E virus
HIV	human immunodeficiency virus
HLA	human leukocyte antigen
HR	Heart rate
HTR	haemolytic transfusion reaction
HV	Haemovigilance
IBCT	incorrect blood component transfused
ICU	intensive care unit
ID	identification
IH	immunohaematology
iv	intravenous
K	antigen/antibody of the Kell blood group
kg BW	kilogram of body weight
LDH	lactate dehydrogenase
ml	millilitre
mm Hg	millimetre mercury column, unit of measurement for (blood) pressure
NAT	nucleic acid testing (means of demonstrating the presence of DNA/RNA of a pathogen, e.g. by PCR)
NM	near miss
NT-pro-BNP	N-terminal brain natriuretic peptide
O_2	oxygen
Op	operating theatre
PC	platelet concentrate (PCa: apheresis-derived; PCb: whole blood-derived)
PI-PC	pathogen-inactivated platelet concentrate
cPC	conventional platelet concentrate
PCR	polymerase chain reaction (means of demonstrating the presence of pathogen DNA/RNA)
pos	positive (e.g. BG Opos = blood group O, rhesus factor positive)
post-	after transfusion
pre-	before transfusion
pRBC	packed red blood cells
prob.	probably
PubMed	database of the US National Institutes of Health
Rh	rhesus (factor)
SCT	stem cell transplantation
SOP	standard operating procedure (guidelines, instructions etc.)
SRC	Swiss Red Cross
S/P	status post
TACO	transfusion-associated circulatory overload
TAD	transfusion-associated dyspnoea
TR	transfusion reaction
TRALI	transfusion-related acute lung injury
T&S	type and screen (to define blood group and detect irregular antibodies)
U/l	unit(s) per litre
VVR	vasovagal reaction
Y	year

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1. Introduction

1.1 Haemovigilance

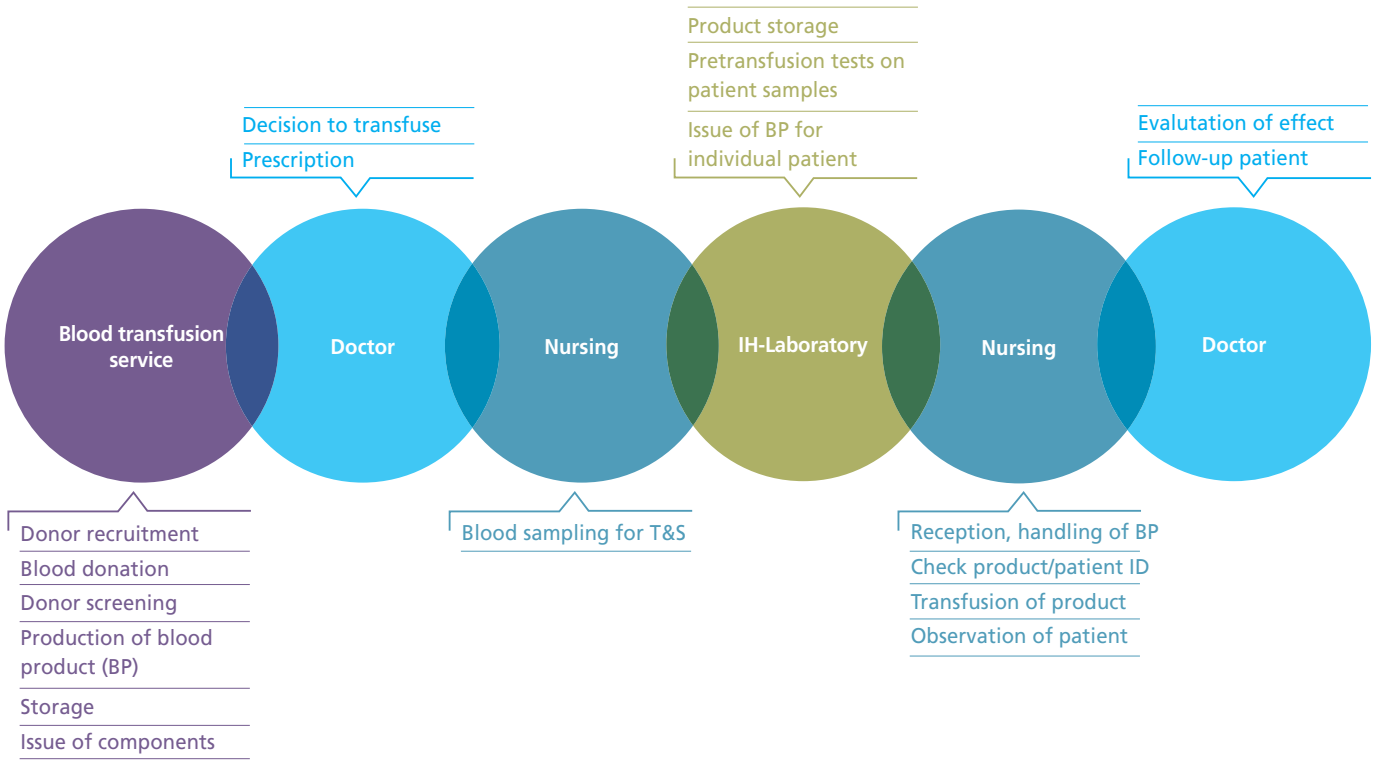
Haemovigilance is a systematic approach to recording adverse events associated with the collection, production and administration of blood transfusions. Its objective is the early detection of new risks and quality defects; at the same time the national haemovigilance system triggers and evaluates preventive measures. In the hospital setting, haemovigilance is closely related to quality assurance in the use of labile blood products.

The Swiss haemovigilance system monitors the following events associated with labile blood products:

- Transfusion reactions (TR)
- Transfusion errors; incorrect blood component transfused (IBCT)
- Near misses
- Donor reactions
- Quality defects and protective measures.

The causes of these events are found throughout the transfusion chain (Figure 1). The figure shows which professions are involved in a transfusion and thus in the prevention of events.

Figure 1:
Transfusion chain



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2. Methods

2.1 Reporting of events

Where and to whom are reports submitted?

The national haemovigilance reporting system (HV system) covers the whole of Switzerland. Under the Therapeutic Products Act, all institutions that transfuse labile blood products ("users") are obliged to report to Swissmedic, the Swiss Agency for Therapeutic Products. This obligation also applies to the manufacturers of blood products including blood banks.

Who submits the reports?

It is mandatory for both users and manufacturers of labile blood products to appoint a responsible person for haemovigilance (haemovigilance officer). This person ensures that events are investigated correctly and that the user and the blood bank or manufacturer work together effectively. This increases the quality of the individual reports.

How are reports submitted?

Report forms are available on the Swissmedic website at Market Surveillance > Blood components > Forms. The reports are either sent directly to Swissmedic by the users or first go to the manufacturer, who adds information about the product history, the history of the donor and additional results of investigations into the incident before passing the report on to Swissmedic. The Swissmedic reviewers obtain additional information from the reporters where necessary and carry out the final assessment. If this assessment deviates significantly from the reporter's assessment, the local haemovigilance officer is consulted.

Definitions:

Transfusion reactions are adverse reactions that occur during or after transfusion of a labile blood product. They are usually characterised by symptoms experienced by the patient. This category also includes alloimmunisation, which is frequently discovered later in the laboratory. Suspected transfusion-transmitted infections must also be reported as transfusion reactions, as should cases involving inadequate efficacy of blood products if this is thought to be due to product-specific factors or there is no other plausible explanation for the lack of effect.

The severity of transfusion reactions is defined as follows:
Grade 1: **non-severe**
Grade 2: **severe**, i.e. one of the following criteria is fulfilled:
- Time in hospital prolonged as a result of the reaction
- Permanent damage (or permanent risk in the case of alloantibodies)
- The reaction must be considered as medically significant for other reasons (e.g. if permanent damage or a fatal outcome was avoided by timely intervention)

Grade 3: **life-threatening**
Grade 4: **death**

Transfusion errors and near misses: Transfusion errors is the term used for all events in which a blood component was transfused that was not intended for that patient or was not optimally suited to the patient to whom it was administered (e.g. intended for another patient, not irradiated, not allo-AB compatible according to the SOP). Classification as a transfusion error is independent of whether or not the patient experienced symptoms or other adverse effects. If adverse effects occur as a result of a transfusion error, the case is recorded in the national haemovigilance system both in the transfusion error database and in the transfusion reaction database.

Near misses are errors or deviations that are discovered and corrected before the transfusion is started or in which no transfusion took place.

Definitions of severity for transfusion errors and near misses:

The definitions of the severity of transfusion reactions are determined by the actual outcome of the reaction. For this reason, they are not identical for transfusion errors and near misses. From July 2015 the following definitions were used for both categories, initially on a trial basis and then definitively:

- **Grade 1** (non-severe): Formal error with no potential for mix-up
- **Grade 2** (severe): Formal error with potential for mix-up or transfusion error involving a suboptimal product
- **Grade 3** (life-threatening): Mix-up occurred at some level in the transfusion chain

Grade 4 (death) is not used for transfusion errors and near misses (if a transfusion error is fatal, the case is recorded as Grade 4 in the transfusion reaction database and as Grade 3 in the transfusion error database).

Table 1:
Examples of severity classification of transfusion errors and near misses

Grade 1 (non-severe): Error with no potential for mix-up	**Grade 2 (severe): Error with potential for mix-up or transfusion error involving a suboptimal product**	**Grade 3 (life-threatening): Mix-up occurred at some level in the transfusion chain**
Examples: • Order form not initialled • Label on sample tubes or order form completed insufficiently • Minor discrepancy between tubes and order form • Deliberate Rhesus conversion in mass transfusions • Handling & storage	Examples: • Labels missing from sample tubes • Another patient's date of birth • Patient ID on sample tube differs from that on form • Transfusion error with unconfirmed allo-AB compatibility according to the SOP	Examples: • Wrong blood in tube* • Discrepant BG determinations • Blood product orders for the wrong patient • Transfusion error ABO-incompatible or ABO-compatible only by chance * *Wrong blood in tube* means that the patient identification on the tube and order form does not match the patient whose blood is in the tube.

Table 1 shows the new severity classification of transfusion errors and near misses with the most important examples. These definitions of severity will be incorporated into the report form when it is next revised. Near misses have not been shown by severity in the results section because the definition of severity was modified during 2015. Transfusion errors, on the other hand, have been classified retrospectively using the modified definition.

Donor reactions are reported to Swissmedic by the blood transfusion services. Severe reactions appear on the report form as individual case reports, the others are compiled into an annual summary in tabular form with no details of individual cases.

Quality defects and protective measures are usually reported to Swissmedic by the manufacturer. In most cases they involve infection markers, i.e. donors who have tested positive. However, quality defects and protective measures may also concern the users. Quality defects in a product are sometimes only detected in the hospital, and the hospitals are also actively involved in protective measures if products need to be traced (look-back procedure).

2.2 Evaluation

Transfusion reactions: All reported cases are recorded in the transfusion reaction database. Each case is classified by:

- **Category** (allergic reaction, haemolytic reaction etc.)
- **Severity 1–4** (see page 4 for definitions)
- **Imputability** (causal connection between transfusion and reaction):
  0 = not evaluabler
  1 = excluded/unlikely: The reaction is definitely/more likely to be due to other causes
  2 = possible: The reaction could be explained by the transfusion as well as by other causes
  3 = probable: The reaction does not appear to be due to another cause
  4 = definite: In all probability the reaction was caused by the transfusion

In the results section, all cases will first be shown in the overview, irrespective of their imputability. In the more detailed analyses, only cases with high imputability (3 and 4) are presented in order to provide the most specific illustration possible of transfusion risks in Switzerland.

In rare cases in which differential diagnosis is difficult, the case is recorded as two database entries – case a) and case b) with two different categories. This approach increases the case numbers since such cases are included twice in the evaluation. This artefact can be ignored because the approach is used for <1% of all cases. In addition, one of the two cases usually has moderate or low imputability and as such is not included in the more detailed analyses.

The Swiss haemovigilance system is based on spontaneous reporting, or in other words it is what is known as a passive surveillance system. The individual professional or haemovigilance officer determines whether a transfusion reaction is investigated and reported. It can therefore be assumed that, in spite of the mandatory reporting requirement, under-reporting occurs to a degree that cannot be precisely quantified.

The number of blood components supplied for transfusion is used for the quantitative evaluation of transfusion risks (with exposure data as the denominator). Transfusion risks may be underestimated as a result of under-reporting, and for this reason the risks described in this report should be understood as minimum figures.

Transfusion errors and near misses: Transfusion errors are analysed by severity, by the area in the transfusion chain in which the deviation occurred and by incompatibility according to the blood group system. In addition to quantitative analyses, anonymised examples are highlighted to enable readers to learn from the mistakes of others. This also applies to near misses.

Donor reactions are summarised briefly in quantitative terms with examples.

Quality defects and protective measures: Manufacturers (including blood banks) are required to report the protective measures adopted when quality defects are identified. The following definitions and approaches to infection markers were agreed by Swissmedic and the manufacturers at the start of 2015.

- Repeat donors: Positive infection markers and the protective measures adopted must be submitted as individual case reports
- First-time donors: The reports must also be submitted as individual case reports if products have been supplied or passed on to third parties. If no products have been supplied, reports can also be submitted annually on a cumulative basis (in 2015 all manufacturers submitted individual case reports)
- Post-donation information not involving positive infection markers does not have to be submitted as individual case reports.

The individual case reports are entered in the Swissmedic database and evaluated both globally and pathogen-specifically.

3. Results

3.1 Reports received: Overview

Table 2:
Reports of adverse events

Type	Number
Transfusion reactions	1,408
Transfusion errors / incorrect blood component transfused (IBCT)	37
Near misses (NM)	1,147
Donor reactions	22
Quality defects and protective measures:	91
Total number of reports evaluated	**2,705**

Table 2 shows the number of reports involving labile blood products received in 2015. A total of 2,702 reports were received, with correction of the data (e.g. reports of more than one transfusion reaction associated with the same transfusion) producing 2,705 evaluable events.

Figure 2:
Events reported by year

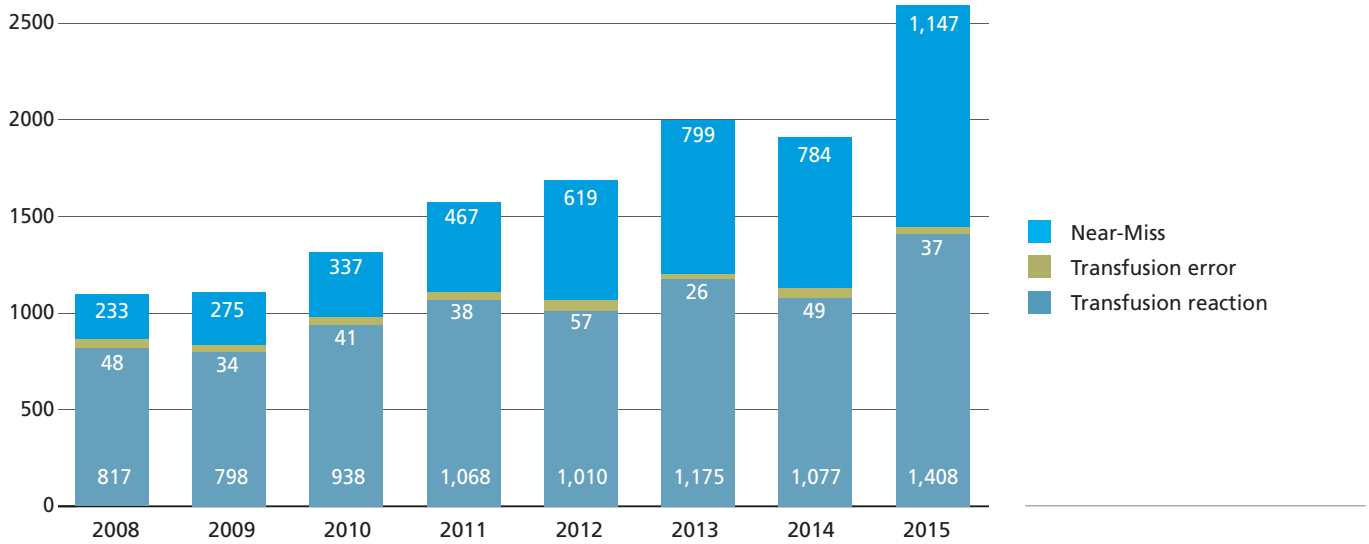


Figure 2 shows the number of events reported compared with previous years. The increase is due to increasing reporting compliance and not to an increased risk of transfusion reactions. The increasing number of near misses is most likely not due to an increased error rate in the transfusion processes, as shown below (Chapter 3.4).

3.2 Number of transfusions and reporting rate

Table 3:
Number of transfusions in Switzerland

Blood components	2008	2009	2010	2011	2012	2013	2014	2015
pRBC	313,587	311,521	308,670	308,627	297,582	279,510	262,953	248,647
FFP (therapy units)	65,800	70,300	61,500	50,063	49,832	44,083	38,183	33,658
PC (products)	27,600	29,600	29,900	33,068	34,265	34,750	35,328	36,439
Total blood components	**406,987**	**411,421**	**400,070**	**391,758**	**381,679**	**358,343**	**336,464**	**318,744**

FFP = Fresh frozen plasma
PC = Platelet concentrates

Table 3 shows the numbers of transfusions given throughout Switzerland in the past 8 years. The figures are based on the number of blood components supplied as shown in the annual statistics of the Blood Transfusion Service of the Swiss Red Cross. There was a decrease of 22% for all blood components during this 8-year period. The biggest decrease was in plasma transfusions (49%), while infusions of platelets increased (32%). 2015 was the first year in which more platelet products than plasma products were used. The proportion of platelet concentrates obtained from whole blood in 2015 was 31%.

The reporting rate can be calculated from the number of transfusions.

Figure 3:
Reporting rate (reports per 1,000 transfusions), all reports

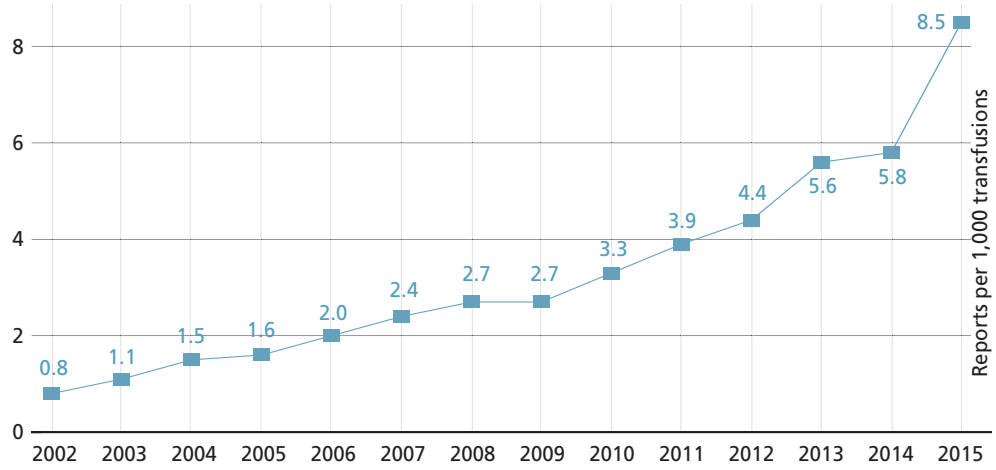
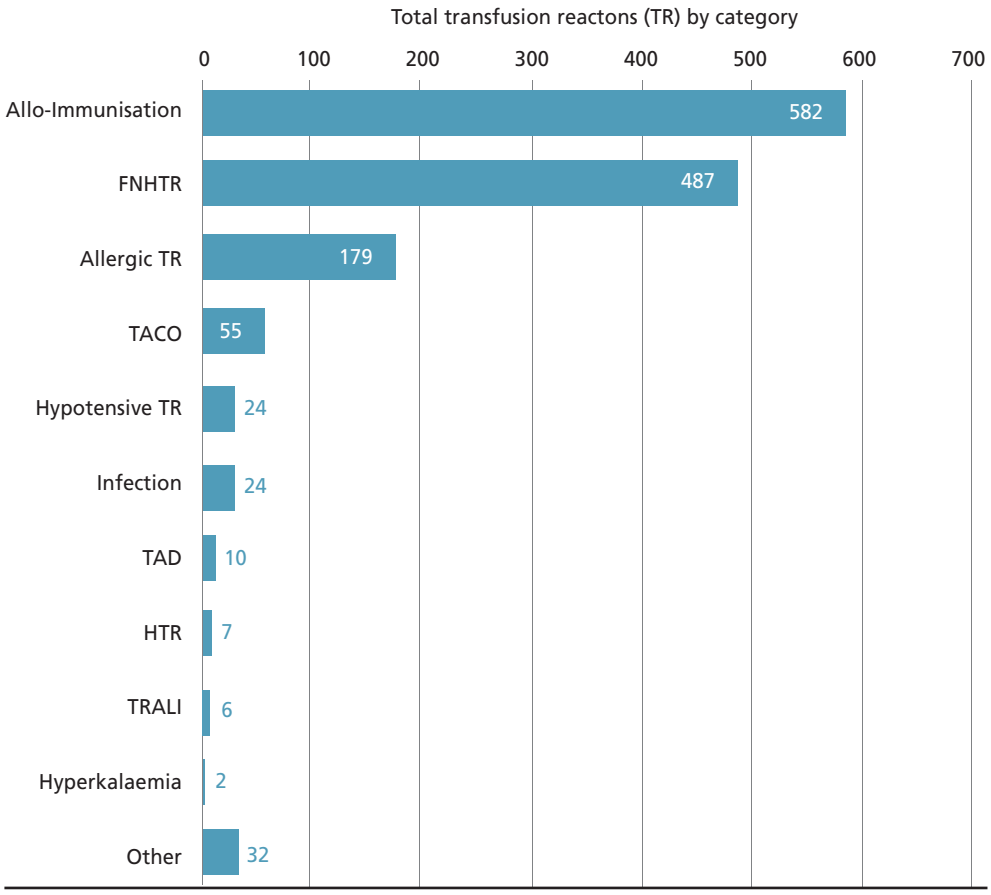


Figure 3 shows the overall reporting rate. It is calculated from the total number of reports per 1,000 transfusions, to be more specific per 1,000 products delivered. The calculation includes all types of reports and all imputability classifications, i.e. all 2,705 reports in 2015. The reporting rate rose sharply in 2015 and currently stands at 8.5 reports per 1,000 transfusions. The increase is due primarily to the higher number of reports and, to a small degree, to the lower number of transfusions. The reporting rate is rather high by international standards[1].

3.3 Transfusion reactions (TR)

Overview

Figure 4:
Transfusion reactions (TR) reported in 2015 by category



N = 1408

FNHTR	Febrile non-haemolytic TR
TACO	Transfusion-associated circulatory overload
TAD	Transfusion-associated dyspnoea
HTR	Haemolytic TR
TRALI	Transfusion-associated acute lung injury

Figure 4 shows the distribution of the transfusion reactions reported in 2015 among the different categories. All 1,408 cases are shown, irrespective of imputability. The cases summarised under "Other" mostly involve unspecific symptoms such as mild tachycardia, nausea or sensations of warmth. They do not include any known transfusion reactions, i.e. in 2015 there were no reported cases of post-transfusion purpura, transfusion-associated graft-versus-host disease or haemosiderosis.

Imputability (relationship to the transfusion)

Table 4:
Number of transfusion reactions (TR) in 2015 by category and imputability

Imputability	all	low	"possible"	high
Alloantibodies	582		3	579 (99 %)
FNHTR	487	55	306	126 (26 %)
Allergic TR	179	4	51	124 (69 %)
TACO	55		22	33 (60 %)
Hypotensive TR	24		17	7 (29 %)
Infection, bacterial	22	20	2	
Infection, viral	2	2		
TAD	10	1	5	4
TRALI	6	2	2	2
H TR: acute	4	1		3
H TR: delayed	3		1	2
Hyperkalaemia	2			2
Other	32	12	12	8
Number of reactions	**1,408**	**97 (7 %)**	**421 (30 %)**	**890 (63 %)**

Low imputability:
causal relationship with the transfusion "excluded" or "unlikely"

High imputability:
causal relationship with the transfusion "probable" or "certain"

Table 4 shows the reports by "imputability" within the categories. Imputability describes the likelihood of there being a causal relationship with the transfusion. The distribution of imputability depends heavily on the reaction. Alloantibodies detected in the laboratory, for example, nearly always have high imputability.

In 2015 high imputability was attributed to 890 reactions (63% of reported TR), i.e. the likelihood of there being a causal relationship with the transfusion was considered to be probable or certain. **Only cases with high imputability are shown below.**

Severity

Table 5:
High-imputability reactions by category and severity

Severity	all	Grade 1	Grade 2	Grade 3	Grade 4
Alloantibodies	**579**		579		
FNHTR	**126**	119	6	1	
Allergic TR	**124**	108	13	3	
TACO	**33**	22	3	6	2*
Hypotensive TR	**7**	4	3		
TAD	**4**	2		2	
Haemolytic TR, acute	**3**	1	2		
HTR, delayed	**2**	2			
TRALI	**2**		1		1*
Hyperkalaemia	**2**			2	
Other	**8**	8			
Total	**890 (100 %)**	**266 (30 %)**	**607 (68 %)**	**14 (1,6 %)**	**3* (0,3 %)**

* A total of 2 patients died in 2015 with "probable" imputability. One patient who died is counted twice in this table; the reaction was classified both as TACO and as TRALI because the patient possibly had both and it was not possible to classify the reaction definitively on the basis of the available data (see case description in Chapter 5.1).

Table 5 shows the severity of the high-imputability cases. There were two deaths in 2015 (Grade 4) and 14 life-threatening transfusion reactions (Grade 3). The vast majority of the severe cases (Grade 2) involved allo-immunisation, which is classified as severe because of the permanent risk and possible difficulties associated with finding a suitable product for a subsequent transfusion.

Life-threatening or fatal transfusion reactions

Figure 5:
Life-threatening or fatal reactions (cases with high imputability)

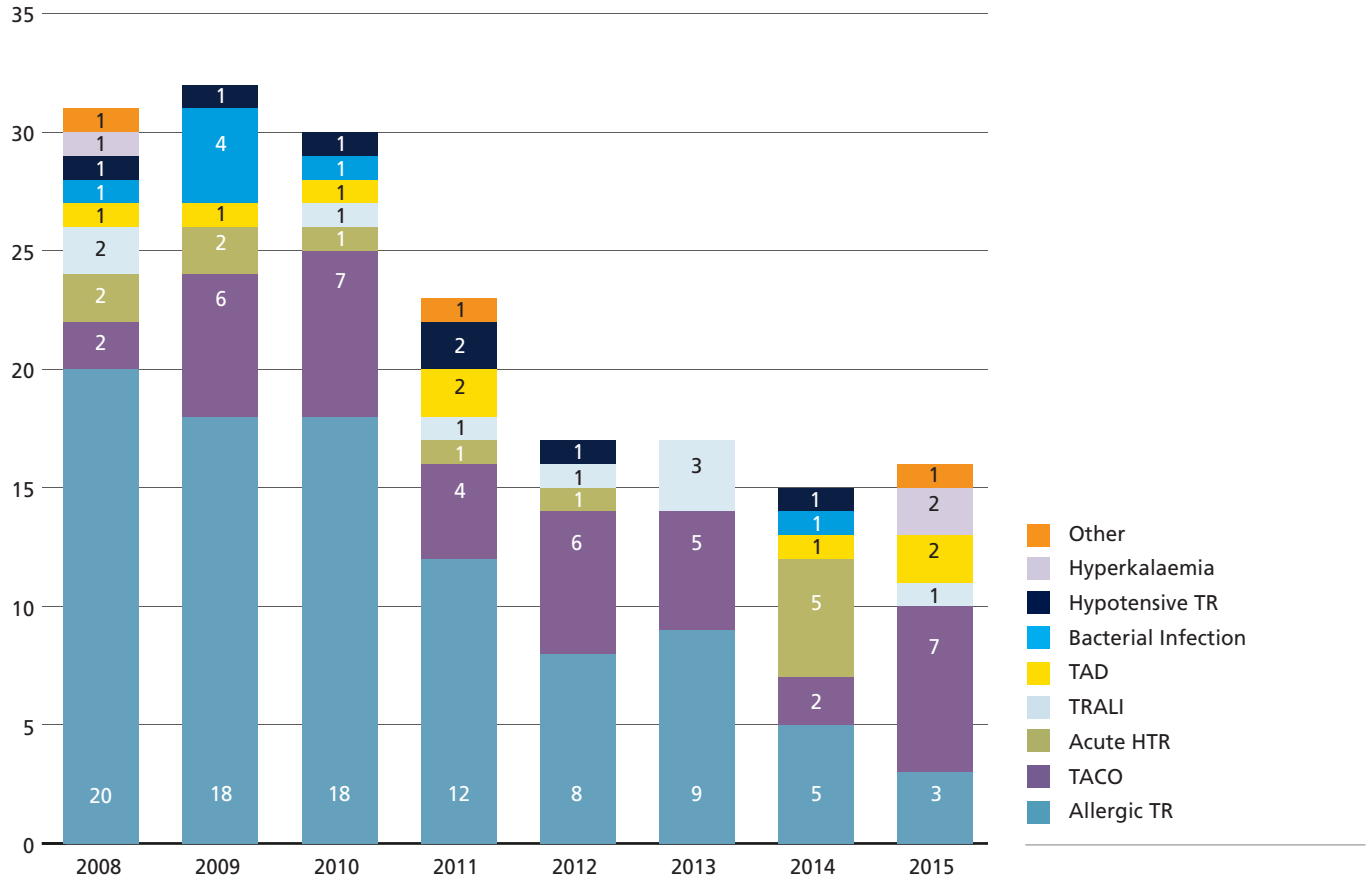
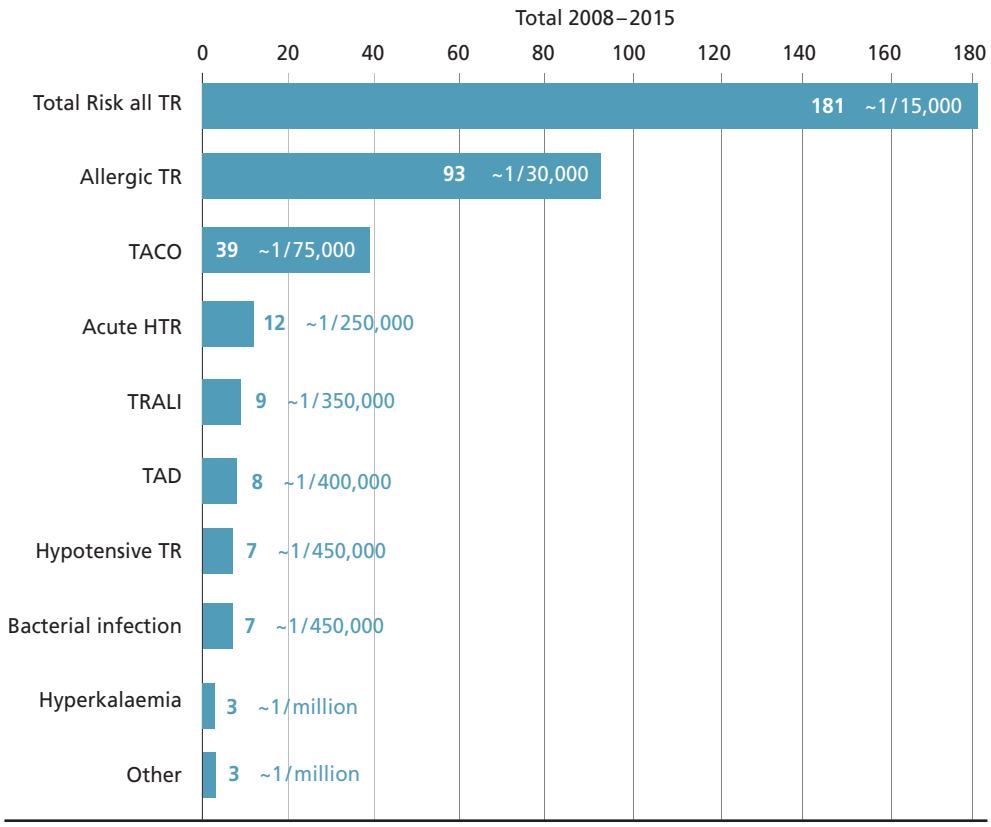


Figure 5 shows the distribution of life-threatening and fatal transfusion reactions over time. Of the 16 cases of life-threatening or fatal transfusion reactions in 2015, 8 occurred in connection with packed red blood cells (pRBC), 4 with platelet concentrates (PC), 3 with plasma (FFP) and 1 with combined products (pRBC, FFP).

Transfusion risks

Figure 6:
Risk of life-threatening and fatal transfusion reactions (TR)



3.0 million products in total administered from 2008–2015

Figure 6 illustrates the risk of life-threatening and fatal transfusion reactions. The risk is related to the products administered. The risk is accordingly higher if a patient is given several products. Between 2008 and 2015, 8 transfusion-associated deaths with high imputability occurred:

- 2008 one TACO after FFP and one TRALI after PC
- 2009 one acute HTR after pRBC and one bacterial infection after PC
- 2012 one TACO after pRBC
- 2014 one acute HTR after pRBC and
- 2015 one TACO after pRBC and one TACO/TRALI after pRBC.

Product-specific risks

Figure 7:
Reporting rates per product, all degrees of severity

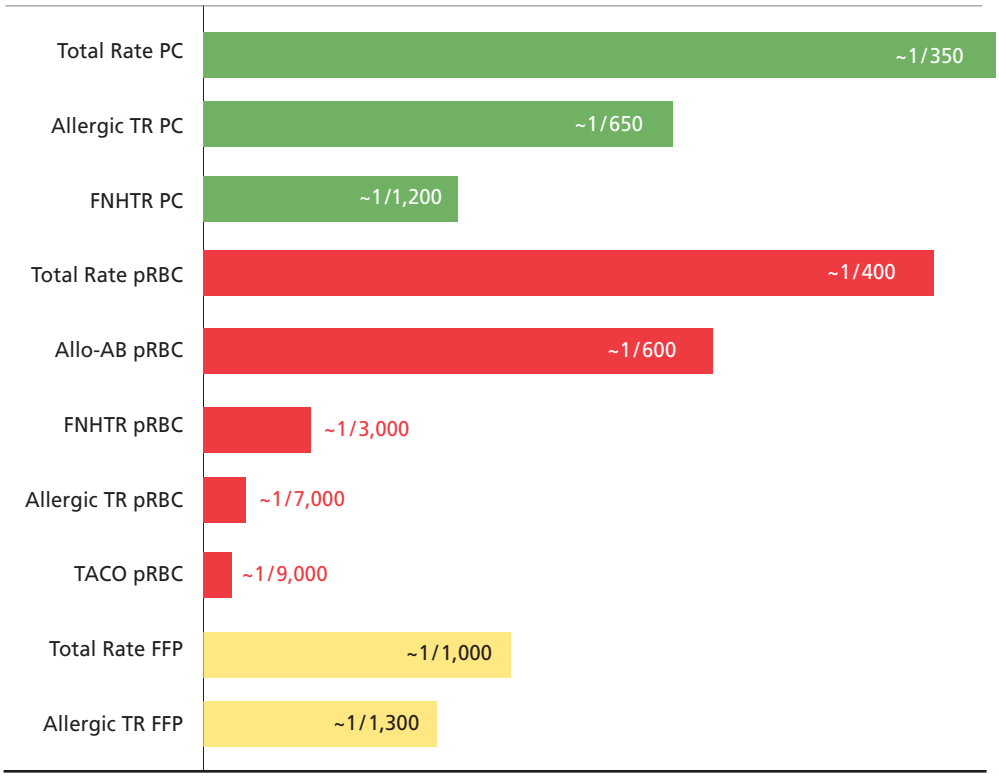


Figure 7 shows the product-specific reporting rates. Transfusion reactions of all degrees of severity (again only those with high imputability) are shown. Reactions reported more than 10 times are shown because events occurring more rarely cannot be reliably expressed on an annual basis as the absolute number of cases is so low.

It should be noted that the number of units administered (bags of product) was used as the denominator when calculating the rates. However, many patients were given more than 1 unit, and for this reason the calculated risk per patient would be substantially greater.

While allergic reactions account for by far the lion's share of reports involving plasma, they account for only a small proportion of reports involving pRBC. Volume overload, on the other hand, occurs predominantly in connection with pRBC transfusions. A good half of reactions involving PC are of an allergic nature.

3.4 Transfusion errors and near misses

37 transfusion errors and 1,147 near misses were reported in 2015.

Transfusion errors by severity/risk to patient

Table 6:
Transfusion errors by severity and risk to patient

Severity/risk	Number
Grade 1: non-severe	**11**
Grade 2: severe	**18**
Grade 3: life-threatening	**8**
Total	**37**

Table 6 shows the classification of the 37 reported transfusion errors by severity and degree of risk to the patient (for definitions see Chapter 2.1). The life-threatening and severe transfusion errors are shown individually below.

Table 7:
Description of Grade 3 and Grade 2 transfusion errors

Transfusion error	Number	Description of error	Localisation of deviation in the transfusion chain	Preventive measures against recurrence
ABO system incompatible	**4**	**Severity/risk Grade 3 life-threatening:**		
		• ABO-incompatible transfusion error of plasma. Patient with BG A undergoing emergency caesarean section at night given 2 FFP with BG O from the laboratory's emergency store. The FFP was labelled correctly, the transfusion rules were not observed.	Administration	In future only plasma with BG AB will be available for emergencies; new SOP.
		• Transfusion error of plasma. Patient with BG AB (before allogeneic SCT) and A (after SCT). 10 blood products were given, including, erroneously, an FFP with BG A instead of BG AB. No one noticed on the ward that the wrong product had been delivered. The FFP was transfused before the blood transfusion centre noticed the error and informed the ward.	Laboratory/ blood bank	Training; supply block set up in the blood transfusion centre's database system.
		Severity/risk Grade 2 severe:		
		• SCT in a previously Apos patient from an Opos SCT donor. Patient was given Apos blood in contravention of the SOP, no symptoms. CT (because of known anti-Cw) was negative.	Laboratory/ blood bank	Modification of software (expansion of options for SCT).
		• Allogeneic SCT in a previously O_{pos} patient from an Apos SCT donor. The patient should then have been transfused with BG O. The BG confirmation in the tube only showed BG A, and the patient was therefore transfused with BG A. Lack of SOP for transfusions after SCT. No signs of haemolysis, DAT positive.	Laboratory/ blood bank	Modification of laboratory IT system; SOP for transfusions in the context of SCT.
ABO system compatible by chance	**6**	**Severity/risk Grade 3 life-threatening:**		
		• Transfusion of a pRBC intended for another patient; the pRBC was taken from the patient's drawer in the refrigerator on the ICU and administered without checking (either electronically or manually) to see that it was intended for the patient.	Administration	
		• pRBC (A_{pos}) for Ms X was delivered to the Op and subsequently administered to Ms Y (A_{pos}) on the ICU. It is no longer possible to ascertain where the mistake happened.	Administration	Switch to a mandatory written-form system for ordering blood; training
		• 2 cases: Transfusion of a PC intended for another patient. Both PC were delivered at the same time and checked together in the office. One PC was given to the wrong patient without checking identity at the bedside. After consulting the blood transfusion service, the other PC was then administered to the second patient. Both products and both patients BG A_{pos}.	Administration	Training with inclusion of the legal service
		• The patient was given 20 ml of an O_{pos} pRBC although he was O_{neg}. After about 20 minutes, the nurse noticed that the name on the product did not match the patient.	Administration	4-eyes principle at the patient's bedside

Transfusion error	Number	Description of error	Localisation of deviation in the transfusion chain	Preventive measures against recurrence
		• Transfusion error with pRBC, ABO compatible only by chance: A 5-year-old child (AB_{pos}) with a body weight at which the contents of the pRBC bag cannot be transfused in one go was transfused on the ICU. At 18.30 the nurse withdrew a syringe of product from the correct AB bag, it was checked correctly using the 4-eyes principle and administered to the child. The bag was stored in a temperature-controlled refrigerator until the next part of the transfusion was given. The second part of the transfusion was given at 20.00 when the shift changed. Because the bag had been checked correctly at 18.30 it was decided that it didn't need to be checked again. A syringe was again filled, but from an O bag that was intended for another child and was also being stored in the fridge.	Administration	The refrigerator used to store blood was divided into sections for each patient; all new employees on the paediatric ICU were trained in transfusions; it was asked whether all new nurses (at the major hospital) could be trained in pre-transfusion checks; the medical director's office was asked whether the check could be "computerised"; pRBC splitting will be investigated as an alternative to syringe withdrawal; the SOP will be improved and a section on checks specific to syringe withdrawal will be added.
Allo-AB compatibility not ensured	**9**	**Severity/risk Grade 2 severe:**		
		• Rh phenotype-incompatible pRBC was transfused due to an error in reservation/release/delivery (female patient born in 1992)	Laboratory/ blood bank	
		• 2 cases: Transfusion of Rh phenotype-incompatible pRBC to patients (both male, born in 1999) following an error in Rh phenotyping of the pRBC.	Laboratory/ blood bank	
		• A B_{pos} patient (male, born in 1970) with Rh phenotype ccDEe was transfused 3 times with O_{neg} and Rh phenotype-compatible for emergency bleeding in the Op, then switched to B_{neg} ccddee, then 5 B_{pos}, 3 of which were positive for C-Ag (lack of sufficiently phenotyped pRBC).	Laboratory/ blood bank	
		• Provision and transfusion of a pRBC that was ABO and Rh phenotype-compatible and took the known anti-K allo-AB into account; however, the anti-C and anti-Kpa that had been identified by the BTO for the first time were not taken into account; CT was negative	Laboratory/ blood bank	
		• Mass transfusion in a young woman (born in 1994) with Rhesus c incompatibility (8 of 26 pRBC)	Laboratory/ blood bank	
		• A Rh phenotype-incompatible pRBC was transfused post-partum to the mother: Patient O CCD.ee, pRBC O CcD.ee	Laboratory/ blood bank	Training
		• A female patient with an anti-K alloantibody was going to be given four pRBC with BG Oneg Ccee, untested, on an emergency basis. During subsequent allocation in the laboratory information system it was discovered that one of the pRBC had the Rh phenotype ccEe, Kell negative	Laboratory/ blood bank	In the laboratory, untested pRBC with BG Oneg are checked again visually before they are issued; BMA trained
		• Antibody known elsewhere not taken into account: AB screening negative, 4 pRBC (CcEe, Ccee) administered to patient with pre-existing alloanti-E and anti-c that were no longer detectable in pre-T&S. Anti-E was detectable again in post-T&S but not anti-c (anti-E boosted).	Other	Request Patient's BG card

Transfusion error	Number	Description of error	Localisation of deviation in the transfusion chain	Preventive measures against recurrence
Administration of suboptimal product	**4**	**Severity/risk Grade 3 life-threatening:**		
		• Delayed use of FFP in haemorrhagic shock in a patient with multiple disorders. The FFP arrived in the shock room 25 minutes after the first order. Various causes, including an erroneous phone call from the shock room saying that the products were no longer needed. The patient subsequently died.	Administration	Personnel in medical shock room trained; possibly modified triage between medical and surgical shock room; finalisation of SOP for massive bleeding; SOP for transfusion in life-threatening emergency updated; SOP for ordering blood products modified: in a resuscitation situation only a doctor may cancel ordered blood products
		Severity/risk Grade 2 severe:		
		• Transfusion of 2 non-irradiated pRBC in a patient who had received an autologous SCT in the context of multiple myeloma. By mistake, the ICU had not ordered irradiated pRBC, the biomedical analyst (BMA) did not see the indication and so did not query the order.	Administration	Discussion at the next meeting of the major hospital's "Risk management" committee.
		• A newborn was erroneously transfused 2 FFP with the same blood group instead of blood group AB as stated in the SOP for children < 3 months.	Laboratory/ blood bank	IT system modified to ensure that only AB plasma can be assigned to newborns under 3 months of age in the system.
		• pRBC administered instead of FFP. In the laboratory, the order was entered manually in the laboratory information system; evidently the wrong product was entered and therefore issued. The early shift did not check the product ordered (orally?) by the doctor.	Laboratory/ blood bank/ administration	Better checking of the order forms in the laboratory and written prescriptions on the ward
Other	**3**	**Severity/risk Grade 2 severe:**		
		• A pRBC was administered even though the numbers in the additional safety identification system did not match. But the patient was still given two pRBC that were correctly intended for him and fully tested. The discrepancy with the safety identification bracelet was noticed when the second pRBC was attached.	Administration	Training with inclusion of the legal service
		• Plasma ordered for patient X but not used was given to patient Y 12 hours later. Both patients and the product had BG A.	Administration	Training, including for senior consultants; blood transfusion service will actively query failure to return empty product bag after 6 hours
		• PC was supplied directly to the ward from the blood bank (order came from an affiliated doctor for an out-patient). The ward asked the laboratory for the BG, the on-call BMA found the type in the system (6 weeks old). After talking to the supervisor, the BMA requested a pre-transfusion blood sample, but the transfusion was already in progress and the typing was done while it was running	Preparation/ laboratory/ administration	
Total	**26**			

Table 7 shows all the Grade 3 (potentially life-threatening consequences) and Grade 2 (potentially serious consequences) transfusion errors. Neither symptoms nor signs of haemolysis were reported in any of these cases.

Transfusion errors: Stage at which the deviation occurred

Table 8:

Stage at which the deviation occurred, by severity

Location	Grade 1 non-severe	Grade 2 severe	Grade 3 life-threatening
Preparation	0	1	0
Laboratory/blood bank	7	11	1
Administration	4	5	7
Other	0	1	0

* P = 0.028
(Fisher exact for 2x3, two-tailed)

Table 8 shows the distribution of all 37 transfusion errors by stage at which the deviation occurred and severity. Deviations in administration are significantly more serious than those that occur in the laboratory. This may be due to the fact that errors in the laboratory were discovered in time when the second blood sample was taken or during the subsequent stages of the process at the administration stage, and thus did not result in transfusion errors. This means that the events are not reported, or are reported only as near misses. Errors in administration, on the other hand, i.e. during the final stages of the process before transfusion takes place, are less likely to be discovered and corrected in time.

Near misses in 2015

Table 9 :

Classification of near misses by stage of the transfusion chain and location of discovery

		Discovery			
Category	**Number**	**Laboratory/blood bank**	**Ward/Op/patient**	**Other/not stated**	**Most important examples**
Preparation	**752**	531	27	194	• Wrong blood in sample tube (WBIT, patients misidentified when taking blood/wrong labels) • Samples and/or order labelled incompletely, discrepantly (e.g. different patient names) or not at all • Mother/child labelling error (obstetrics)
Laboratory	**99**	72	9	18	Wrong BG typing or interpretation, or entry of results
Administration	**264**	51*	4	209	• Products not transfused after all • Temperature deviations
Other	**22**	8	1	13	pRBC older than 14 days were irradiated
Could not be determined	**10**	10	0	0	Blood group discrepancy with previous finding
Total	**1,147**	**672**	**41**	**434**	

* especially when returned

Table 9 shows the localisation of the near misses. The lines are arranged according to where in the transfusion chain the errors occurred. The columns show where the error was discovered and therefore corrected, thus avoiding a transfusion error. Near misses were reported by 39 institutions in 2015. (2014: 32, 2013: 30, 2012: 14, in 2011 there were 4).

Trends in near misses and transfusion errors

Figure 8:
Number of near misses reported by year 2008-2015

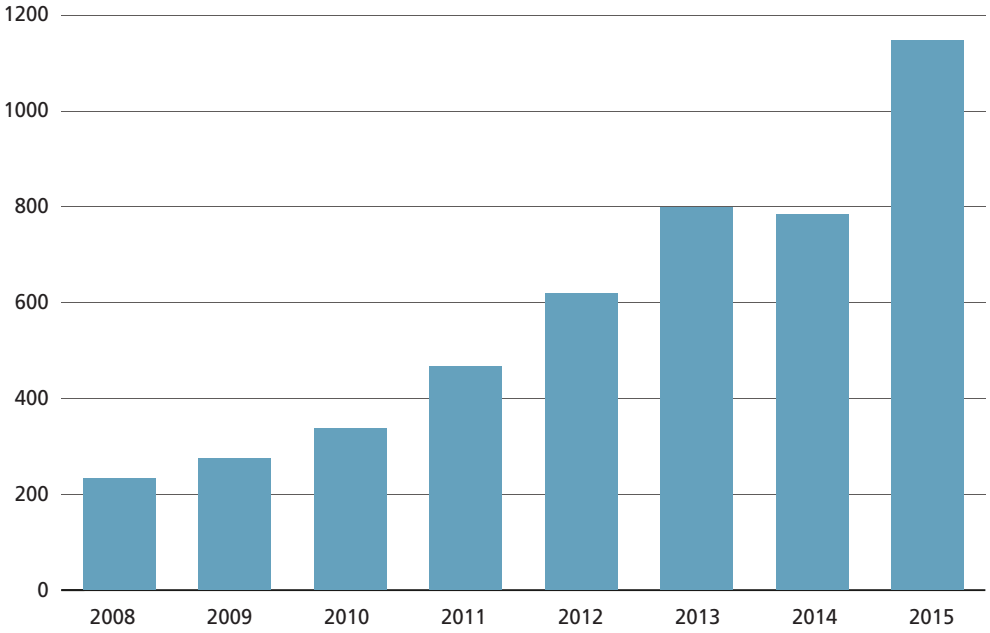


Figure 8 shows the number of near misses reported each year since 2008. The continuous increase in the number of events reported is paralleled by the increase in the number of transfusion reactions reported.

Unlike transfusion errors, near misses are discovered and corrected before the transfusion takes place. What trend is emerging over time for transfusion errors?

Figure 9:
Number of transfusion errors reported by year 2008-2015

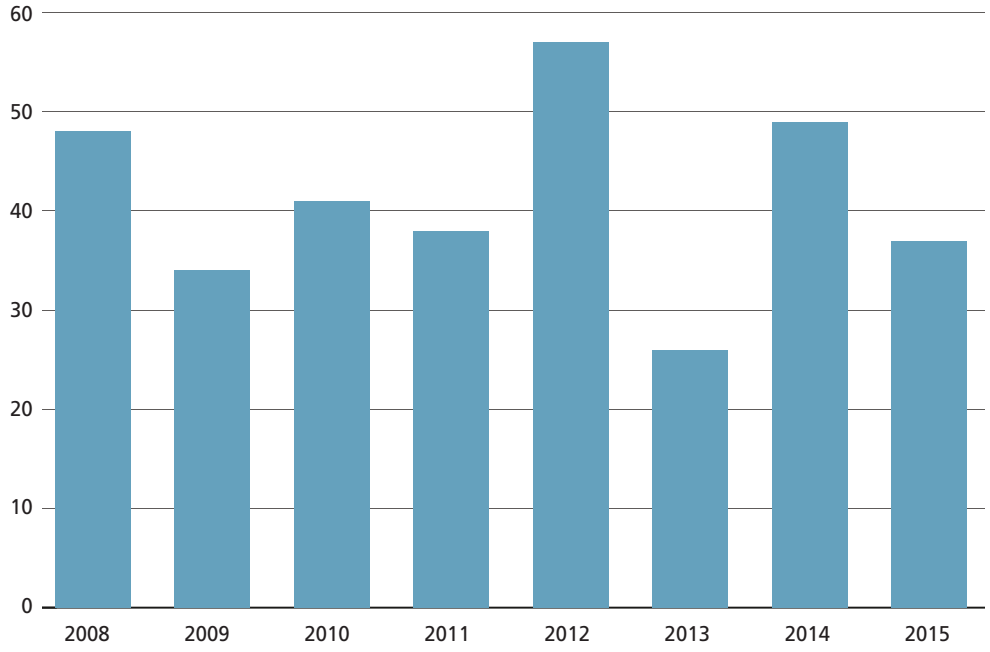


Figure 9 shows the number of transfusion errors reported by year. In contrast to near misses, there has been no increase in the reporting rate. This indicates that the increase in near misses mentioned above is not associated with an increased risk for patients; in fact it is more likely to indicate improved awareness of quality or reporting behaviour.

ABO-incompatible transfusions represent the highest-risk transfusion errors. What is the trend here?

Figure 10:
Reported ABO-incompatible transfusion errors by year 2008-2015

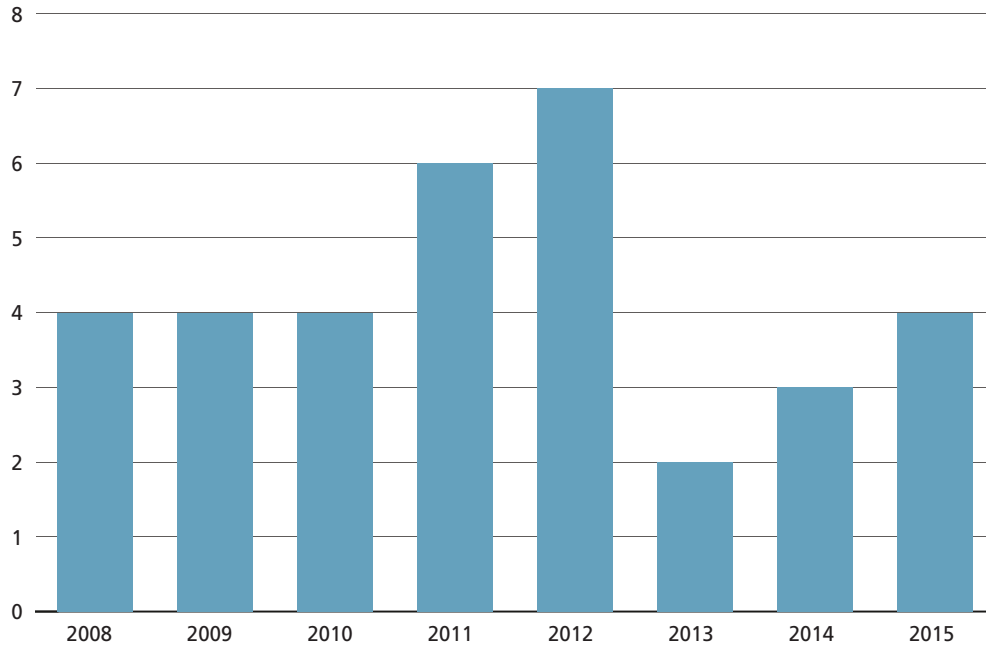


Figure 10 shows the trend for ABO-incompatible transfusion errors between 2008 and 2015. Here, too, there seems to be no increase in the reporting rate and in fact there is a slightly downward trend. However, the low numbers do not permit definitive conclusions to be drawn.

3.5 Donor reactions

Table 10:
Individual case reports of donor reactions

Category	Number	of which serious	Examples
A1.2 Artery punctured	1	0	Artery punctured, noticed because of colour of blood and speed of donation.
B1 Vasovagal reaction (VVR), immediate type All connected with donation of whole blood	10	8	After an uncomplicated donation, donor felt unwell, weak, vomited repeatedly. No improvement despite volume replacement (2 x 500 ml Ringer's solution). Cold, shivering with no temperature increase (36.1°C), persistent nausea. Blood pressure/pulse good throughout (BP around 110/65, pulse around 60/min). After 100 minutes the donor was admitted to the cantonal hospital as she had still not recovered. There only volume replacement was given with a further 1,000 ml, discharged after four hours. Felt well the next day, no infection. The donor had not slept the night before he gave blood (policeman on night shift). He collapsed after the donation (twice with convulsions). Passed two soft stools and vomited twice. Vital signs (blood pressure, pulse) were normal. In the blood transfusion service the donor received 2 x 500 ml 0.9% NaCl and other measures to treat collapse. He was transferred to the A&E department after about 1.5 hours and discharged home from there after about 2 hours of observation.
B2 VVR, immediate type with injury	4	4	The donor collapsed in the café after her second donation and fell. She sustained a laceration about 2 cm long to the head (right forehead). The patient was immediately taken to the A&E department of the regional hospital for wound care and to exclude concussion. The wound was managed with Steristrips and the patient was discharged the same day. When asked the next day, she felt well again and was keen to continue giving blood. She was stressed when she gave blood the previous day and would not do that again.
B3 VVR delayed	3	2	Approx. 7 hours after giving blood, dizziness, weakness, perspiration and hyperventilation developed during physical exertion; no loss of consciousness. The donor was taken to the A&E department in an ambulance and given i.v. fluids. He was discharged 3 hours later.
B4 VVR, delayed, with injury	2	2	After giving blood that evening, the donor got out of bed during the night, collapsed and broke her nose.
D2 Other	2	1	Pain in left side of chest, following investigation musculoskeletal chest pain was diagnosed.
Total	**22**	**17**	

Table 10 shows the categories of donor reactions reported as individual cases. 1–2 examples are given for each category.

Non-severe donor reactions reported cumulatively in tabular form are not shown in this annual report since only two of the twelve regional blood transfusion services reported them.

3.6 3.6 Quality defects and protective measures

Reports received: Overview

Figure 11:
Reports received of protective measures in response to positive infection markers

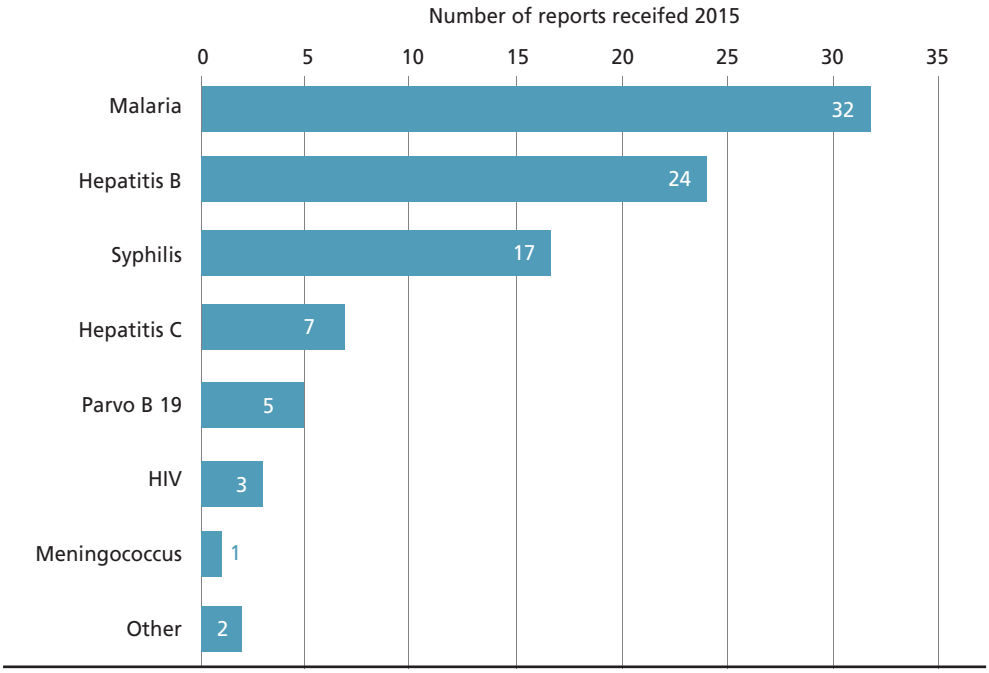


Table 11 shows the reports of infection markers discovered in donors. All reports are shown together, i.e. those involving first-time donors and repeat donors. The two reports under "Other" are one case of borreliosis and one involving an earlier blood transfusion not mentioned on the questionnaire (recipients of blood transfusions are not permitted to give blood to prevent emerging or unknown diseases being propagated in the recipient-donor cycle).

All the reports of quality defects and protective measures in 2015 involved infectious diseases. No other reports of quality defects were received.

Protective measures taken

Table 11:
Measures taken for first-time donors

Pathogen	Number of first-time donors	Measures	Comments
HIV	1	Donor deferred for 3 months	Test result evaluated as questionable
Hepatitis B	18	Donor permanently deferred	
		Temporary deferral	With certain test constellations temporary deferral is followed by repeat testing
Hepatitis C	6	Permanent deferral	
		Temporary deferral	Deferred for one year because of unspecific test reaction
Syphilis	11	Permanent deferral	
Malaria	28	Deferred for 3 years	Antibody test that also demonstrates semi-immunity

Table 11 shows the protective measures taken for first-time donors. These are generally limited to deferring the donor since the products have not usually been administered at this stage and therefore no look-back procedure is necessary.

Table 12:
Measures taken for repeat donors

Pathogen	Number of repeat donors	Measures	Comments
HIV	2	Informing blood transfusion service abroad Permanent deferral	Donor giving for the first time in CH but has previously given abroad No donation (donor came for confirmatory typing for SCT)
Hepatitis B	6	Look-back procedure Informing blood transfusion service abroad	 For first-time donors in CH who have previously given abroad
Hepatitis C	1	Look-back procedure	
Syphilis	6	Permanent deferral Temporary deferral Informing abroad	No look-back as *Treponema pallidum* does practically not survive modern manufacturing methods.
Malaria	4	Permanent deferral Temporary deferral	No look-back in cases where donor had malaria a long time ago
Parvovirus B19	4	Products destroyed	

Table 12 shows the protective measures taken for repeat donors. A look-back procedure is usually initiated if infection markers are found in repeat donors because the previous donation may have been given during the diagnostic window period.

4. Findings and prevention

4.1 Transfusion-associated circulatory overload (TACO)

Almost half the life-threatening or fatal reactions reported in 2015 involved transfusion-associated circulatory overload (TACO), including the two reported deaths. TACO has also been the second most common cause of life-threatening and fatal reactions in the global statistics since 2008. Since it is not generally possible to avoid allergic reactions, TACO is therefore the major avoidable transfusion risk.

Volume is not the only factor

There is evidence that the transfusion volume alone is not the only reason why transfusion-associated circulatory overload is so dangerous[2]. Relatively small volumes (e.g. 1 unit of pRBC) can also cause severe reactions.[3] Another striking feature is that TACO is more frequently associated with pRBC than with PC[4, +own data] even though the latter are administered at considerably higher transfusion rates in many hospitals. It is therefore conceivable that other pathophysiological processes, possibly specific to pRBC, are involved in addition to the volume overload as such.

This shows that the preventive measures published in 2013 are still just as relevant today.[5]

- The transfusion rate should be adapted to the situation. A transfusion rate of **4 ml/min** should not be exceeded in patients with stable circulation
- This must be reduced (**1 ml/kg BW/h**) in patients with impaired volume tolerance
- The volume status must be evaluated before and after a transfusion.

4.2 Pathogen inactivation of platelet concentrates (PC) using the Intercept procedure

Since 2011, all platelet concentrates (PC) in Switzerland have been pathogen-inactivated using the Intercept procedure. The purpose of this procedure is to avoid transfusion-transmitted infections, particularly those due to bacterial contamination. This measure is evaluated using the haemovigilance data.

As in previous years, in 2015 there were again no reports of high-imputability transfusion reactions to bacterially contaminated PC. Since the pathogen inactivation process was introduced for all PC in Switzerland, no high-imputability cases of sepsis due to PC have been reported. However, there was one case with the imputability possible in 2015: possible transmission of Klebsiella pneumoniae evaluated as severity grade 2 (severe), imputability 2 (possible). Despite extensive investigation, it was not possible to determine conclusively whether this was a case of retrograde contamination of the PC bag or transmission of the pathogen to the patient. The case report is expected to be published in a scientific journal in the near future. We will not go into details here in order not to prejudice the publication.

The introduction of the PI process was also associated with a reduction in the number and severity of non-infection-related transfusion reactions following transfusion of PC. The figures for 2015 again confirm the difference. The likeliest explanation for this is the generally lower plasma content of PI-PC, which reduces allergic and febrile TR to plasma components (Table 13).

Table 13:

Reported transfusion reactions involving conventional and pathogen-inactivated PC

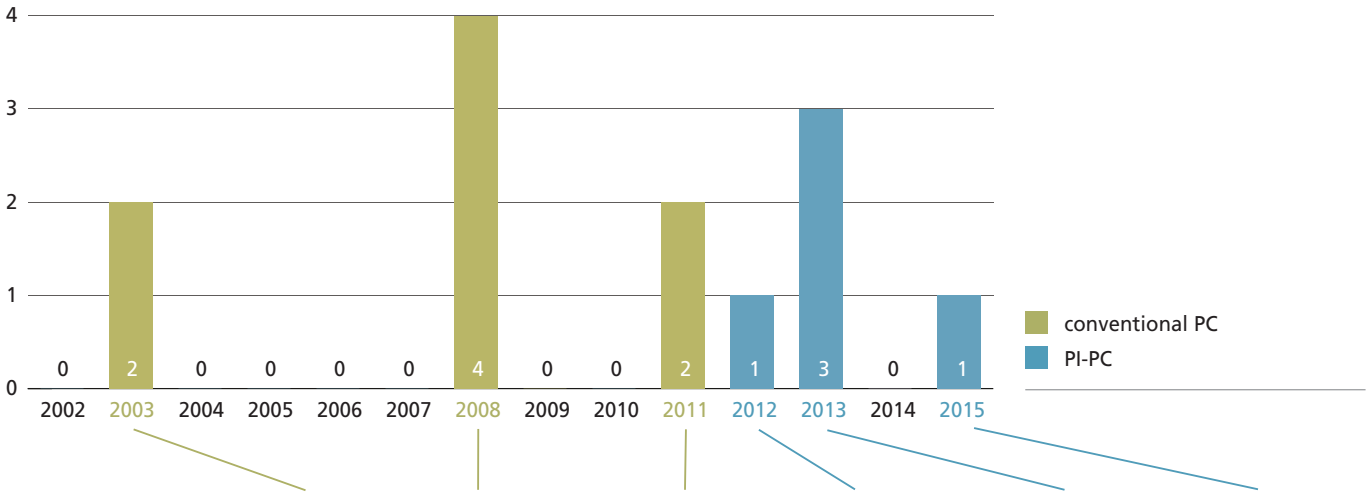
Transfusion reactions	2008 – 2011 kTK		2011 – 2015 PI-TK		
Units transfused	93 600		167 200		
Risk = 1 reaction per x PC	Reports	Risk	Reports	Risk	
All high-imputability reports	344	~ 1/270	448	~ 1/375	P<0.001
High-imputability reports, Grade 3 & 4	33	~ 1/2,800	19	~ 1/8,800	P<0.001

cPC = conventional platelet concentrates
PI-PC = pathogen-inactivated platelet concentrates

TRALI

Studies had provided evidence that pathogen-inactivated PC may constitute a higher risk of TRALI than conventional platelet concentrates[6, 7]. For this reason the Swiss TRALI cases involving PC are shown separately in the annual reports (Figure 12).

Figure 12:
Reported TRALI cases in Switzerland associated with PC transfusion



Year	2003 (2 cases)	2008 (4 cases)	2011 (2 cases)	2012 (1 case)	2013 (3 cases)	2015 (1 case)
Imputability	Certain Probable	Possible/unlikely Possible Probable Possible	Possible Probable	Probable	Probable Probable Probable	Probable
Immunogenic vs non-immun. TRALI	Immunogenic Non-Immun.	Unknown Unknown Immunogenic Immunogenic	Immunogenic Immunogenic	Immunogenic	Non-Immun. Immunogenic Immunogenic	Immunogenic
Product(s) administered	PC FFP + PC	PC (apheresis) + pRBC PC (apheresis) + FFP + pRBC PC (apheresis) PC (apheresis)	PC + pRBC PC (apheresis)	PC (apheresis)	PC (buffy coat) PC (buffy coat) PC (apheresis)	PC (apheresis)
Severity 2 = severe 3 = life-threatening 4 = death	3 3	3 3 4 3	3 3	3	3 3 2	2

Explanation: High and moderate imputabilities are shown, i.e. cases that are "certain", "probable" and "possible". The figure shows not only the "pure" PC cases but also those involving a combination of products, e.g. PC and pRBC. The cases are listed by year; the order within the individual sections is unchanged.

Example (how to read the table): In the second TRALI case in 2003, the imputability was "probable"; it was a non-immunogenic TRALI, the patient had been given FFP+pRBC, the severity was 3 (life-threatening).

Between 2002 and 2011 a total of 247,700 conventional PC were transfused and 8 TRALI (5 immunogenic TRALI, 2 TRALI with unknown aetiology and one non-immunogenic TRALI) were reported, while between 2011 and 2015 167,200 pathogen-inactivated PC were transfused and there were 5 TRALI reports (4 immunogenic TRALI and one non-immunogenic TRALI). This is equivalent to a TRALI rate of approx. 1:31,000 conventional and 1:33,000 pathogen-inactivated PC. The Swiss haemovigilance data therefore provide no evidence of an increased TRALI risk as a result of the Intercept pathogen inactivation of PC.

Efficacy

Possible effects of the PI process on platelet stability and functionality have long been the subject of research. There were no reports of lack of efficacy in 2015.

4.3 Transfusion errors and quality assurance in hospitals

There has been a continual increase in the reporting rate for near misses since the Swiss haemovigilance system was set up. There was a particularly sharp rise in 2015, from 784 reports in 2014 to 1,147 in 2015. By definition, in near misses the error is discovered and corrected before the transfusion is given and a transfusion error occurs. The increase in reporting may therefore be the result of a larger number of quality assurance measures such as intensified event reporting, greater awareness of quality assurance in general, or an increase in willingness to report. These developments in quality assurance are also reflected in the number of transfusion error reports which, in contrast to near misses, have not increased. In particular, the reporting rate for the highest-risk transfusion errors, i.e. ABO-incompatible errors, seems to be stable or trending slightly downward, something that has also been observed in other countries[8].

The Therapeutic Products Act requires institutions that transfuse blood to establish a quality assurance (QA) system. The function of the QA system is to define a framework for preventing avoidable transfusion reactions as far as possible and identifying unavoidable transfusion reactions in good time. However, the legislation defines neither the structure nor the scope of the QA system. In response to many requests, a working group was set up in 2014 to produce guidelines for quality assurance in the practical transfusion setting. The guideline is intended to stipulate what a QA system should regulate and what the minimum requirements are. Hospitals can also use it as a checklist for updating/refining their QA systems. The working group comprises members of the following professional groups:

- Cantonal pharmacists (“Kantonsapotheker”)
- Cantonal medical officers (“Kantonsärzte”)
- Haemovigilance officers
- Swissmedic.

4.4 Protective measures for positive infection markers

There were substantially more reports of protective measures being taken in 2015 than the year before. The number increased from 12 reports in 2014 to 91 in 2015. The main explanation for this increase is the fact that Swissmedic and the manufacturers confirmed the definitions and procedures at the start of 2015 (described in Chapter 2.2). This resulted in a higher reporting rate.

The objectives of protective measures are as follows:

- To protect recipients against transfusion products with quality defects, particularly transfusion-transmitted infections
- To protect recipients against the consequences of infectious diseases if transmission has already occurred by identifying the undetected transmission, and to prevent potential subsequent transmission
- To monitor and evaluate the testing strategies and donor suitability criteria used in Switzerland.

Classical transfusion-transmissible pathogens (HIV, HBV, HCV):

The most important protective measures adopted for positive infection markers are destruction of the donated blood, deferral of the donor and look-back procedure. The testing strategies, donor suitability criteria and protective measures currently in use – provided that they are applied rigorously – produce an excellent level of recipient safety. The last identified HIV infection associated with a transfusion in Switzerland occurred in 2001[9].

Zika virus

There were no single case reports of protective measures relating to Zika virus. The virus is, however, a challenge that is new in the field of blood safety[10]. The following measures and donor suitability criteria currently ensure a high level of safety in Switzerland (Status 15 August 2016):

Ongoing risk analysis by the Blood Transfusion Service of the Swiss Red Cross and by the FOPH

- Ongoing epidemiological monitoring of countries with autochtonous Zika cases and active transmission of Zika virus with corresponding continuous revision of donor suitability criteria
- FOPH provides ongoing information about national developments to the Blood Transfusion Service of the Swiss Red Cross

Adaptation of the donor suitability criteria on the basis of the currently available data

- Donors who have spent time in an epidemic country will be rejected for 1 month after their return
- Sexual partners of returning travellers will not be rejected; theoretical risk calculations have estimated the risk of a viraemic donor following sexual transmission by a returning traveller at 1 in 10 million or less
- Donors diagnosed with or suspected of having Zika disease will be rejected for 1 month after the symptoms have subsided

Testing

- Global donor screening is not done. PCR testing systems are being evaluated in studies.

Post-donation information

- Donors are requested to inform the regional blood transfusion service as soon as possible if they develop a high temperature or if an infectious disease is diagnosed after they have given blood.

Development and future plans

- A plan of action has been developed in case the Zika virus becomes endemic in Switzerland or Europe. The objective of the plan is to ensure the adequate provision of safe blood in Switzerland.

Oversight and monitoring

- Swissmedic checks whether the measures adopted are in keeping with the current state of science and technology and whether the market surveillance data indicate that additional measures are necessary to protect the recipients of blood products.

Hepatitis E (HEV)

In 2015 there were again no reports of transfusion-transmitted hepatitis E in Switzerland. A patient-specific look-back was triggered for one patient with hepatitis E, but this proved to be negative. This means that the patient must have acquired hepatitis E by a route other than blood transfusion. In recent years, increasing attention has focused on the problem of HEV both in Switzerland and internationally. Immunosuppressed patients, particularly transplant recipients, are at risk of chronic hepatitis E that can lead to cirrhosis of the liver. Infection can occur both through blood products and "naturally" (the latter probably through foodstuffs). The prevalence of chronic hepatitis E among transplant recipients is estimated at about 1-3 percent[11, 12, 13, 14, 15]. It is more difficult to estimate the prevalence in other patient groups with immunosuppression, possibly because it is lower.

It is recommended to test immunosuppressed transplant recipients for the hepatitis E pathogen (NAT) if liver transaminases are elevated. This is because hepatitis E can be successfully treated or eliminated in the majority of cases. An interdisciplinary working group has been set up in Switzerland to focus on the prevention of (blood-borne) hepatitis E and its sequelae.

Creutzfeldt-Jakob disease (CJD)

The individual manufacturers did not report cases of CJD because the FOPH and the focal point ("Meldestelle") of the Blood Transfusion Service of the Swiss Red Cross consult directly to determine whether patients with CJD in Switzerland were blood donors. Classic forms of CJD, such as the sporadic form, are nowadays not considered to be transmissible in blood. For this reason, further look-back procedures are not done in Switzerland other than to inform the hospital that performed the transfusion.

Tick-borne encephalitis (TBE)

Following a case report from Finland[16] and the possibility of blood donors harbouring latent forms, it can be assumed that TBE is transmissible in blood in principle. From 2017 the intention is therefore to ask TBE patients whether they had a blood transfusion (labile blood products) during the four weeks before the onset of the disease. Donor samples will then be re-tested with the aim of identifying (rare) cases of blood-borne TBE and taking appropriate action as necessary.

5. Sample case reports

Deaths

TACO
(pRBC, imputability probable, Grade 4)

A 76-year-old patient with symptomatic anaemia of unclear origin (she refused to be examined), chronic right-heart failure with ascites and pleural effusion, aortic stenosis and stable chronic renal failure was given 2 pRBC. Dyspnoea and mild tachycardia developed approx. 4.5 hours after the start of the pRBC transfusion (1.5 hours after the second bag was started). The patient was treated with 20 mg furosemide iv. The transfusion was not discontinued, both bags were administered within 6 hours. At the end of the transfusion her blood pressure rose from 120/76-->150/95 mm Hg, HR 112/min. One hour after the end of the transfusion the patient was subfebrile at 37.7°. The first signs of shock developed a further hour later with BP 90/25, HR 115; repeat treatment with 20 mg furosemide iv, methylprednisolone 125 mg iv, inhaled ipratropium bromide/salbutamol and budesonide and O2. Blood pressure rapidly improved to 120/70 with a fluctuating level of consciousness. Neither the patient nor her family wanted her to be transferred to the acute ward. She died two days after the transfusion.

Investigation: Review of the documentation (blood group comparison) showed nothing abnormal, nor did the immunohaematology apart from known anti-C and anti-e antibodies. IgA was in the normal range. The blood cultures from both product bags were sterile. LDH was greatly elevated the day after the transfusion at 5,141 U/l, as was conjugated bilirubin at 192 µmol/l. Haptoglobin was low (<0.1 g/l). Haemoglobin rose from 7.5 prior to the transfusion to 11.4 g/dl the next day. No chest X-ray was done. NT-pro-BNP and the donor's anti-HLA antibodies were not determined.

Assessment: The initial increase in blood pressure, the partial good response to diuretics and the patient's substantial risk factors are commensurate with a TACO. A TRALI cannot be excluded, although the criteria put forward by the Consensus Panel [17] are not met in the absence of a chest X-ray and the existing signs of volume overload. The laboratory findings are typical of haemolysis; however, the patient was already in shock when the tested blood was drawn. Relevant haemolysis is negated by the sharp increase in haemoglobin and the otherwise normal results of immunohaematological testing.

The case was classified as TACO, Grade 4 with "probable"imputability.

TACO/TRALI
(pRBC, imputability probable, Grade 4)

An 85-year-old patient with prostate cancer with bone metastasis treated with 20 mg prednisone and anaemia with dyspnoea requiring transfusion was given two pRBC concentrates. His dyspnoea worsened after about 10% of the second bag and his temperature subsequently rose, blood pressure rose from 126/50 –> 170/73 mm Hg, HR increased from 86 –> 113/min. His dyspnoea got progressively worse, O_2 saturation was 93% with 4 litres of O_2. A chest X-ray showed bilateral shadows compatible with ARDS; a cardiac component was not excluded. CT excluded pulmonary embolism. The next morning he had moderate dyspnoea and was afebrile. The dyspnoea persisted and the patient died after 4 days.

Investigation: Review of the documentation (blood group comparison) showed nothing abnormal, the following laboratory findings were recorded: haemoglobin 8.9 g/dl before and 10.8 g/dl after the transfusion. LDH rose to 1,061 IU/l, haptoglobin 2.66 g/l, blood cultures negative to date, no leukocytosis. Class I and II HLA antibodies were found in the female donor of the second pRBC.

Assessment: The first differential diagnosis was volume overload, suggested by the increase in blood pressure and the risk factors age, moribund state and pre-existing (cardiac?) dyspnoea. A TRALI cannot be excluded in view of the HLA antibodies found in the donor of one of the two products, nor can a combined cause of the infiltrates. The case was classified both as TACO and as TRALI, Grade 4, with "probable" imputability.

Addition to a case from 2014: Acute Chagas disease (PC, possible imputability, Grade 4)

This case has been recorded under 2014 because the possible connection with a PC transfusion given in 2008 was identified and reported in 2014. A publication, which is now 'in press', details the aspects of Chagas-Screening in Switzerland and of this case[18].

The patient had received seven PC transfusions between 2005 and 2008. One of them, given in 2008, had originated from a donor who tested positive in Chagas serology in 2013 (testing of donors at risk was introduced in 2013).

The patient developed acute Chagas myocarditis with a fatal course in 2010, 4 months after he had undergone a kidney transplantation with a triple-therapy immunosuppressive regime[19]. Transmission by the transplanted kidney was excluded, and it was confirmed that the immunosuppression had reactivated an existing infection.

The case was assigned the imputability "possible" since a pure chance connection is very unlikely, yet on the other hand the possibility that the infection took place during one of the patient's trips to South America cannot be excluded. However, Chagas infections are extremely rare in travellers[20].

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