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Haemovigilance Annual report 2016

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The annual report was written by

Swissmedic, Swiss Agency for Therapeutic Products
Safety of Medicines Department
Haemovigilance Unit
Hallerstrasse 7
P.O. Box
3000 Berne 9
Switzerland

haemovigilance@swissmedic.ch
www.swissmedic.ch/haemovigilance-report

Contact
Lorenz Amsler, Clinical Reviewer

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

Version 2-0
Corrections (Table 3) from 15.01.2018

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Abbreviations

°C	degrees Celsius
AB	antibodies
ABO	ABO blood group system
Ag	antigen
BD/BTO	blood donation/blood transfusion organisation
BG	blood group
BMA	biomedical analyst
BP	blood pressure
BPr	blood product
CcEe	rhesus antigens in the rhesus system (in addition to rhesus D)
CH	Switzerland
CMV	cytomegalovirus
cPC	conventional platelet concentrate
CT	compatibility testing
DAT	direct antiglobulin test, also known as direct Coombs test
e.g.	for example
emp	employee
FFP	fresh frozen plasma
FNHTR	febrile non-haemolytic transfusion reaction
g/l	grams per litre
Hb	haemoglobin
HBV	hepatitis B virus
HCV	hepatitis C virus
HEV	hepatitis E virus
HIV	human immunodeficiency virus
HLA	human leukocyte antigen
HPC	Health Professional Communication
HTR	haemolytic transfusion reaction
HV	haemovigilance
IBCT	incorrect blood component transfused
ID	identification
IH	immunohaematology
ITP	immune thrombocytopenia
iv	intravenous
K	antigen/antibody of the Kell blood group
LDH	lactate dehydrogenase
LIS	laboratory information system
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
O_2	oxygen
Op	operating theatre
PC	platelet concentrate (PCa: apheresis-derived; PCb: whole blood-derived)
PI-PC	pathogen-inactivated platelet concentrate
pos	positive (e.g. tested positive for an infection marker)
PR	medical history (patient records)
pRBC	packed red blood cells
prob.	probably
Rh	rhesus (factor) e.g. Rh+ = rhesus positive
SCT	stem cell transplantation
SOP	standard operating procedure (guidelines, instructions etc.)
SRC	Swiss Red Cross
T&S	type and screen (to define blood group and detect irregular antibodies)
T. cruzi	Trypanosoma cruzi (causative agent in Chagas disease)
TACO	transfusion-associated circulatory overload
TAD	transfusion-associated dyspnoea
TR	transfusion reaction
TRALI	transfusion-related acute lung injury
U/l	unit(s) per litre
VVR	vasovagal reaction
WBIT	wrong blood in tube (wrong patient with wrong blood/label in/on the blood tube)
Y	year

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List of contents

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1. Introduction

The haemovigilance annual report provides a regular update on facts and developments relating to transfusion safety. To produce a report that stands on its own, certain aspects and sections of text from previous annual reports are taken over, particularly into the sections Introduction and Methods.

1.1 Haemovigilance

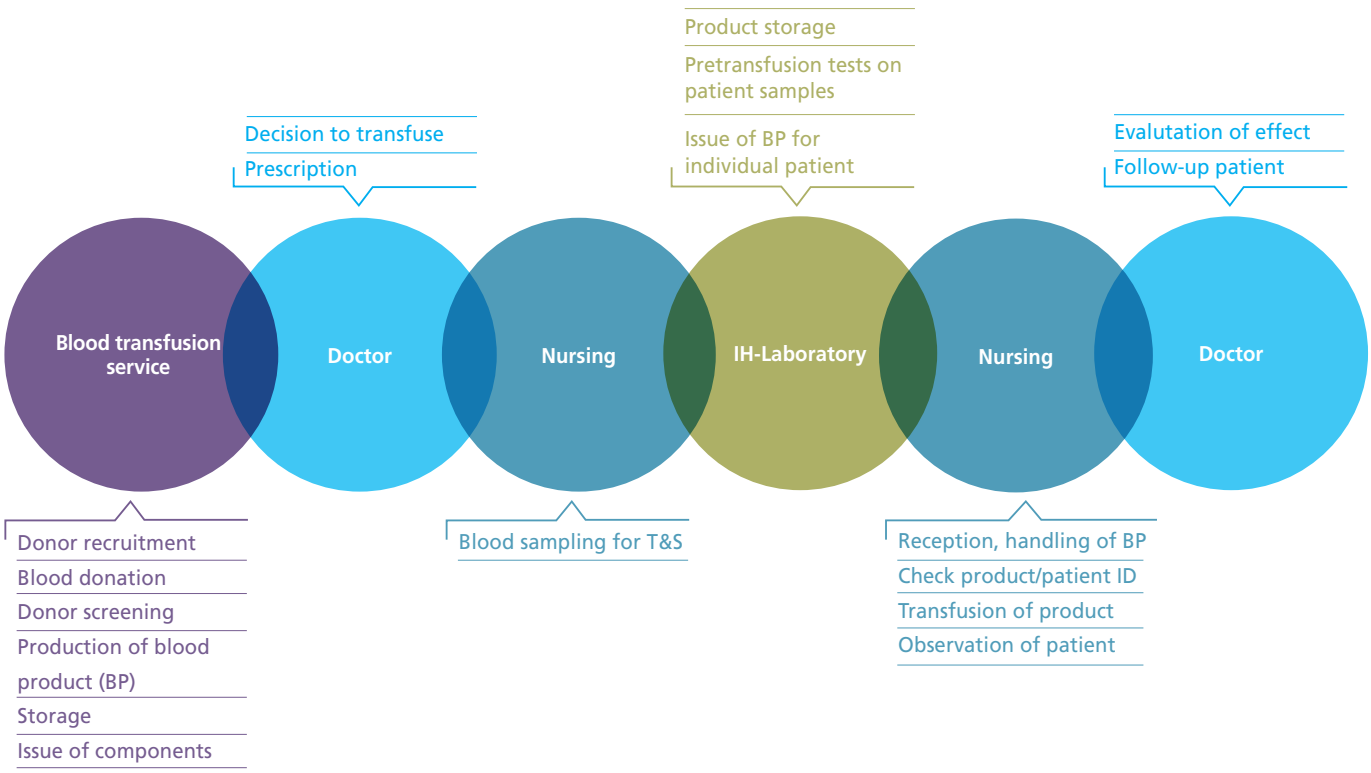
Haemovigilance is a systematic approach to recording adverse events associated with the collection, production and administration of blood transfusions. Its objective is the early detection of new risks and quality defects; at the same time the national haemovigilance system triggers and evaluates preventive 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



2. Methods

The expanded definitions of TR severity and the section on transfusions in children did not appear in the 2015 annual report and are new in this edition.

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 stores.

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 store 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 www.swissmedic.ch/haemovigilance-reporting.

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 undesirable effects of a transfusion 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::

- Permanent damage (or permanent risk in the case of alloantibodies)
- The reaction must otherwise be evaluated as medically significant: If the following symptoms or findings are present, a transfusion reaction should be classified at least as severe:
  - **Fever > 39° C and > 2° C increase**
  - **Dyspnoea / hypoxia** (other than a very mild form)**, pulmonary oedema**
  - **Drop in blood pressure** (other than a very mild form)**, loss of consciousness**
  - **Suspected haemolytic transfusion reaction**
  - **Suspected bacterial contamination / infection as a result of the transfusion**
  - **Positive blood cultures in patient or blood product**
  - Timely intervention is necessary to avoid permanent damage or a life-threatening course

Grade 3: life-threatening

Grade 4: death

The severity of a transfusion reaction is evaluated independently of its possible connection with the transfusion (imputability). For example, suspected cases of bacterial contamination or other infections should be classified as severe – and should remain so – even if the imputability is classified as 'unlikely' in the final evaluation.

Imputability (causal connection between transfusion and reaction):

0 = **not evaluable**
1 = **excluded/unlikely**: The reaction is definitely/more likely to be due to other causes
2 = **possible:** The reaction can be explained both by the transfusion and 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

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 of this kind 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. The following definitions apply to near misses and transfusion errors:

- **Grade 1** (non-severe): Formal error with no potential for use by mistake
- **Grade 2** (severe): Formal error with potential for use by mistake or transfusion error involving a suboptimal product
- **Grade 3** (life-threatening): Use by mistake 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 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).

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 above for definitions)
- **Imputability 0-4** (see above for definitions)

IIn 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, which is referred to as a "passive monitoring 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.

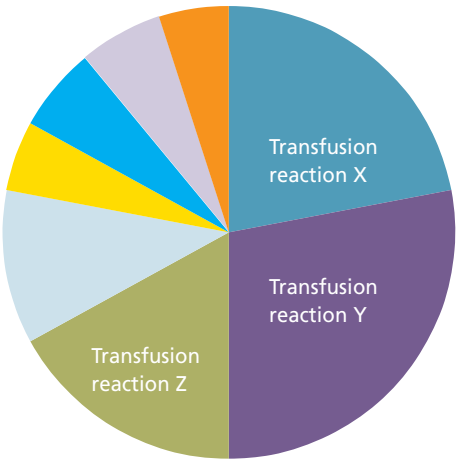
Transfusions in children: Comparison of acute transfusion reactions in adults and children

The Swiss HV database contains more than 10,000 TR reports submitted since 2008, over 700 of which occurred in children (<18 years old). The data from adults and from children are compared to identify the differences in the reaction profile. It is not possible to compare the reporting rates directly since it is not known how many of the approximately 300,000 transfusions per year are administered to children. This is why a method known as disproportionality analysis is used[1,2]. In this method the proportion of specific transfusion reactions is determined and compared between adults and children.

The reaction profiles of adults and children can be illustrated in the form of pie charts, and the size of the individual slices is compared (Figure 2).

Figure 2

Example: Reaction Profile, children



Example: Reaction Profile, adults

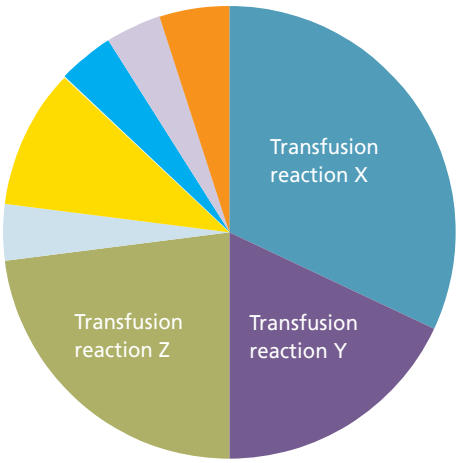


Figure 2 shows the principle of disproportionality analysis with the comparison of the reaction profiles. This method can be used to identify differences between two groups, or in other words to find out which group has the greatest proportion of which reaction.

The total reporting rate (size of pie) must be compared to confirm differences between the risk for adults and the risk for children identified by this analysis. The risks are estimated on the basis of the scientific literature. In addition, the total reporting rates for adults and children have been estimated at Basel University Hospital for comparison purposes on the basis that the same internal reporting system is used there for both adults and for paediatric patients.

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 stores) are required to report the protective measures adopted when quality defects are identified. In most cases this involves donors who have tested positive for infection markers.
The individual case reports are entered in the Swissmedic database and evaluated both globally and pathogen-specifically.

Statistics: Fisher's exact test is used for categorical data (2x2 table). Statistical significance means $p<0.05$ (two-tailed).

3. Results

3.1 Reports received: Overview

Table 2
Reports of adverse events

Type	Number
Transfusion reactions	1,777
Transfusion errors / incorrect blood component transfused (IBCT)	36
Near misses (NM)	1,168
Donor reactions	24
Quality defects and protective measures:	122
Total number of reports evaluated	**3,127**

Table 2 shows the number of reports involving labile blood products received in 2016. A total of 3,127 reports were received.

Figure 3
Events reported by year

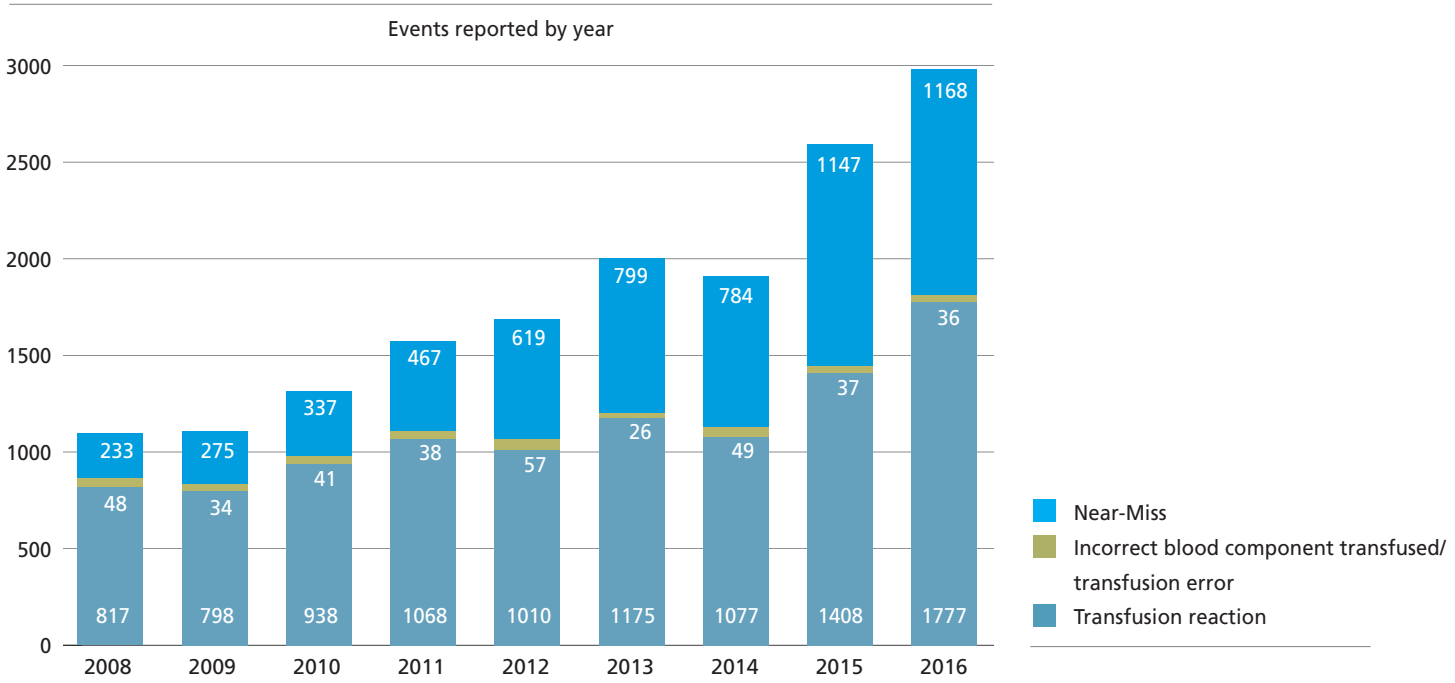


Figure 3 shows the number of events reported compared with previous years. The increase in transfusion reactions is due largely to the increase in the reported alloantibodies, as explained below (Chapter 3.3).

3.2 Number of transfusions and reporting rate

Table 2
Number of transfusions in Switzerland

Blood components	2008	2009	2010	2011	2012	2013	2014	2015	2016
pRBC	313,587	311,521	308,670	308,627	297,582	279,510	262,953	248,647	239,890
FFP (therapy units)	65,800	70,300	61,500	50,063	49,832	44,083	38,183	33,658	33,310
PC (products)	27,600	29,600	29,900	33,068	34,265	34,750	35,328	36,439	38,374
Total blood components	**406,987**	**411,421**	**400,070**	**391,758**	**381,679**	**358,343**	**336,464**	**318,744**	**311,574**

FFP = Fresh frozen plasma
PC = Platelet concentrates

Table 3 shows the number of transfusions given throughout Switzerland in the past 9 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. While packed red blood cells and plasma are still showing a declining trend, consumption of platelets is increasing slightly but steadily.

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

Figure 4
Reporting rate (reports per 1,000 transfusions), all reports

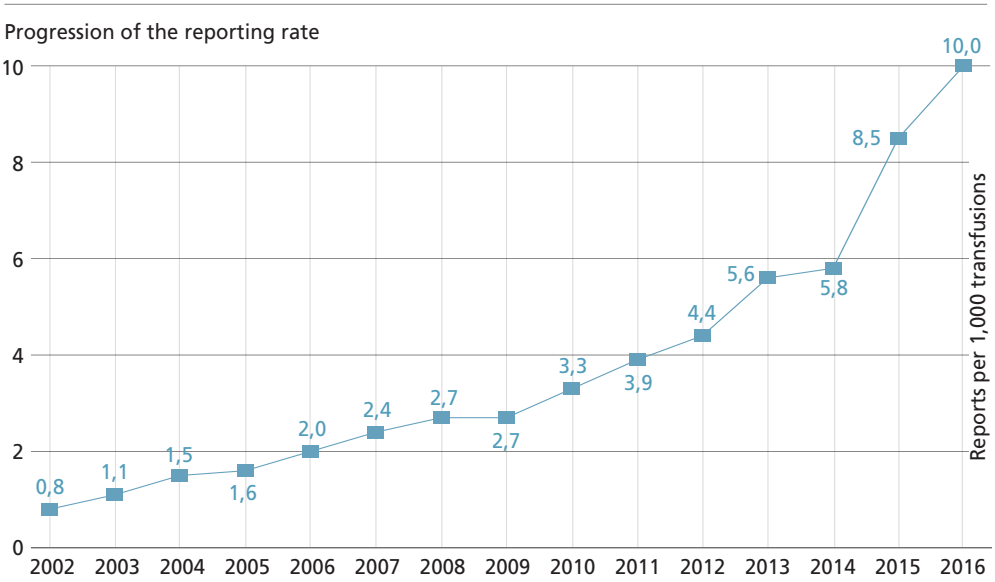


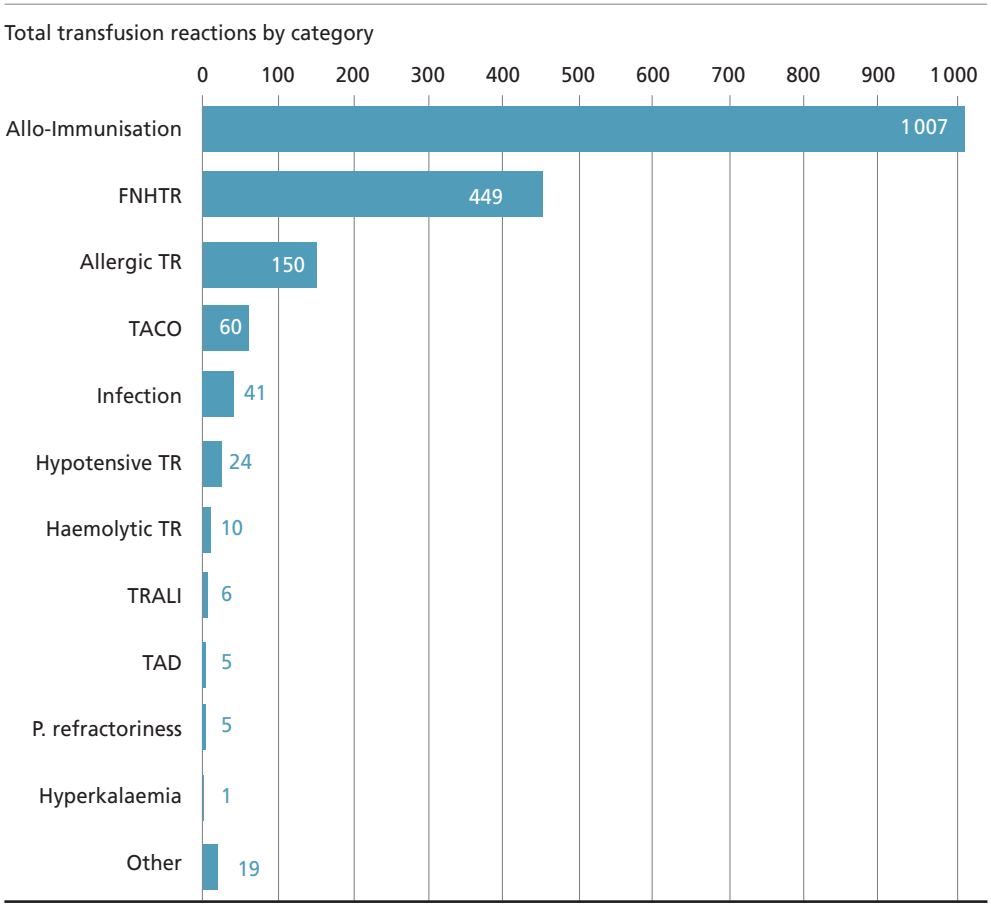
Figure 4 shows the overall reporting rate. It is calculated from the total number of reports per 1,000 transfusions or, more precisely, per 1,000 product bags supplied. The calculation includes all types of reports and all imputability classifications, i.e. all 3,127 reports in 2016. The reporting rate rose again in 2016 and currently stands at 10.0 reports per 1,000 transfusions. The reporting rate is very high by international standards[3].

3.3 Transfusion reactions (TR)

Overview

A total of 1,777 transfusion reactions were reported.
Figure 5 shows their distribution by reaction category.

Figure 5
Transfusion reactions (TR) reported in 2016 by category



N = 1,777

FNHTR	Febrile non-haemolytic transfusion reaction
TACO	Transfusion-associated circulatory overload
TAD	Transfusion-associated acute lung injury
TRALI	Transfusion-associated dyspnoea
P	Platelet

Figure 5 shows the distribution of the transfusion reactions reported in 2016 among the different categories. All 1,777 cases are shown, irrespective of imputability. With the exception of 2 cases with 'possible' imputability, all 41 cases of infections were suspected cases which were classified with low imputability following investigation. The cases summarised under 'Other' mostly involve unspecific symptoms such as nausea or increased blood pressure. They do not include any known transfusion reactions, i.e. in 2016 there were no reported cases of post-transfusion purpura, transfusion-associated graft-versus-host disease or haemosiderosis.

Deaths

Table 4
Reported deaths in 2016 by category and imputability

Number	Category	Imputability	Product
3	Infection, bacterial	unlikely	pRBC
2	TACO	possible	pRBC
1	Other (seizure, respiratory arrest)	unlikely	pRBC
1	Infection, viral	excluded	pRBC

pRBC = packed red blood cells

Table 4 shows all the deaths reported in 2016. With the exception of the two cases of TACO, the imputability of which was 'possible', all the deaths had low imputability, i.e. a causal relationship with the transfusion is unlikely.

Imputability (relationship to the transfusion)

Table 5
Number of transfusion reactions (TR) in 2016 by category and imputability

Transfusion reaction	All	Low	'Possible'	High
Allo-AB	1,007	2	284	721 (72%)
FNHTR	449	66	262	121 (27%)
Allergic TR	150	5	42	103 (69%)
TACO	60	2	20	38 (63%)
Hypotensive TR	24	4	9	11 (46%)
Infection, bacterial	39	37	2	
Infection, viral	2	2		
TAD	5		3	2
TRALI	6	3	2	1
HTR, acute	9	1	1	7
HTR: delayed	1			1
Hyperkalaemia	1			1
Platelet refractoriness	5		1	4
Other	19	6	12	1
Number of reactions	**1,777**	**128 (7%)**	**638 (36%)**	**1,011 (57%)**

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

High imputability:
causal relationship with the transfusion 'probable' or 'certain'.

Table 5 shows the reports by 'imputability' within the categories. Imputability describes the likelihood of there being a causal relationship with the transfusion. The degree of imputability is highly dependent on the reaction. Alloantibodies detected in the laboratory, for example, nearly always have high imputability.

In 2016 high imputability was attributed to 1,011 reactions (57% 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 6
High-imputability reactions by category and severity

Severity	All	Grade 1	Grade 2	Grade 3	Grade 4
Allo-AB	721		721		
FNHTR	121	118	3		
Allergic TR	103	83	16	4	
TACO	38	14	17	7	
Hypotensive TR	11	6	4	1	
HTR, acute	7	4	3		
HTR, delayed	1		1		
Platelet refractoriness	4		4		
TAD	2	2			
TRALI	1		1		
Hyperkalaemia	1	1			
Other	1	1			
Total	**1,011(100%)**	**229 (23%)**	**770 (76%)**	**12 (1.2%)**	**0**

Table 6 shows the severity of the high-imputability cases. There were no deaths in 2016 (Grade 4) but 12 life-threatening transfusion reactions (Grade 3).
These are shown in Figure 6.
The vast majority of the severe cases (Grade 2) involved allo-immunisation, which is classified as severe because of the permanent risk or possible difficulties associated with finding a compatible product for a subsequent transfusion. The sharp increase in reports of allo-immunisation (2014: 285, 2015: 579, 2016: 721) indicates a high level of reporting compliance in the hospitals.

Life-threatening or fatal transfusion reactions

Figure 6
Life-threatening or fatal transfusion reactions

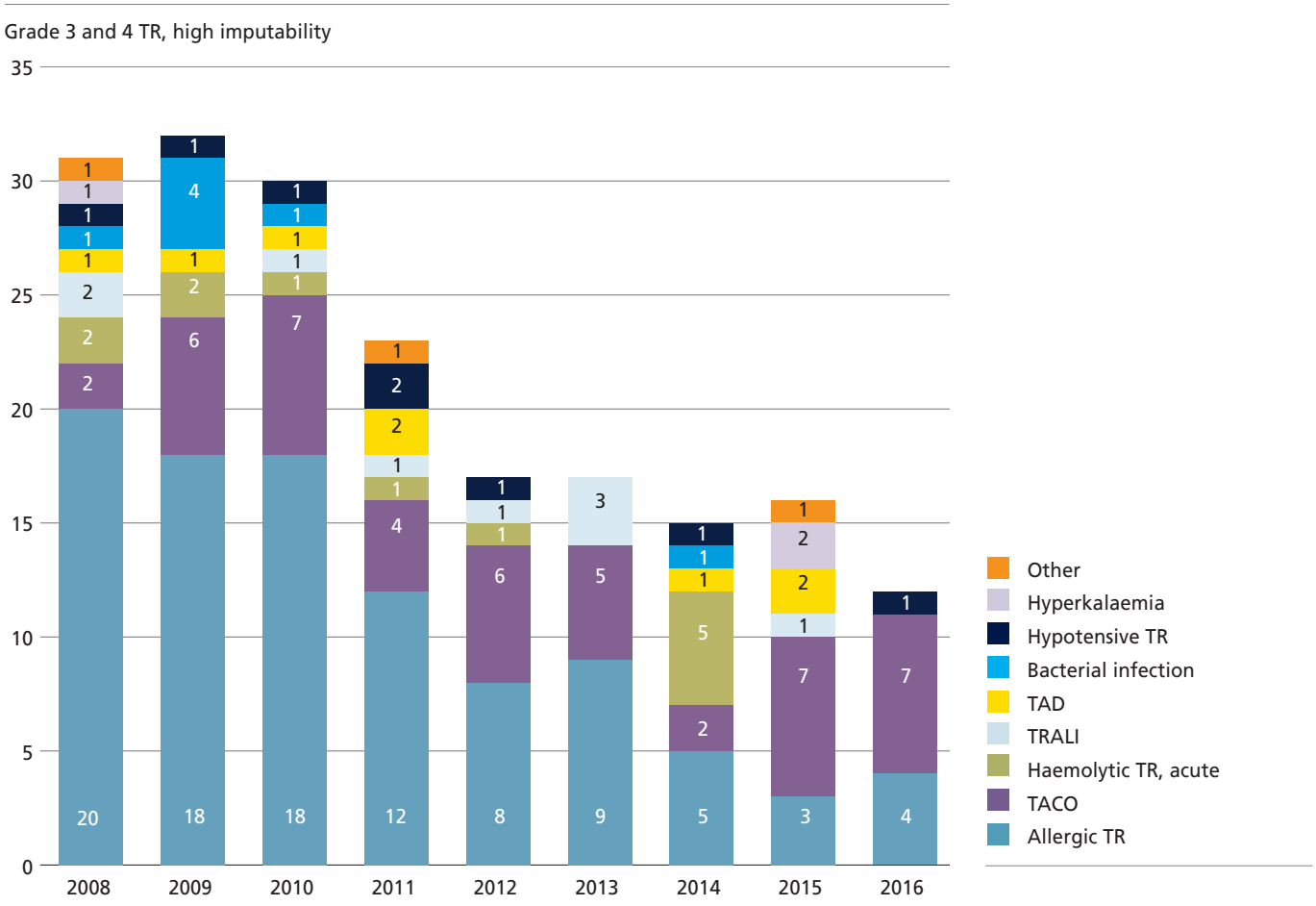


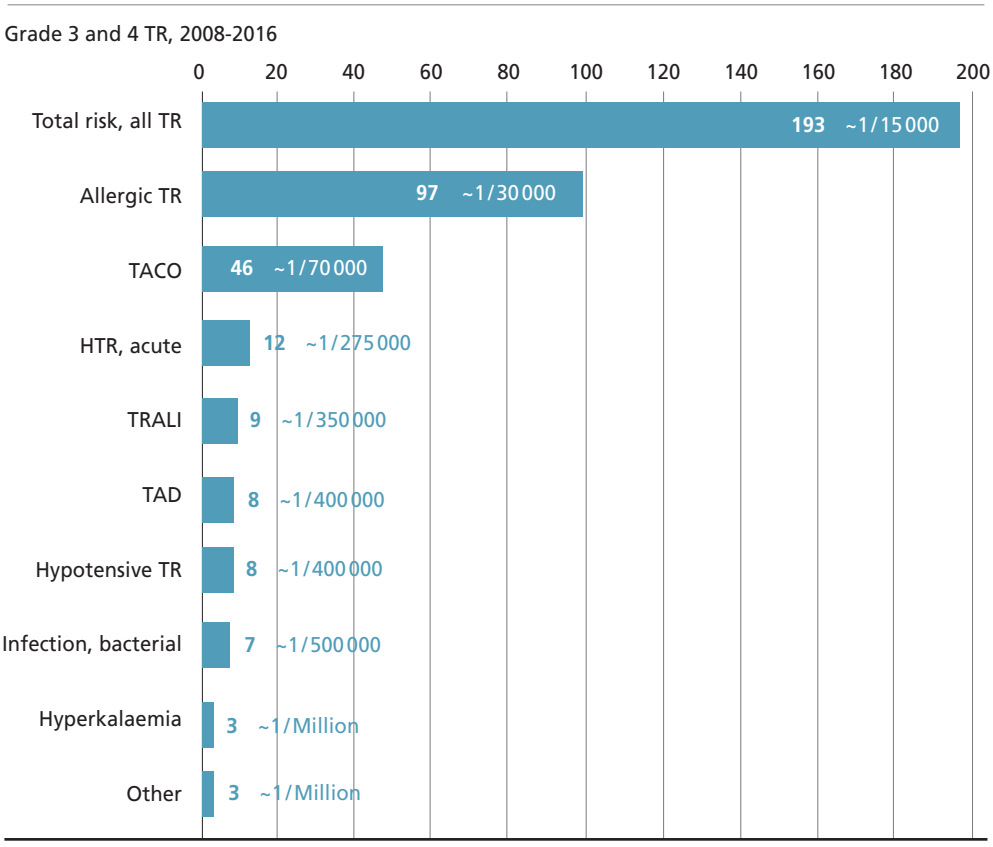
Figure 6 shows the distribution of life-threatening and fatal transfusion reactions over time. Of the 12 cases of life-threatening transfusion reactions in 2016, 6 occurred in connection with packed red blood cells (6 TACO cases) and the remaining 6 with platelet concentrates.
As reports of life-threatening allergic TR are declining constantly, TACO is currently the most frequent Grade 3 or 4 TR[i].

[i] There are several reasons for the decline in allergic TR: declining use of plasma; pathogen inactivation of platelet concentrates (see evaluation in the Annual Report 2015); possibly others (monitoring, therapy).

Transfusion risks

Transfusion risks are the number of reported cases per number of administered transfusions, compared for each type of transfusion reaction.

Figure 7
Risk of life-threatening and fatal transfusion reactions (TR), all blood products



3.3 million products in total administered from 2008-2016

Figure 7 illustrates the risk of life-threatening and fatal transfusion reactions. The risk is related to the products administered. in Switzerland. There were no high-imputability deaths in 2016. 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 8
Reporting rates per product, all degrees of severity

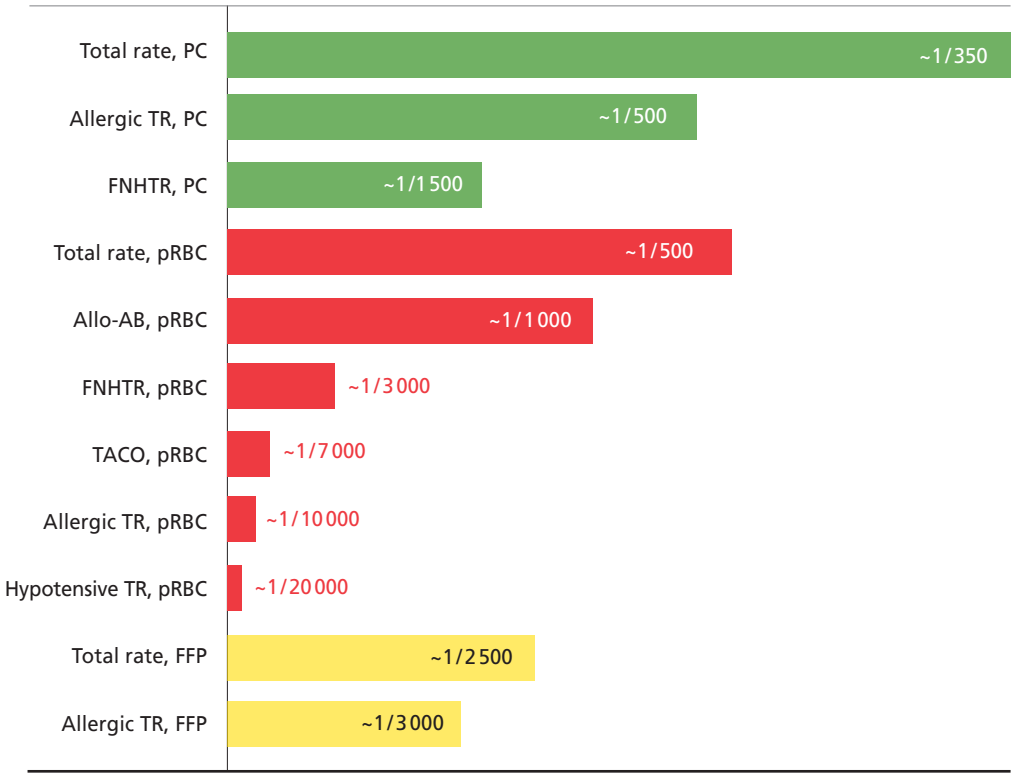


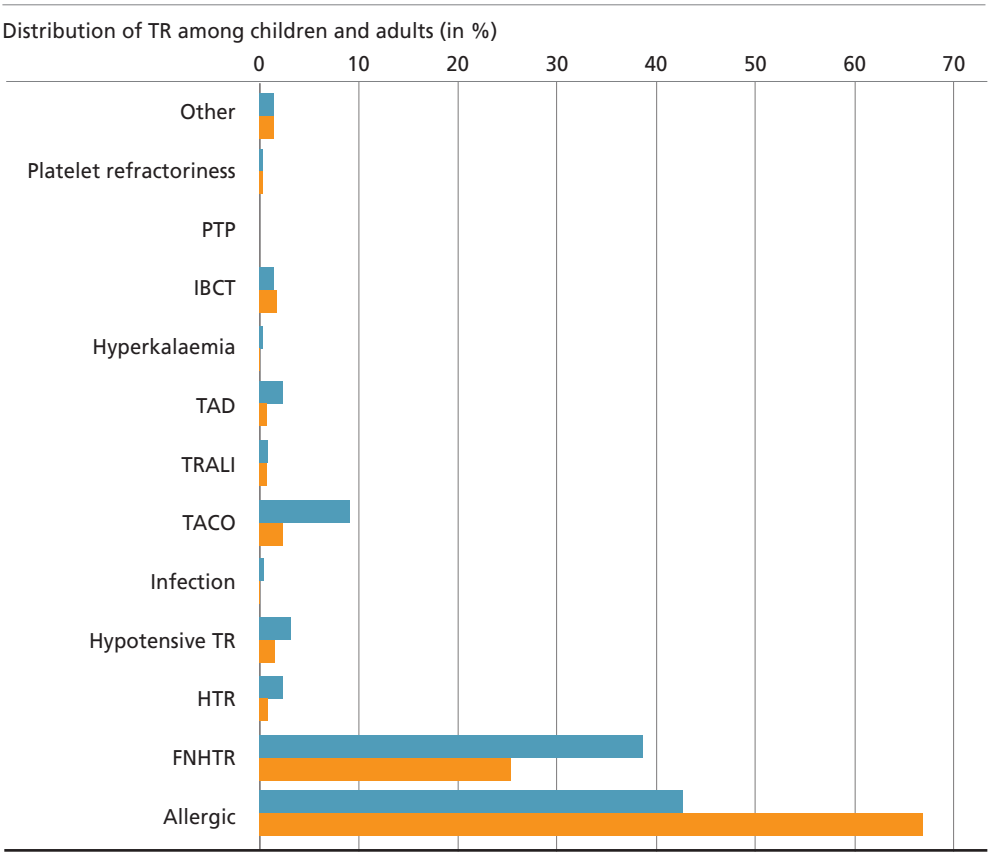
Figure 8 shows a comparison of the product-specific reporting rates. Transfusion reactions of all degrees of severity (again only those with high imputability) are shown. Only reactions reported at least 10 times are shown because events occurring more rarely cannot be reliably expressed on an annual basis as the absolute number of cases is so low.
Allergic reactions account for by far the majority of the plasma-related reports. More than half of reactions involving PC are also of an allergic nature. They account for a small proportion of reactions involving pRBC.
One case of TRALI with high imputability occurred in connection with a pRBC transfusion. (In addition, 2 possible TRALI cases were reported, one with pRBC and plasma, the other with pRBC.)

Comparison of adults and children

The disproportionality analysis (described in Chapter 2.2) was used to compare the acute transfusion reactions in adults and in children.

Figure 9

Proportions of individual acute transfusion reactions in adults and children (figures in per cent; only high imputability)



PTP	Post-transfusion purpura
IBCT	Incorrect blood component transfused (= transfusion error)
TAD	Transfusion-associated dyspnoea
TRALI	Transfusion-associated acute lung injury
TACO	Transfusion-associated circulatory overload
HTR	Haemolytic transfusion reaction
FNHTR	Febrile, non-haemolytic TR

Figure 9 shows the percentage distribution of acute transfusion reactions in adults and children. Significant differences are in TACO and allergic reactions.

TACO

Children experience proportionally fewer TACO than adults. It is not possible to state reliably on the basis of these figures whether the lower proportion also means a lower risk because the overall reporting rate (all reactions) is higher for children[2]. Since 2008 only 6 paediatric TACO cases with high imputability have been reported. The cases confirm the information in the scientific literature about TACO[4,5,6] that, among children, the under 3 year-olds are at greatest risk (Table 7).

Table 7
Cases of TACO with high imputability in children

Age	Number	Product, severity
Newborns (< 1 month)	**2**	**pRBC, non-severe** **FFP, severe**
Infant (< 1 year)	**1**	**PC, life-threatening**
1 to < 3 years	**2**	**pRBC, severe** **pRBC, severe**
3 to < 18 years	**1**	**PC, non-severe**

Table 7 shows the age distribution and severity of the 6 TACO cases in children. Five of the six cases occurred in children under 3 years. This distribution differs to a statistically significant degree from the age distribution of all paediatric cases in the HV database (nearly 1/3 under 3 year-olds).

Allergic reactions
The distribution of transfusion reactions in children shows a substantially higher proportion of allergic reactions (Figure 9). Since children have transfusion reactions more frequently in general[2], this higher proportion also equates to a higher risk. This means that there is a higher probability of allergic TR occurring in children than in adults.

3.4 Transfusion errors and near misses

36 transfusion errors and 1,168 near misses were reported in 2016.

Transfusion errors by severity/risk to patient

Table 8
Transfusion errors and near misses by severity and risk to patient

Severity/risk	Number of transfusion errors	Number of near misses
Grade 1: non-severe	**7**	**544**
Grade 2: severe	**18**	**474**
Grade 3: life-threatening	**11**	**150**
Total	**36**	**1,168**

Table 8 shows the classification of the reported transfusion errors and near misses 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 9).

Table 9

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	**1**	**Severity/risk Grade 3 life-threatening**		
		Only a few minutes after (approx. 10-15 ml) of the second pRBC transfusion the patient complained of dizziness and profuse sweating; he was also somnolent (but arousable). His vital parameters were stable a few minutes later, there was no bronchospasm or exanthema. Mild signs of haemolysis* in the laboratory. The ward noticed the mistake by the symptoms and prompt action prevented a further transfusion error. A patient with blood group AB was given pRBC intended for a patient with blood group O and vice versa; each received 2 pRBC. The first pRBC were assigned correctly using the 4-eyes principle, but the second were mixed up; the products had not been checked when the second pRBC were attached.	Administration *Total bilirubin 81 umol/l (previous day 61), LDH 173 U/l (previous day 111), haptoglobin 0.23 g/l (back to 0.67 the following day). DAT negative. Hb from 57 to 73 g/l.	Process analysis and team training
	2	**Severity/risk Grade 2 severe**		
		• 63-year-old female patient (O Rh+ Ccee K-neg) following a SCT (donor A Rh- Ccee K-neg CMV pos). According to instructions was supposed to be given O Rh+ blood, was actually given 2 A Rh+ pRBC with no clinical consequences. Blood group had tested as A, and this had also been entered in the LIS after the SCT. It was also stated in the LIS that the patient should be given O Rh+. This was evidently ignored when the product was issued.	Laboratory, administration	Instructions in the LIS should be able to block incorrect issue. Special BG card for allogeneic SCT recipients. Warnings in the clinical IT system. Production of an SOP for allogeneic SCT and labile blood products.
		• An FFP with BG O was administered to a newborn instead of AB as required by the guidelines.	Laboratory	Training
ABO system compatible by chance	**8**	**Severity/risk Grade 3 life-threatening**		
		• Patient was transferred from a hospital abroad. The only information provided on transfer was that the patient had already been given a pRBC. The patient showed a mixed-field reaction on blood typing, between A/O and Rh+/-. The lab technician assumed that the patient had previously been transfused an O Rh- pRBC. The patient was given an A Rh+ pRBC on the basis of this assumption. The information that the patient had previously been given an O Rh+ pRBC was only provided later.	Laboratory	No information. Information passed on to laboratory manager and director of medical services.
		• 2 pRBC for 2 different patients were fetched at the same time and checked on the ward using the 4-eyes principle. A further employee, who had not performed the check, attached the wrong pRBC to the female patient (born in 1992). The pRBC was ABO compatible by chance, but the patient was known to be partial D and the pRBC was Rh+.	Administration	Attention drawn to SOP and compliance with processes.
		• Two patients were each supposed to be given one PC. The PC for patient X was attached to patient Y. The patient with BG AB Rh+ was given a PC with BG A Rh+. Patient identification was not performed. When the error was analysed it was found that insufficient attention had been paid to active patient identification because the nurse had been caring for the patients for a long time and knew them well.	Administration	Attention drawn to SOP and compliance with processes.

Transfusion error	Number	Description of error	Localisation of deviation in the transfusion chain	Preventive measures against recurrence
		• The laboratory erroneously supplied a pRBC for a patient with a similar name. This mistake was not noticed during the check on the ward as the patients had the same BG. The mistake was only noticed when the laboratory phoned the ward approx. 15 minutes after the transfusion had started. The pRBC had been ordered orally and the laboratory did not get the form until later.	Laboratory	Attention drawn to SOP and compliance with processes. In future it will not be possible to order orally.
		• The wrong blood product was administered in the intensive care unit. The patient was given an FFP intended for another patient. The patients had the same BG by chance. The error was not noticed until later, so a further transfusion error happened.	Administration	Attention drawn to existing SOP.
		• The wrong blood product was administered in the intensive care unit. The patient was given an FFP intended for another patient. The patients had the same BG by chance (see above case).	Administration	Attention drawn to existing SOP.
		• 2 PC ordered under the wrong patient's name but administered to the intended patient. The error was not corrected earlier in an emergency situation.	Administration	No information
		• An FFP was issued without valid test blood. The employees assumed that the test blood was valid for 28 days.	Laboratory	Training
	1	**Severity/risk Grade 2 severe**		
		• The nurse was supposed to take a pRBC with BG O Rh- from the emergency reserve; as she was new on the ward, she took a pRBC O Rh- from the refrigerator that had nominally been tested and reserved for another patient.	Administration	Training
Allo-AB compatibility not ensured	9	**Severity/risk Grade 2 severe**		
		• Rhesus conversion in a young female patient (born in 1995) in the course of a mass transfusion as O Rh- supplies were at a critical level.	Laboratory	n.a.
		• Patient with positive AB screening test with unspecific reaction. 4 pRBC with CT were tested, 3 of which were negative and one positive. While one BMA was still discussing this with the BTO on the phone, the other gave the bags to someone who had come from the ward to pick them up. The first bag to be transfused was the one with the positive CT. The patient had no symptoms or haemolysis. An anti-Yt(b) AB was found eight days later.	Laboratory	Attention drawn to SOPs and retraining.
		• The patient was given a total of 10 FFP, 6 PC and 16 pRBC following massive bleeding after giving birth. One of the pRBC was Rhesus phenotype-incompatible.	Laboratory	n.a.
		• The patient, in whom anti-E alloantibodies were no longer detectable, was given a pRBC with phenotype Ee. A transfusion reaction with fever occurred. It was not discovered until the cause of the transfusion reaction was being investigated that the patient was known to have anti-E.	Laboratory	No information
		• Patient with known anti-Kp(a) alloantibodies for whom the allo-AB were not taken into account as the AB screening was negative. The IT system did not issue an alert and also did not block the products. No transfusion reaction occurred.	Laboratory	Software update

Transfusion error	Number	Description of error	Localisation of deviation in the transfusion chain	Preventive measures against recurrence
		• Known AB were not taken into account in an emergency situation. The pre-existing anti-E were subsequently reconfirmed and the information has been in the system since 2008. The last transfusion was 3 months previously. The ward was notified of the result at the end of the transfusion, the patient was subsequently observed closely.	Laboratory	Attention drawn to SOPs and retraining.
		• Emergency transfusion of 8 pRBC. One of the pRBC was anti-M-positive. The patient has been registered in the system since 2000 as having anti-M. The error was discovered by the person responsible for HV in the context of a transfusion reaction (FNHTR).	Laboratory	No information
		• The female patient (born in 1930) with positive AB screening and known anti-Fy(a) alloantibody was given 1 pRBC without taking the antibody into account. The error was noticed when a second stored blood product was ordered. Allocation of the blood product on the basis of T+S was not blocked by the laboratory software even though AB screening was positive and the anti-Fy(a) alloantibody was known.	Laboratory	Detailed investigation of why the laboratory software had not blocked the product and implementation of corrective actions.
		• Female patient (born in 1953), known to have allo-anti-E, was given 2 out of 4 PC with phenotype Ee. Rhesus phenotype was not taken into account.	Laboratory	Attention drawn to SOPs and retraining.
Administration of a sub-optimal product	**1**	**Severity/risk Grade 3 life-threatening**		
		• Following an allergic reaction to the first bag of PC, the second bag of PC from the same donor was correctly blocked for the patient in the system. However, the electronic release was bypassed for the second PC transfusion and the product was released manually. The error was not noticed until the product was released retrospectively in the system, after transfusion.	Administration	Attention drawn to SOP and compliance with processes.
	5	**Severity/risk Grade 2 severe**		
		• Transfusion of an unirradiated pRBC to a patient receiving chemotherapy. Irradiation was not prescribed. The error was noticed after the second pRBC had started. The indication was noted in the patient's records but not in the laboratory information system.	Laboratory	Inclusion in the laboratory database and training.
		• Two pRBC were administered to a female patient known to have cold antibodies. The second pRBC had not been warmed despite the information on the bag. The patient developed dyspnoea (O2 saturation 92%), tachycardia, a drop in blood pressure (mean BP 53) and fever (38.7°). No signs of haemolysis. Observed overnight then discharged home.	Administration	No information
		• A male patient with known cold agglutinins was given a pRBC that had not been warmed before transfusion. The haematologist had not stated the indication, but the need for warming was stated on the PC bag. The instruction was ignored and the doctor was not consulted. It subsequently emerged that the intensive care unit has no facility of warming pRBC prior to transfusion.	Administration	In future it will be possible for pRBC to be warmed in the intensive care unit.
		• Transfusion of an unirradiated to patient receiving chemotherapy. The ward had not ordered irradiated pRBC by mistake, as the need was not evident from the classification scheme.	Administration	Modification and updating of the classification scheme and list of diagnoses.

Transfusion error	Number	Description of error	Localisation of deviation in the transfusion chain	Preventive measures against recurrence
		• Transfusion of an unirradiated pRBC. The assistant doctor noticed the error during the transfusion and stopped it. He had not looked at the patient's medical records until the transfusion had already started.	Administration	Attention drawn to SOP and compliance with processes.
Other	**1**	**Severity/risk Grade 3 life-threatening**		
		• Patient with immune thrombocytopenia (ITP) with no bleeding risk was given a PC. The PC was contraindicated in this case.	Administration	No information
	1	**Severity/risk Grade 2 severe**		
		• Two pRBC were administered in same time parallel through two accesses. The error was noticed after the anaesthetist had handed over the patient.	Administration	Attention drawn to SOP and compliance with processes.
Total	**29**			

Table 9 shows all the Grade 3 (potentially life-threatening consequences) and Grade 2 (potentially serious consequences) transfusion errors. No signs of haemolysis were reported in any of the cases apart from the first one.

Transfusion errors: Stage at which the deviation occurred

Table 10

Stage at which the deviation occurred, by severity

Location	Grade 1 non-severe	Grade 2 severe	Grade 3 life-threatening
Preparation	1	2	0
Laboratory/ blood store	0	7	2
Administration	2	9	9
Other	4	0	0

Table 10 shows the distribution of all 36 transfusion errors by stage at which the deviation occurred and severity. Deviations in administration tend to be more serious than those that occur in the laboratory. Errors at the final stage of the transfusion chain, when the transfusion is attached, are the most critical since they cannot be corrected at a subsequent stage.

Near misses in 2016

1,168 near miss reports were received in 2016. Table 9 shows the stage of the transfusion chain at which the errors occurred and where they were discovered.

Tabelle 11:
Einteilung der Near-Miss Ereignisse nach Lokalisation und Entdeckung der Abweichung

		Discovery			
Category	**Number**	**Laboratory/blood bank**	**Ward/Op/patient**	**Other/not stated**	**Typical examples**
Preparation	**547**	391	29	127	• 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	**192**	146	16	30	Wrong BG typing or interpretation or entry of results
Administration	**301**	126*	12	163	Products outside the cold chain or thawed and then not transfused after all
Other	**25**	11	1	13	Patient identified wrongly on admission
Could not be determined	**103**	9	0	94	Blood group discrepancy with previous finding
Total	**1,168**	**683**	**58**	**427**	

* especially when returned

Table 11 shows the location 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 how it was corrected, thus avoiding a transfusion error.

3.5 Donor reactions

In 2016 there were 24 reports of donor reactions.

Table 12
Individual case reports of donor reactions

Category	Number	of which serious	Example
A Local symptoms due to puncture	2	1	The donor experienced an electrifying pain in her right arm when the vein was punctured. Phlebotomy was stopped immediately. Unpleasant, electrifying and movement-related sensations subsequently persisted, leading the donor to seek medical advice repeatedly. The donor was not completely symptom-free even one year after the event (sensations occurring several times a day that did not impair function but were considered unpleasant).
B1 Vasovagal reaction (VVR), immediate type	9	3	Vasovagal reaction with no loss of consciousness accompanied by malaise, severe abdominal pain (8/10) and vomiting, no improvement in response to 1000 ml NaCl. An ambulance was called and the donor was observed for several hours in hospital. The donor had exerted herself physically before giving blood.
	3	3	After giving blood at the donation venue, the donor collapsed, falling on her head; tonic-clonic seizure, unconscious for approx. 3 minutes; subsequently responsive, oriented, grossly neurologically normal; no pain, small laceration on back of head.
B2 VVR, immediate type with injury	5	1	First-time donor with elevated blood pressure prior to donation: 146/98 mm Hg, pulse 56. Shortly after 450 ml of whole blood had been taken he collapsed, no response to voice for a short time. The blood donation team called the emergency service, systolic blood pressure measured by the resuscitation team was under 80. An infusion and ephedrine were given, and it was possible to discharge the donor 75 minutes later.
B3 VVR, delayed	4	4	The donor collapsed on the way home, 30 minutes after leaving the donation venue, while getting out of a bus and lost consciousness. He was taken by ambulance to the emergency department, where wounds on his eyebrow and hand had to be sutured. He was barred from giving blood because of his age (72).
B4 VVR, delayed, with injury	1	1	Death: The donor died during the night after giving blood at a mobile donation venue. There was no indication before, during or after the donation that the donor had any health problems. The donor died at home. A review of the questionnaire showed no issues indicative of a medical risk for the donor. An enquiry to the attorney general found that an autopsy had not been performed. The exact cause of death could not be determined.
D2 Other	**24**	**13**	**All the reported causes occurred in connection with whole blood donations.**

Table 12 shows the categories of donor reactions reported as individual cases. 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 Quality defects and protective measures

Reports received: Overview

In 2016 a total of 122 reports were received concerning protective measures for positive infection markers and quality defects. Figure 10 provides an overview of the received reports.

Figure 10
Protective measures for positive infection markers and quality defects

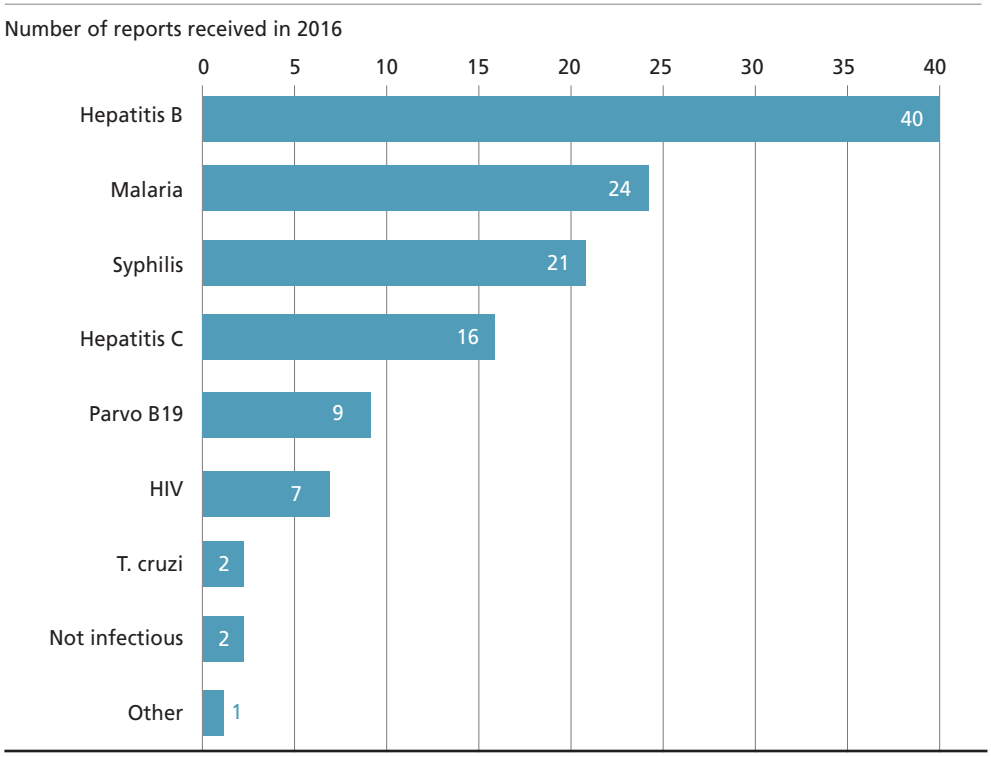


Figure 10 shows the reports of infection markers discovered in donors. All reports are shown together, i.e. those involving first-time donors and repeat donors. The two non-infectious reports concerned post-donation information: corticosteroid injection and iron storage disease. The report under 'Other' concerned a case who had received a blood transfusion in the past that was not mentioned in the questionnaire.
There was an increase in the number of reports of positive hepatitis B markers: 40 reports in 2016 compared to 24 reports in 2015. This increase is due to greater test sensitivity as a result of the switch from pool testing to single-donation testing at several blood donation centres.

Measures taken for first-time and repeat donors

Table 13
Measures taken

Donors	Number	Most frequent measures	Comments
First-time donors	70	Product destroyed and donor deferred	
First-time donor in CH, had previously given abroad	3	Product destroyed and donor deferred	In all three cases it was not appropriate to inform the blood donation service abroad.
Repeat donors	46	As above, plus look-back procedure	
Unknown	3	Recipient/doctor informed	Post-donation information passed on

Table 13 shows the protective measures taken for 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.

Patient-specific look-back procedure

All the completed look-back investigations showed a negative result, i.e. the patients had not acquired the infection as a result of the transfused blood product but by some other route.

Table 14
Patient-specific look-back procedures

Infection	Number	Result
Hepatitis C	5	4 negative, 1 still being processed
Hepatitis E	1	negative

Table 14 shows the reported look-back procedures triggered by a patient with an infectious disease. It was ascertained by means of the look-back whether the patient had acquired the infectious disease as the result of a blood transfusion.

4. Findings and prevention

4.1 Transfusion reactions in children

Published figures for transfusion reactions often refer to the total number of reports. Since more than 90% of these involve adults, the results may not be applicable to children. For this reason the differences between adults and children were discussed specifically in Chapter 3.3 Transfusion reactions.

Comparison of the proportions of transfusion reaction types accounted for children shows that TACO occurs less often in children while allergic TR occur more frequently. In order to determine differences in the risks, it is also necessary to compare the total reporting rates for adults and children. Oakley[2] et al. have shown that the general incidence of transfusion reactions is higher in children. Comparison of the HV reporting rates from Basel University Hospital has also shown a higher reporting rate for paediatric patients in the same reporting system used throughout the hospital.

TACO: The lower proportion of TACO reports accounted for children may therefore be made up by the generally higher reporting rate. However, the risk for children is assumed to be similar to adults. Overall, only 6 cases of paediatric TACO were reported between 2008 and 2017 [accessed June 30, 2017]. Nevertheless children under 3 years are disproportionately higher representedin these cases. This tendencyis also be found in other analyses[2,7]. It is therefore particularly important to ensure an appropriate transfusion rate in children under 3 years:

Where risk factors for volume overload exist (e.g. heart failure, kidney failure, hypoalbuminaemia, hyperhydration), the transfusion rate should be reduced to 1 ml/kg/h.

Allergic transfusion reactions: These are more common in children than in adults. Particular attention must therefore be paid to systematic monitoring during the transfusion and premedication if necessary.

4.2 Transfusion errors and quality assurance in hospitals

36 transfusion errors and 1,168 near misses were reported in 2016. By definition, in near misses the error is discovered and corrected before the transfusion is given and a transfusion error occurs. The high number of reported near misses is indicative of a good approach to dealing with errors in Swiss hospitals. 11 of the transfusion errors and 150 of the near misses were classified as "potentially life-threatening", most of them errors involving imminent ABO-incompatible transfusions. The majority of these errors are found especially in the Sampling and Application steps in the Transfusion chain, , i.e. while they were being prepared on the ward (when pre-transfusion blood was taken) or while attaching the transfusion. Therefore it is mandatory to define a framework for preventing avoidable transfusion reactions as far as possible and identifying unavoidable transfusion reactions in good time.

In 2014 Swiss "Quality Assurance in the Use of Blood Products" working group was established to produce guidelines for quality assurance in the practical transfusion setting. The working group published the Guidelines for quality assurance in transfusion practice in June 2017. The guidelines are available on the website of the following bodies that are responsible for monitoring transfusion activities:

- Association of Cantonal Pharmacists
- Association of Cantonal Medical Officers in Switzerland
- Swissmedic
- Swiss Transfusion Medicine Association

The guidelines define the requirements that must be met by the mandatory quality assurance (QA) system and personnel involved in transfusions. They explain the aspects of the process steps in the transfusion chain "Decision to transfuse, Prescription, Ordering, Handling of blood components, Pre-transfusion checks, Administration and Monitoring" which have to be regulated in the QA system and what the minimum requirements are. Institutions can also use it as a checklist for updating/refining their QA systems.

4.3 Infectious diseases and protective measures

122 protective measures were reported in 2016. Nearly all (120) involved infectious diseases.

Pathogens classically transmitted in blood (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.

Hepatitis B: The increase in the number of donors testing positive for hepatitis B mentioned in Chapter 3.5 is due to a change in the testing system. Several centres have switched from pool testing to single-donation testing. Most of the positive donors detected by the greater testing sensitivity of this approach are so-called occult hepatitis B carriers. These donors have a very low titre of hepatitis B virus that over time may also fluctuate around the limit of detection, i.e. it is sometimes detectable and sometimes not. It is not known whether hepatitis B titres this low are transmissible or not. If these donors are repeat donors, a look-back procedure to earlier donations is started. Transmission has not been identified in any of the procedures completed so far [accessed July 2017].

Hepatitis E Virus (HEV): Hepatitis E (HEV): In 2016 there were again no reports of transfusion-transmitted hepatitis E in Switzerland. However, the donor pathogen prevalence is estimated as being in the order of 1 viraemic donation per approx. 2,000 donations[8,9]. This means that a high level of under-reporting of (often asymptomatic) transfusion-related transmission is likely. The disease can lead to complications in immunosuppressed patients or those with pre-existing liver disease, e.g. as a result of cirrhosis of the liver.

A Swiss working group has developed recommendations for the prevention of (transfusion-related) hepatitis E. Its first step was to publish a Health Professional Communication (HPC) warning of the possible complications in immunosuppressed patients, particularly those who are transplant recipients (HPC – Hepatitis E in transplant recipients; published in German and in French).

The working group has also recommended HEV testing (not relevant for release) of all blood donations in 96-donation pools. This would mean that the results of an estimated 80% of blood components would be known before the transfusion took place, and that a large proportion of positive products could be destroyed in good time. This type of testing in pools of 96 donations does not detect contaminated blood products with a viral load below approx. 2000 IU/ml. Overall, this residual risk attached to undetected low viral loads would appear to be acceptable since the likelihood of a patient being infected by foodstuffs is substantially greater.

Internationally, comprehensive hepatitis E testing is done only in Ireland and in the United Kingdom of Great Britain and Northern Ireland (UK). All donations are tested in Ireland. In the UK testing was initially done only on donations for high-risk patients (e.g. immunosuppressed individuals), but this turned out to be more time-consuming and expensive than comprehensive testing because of the logistics involved. For this reason the competent committee in the UK published a recommendation that testing should be switched to comprehensive testing . The introduction of this form of testing is under discussion in many other European countries (e.g. the Netherlands, France, Germany; status July 2017).

MHM as a criterion for donor suitability

In 2016, Swissmedic was asked by the Blood Transfusion Service of the Swiss Red Cross for permission to modify the donor suitability criterion "men having sex with men (MHM)". The request foresaw the deferral of MHM donors for 12 months after their last same-sex sexual contact instead of deferring them indefinitely. Swissmedic approved this request, imposing two conditions (to ensure confidentiality when taking the donor's history and during monitoring) and a number of items that had to be fulfilled.

This decision was taken, among other things, on the basis of new data from countries which had already introduced this or similar measures. In these countries there has been no evidence of an elevated risk overall for recipients of blood[11,12].

The modified donor suitability criterion was introduced by the Blood Transfusion Service of the Swiss Red Cross on 1 July 2017.

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