TRIP REPORT 2016

Hemovigilance

Extended version

TRIP
Hemo-en biovigilantie

TRIP REPORT 2016

Hemovigilance

Extended version

TRIP report 2016, hemovigilance, extended version, is published under the responsibility of TRIP Foundation (Transfusion and Transplantation Reactions in Patients)

TRIP
Hemo- en biovigilantie

TRIP Executive Board — On behalf of

M.R. Schipperus	President, TRIP Foundation
J.W.P.H. Soons	Society for Hematological Laboratory Investigation, TRIP hon. Secretary
K.M.K. de Vooght	Dutch Society for Clinical Chemistry, TRIP treasurer

Hemovigilance Advisory Board

E.A.M. Beckers	Dutch Society for Hematology
P.A.W. te Boekhorst	Hematology and transfusion medicine
M.R. van Bohemen-Onnes	Nurses and nursing care professionals (Verpleegkundigen & Verzorgenden Nederland)
C.C. Folman	Immunohematology
E.J. Huisman	Dutch Association for Pediatrics
M.M.W. Koopman	Sanquin Transfusion Medicine Unit
A.W.M.M. Koopman-van Gemert	Dutch Society for Anaesthesiology and Intensive Care Medicine, Hemovigilance advisory board chair
E.C.M. van Pampus	Dutch Society for Blood Transfusion, Hemovigilance advisory board vice-chair
J. Slomp	Society for Hematological Laboratory Investigation
D. Versteeg	Dutch Society for Medical Microbiology (from June 2016)
J.J. Zwaginga	Dutch Society of Specialists in Internal Medicine

Advisory Board

R.M.Y. Barge	Dutch Association of Hospitals
J.R. van Diermen	(reading member) Healthcare Inspectorate (from May 2016)
J.T. Tamsma	Dutch Federation of University Hospitals
H.J.C. de Wit	Sanquin Blood Bank (till August 2016)
D. C. Thijssen-Timmer	Sanquin Blood Bank (from March 2017)

Patroness

E.J.G.M. Six – Baroness van Voorst tot Voorst

TRIP Office

A.G. Bokhorst	Director
J.C. Wiersum-Osselton	National coordinator
A.J.W. van Tilborgh-de Jong	Senior hemovigilance physician
P.Y. Zijlker-Jansen	Hemovigilance and biovigilance physician
M.J. Happel-van 't Veer	Biovigilance coordinator
I.C. van Veen-Rottier	Office Manager
S.M. van Walraven	Biovigilance Staff member (from May 2017)
M. Wilson	PhD student

Contents

Foreword

The annual extended TRIP hemovigilance report describes the state of transfusion safety in The Netherlands based on the reports submitted to the national hemovigilance and biovigilance office. Through hemovigilance reporting, problems which arise when changes are made in the transfusion chain can come to light, and new epidemiological transfusion risks can be discerned. This year issues emerged in relation to introduction or updating of IT systems in the hospitals – systems for electronic patient dossiers, laboratory information systems and links, for example with "TRIX", the national database of irregular antibodies and crossmatch problems. Following such modifications problems can arise in selecting appropriate blood components and can lead to transfusion of an incorrect blood component.

The number of infectious complications is very low, with an incidence in the order of one confirmed transfusion-transmitted bacterial infection per 180,000 units and an even lower incidence of viral infections. The overall picture, with a rate of less than one serious transfusion reaction per 5000 administered blood components demonstrates that there is a high level of safety in the Dutch transfusion chain.

In 2016 TRIP introduced a new electronic reporting system, which was well received by the hospital contact people. The objectives of the new reporting system were to improve user-friendliness and provide clearer information about what extra information, such as results of investigations, should be provided, particularly with serious cases, in order to facilitate quicker and better assessment and analyses of the reports. This will improve the quality of the TRIP data and reports.

The data collected by TRIP now cover a period of over 14 years. TRIP is open to receiving requests for anonimised data for researching relevant questions. TRIP is a partner in the Dutch Consortium for blood transfusion-related research and will supply transfusion reaction data from participating hospitals to the Dutch Transfusion Data warehouse if (written) permission is given. We will be glad to consider other possible uses of data in monitoring quality and safety of blood transfusion.

As each year, this report could not have been compiled without the essential contribution of the hemovigilance officers and hemovigilance assistants, other professionals in the transfusion chain, the TRIP experts and the members of the Hemovigilance Advisory Board. I hope it will support your activities, with which I wish you every success.

Dr. Martin R. Schipperus
President, TRIP Foundation

CHAPTER 1

Main 2016 findings

1.1 Hemovigilance trends in 2016

In 2016 the total number of reports was roughly stable in comparison to 2015 and earlier years. The use of red blood cell concentrates was 2% lower than in 2015 and that of platelet concentrates unchanged from recent years. In 2016 the progressive transition from quarantaine fresh frozen plasma to the solvent-detergent treated pharmaceutical plasma product Omniplasma® as the standard product for transfusion, launched by the national blood service Sanquin in 2014, was almost complete (Figure 1 on page 10).

Errors and incidents

The reports of incorrect blood component transfused (IBCT) are classified by TRIP according to the type of risk for the patient. Since 2013 the largest number of IBCT reports have been cases where the patient received blood without observance of the recommendations for prevention of new allo-antibodies. An important group is that of IBCT where the patient could received (and in some cases did receive) an ABO incompatible unit: the number of these has been lower in recent years than it was before 2013. Two noteworthy IBCT cases in the group with ABO risk concerned mistakes in the blood testing prior to transfusion (blood group determination and irregular antibody screening) which were not picked up by the finding of a blood group discrepancy in the routine blood group check. These are dangerous errors because the normal checks in later stages of the transfusion chain will not detect the error. If the patient has a transfusion reaction, the administrative checks will not reveal the error because the patient's identity details correspond to those on the compatibility label.

Among the reports of other incident, the subgroups of unnecessary transfusion (overtransfusion) and delayed transfusion (undertransfusion) carry a potential risk for the patient. Several cases in 2016 were associated with adverse consequences for the patient.

Hospitals are increasingly introducing electronic blood order systems along with other IT applications. Several IBCT reports (n=4) and one near miss report arose from non-functioning links between the laboratory information system and other information systems or from failure to display information which had been correctly entered. Among the other incidents, 11 reports of delayed transfusion involved (technical) problems with electronic blood requests, which as a result were not responded to at the transfusion laboratory in timely fashion. These reports show that IT applications can also be a source of errors and failures which may continue for some time before being detected, potentially endangering several patients.

Infectious transfusion complications

Four reports of post-transfusion bacteremia/sepsis in 2016 and one late 2015 report (1x grade 1, 2x grade 2, 2x grade 3) were accompanied by bacteriological culture results showing the same type of bacteria in the administered blood unit as in the patient's blood culture. These reports were formally assessed by the Expert Committee. Four out of the five were judged to be cases of transfusion-transmitted bacterial infection (TTBI), see Table 13 on page 27 In addition, following a recall by Sanquin of a platelet concentrate which had already been administered, the recipient was found to have had a serious reaction. Blood culture results from the patient remained negative, however this could be explained by ongoing antibiotic treatment. Bacteriological screening of platelet concentrates is an important safety measure but it cannot fully eliminate TTBI through platelet concentrates or associated RBC concentrates.

Two reports of hepatitis E following administration of blood components were registered in de category of post-transfusion viral infection. In one of these two cases genetic typing confirmed transmission from a

single donor apheresis platelet unit (at the time of going to print the investigation of the other case had not concluded). Hepatitis E can take a serious course in patients who are immune suppressed. Given the current risks, in consultation with the Ministry of Health, Welfare and Sports, Sanquin introduced a (minipool) NAT screening test for HEV in 2017 for donations processed into labile blood components for transfusion.

Transfusion-associated circulatory overload, TRALI and TAD

The annual number of reports of transfusion-associated circulatory overload (TACO) continues to rise. The number of cases of severity grade 2 or higher (n=25) is lower than last year (32) but TACO remains the category with the highest number of serious reports. Preventive measures can be applied against this transfusion complication, such as a slower rate of transfusion, administration of diuretics and careful evaluation of the patient's clinical condition after each unit. To guide this process TRIP has drafted a tool which can support prescribing physicians in assessing whether a patient has an increased risk of developing TACO. TRIP and the hemovigilance advisory board are planning a possible pilot of the feasibility of this tool in practice.

The number of reports of transfusion-associated acute lung injury (TRALI) was unchanged in 2016 in comparison to recent years. In the newly introduced category of transfusion-associated dyspnoea (TAD) eight reports were registered, none of them serious. Hitherto such reports were registered in the category of other reaction.

The assessment of reactions with respiratory problems is complex. X-ray or other imaging of the chest is important in differentiating between possible causes. An optimal assessment of images by the radiologist requires adequate information in the imaging request – in any case the request should state that the patient has respiratory compromise following a blood transfusion. For TRIP and the TRIP experts assessing the cases it is important that reports include the signs and symptoms, the clinical findings and assessment of the treating physician as well as the date and time and full reports of investigations.
The new digital reporting system offers different means for reporters to enter this information, including the possibility of secure uploading of attachments.

Blood management techniques (BMT)

The reports of adverse reactions and incidents in relation to blood management techniques since 2011 have all been associated with the use of drain blood. The annual number of reports has declined and was five in 2016, all reports coming from one hospital. From the incomplete figures about the application of autologous BMT, the use of drain blood appears to be decreasing. Since TRIP started asking hospitals for figures on the use of drain blood, the number of hospitals able to provide figures has never been over 50%, despite the recommendations in the (2011) national "CBO" transfusion guidelines. TRIP and the hemovigilance advisory board have decided to drop the annual collection of these denominators. Hospitals are however requested to continue to report reactions and incidents associated with the use of autologous blood management techniques to TRIP.

New TRIP reporting system and reporting categories

TRIP's new digital reporting system was taken into use from January 2016. The transition gave no significant problems. Groups of hemovigilance professionals paraticipated in workshops to discover the system's new functions, however the reporters are not yet all using these to their best advantage. TRIP provides personalised tips to the reporters when relevant when corresponding about their cases. Among the reporting categories, the new categories of Transfusion-associated dyspnea (TAD) and calculated risk have been added. These are discussed in the relevant chapters of this report.

TRIP and TRIX

It is a good development that in 2016 nearly all the hospitals had started actively using TRIX, the Dutch "Transfusion Register of Irregular antibodies and cross(X)match problems". As a consequence, hospitals which also report new allo-antibodies to TRIP are now reporting in two different systems. In TRIX no information is recorded to indicate whether a new allo-antibody could have been caused by a blood transfusion. Conversely, not all hospitals report allo-antibody formation to TRIP. Information extracted from TRIX could potentially take the place of information based on reports to TRIP. It is important for hospitals to (continue to) report cases of new allo-antibody formation to TRIP if they are detected in transfused patients for whom national transfusion guidelines recommend preventive matching: women younger than 45 years, multiply transfused patients (hemoglobinopathy, MDS) and patients who already have one or more allo-antibodies. These reports to TRIP can provide insight into the effectiveness and difficulties of the preventive policies relating to prevention of allo-immunisation after blood transfusion.

1.2 Recommendation	Who?
1 IT When new IT applications relating to blood transfusion are implemented a prospective risk inventarisation should be done. When applications are installed or updated the validation protocol should ensure that relevant links work as intended.	Blood transfusion committees, IT departments of hospitals, hemovigilance officers and hemovigilance assistants (transfusion safety officers)
2 Reporting allo-antibody formation New irregular antibody formation after transfusions in patients for whom preventively antigen-matched RBC units have to be selected according to the CBO guideline – these should be reported to TRIP.	Hemovigilance officers and hemovigilance assistants
3 Transfusion reactions with respiratory feaatures A. in the request for imaging, mention that the patient has dyspnea following transfusion. B. Include relevant findings of physical examination and the treating team's clinical diagnosis in the report to TRIP, and also the full report of chest X-ray if performed as well as other relevant investigations such as NT-pro-BNP or tryptase with details of date and time of the blood sample.	Members of the clinical team; hemovigilance officers and hemovigilance assistants to promote this in teaching Hemovigilance officers and hemovigilance assistants

CHAPTER 2

Overview of 2016 hemovigilance results

2.1 Overview of 2016 hemovigilance data in comparison with previous years

The definitions of categories of incidents, transfusion reactions, severity, imputability etc. can be found on www.tripnet.nl/ under hemovigilance/supporting materials and in the relevant sections of this report. The reported data are presented in the following tables and figures:

** Supplementary tables available as online annexe*

Table 1. Incidents reported to TRIP, 2010-2016

Incident	2010	2011	2012	2013	2014	2015	2016	No. of hospitals with reports in 2016
Incorrect blood component transfused (IBCT)	58	43	51	43	71	53	42	24
Near miss	71	45	50	39	33	40	52	17
Other incident	118	138	139	107	120	93	106	35
Calculated risk situation#	-	-	-	-	-	-	7	6
Hemolysed product	0	2	0	0	1	0	0	0
Totaal	**247**	**228**	**240**	**189**	**225**	**186**	**207**	**45**

* *Separate category of calculated risk introduced in 2016 (previously a few reports of calculated risk in category IBCT); in the table the reports classified as calculated risk in years up to and including 2015 have not been included*

Table 2. Transfusion reactions per reporting category, 2010-2016

Reactie	2010	2011	2012	2013	2014	2015	2016	Severity grade 2 or higher[#]	No of hospitals with reports in
Post-transfusion bacteremia/sepsis	41	61	50	47	56	79	64	10	37
Post-transfusion viral infection	1	5	2	5	0	2	3	2	2
TRALI	17	12	9	9	6	9	6	5	4
TACO	47	39	56	69	76	76	87	25	39
Transfusion-associated dyspnea (TAD) +	-	-	-	-	-	-	8	0	7
Anafylactic reaction	73	67	59	70	53	43	60	19	27
Other allergic reaction	184	191	180	193	153	151	123	0	35
AHTR	21	17	7	11	17	18	18	7	15
DHTR	7	9	8	4	5	6	8	1	7
New allo-antibody	814	831	851	849	763	697	637	0	63
NHTR	506	504	456	442	419	448	396	8	71
Mild non-hemolytic febrile reaction	363	366	383	340	311	336	360	4	62
Other reaction	164	218	225	221	191	205	207	19	63
Other small categories of TR	4	5		5	17	3	4	1	4
Total TR	**2242**	**2325**	**2287**	**2265**	**2067**	**2073**	**1982**	**101**	**88**
Total grade 2 or higher[#*]	93	101	100	108	96	112	105		
Total reports*	**2594**	**2630**	**2580**	**2504**	**2318**	**2289**	**2199**		

[#] *Imputability certain, probable, possible*

[+] *New reporting category introduced in 2016, see discussion in Chapter 3*

[*] *Total including transfusion reactions following an incident or other occurrence such as hospital finding of bacterially contaminated blood component*

Abbreviations: TRALI=transfusion-related acute lung injury; TACO=transfusion-associated circulatory overload; AHTR=acute hemolytic transfusion reaction; DHTR=delayed hemolytic transfusion reaction; NHTR=non-hemolytic transfusion reaction; TR=transfusion reaction

Table 2a. Transfusion reactions in small categories, 2010-2016

Table 3. Reports per type of blood component in 2016

Type of blood component (bc)	Units distributed	Units transfused	No. of reports		Reports per 1000 bc distributed	
			All	Serious[#]	All	Serious[#]
Red blood cell concentrate	418384	365751	1749	58	4,18	0,14
Platelet concentrate	55514	44100	286	36	5,15	0,65
Fresh frozen plasma	2491	747	1	-	1,34[1]	0,00[1]
SD-plasma[2]	64124	50715	18	2	0,35[1]	0,04[1]
Blood management techniques[3]			5	-		
Combinations			59[4]	9		
Not stated			81	0		
Total	**540513**		**2199**	**105**	**4,07**	**0,19**

[#] *Imputability definite, probable or possible*

[1] *Calculated using numbers of units transfused, see chapter 3.5*

[2] *SD = solvent-detergent (Omniplasma®)*

[3] *See chapter 3.4*

[4] *Including combinations with SD-plasma*

Table 3a Types of blood component for each type of reaction or incident in 2016

Table 3b Types of reactions and incidents for each type of blood component in 2016

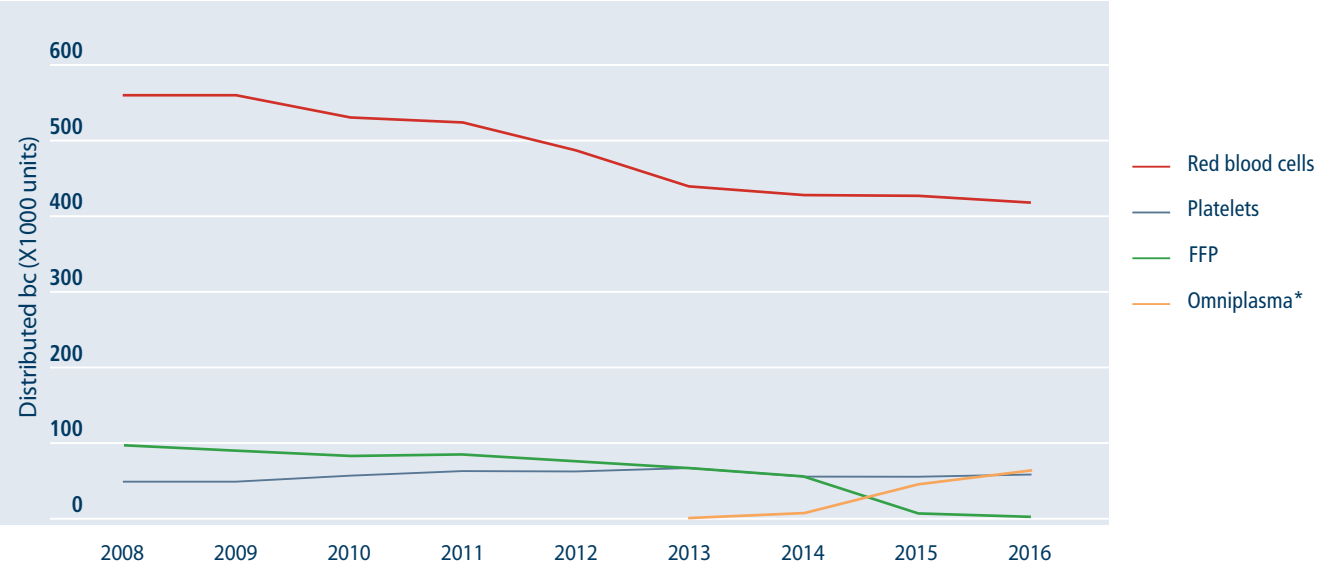


Figure 1. Distributed units of blood components, 2008-2016

* *For SD-plasma (Omniplasma®) the distributed units have been used in 2013-2015 because of the transition (Data from Sanquin for the annual TRIP report)*

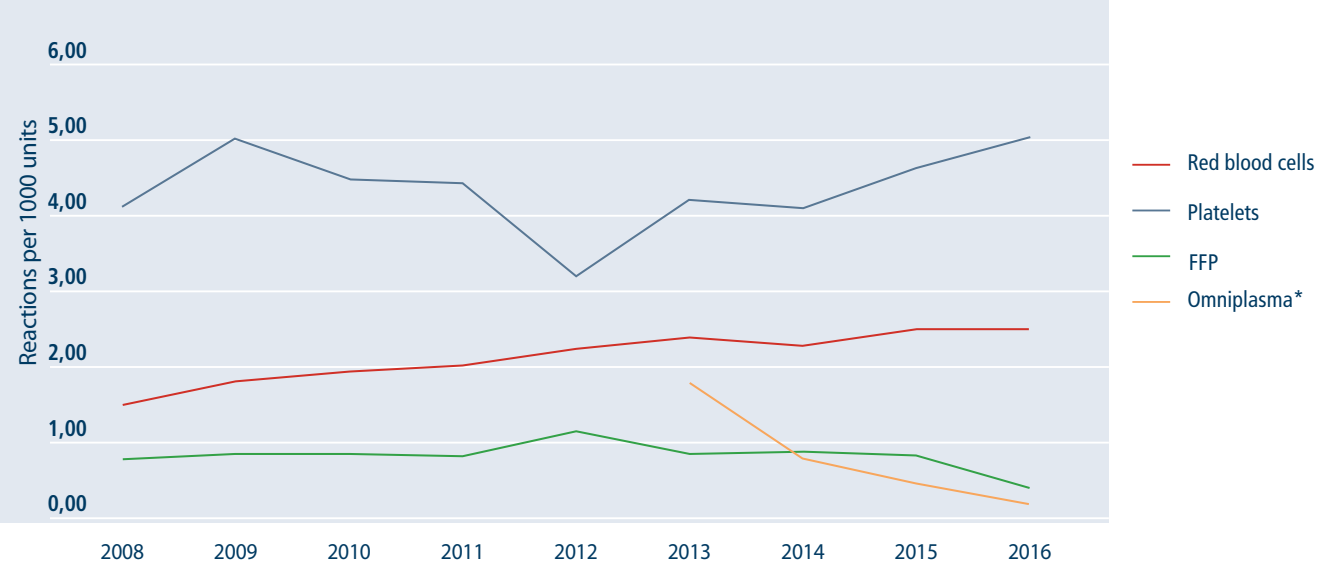


Figure 2. Transfusion reactions excluding new allo-antibodies per 1000 units, 2008-2016

* *Omniplasma (SD-plasma): in 2013-2015 transfused units used as denominator during phase of rolling out*

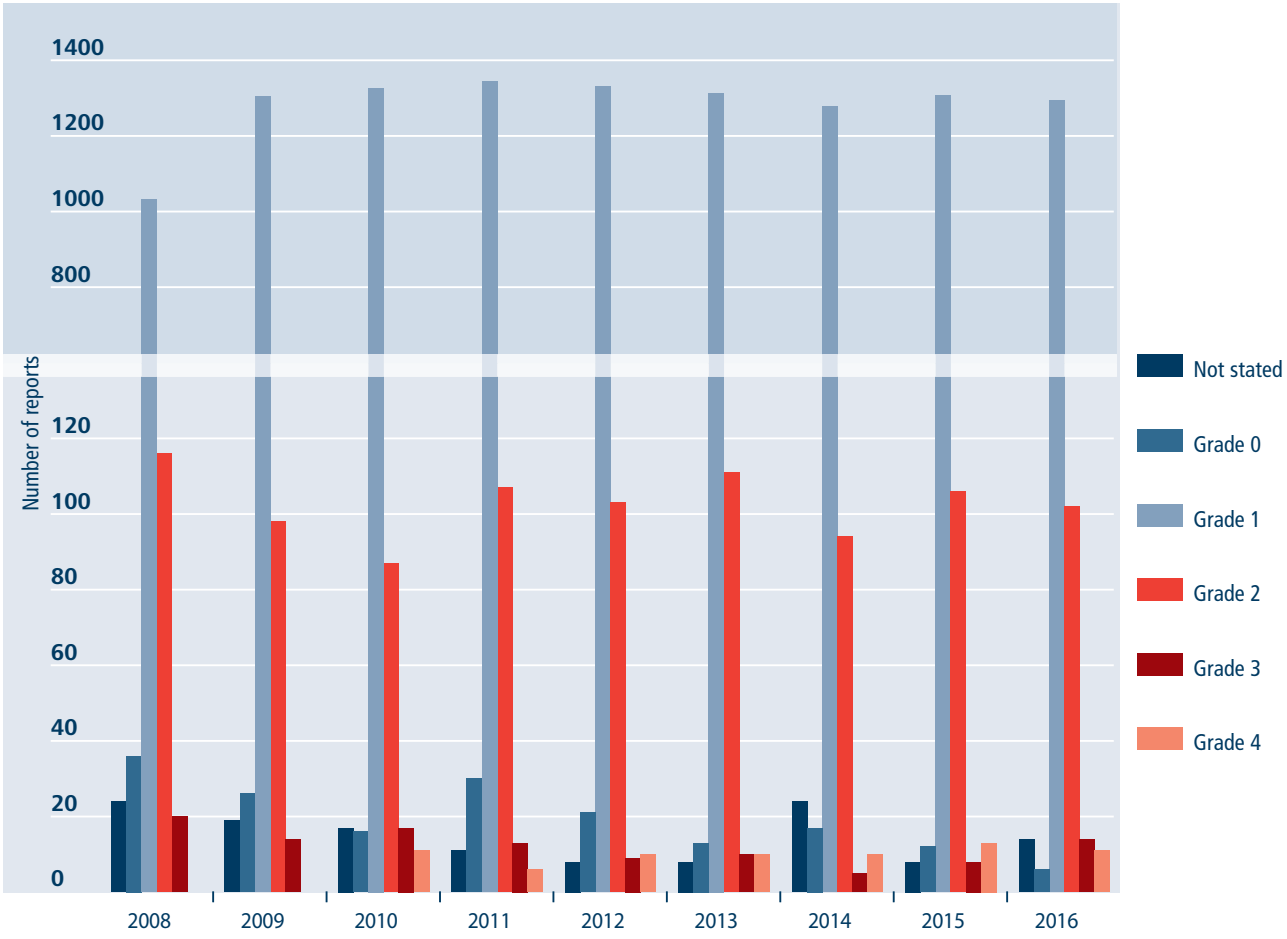


Figure 3. Severity of the transfusion reactions, 2008-2016

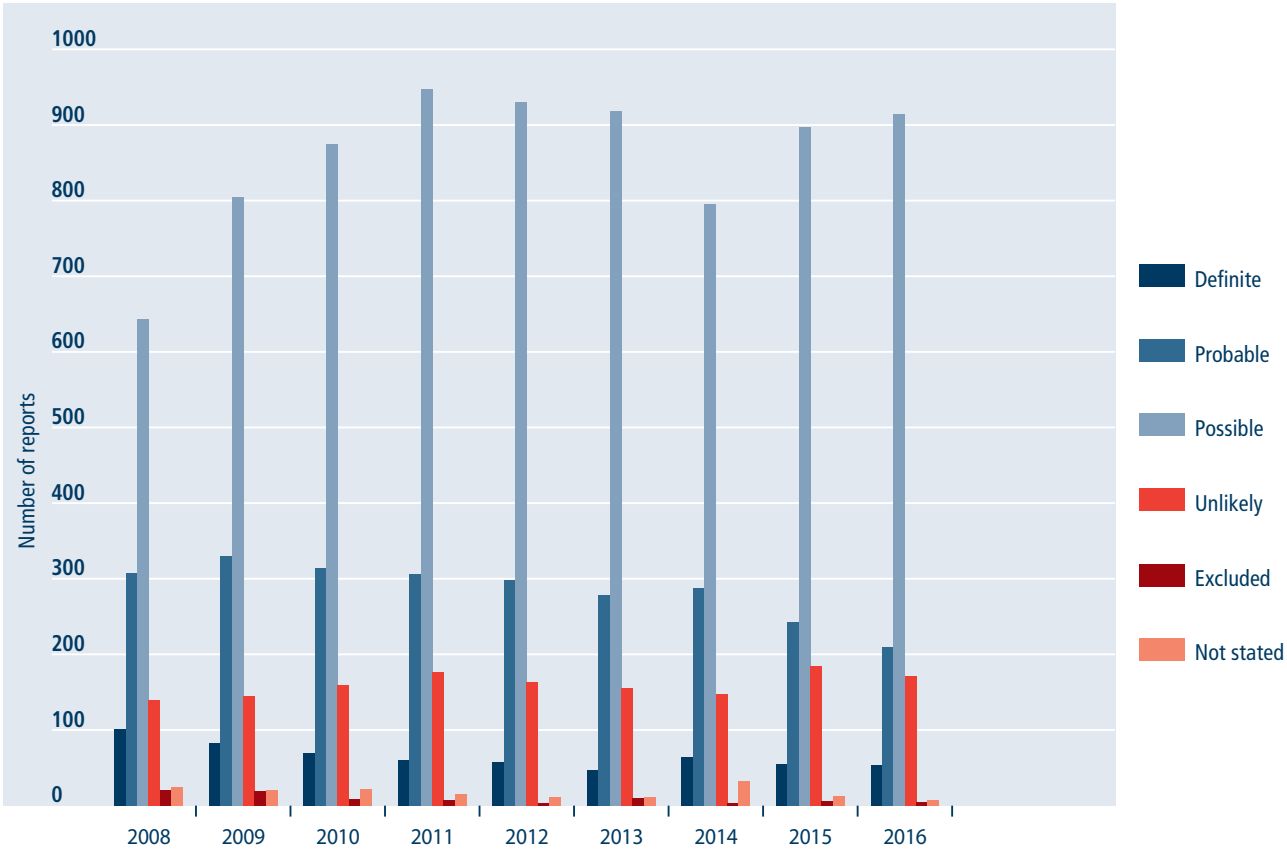


Figure 4 Imputability of the transfusion reactions, 2008-2016

2.2 Overview of mandatory reports of serious transfusion reactions

Each year TRIP compiles an overview of serious transfusion reactions (Grade 2 or higher) and incidents in the transfusion chain for the European Commission.

The European Commission gives the following guidance in the "Common Approach" document:

- Reactions with definite, probeble and possible mputability are to be reported.
- Reactions following transfusion of an incorrect blood component or an other incident are included in the appropriate category.
- Hemolytic reactions are subdivided into immunological (ABO), other immunological (irregular antibodies) or non-immunological (e.g. infusion together with hypotonic solution).
- Reactions with (only) SD-plasma are not included because of its different legal status and vigilance requirements.
- The reactions are reported in a form which provides for breakdown between the types of associated blood component.

Table 4 shows the serious reactions in 2016 as submitted to the European Commission. The febrile reactions in the table were counted as serious reactions because of (prolongation of) hospital admission.

Table 4. Number and imputability of reports of grade 2 and higher in 2016

Severity	2			3			4	
Imputability	Definite	Probable	Possible	Definite	Probable	Possible	Probable	Possible
Hemolytic transfusion reaction (ABO)	1	-	2	-	-	-	-	-
Hemolytic transfusion reaction (immunologic, non ABO)	5	-	1	-	-	-	-	-
Anaphylactic reaction	3	7	5	1	1	1	-	-
Mild non-hemolytic febrile reaction	-	1	3	-	-	-	-	-
Non-hemolytic transfusion reaction	-	2	6	-	-	-	-	-
Other reaction	2	2	16	-	-	1	1	-
Transfusion-transmission of bacterial infection	-	1	1	-	-	1	-	-
Post-transfusion viral infection	1	-	1	-	-	-	-	-
Post-transfusion purpura	-	-	1	-	-	-	-	-
TRALI	-	-	-	-	1	2	-	1
Transfusion-associated circulatory overload	1	11	10	-	-	1	-	3
Total	**13**	**24**	**46**	**1**	**2**	**6**	**1**	**4**

2.3 Transfusion reactions with fatal outcome (Grade 4)

In 2016 a total of 11 transfusion reaction reports were of grade 4 severity and there was one other incident in the transfusion chain where the patient died. The reports are summarised in Table 5. Five of the 11 reactions were judged to be probably or possibly caused by the transfusion.

Table 5. Reports with fatal outcome

Reporting category	Gender, age	Blood component	Imputability	Clinical situation
Other reaction	M, 82	Platelets (pooled)	Probable	Operation for AAAA, clinical features suggestive of sepsis after transfusion of unit which later showed positive bacterial screening result with Gram + cocci and group G hemolytic streptococci, see case description in chapter on bacterial problems
Other incident	F, 62	Red blood cells		Tf ordered but administration deferred till the next morning. The patient suffered an ischaemic CVA; case discussed in chapter on other incidents.
Transfusion-associated circulatory overload	F, 79	Red blood cells	Possible	Cardiac history and renal insufficiency. Tf for Hb 4.4 mMol/L, clinical deterioration with dyspnea and rise in BP, high dose of furosemide given, dialysis started for fluid removal
Transfusion-associated circulatory overload	F, 85	Red blood cells	Possible	Bleed from intestinal diverticulum. Dyspnea and rise in BP after 2 units. Poor response to diuretics and oxygen, patient declined IC treatment.
Transfusion-associated circulatory overload	M, 88	Red blood cells	Possible	Bone marrow failure and renal insufficiency. Clinical deterioration and drop in saturation in night after 2 units, very high BNP.
TRALI	F, 55	Platelets (pooled)	Possible	Small cell lung carcinoma, chemo. Respiratory deterioration several hours after Tf, CXR showed lung oedema and increase of pleural fluid, patient died 2d later.
Transfusion-associated circulatory overload	M, 72	Red blood cells	Unlikely	Admitted with dyspnoea and congestive heart failure, Hb 4.6 mMol/L. Clinical deterioration after infusion of (approx.) 30 ml.
Other reaction	M, 78	Red blood cells	Unlikely	Bleed after removal of tumor in patient with cardiac history. Temp and increase of oxygen requirement after Tf, patient was dyspneic before Tf. CXR showed no clear changes.
Other reaction	F, 14	Red blood cells	Unlikely	Seriously ill patient with neurological symptoms, cachexia and infected pressure ulcers. Temp and drop in BP after Tf.
Other reaction	M, 0 yrs	Red blood cells	Unlikely	Premature baby, deterioration soon after commencement of Tf: necrotising enterocolitis
Other reaction	F, 18	Red blood cells	Unlikely	Recovering from sickle crisis, uneventful Tf. Found dead in bed less than 24 hours later.
TRALI	M, 75	Red blood cells	Unlikely	Leukemia and myocardial infarction. Tf stopped soon after 2nd unit because of rise in temp followed by dyspnea. Chest X-ray appearances could represent TRALI. No improvement following administration of diuretics.

Abbreviations: AAAA= atherosclerotic aneurysm of abdominal aorta; Tf=transfusion; CVA=cerebrovascular accident; BP=blood pressure; BNP=Brain-type natriuretic peptide; pt=patient

Table 6 summarises the grade 4 reports to TRIP with definite, probable or possible imputability from 2010. The most important categories are circulatory overload (12), other reaction (10) en TRALI (6), followed by acute hemolytic transfusion reaction (4) and post-transfusion bacteremia/sepsis (3). The imputability of the reports of other reaction was possible in all cases, never probable or definite.

Table 6. Grade 4 reports (certain, probable or possible imputability), 2010-2016

Reaction	2010	2011	2012	2013	2014	2015	2016	Totaal
AHTR		1	1			2		4
Other reaction	3	1	1	2		1	1	9
Post-transfusion bacteremia/sepsis*			1		2			3
Post-transfusion purpura					1			1
TRALI	2		1			2	1	6
Transfusion-associated	2	1	1		3	2	3	12
circulatory overload	7	3	5	2	6	7	5	35
Total								

* *Only one case (in 2014) was a case of Transfusion-Transmitted Bacterial Infection on the basis of culture results on patient blood culture and unit*

2.4 Variation between hospitals in number of reports in relation to transfused blood components

The last two TRIP reports highlighted considerable variation between hospitals in the number of reported reactions in relation to the number of transfused units. This was examined for the largest hospitals because the variation through chance alone is less. The data up to and including 2016 are shown in Figure 5A (transfusion reactions excluding new allo-antibodies and mild non-hemolytic febrile reactions) and B (serious transfusion reactions). On analysing the reports of all severity levels it appears that certain hospitals report fewer cases in relation to the number of transfused units than others. This can adversely affect the generalisablitiy of the collected data. The rate of reported serious reactions, however, shows less variation and it does not appear that some hospitals consistently have a higher rate or lower rate of serious reports. TRIP will continue to monitor this.

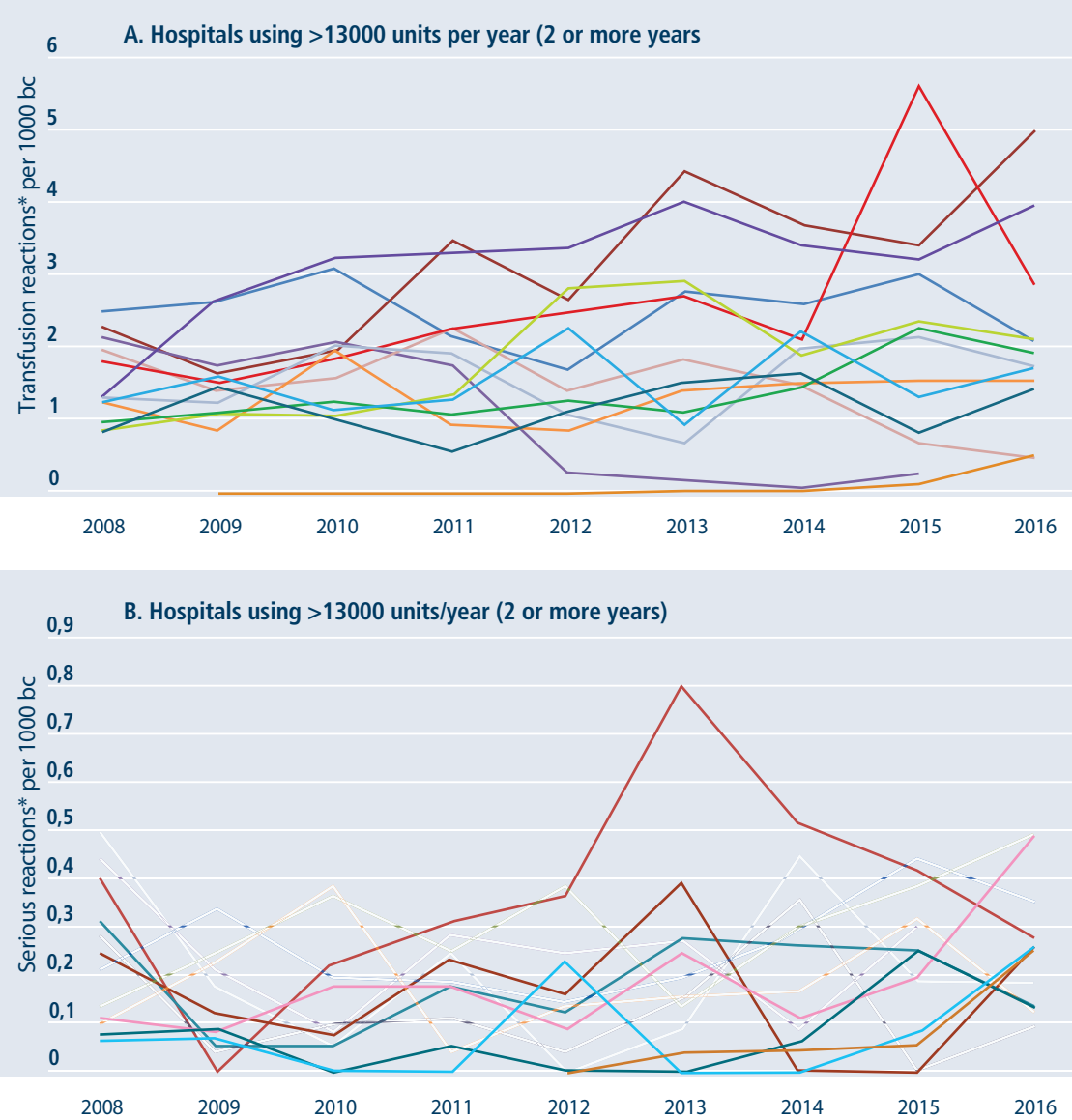


Figure 5 A and B. Reported transfusion reactions per year in relation to blood use in hospitals with high blood use; A all severity levels; B serious reports, grade 2 or higher

* *Reports of certain, probable or possible imputability, excluding new allo-antibody formation and mild non-hemolytic febrile reaction, as these are not systematically reported by all hospitals*

2.5 Late reports from 2015

Apart from variability in reporting level, submission of reports after the closing date also affects the annual figures which are reported and the potential for valid analyses and recommendations.

Because of the transition to the new reporting system, TRIP actively approached reporters to ask them to conclude any non-finalised reports from earlier years. In in 2016 several reports (8) from before 2015 were concluded. A total of 42 2015 reports from nine hospitals were received after the closing date for the 2015 report (late 2014 reports in the 2015 annual report: 56). Among these 5 (12%) were of severity grade 2 or higher (Table 7), whereas only 5% of the timely reports were serious. The late reports have all been formally assessed and are included in the relevant figures and tables of this annual report.

Table 7. Late 2015 reports

Reporting category	Severity					No reaction, severity not applicable
	Not stated or 0	1	2	3	4	
Other incident						2
Incorrect blood component transfused						1
Anaphylactic reaction			1			
Other allergic reaction		8				
Mild non-hemolytic febrile reaction		7				
Non-hemolytic transfusion reaction		12				
New allo-antibody formation	5					
Other reaction		2	2			
Post-transfusion bacteremia/sepsis (TTBI, possible)				1		
TRALI			1			

CHAPTER 3

Discussion of reports per category

3.1 Incidents in the transfusion chain

Incorrect Blood Component Transfused (IBCT)

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

As in previous years, TRIP assessed all the reports of incorrect blood component transfused to establish which was the worst potential risk to which a patient was exposed through transfusion of an incorrect blood component. For instance in the case of a mix-up of units intended for two patients, if patient X receives the blood which was intended for patient Y the worst risk is that the unit could be ABO incompatible – though it may happen to be ABO compatible. Before 2013, IBCT cases where the patient could have received an ABO incompatible unit constituted the largest subgroup. From 2013, the largest subgroup has been that of IBCT reports of failure to provide units in accordance with recommended preventive Kell and rhesus phenotype matching for patients in defined at risk groups (Figure 6).

The descriptions of the risk groups which TRIP includes in this analysis can be found on www.tripnet.nl (under hemovigilance, tools). In addition the reports are classified according to the first error (in time) which led to the transfusion of an incorrect unit: this first error is classified according to the type of error, such as identification error, communication error, selection error. The step in the transfusion chain when the first error occurred is also noted; see the TRIP diagram representing the transfusion chain on www.tripnet.nl.

- 42 reports from 24 hospitals (26%), 1-6 reports per hospital.
- 6x a reaction was reported as an additional category (1x AHTR, 1x DHTR, 1x mild NHFR, 3x new allo-antibody formation), see Table 8.
- 3 reactions led to the discovery that an error had been made: 1x DHTR, 2x allo-antibody formation, leading to the recording of IBCT or IBCT in the past as an additional category, see Table 9.
- 7x analysis of an IBCT led to the discovery that the same or a similar error had been made for that patient (and not been reported at the time) and IBCT had occurred in earlier transfusion episodes: reported as an additional category of IBCTin the past, see Table 9.
- 1 reported other incident involved a once-off error which had led to administration of plasma stored at too high a temperature to 4 patients: recorded as IBCT as an additional category, see Table 9.

Table 8. Clinical symptoms after transfusion of an incorrect blood component in 2016

IBCT Risk group	Blood component	Reaction (additional category)	Imputability*	Severity*
ABO	RBC	AHTR	definite	2
	RBC	New allo-antibody	definite	
		Anti-Cw; anti-K		
Irrab	RBC	DHTR	definite	1
Prevention Irrab	RBC	Mild NHFR[$]	unlikely	1
		New allo-antibody:		
	RBC	Anti-K[&]	definite	
	RBC	Anti-E	definite	

* *Imputability and severity grade apply to clinical symptoms of a transfusion reaction; new allo-antibody formation is severity grade 0 by definition*

[$] *Mild increase in temperature in patient with septic arthritis*

[&] *Female patient < 45y*

Abbreviations: AHTR = acute hemolytic transfusion reaction; irrab=irregular antibodies; DHTR = delayed hemolytic transfusion reaction; mild NHFR = mild niet-hemolytic febrile reaction

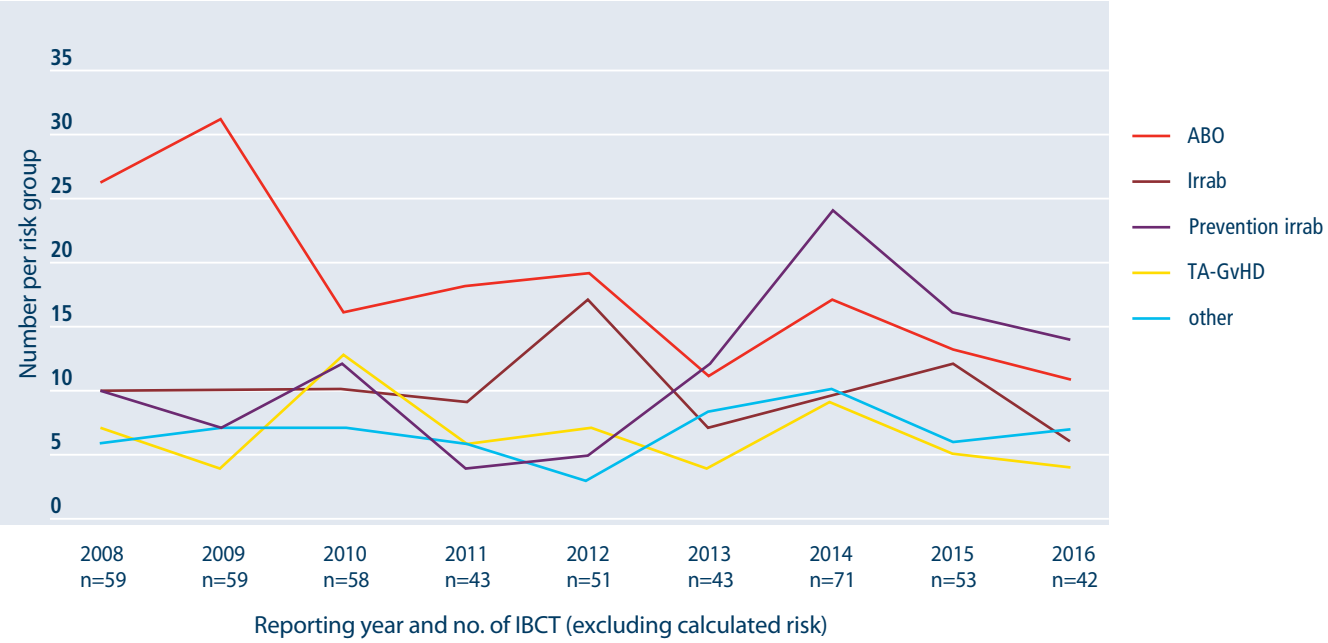


Figure 6. Incorrect blood component transfused broken down according to risk group, 2008-2016

Abbreviations: ABO = risk of an ABO incompatible blood transfusion
Irrab = risk of an irregular antibody incompatiblee transfusion
Prevention irrab = guidelines not followed with regard to prevention of irregular antibody formation
TA-GVHD = risk of transfusion-associated graft versus host disease (after transfusion of a non-irradiated blood component)

- 9 out of the 11 ABO risk cases arose from a mix-up of blood bags, patients of patient identification details.
- Once part of an ABO incompatible RBC unit was administered (A neg RBC to an O pos patient), this mistake led to an AHTR.
- Twice incompatible SD-plasma was transfused in an emergency to patients with massive blood loss (O plasma to an A pos and a B pos patient). In one of these cases group O Omniplasma was wrongly selected instead of AB. In the other case the wrong case notes were sent to theatre with the patient leading to the wrong patient identifiers being used for the request for plasma and for the electronic check prior to administration. In neither of these cases was a transfusion reaction reported.
- in 7 cases (64%) the unit happened to be ABO compatible and in 6 of these it was also rhesus D compatible. Once new allo-antibody formation was reported after administration of a small amount of blood to a patient who did not need transfusion. Once rhesus D incompatible O pos RBC were administered to a group B neg patient.
- Once the error was only reported to the hemovigilance assistant (transfusion safety officer) and laboratory after investigation by the patient safety committee, and without patient identifiers so the unit and patient blood group details are not known.
- In the 6 cases with irregular antibody risk, twice the unit happened to be compatible for the known antibody, once the product had not been typed for the cognate antigen, while in the remaining 3 cases the product was not compatible. In cases where antibody incompatible RBC were transfused, once a DHTR was reported. This case involved 2 c pos RBC, the irregular antibody screening was negative but the patient had previously been reported to have an anti-c and this information was recorded in the "TRIX" national database of irregular antibodies.

Two reports of IBCT with ABO risk involved errors in the blood group determination and irregular antibody screening which were not detected through discrepancies with previous results. These are dangerous situations because the normal checks in the subsequent stages of the transfusion chain will not lead to detection of the mistake. In the event of a reaction to the transfused unit, the possibility of incompatibility will not be readily picked up because the details on the compatibility label and the accompanying form correspond to the patient receiving the unit.

In one of these cases, a mistake was made in the identification of the patient when taking the blood group sample and as an additional error, the second sample which was provided to the lab was not collected independently from the first. This led to blood group A rhesus D positive being incorrectly recorded as the confirmed blood group, whereas the patient actually was O positive. During administration of an A neg RBC unit, the patient developed symptoms and on re-checking the blood group the discrepancy was discovered.

In the other case the result of the blood group determination was erroneously entered into the computer system as O pos although the result had been AB pos. An O pos RBC unit was administered without adverse effect. A week later on repeat determination, a blood group discrepancy was found. In-depth investigation by the hemovigilance assistant showed that the mistake had been made when manually determining and recording the blood group without checking by a second staff member. This case underlines the importance of unbiased analysis of incidents, systematically checking all the steps of the transfusion chain. Initially it had been assumed that there had been a sample identification error and it was only the extensive investigation which revealed what had actually happened. Active participation by the hemovigilance officer and/or the hemovigilance assistance can help to avoid "tunnel vision". In this case the analysis revealed other unsafe aspects which were analysed and tackled at the level of the whole hospital. A more extensive description of the case was published (in Dutch) in the August 2017 Report of the Month.

Problems with IT applications, notably problems with links between different IT systems, led to 4 reports of IBCT arising when requesting or selecting blood units. They led to failure to take important information into account about medication (indication for irradiated blood components), irregular antibodies which had previously been detected at a different hospital or the patient's medical condition (indication for preventive matching). In each of these cases a single error or oversight can create a risk of repetition for the same or for several patients (see Table 9).

IBCT case descriptions can be found (in Dutch) on www.tripnet.nl under Report of the Month:
February 2017: M/F?
https://www.tripnet.nl/melding-van-de-maand-februari-2017/
July 2016: Communication about preventive matching for at-risk patient groups
https://www.tripnet.nl/melding-van-de-maand-juli-2016-communicatie-bij-preventief-beleid-voor-doelgroepen/
August 2017: Identification error?
https://www.tripnet.nl/melding-van-de-maand-augustus-2017/

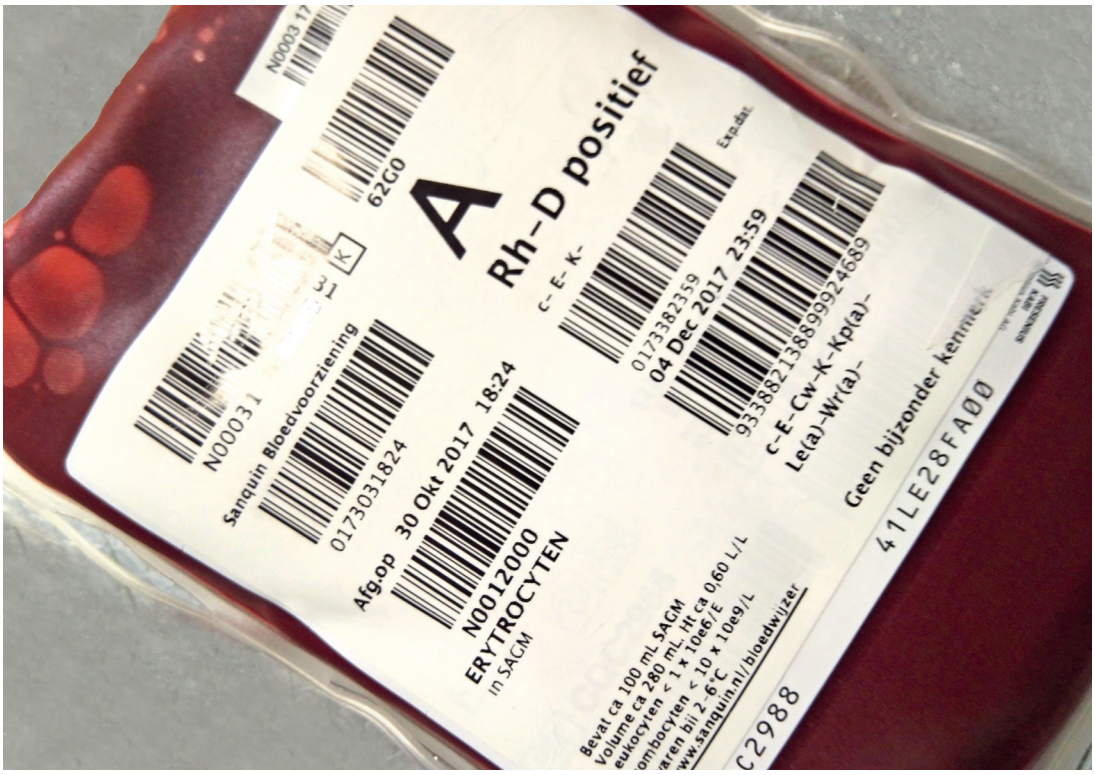


Table 9. Reports in 2016 with IBCT/IBCT in the past as an additional category*

Reaction category	IBCT risk group (additional category)	Description: Analysis following the reaction reveals	Number of IBCT (additional category)
Delayed hemolytic transfusion reaction (severity grade 1, improbable)	Prevention irrab (new allo-antibody formation also reported)	Lab. procedure error → failure to provide rhesus sub-fenotype compatible units for patient with irregular antibody	1
New allo-antibody	Prevention irrab	Assessment error → failure (in the past) to record requirement for preventive Kell matching for a patient with irregular antibody	2
		Selection error → failure to provide rhesus and Kell compatible units for woman <45 years old.	1
Incorrect blood component transfused	TA-GVHD	Communication error → previous inappropriate removal of indication for irradiated blood	1
	Prevention Irrab	Communication error → patient previouly not registered as multiply transfused	9
		Communication error → patient previouly not registered as multiply transfused and not phenotyped	1
		Technical error → in the past, patient's diagnosis not displayed in blood request module of laboratory information system, and patient not phenotyped appropriately in connection with hemoglobinopathy.	1
		Assessment error → in the past, failure to take account of special transfusion requirements in connection with stem cell transplantation	1
		Assessment error → in the past, failure to take account of special requirements in connection with patient's diagnosis	4
	B19 prevention	Communication error → in the past, failure to request B19-safe blood and failure to record special Tf requirements for pregnant patient	1
Other incident	Damage /quality	Storage error → temperature in freezer with SD-plasma found to briefly have been above 0°C, several units transfused to 4 patients before error detected.	4

Abbreviations: IBCT=incorrect blood component transfused; prevention irrab = guidelines not followed with regard to prevention of irregular antibody formation; TA-GVHD = risk of transfusion-associated graft versus host disease (after transfusion of a non-irradiated blood component); B19 prevention=failure to provide Parvovirus B19-safe units; Tf=transfusion

** IBCT or IBCT in the past is recorded as an additional category if the error was detected after a reaction or*

Near miss

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

- 52 reports from 17 hospitals (18%), range 1-10 reports per hospital.
- In 40 cases there was (presumably) a mix-up of patients or patient identifiers, labels, blood samples, units, testing materials etcetera. In four of these cases a discrepancy was found between the historic confirmed blood group (note that according to Dutch guidelines, the historic blood group should have been determined twice on independent samples) and the new result, and repeat determination of the blood group demonstrated that to be correct; the hospital was no longer able to establish what had gone wrong in the past. A further 7 reports of blood group discrepancy against an earlier result were received in a "bulk" report which did not detail the results of investigation.
- In 42 reports to TRIP there was a potential ABO risk, and in 25 of these the mistake was detected through the finding of a blood group discrepancy. These led to discovery of 24 (presumed) mix-ups and one incorrect laboratory result of a first blood group determination (an "ordinary" blood group A was recorded whereas the patient was found to be of a group A subgroup).
- In one case a product problem was reported: on entering the unit into stock the hospital determined and confirmed the blood group as O positive, whereas the label indicated A pos.
- One report concerns IT: following an update of the laboratory system, the link to the patient's medication list no longer worked, leading to issue of a non-irradiated unit to a patient who should have had irradiated blood.

In the 2015 TRIP report we recommended that near miss cases should always be reported if investigation reveals an unexpected cause or the problem results in measures being implemented, so that the issues can be brought to the attention of a wider audience. In two linked cases involving patients admitted to the same ward on the same day (one near miss, one IBCT), the hospital carried out an extensive investigation and introduced safety measures. The cases are described (in Dutch) in the August 2017 Report of the Month.

In 2008-2016 approximately half of the Dutch hospitals (46) reported one or more near misses. One large hospital reported a total of 103 cases, followed by a medium-sized hospital which reported 42 near miss cases. It seems reasonable to conclude that near miss cases are not consistently reported to TRIP. This makes it difficult to perform meaningful analyses at the national level. We have to assume that the hospitals have systematically reported and investigated near miss cases internally since the introduction of the mandatory safe Incident reporting systems (veilig incident meldsystemen, VIM), however TRIP has no access to these data.

Table 10. Near miss reports, 2008-2016

	2008	2009	2010	2011	2012	2013	2014	2015	2016	totaal
No. of reports	55	72	71	45	50	39	33	40	52	457
Reporting hospitals	14	20	21	16	18	15	16	15	17	45
Range per hospital	1-24	1-12	1-15	1-8	1-19	1-17	1-5	1-9	1-10	

It has also been suggested that thematic national collection of particular types of near miss events could provide evidence to support the introduction of specific measures, such as the use of electronic identification when collecting blood samples. In the new TRIP reporting system it is possible to submit so-called

bulk reports, providing the number of a particular type of event without details per individual case. This proposal has not yet been implemented by TRIP and the hospitals, apart from one hospital having submitted a bulk report of 7 blood group discrepancies. Depending on the particular issue, guidance will be needed as to which reports can be grouped and what minimum information is required.

Near miss case material (in Dutch) from 2016 can be found on www.tripnet.nl in the Report of the Month series:
June 2017: What is in a name?

Other incident (OI)

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

- 106 reports from 32 hospitals (34%), range 1-13 reports per hospital
- 7 OI which were associated with a reaction (registered as an additional category): 2x TACO, 2x Other reaction, 2x mild non-hemolytic febrile reaction, 1x NHTR
- 19 reports of reactions have an additional category of OI: 9x mild non-hemolytic febrile reaction; 3x NHTR; 4x TACO; 2x Other reaction and 1x TAD

A large subcategory of OI in 2016 is that of incidents with a (considerable) chance of delayed transfusion with potential clinical consequences from undertransfusion (n=22). It is noteworthy that half of the reports of delayed transfusion involved (technical) problems when electronically ordering blood, and the request not being noticed in timely fashion at the laboratory. Several hospitals reported this type of incident. In two cases, after prescription of the blood and a decision to give the transfusion the next day, the patient developed a condition which might have been linked to undertransfusion. One of the reports was involved a patient who suffered an ischemic CVA and the other was admitted to hospital in the night with a myocardial infarction. In four further cases involving delay, one or more blood unit was (largely) wasted; in one case only part of the blood was administered owing to repeated venous access problems.

Another subgroup consists of (nearly) unnecessary transfusions (n=23), including 3 cases where the error was detected before administration of the unit, but in two cases the blood unit had to be discarded because of delay in returning it to the laboratory. In a fourth case, a blood sampling error (clot formation in the syringe which was used to collect the sample) two platelet concentrates were unnecessarily administered to a bleeding patient and a third platelet concentrate expired avoidably. In a further four reports, investigation of a transfusion reaction led to the discovery that the patient had been unnecessarily transfused: these cases are registered with an additional category of other incident, see Table 11.

In 2016, as in previous years, wastage or wastage of a large part of a blood component, other than in the above cases of delay or unnecessary transfusion, constitutes the largest group of reported other incidents (n=27). In 17 of these cases the wastage of the unit can be regarded as avoidable, notably in cases where the pre-transfusion observations required action and the blood units were not returned to the laboratory, or not returned in timely fashion. In two of these cases the blood unit is reported to have been spiked before the observations were performed. Among the other 10 cases, where the wastage of the unit was judged to be inevitable, 4x the bag was accidentally spiked when connecting the unit and twice units were sent with a patient on transport to a different hospital.

Further small clusters of reports were received where there had been errors or problems at administration of a blood component (n=18) such as infusion together with an unsuitable IV solution or with medication (8x), infusion into the subcutaneous tissue after displacement of the IV cannula (2x), too slow (>6 hours) or too rapid infusion (2x); incorrect or non-performance of the vital parameter observations (6x) and wrong, incorrectly completed or forgotten forms (3x).

The great majority of reports where other incident has been recorded as an additional category (n=14) concern failure to report a transfusion reaction to the laboratory or cases where the report was late or incomplete.

Table 11. Respiratory symptoms (reactions) in combination with other incidents in 2016

Reporting category	Subgroep of OI	Type of error and brief description	Additional category
TACO	Unnecessary Tf	IIdentification error → dyspnea and chest pain several hours after Tf. In a patient's electronic medical dossier(Hb 6.6 mMol/L) a Tf order intended for a different patient (Hb 5.0) has been recorded	Other incident
		Assessment error → Increase of pre-existing congestive heart failure after administration of 2nd RBC unit to a patient with cardiac history. Hb was 5.5 mMol/L after 1st RBC; after diuresis post-transfusion Hb was 6.5 mMol/L.	
		Assessment error → dyspnea, vomiting and mild rise in temperature after administration of 4 RBC units to a 92 year old man with chronic symptomatic anemia (4.2 mMol/L). Post-transfusion Hb after diuresis was 4.2 mMol/L.	
	Reaction not reported to blood transfusion labora-tory	Communication error → dyspnea and stridor during administration of a RBC unit. Transfusion was temporarily halted, patient received diuretic treatment and then Tf continued more slowly. Laboratory investigations required by transfusion reaction protocol were not performed.	
TAD	Unnecessary Tf	Communication error → 1 RBC unit administered to patient with Hb 5.6 mMol/L whereas trigger of <5.0 mMol/L had been set for that patient. Patient showed desaturation.	Other incident
Other incident	Damage/quality	Administration error → recurrence of congestive cardiac failure after trasfusion of 1 RBC unit; the prescribed premedication with furosemide was administered intravenously together with the unit instead of before the tranfusion.	TACO
	Speed of transfusion	Administration error → RBC unit transfused in 1h 15 minutes instead of 4 hours, the 87 year old patient developed dyspnea and chest pain.	TACO
	Reaction not reported to laboratory	Communication error → transfusion form states that patient had dyspnea and chest pain during ad-ministration of RBCs but this was not reported to lab.	Other reaction

A case of other incident can be found (in Dutch) on www.tripnet.nl under the Report of the month: September 2016: The patient has a temperature, should we start the transfusion?
https://www.tripnet.nl/melding-van-de-maand-september-2016-de-patient-heeft-koorts-transfusion-starten/

Calculated risk situation

A situation where the clinician knowingly decides to proceed with transfusion in the presence of an increased risk or anticipated side effect of the transfusion and where the intended benefit from transfusion is deemed to justify the risk of harm and its possible severity.

- 7 reports from 6 hospitals (6%), range 1-2 reports per hospital
- 1x with additional category of acute hemolytic transfusion reaction
- 2 reports of new allo-antibody formation with an additional category of Calculated risk situation

These reports concern situations where the urgency of transfusion made it impossible to meet a requirement to supply antibody-compatible units or follow recommendations for preventive (extensive) matching units for specific patient groups.

Case examples of Calculated risk situations can be found (in Dutch) in the Report of the Month series:
March 2017: 3 calculated risk situations (problems complying with preventive transfusion advice for patient groups)
https://www.tripnet.nl/melding-van-de-maand-maart-2017/
July 2017: calculated risk with acute hemolytic transfusion reaction
https://www.tripnet.nl/melding-van-de-maand-juli-2017/

3.2 Infectious transfusion complications

Bacterial problems associated with blood transfusion

Post-transfusion bacteremia/sepsis

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

Bacterial contamination of blood product

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

If post-transfusion symptoms indicate blood culture and the presence of bacteria in the patient's blood is confirmed, a post-transfusion bacteremia/sepsis is said to have occurred (as long as the specified bacterium was not previously observed in the patient). If the same bacterium is cultured from the administered blood product, the possibility of transfusion transmitted bacterial infection (TTBI) should be considered. Four reports of post-transfusion bacteremia from 2016 and one late report from 2015 (1x grade 1, 2x grade 2, 2x grade 3) confirmed the same micro-organism in the patient as in the administered blood product. The reports were evaluated by the Expert Committee which categorized four of the five as 'possible' or 'probable' transfusion-transmitted bacterial infections (see Table 13).

Additionally, one patient receiving a platelet unit, later recalled by Sanquin, experienced a serious transfusion reaction. Blood culture on the patient, who was receiving antibiotic therapy, resulted in no growth. The report was categorized as a bacterial contamination of the blood product, with a secondary diagnosis of other transfusion reaction (subgroup unconfirmed sepsis), and is described as a case in the section on bacterial contamination of blood products. Bacterial screening of platelet units is an important safety measure but it cannot completely eliminate the risk of TTBI following platelet transfusion.

Table 12 shows the numbers of reports of bacterial problems associated with blood transfusion in the years 2010-2016. The use of the different reporting categories and additional categories relating to bacterial problems is further explained in a diagram on www.tripnet.nl under hemovigilance, additional materials. The flow diagram also shows how the results of the investigations are used to judge whether a report might represent a case of transfusion-associated bacterial infection (TTBI). Figure 7 illustrates the process using the numbers of reports in 2016.

Table 12. Overview of reports from hospitals relating to bacterial problems, 2010-2016

	2010	2011	2012	2013	2014	2015	2016
Post-transfusion bacteremia/sepsis	41	61	50	47	55	79	64
(cases of TTBI as assessed by experts)	(3)	(2)	(1)	(2)	(2)	(2)	(3)
Post-transfusion bacteremia/sepsis as additional category (not TTBI)	17	13	14	6	10	4	2
Bacterial contamination of blood component (including positive bacterial screening)	44	43	42	25	12	15	10
Bacterial contamination of blood component (including reports of positive bacterial screening) as additional category	17	19	16	10	14	7	16

Post-transfusion bacteremia/sepsis

- 64 reports from 37 hospitsls (39%), 1-6 reports per hospital
- 5x with additional category of Bacterial contamination of blood component
- 2 reports (bacterial contamination of blood component and TACO respectively) with Post-transfusion bacteremia/sepsis as additional category

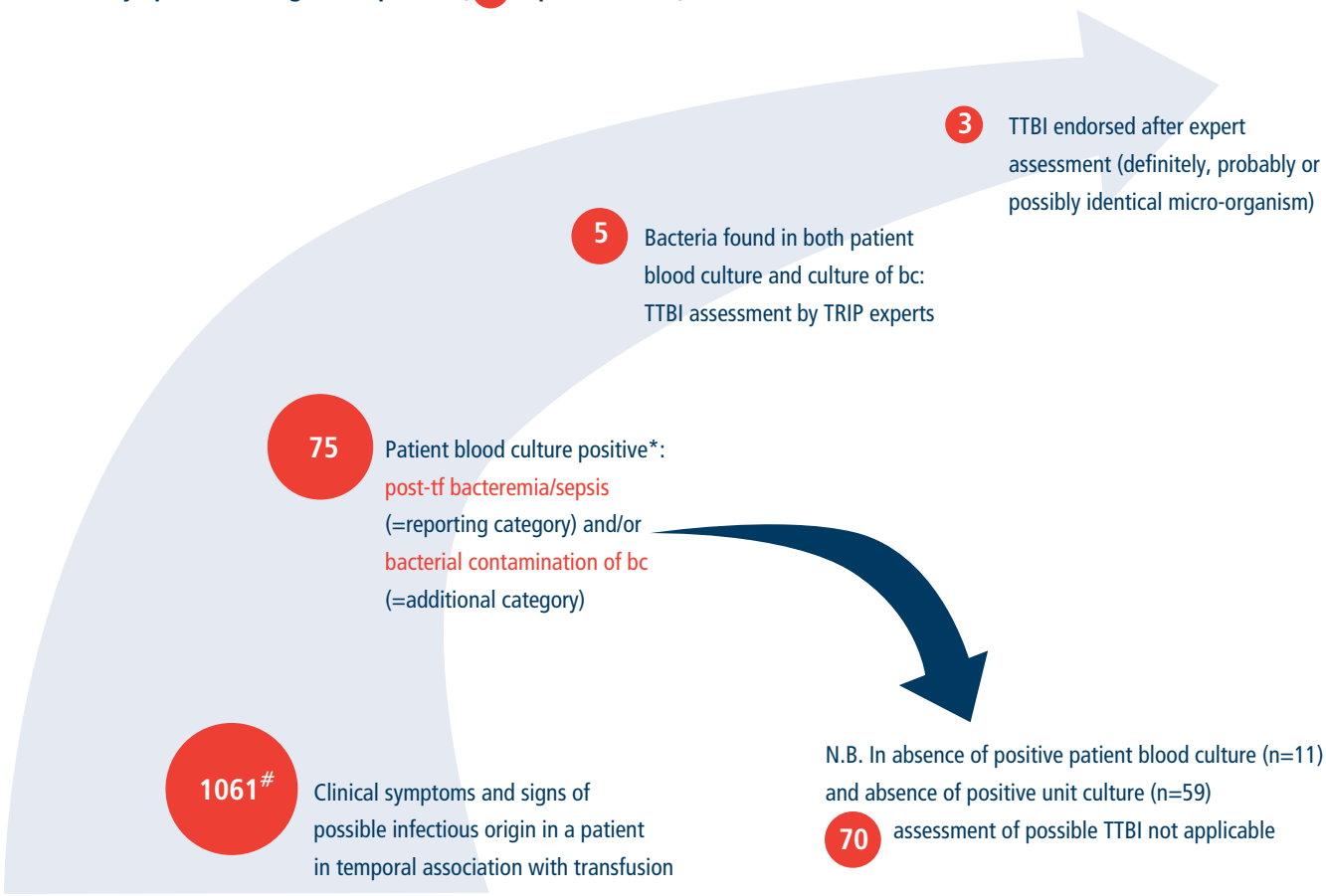


Figure 7. TTBI assessment, route A*

Abbreviations: pt=patient; bc=blood component; tf=transfusion; TTBI=transfusion-transmitted bacterial infection

 # Number of reports in 2015 (in relevant categories: non-hemolytic TR, mild non-hemolytic febrile reaction, post-tf bacteremia/sepsis, transfusion-associated circulatory overload, transfusion-associated acute lung injury, anaphylactic reaction, acute hemolytic TR, other reaction

** Culture result should be deemed relevant*

Table 13. Assessment of potential 2016 TTBI reports in TRIP Expert meeting, April 2017

Patient blood culture	Unit (culture result in hospital)	BactAlert / culture by Sanquin	Reporting category	Severity	Imputability of reaction	Bc	TTBI assessment
Enterococcus faecalis	Enterococcus faecalis	Negative	Post-Tf bact/sepsis*	3	definite	Plts	possible*
Staph. epidermidis	Staph. epidermidis	No notification received	Post-Tf bact/sepsis	3	definite	Plts	possible
Staph. epidermidis	Staph. epidermidis	Negative	Post-Tf bact/sepsis	2	probable	Plts	possible
Strept. dysgalactiae	Strept. dysgalactiae	Negative	Post-Tf bact/sepsis	2	probable	Plts	probable
Staph. epidermidis	Staph. epidermidis	Not stated	Post-Tf bact/sepsis	1	definite	RBC	no information re typing by hospital
Staph. epidermidis	Not performed	Propionibact. acnes	Bact. contaminatie bc		not applicable	Plts	not applicable
Staph. epidermidis	Not performed	Propionibact. acnes	Bact. contaminatie bc		not applicable	Plts	not applicable
Strept. pyogenes	Strept. oralis	Not stated	Post-Tf bact/sepsis	1	probable	RBC	not applicable

** Late 2015 report*

Case 1 post-transfusion bacteremia/sepsis (TTBI)

A young patient receives an irradiated platelet concentrate five days following stem cell transplantion because of a T-cel lymphoma. During the transfusion he develops chills and dyspnea and subsequently the blood cultures which were performed were found to be repeatedly positive for Staphylococcus epidermidis (positive within 1 day after collecting the blood culture) and the culture of the platelet concentrate also showed growth of Staphylococcus epidermidis. The patient is assessed and monitored by the intensive care specialist but remains on the hematology ward. The patient recovers and blood cultures on the second day after the reaction are all negative. The antibiograms of the bacterial strains are identical. DNA typing is performed using the PFGE technique) and also yields identical results for the strains isolated from the patient's blood culture and the platelet unit.

TRIP report:

Post-transfusion bacteremia/sepsis, severity 3, imputability definite.
TTBI likelihood: possible

Casus 2 Post-transfusie bacteriëmie/sepsis (TTBI)

A 63 year old patient with acute myeloid leukemia receives an irradiated platelet concentrate in the day care ward through a new giving set – the patient does not have a central venous line. Approximately 20 minutes after the transfusion the patient shows a rise of temperature to 39.0°C with chills; dyspnea; increase in blood pressure; tachycardia, chest heaviness and pain. Before transfusion the patient had no signs suggestive of an infection. The patient is admitted from the day ward and antibiotic treatment is started. The blood cultures taken after the reaction yield growth of haemolytic streptococci. The cultured remnant of the platelet concentrate is also positive for streptococci. The antibiograms are identical. The patient recovers from the reaction and is discharged home after three days. Serotypes of the bacterial strains are identical, they are Lancefield group C haemolytic streptococci, further typed as Streptococcus dysgalactiae. Sanquin recalled the associated red blood cell concentrates: 1 RBC had already been transfused uneventfully. The other four RBC units were cultured and no bacterial contamination was detected. The (Bactalert) screening sample from the implicated platelet concentrate had already been disposed of at the time of the notifiction to Sanquin.

TRIP report:

Post-transfusion bacteremia/sepsis, severity 2, imputability probable
TTBI likelihood: probable

A third case illustrating the reports of post-transfusion bacteremia/sepsis is described on www.tripnet.nl in the Report of the month series (in Dutch):
January 2017: reactions with nausea and vomiting (case 3)
https://www.tripnet.nl/melding-van-de-maand-januari-2017/

Bacterial contamination of blood component

- 10 reports of positive bacterial screening from 9 hospitals (10%), range 1-2 reports per hospital (Table 12)
- 2x with an additional category (1x post-transfusion bacteremia/sepsis and 1x other reaction, zie case description)
- 16 reports (6x other reaction, 5x NHTR and 5x post-transfusion bacteremia/sepsis) with additional category Bacterial contamination of blood component (Figure 7, Tables 12 and 14)

Reports in this category represent instances where a hospital informs TRIP of a notification from Sanquin about a positive bacterial screening result on a unit which has already been transfused at the time when the notification is received. TRIP also receives overall figures from Sanquin (Table 15). Hospitals are requested to report cases where (sometimes only with hindsight) a patient had symptoms during or after the transfusion or where the notification of a (probably) contaminated transfusion had medical consequences for the patient who had received the unit. For instance, the patient may receive prophylactic antibiotics or undergo extra investigations.

The additional category of bacterial contamination of a blood component is registered if (usually in the hospital) a positive bacterial culture result is returned on a component which has (partly) been transfused and which is tested in the context of a suspected transfusion reaction.

Table 14. Overview of reactions (excluding post-transfusion bacteremia/sepsis) reported with an additional category of bacterial contamination of a blood component

Remarks (TR*/patient#)	Culture of bc$ (performed in hospital) In no case was the Sanquin screening positive	Reporting category	Total	Patient blood culture
				No growth
Patient without pre-existing infection	Staphylococcus sp. (not Staph. aureus)	Other reaction	4	4x
	1x plts 4x RBC	NHTR	1	x
	Citrobacter freundi; Enterococcus faecalis (RBC)	NHTR	1	x
	Propionibacterium acnes (plts)	Other reaction	1	x
Patient already on AB	Staphylococcus sp. (plts) (not Staph.aureus)	NHTR	1	x
	Streptococcus sp. (RBC)	Other reaction	1	x
Patient with pre-existing infection/on AB	Coryne-Propionibact. (RBC)	NHTR	1	x
	Micrococcus Luteus (plts)	NHTR	1	x
	Total		11	

* *all cases had TR with rise in temperature and/or chills and in some cases there were additional symptoms*
\# *all patients were oncology patients (6x AML)*
$ *bc: 7x RBC, 4x plts*
Abbreviations: TR=transfusion reaction; bc=blood component; sp=species; AB=antibiotics; RBC=red blood cell concentrate; Plts=platelet concentrate; AML=acute myeloid leukemia

Table 15. Overview of bacterial screening of platelet concentrates by Sanquin, 2010-2016

Total numbers (Sanquin)	2010	2011	2012	2013	2014	2015	2016
Platelet concentrates with initial positive result	332	321	238	165	214	190	218
Units already transfused (Platelet concentrates and associated red blood cell units)	106	125	90	83	80	82	79 *

* *1x Sanquin was informed that the patient had had a serious reaction (case of bacterial contaminatuin of blood component described below); 5x mild reaction; 6x no information to Sanquin following the notification*

Case: Bacterial contamination of blood component

Early in the morning the hospital laboratory is informed by Sanquin of an initial positive bacterial screening result on a platelet concentrate. The unit had been given to a patient the previous evening following an uncomplicated emergency operation (classical abdominal aorta prosthesis). Shortly after transfer to the ICU at 22:19 hrs, approximately 1½ hours after transfusion of the platelets, the patient had developed signs suggesting sepsis and shock. At the operation prophylactic antibiotics (Kefzol) had been initiated according to the standard protocol; after the recall notification this was changed to gentamycin, Tazocin, vancomycin). The bacterial screening sample yielded growth of group G hemolytic streptococci. The patient's blood cultures gave negative results (the first culture was taken the morning after surgery at 8:29 hrs), however it must be noted that the patient was receiving antibiotics at the time. Cultures of sputum, pleural and intra-abdominal fluid were also negative. During the ICU period, the patient required hemodynamic support and full ventilation. Finally, more than two months after the operation the patient died from sepsis with an unclear focus, possibly an infected prosthesis. Post-mortem cultures showed growth of various pathogens but not of group G hemilytic streptococci.

TRIP report:

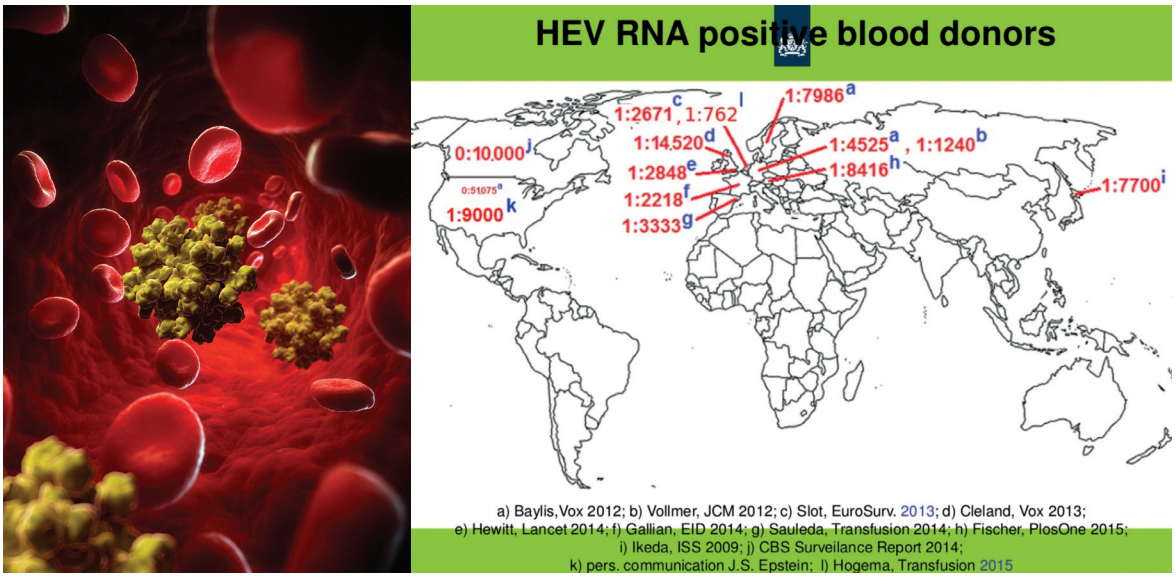
Bacterial contamination of blood component
Following review by the Expert Committee an additional category of other reaction was recorded: subgroup of nonconfirmed sepsis, severity grade 4, imputability probable.

Post-transfusion viral infection

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

Information from the hospitals

In 2016 there were three reports of post-transfusion viral infection. One of these was a case of acute hepatitis E which was diagnosed in a stem cell transplant recipient approximately 6 weeks after administration of RBC and platelet concentrates. Further investigation confirmed transmission by an apheresis platelet unit (definite imputability). Investigation of a second case of post-transfusion hepatitis E had not been concluded when the TRIP report was published.



Science Photo Library / Alamy Stock Photo *ECDC-HEV-expert meeting, Stockholm december 2015, presentation Wilfrid van Pelt (RIVM)*

Hepatitis E can take a serious course in immunosuppressed patients. For this reason in mid 2017, in consultation with the Dutch ministry of health, Sanquin introduced a (minipool) NAT test for hepatitis E virus (HEV) for donations used in the production of labile blood components. The main source of hepatitis E is the food chain. Healthy people generally remain asymptomatic when infected but can be viremic for several weeks. If a donation is found to be viremic the donor will be notified by letter and informed that the next donation will be deferred for three months.

The third report of post-transfusion viral infection was of cytomegalovirus (CMV), found in a premature neonate who had been transfused with several units of RBC and platelets. In principle blood components which have been leukoreduced are regarded as safe with respect to CMV for nearly all clinical indications; infection from the surroundings is also possible. The imputability of this case was rated as possible.

Look-back by the blood establishement

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

In 2016 there was one report from a hospital about look-back notification from the blood establishment Sanquin. In this case the donor had had a bacterial infection in the days after the donation. The patient who received the red blood cell unit did not show any symptoms suggestive of a bacterial infection. The recipient was already receiving antibiotic treatment at the time of transfusion because of the clinical situation.

Information from Sanquin

In 2016 there were 8 seroconversions (3x HBV, 1x syphilis, 2x HIV and 2x anti-hepatitis B core). Look-back investigations were performed according to the protocol and no transmissions were uncovered. (One case of HIV seroconversion had not yet been closed at the time of publication of this report.

Infectious transfusion complications: conclusion

As in previous years there were very few confirmed transmissions of bacterial or viral infection by blood transfusion: 1 per +/- 90.000 transfused units. In 2016 a transmission of hepatitis E was confirmed for the first time. Minipool NAT screening for hepatitis E will be introduced in 2017. Transfusion-transmitted bacterial infection remains a small but real risk of transfusion of platelets.

3.3 Non-infectious transfusion reactions

Transfusion-associated circulatory overload, TACO

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

- 87 reports from 39 reporting hospitals (41%), 1-4 reports per hospital
- 4 reports have an additional category of other incident (3x unnecessary Tf; 1x reaction not reported to blood transfusion laboratory)
- 4 reports have TACO recorded as an additional category (2x other incident; 1x TRALI and 1x mild NHFR)

In 2016 87 reports of transfusion-associated circulatory overload were submitted (2015: 76): the annual number of cases shows a rising trend but the number of serious reports of grade 2 and higher (n=25 of definite, probable or possible imputability) is lower than last year. TACO remains the type of reaction with the largest number of serious reports. The breakdown of severity and imputability is shown in Table 16.

The majority of cases of TACO are associated with administration of one or more RBC concentrates (n=75) or RBCs with platelets or plasma (n=3). Only a few cases are associated with exclusive administration of platelets (n=6) or with multiple types of blood component to patients with major blood loss (n=3). In six cases there was also an other incident, see Table 11 (in the other incident paragraph in chapter 3.2). In two reports of other incident, TACO is recorded as an additional category because it could have been caused by an error in administration of the blood component. Once an RBC unit was transfused in 1 hour and 15 minutes instead of 4 hours as prescribed; in the other case furosemide was given by continuous infusion together with the transfusion rather than before the unit was started. Unnecessary transfusion followed by development of TACO was reported three times and once staff failed to report the reaction to the lab.

A TACO case description (in Dutch) can be found on www.tripnet.nl in Report of the month series:
May 2017: mix-up of patients' case notes
https://www.tripnet.nl/melding-van-de-maand-mei-2017-verwisseling-patientdossier/

Table 16. Severity and imputability of TACO cases in 2016

Imputability	Total reports*	Severity			
		1	2	3	4
Definite	2 *	1	1 *		
Probable	30 #	18	11		
Possible	52 *	38 *	10	1	3
Unlikely	5 $	2	1		1
Total	**89 ***	**59 ***	**23 ***	**1**	**4**

* *including TACO reported as an additional category with an Other incident*
\# *1x the severity was listed as not assessable in a patient on palliative treatment who died a day after the reaction*
$ *1x the severity was not assessed in a patient who had just been admitted with bilateral pneumonia and who died within hours of onset of the reaction.*

The assessment of reactions with a respiratory component is complex. For TRIP and the TRIP experts to be able to assess the reports properly it is important that they provide information about clinical findings and the results of laboratory and other investigations. The new TRIP reporting system offers extra ways to include this information. Radiographic and other imaging of the chest can be essential in the differentiation between different causes. In order for the radiologist to report optimally the indication for the investigation should be comprehensive and notably should mention that there are respiratory problems associated with a blood transfusion. When providing results to TRIP please give the whole report and include the date and time when the investigation was performed.

Internationally it is also recognised that TACO is an important problem among the transfusion complications, and is a problem which is amenable to mitigating measures. The hemovigilance working party of the International Society for Blood Transfusion has noted that the 2011 definition for TACO is not satisfactory because (http://www.isbtweb.org/fileadmin/user_upload/Proposed_definitions_2011_surveillance_non_infectious_adverse_reactions_haemovigilance_incl_TRALI_correction_2013.pdf) many reported cases which are endorsed as TACO by hemovigilance systems do not meet all the required (2011) criteria. In collaboration with the International Haemovigilance Network and AABB (formerly: American Association of Blood Banks) a revised set of criteria is undergoing validation at the time of publication of this report in 2017. TRIP is actively involved with this process.

A study of the risk factors in a cohort of patients whose TACO reactions were reported to TRIP confirmed that nearly all patients had several of the recognised risk factors (Presentation by A. van Tilborgh, NVB-TRIP Symposium 2017). Together with members of the TRIP hemovigilance advisory board TRIP will examine which risk factors are suitable for inclusion in a so-called TACO tool: an aid to support doctors prescribing blood components by triggering awareness that patients may be at increased risk of TACO so that an appropriate speed of transfusion and maybe prophylactic medication can be prescribed when ordering blood.

TRALI

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

In 2016 six cases of TRALI were reported to TRIP: two of severity grade 4, four of grade 3. After the closing date for the 2015 an additional case of TRALI was reported and this was assessed by the experts with the 2016 reports.

- The imputability of five of the six TRALI reports was assessed as definite, probable or possible
- Figure 8 shows the types of blood components which were associated with the reported cases from 2012.
- In 2016 one TRALI was reported after transfusion of a relatively large volume of SD-plasma, imputability possible; RBC and platelets were also transfused but that was outside the window of 6 hours before onset of the respiratory problems. The 3-year old patiënt, a stem cell transplant recipient, had various problems which are predisposing factors for developing 'ALI' (acute lung injury). As far as TRIP is aware TRALI in the absence of ALI risk factors has not been reported in association with trans-fusion of exclusively SD-plasma. The Expert Committee was of the opinion that TACO could not be excluded and in accordance with this advice TACO has been recorded as an additional category. The reporter did not endorse this modification.
- The two grade 4 cases are briefly described in Table 5; one case (following the admniistration of a pooled platelet concentrate with platelet additive solution) was judged to be of possible imputability, one case unlikely (red blood cells).
- Since the introduction of male only plasma (2007) a total of four TRALI cases have been reported in association with transfusion of plasma alone (quarantine fresh frozen plasma).

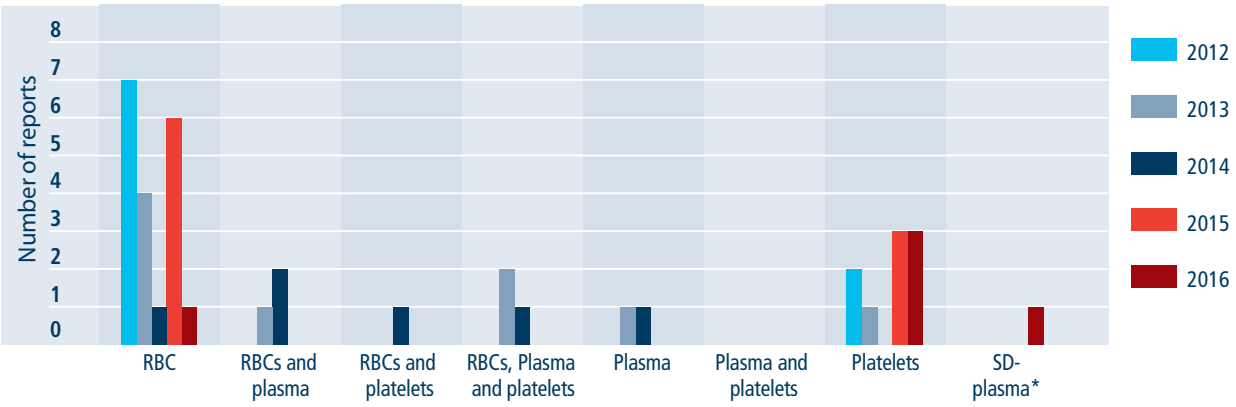


Figure 8. Type of blood component in TRALI reports of certain, probable or possible imputability, 2012-2016

* *See comment in text*

Transfusion-associated dyspnea (TAD)

Shortness of breath or hypoxia during or within 24 hours after a blood transfusion, and the criteria for TRALI, circulatory overload, anaphylactic or other allergic reaction are not met. Respiratory problems are the most prominent feature and they cannot be explained by the patient's underlying pathology or other known specific causes.

Transfusion-associated dyspnea (TAD) was introduced as a reporting category in 2016. The true nature of these reactions is not clear. Are some of these reactions maybe milder TRALI of TACO cases, or cases where pulmonary oedema had not yet become radiographically visible on the chest X-ray at the time when it was taken? In the past these cases were registered as other reaction (in the subgroup of reactions with dyspnea). Eight reports of TAD were submitted in 2016.

Table 17 gives information about the patients and transfused blood components for different categories of reaction where dyspnea is observed following transfusion. For TAD the average age (56) is closer to TRALI (average 53) than TACO (average 73); the severity is grade 1 in all reports of TAD. In the remaining cases of other reaction with dyspnea the average age is higher. TAD started on average 1 hour and 15 minutes after the beginning of the transfusion (median 55 minutes). .

Table 17. Patient characteristics and associated blood components in reactions with dyspnea in 2015and 2016

Category	TRALI*	TACO	TAD	Anaphylactic reaction	Other reaction with dyspnea#
Total cases	27	163	13	103	64
Patient					
Age (minimum)	3	0	14	0	0
Age (maximum)	81	95	81	95	91
Age (average)	53	73	56	52	71
% female	46%	52%	62%	44%	50%
Severity average	2,6	1,5	1,0	1,4	1,1
% serious	100%	37%	0%	37%	14%
Imputability					
Definite	2	5	0	16	2
Probable	5	60	5	43	8
Possible	19	92	8	42	46
Unlikely	1	6	0	2	8
Product					
RBC	12	140	12	22	52
Platelets	8	9	1	72	11
Plasma (FFP)	2	0	0	1	0
SD-plasma (Omniplasma)	1	2	0	5	0
Combination	4	12	0	3	1
% RBC	46%	87%	92%	21%	81%
% platelets	27%	5%	8%	70%	17%

* *For TRALI all 2016 dases have been included and the 2013-2015 cases with definite, probable or possible imputability*

\# *Reports of other reaction which did not meet criteria for TACO, TRALI, TAD or anaphylactic reaction (e.g. patient with dyspnea before transfusion and it was unclear whether dyspnea worsened following transfusion)*

Internationally, hemovigilance systems handle classification of reports in the category of TAD in different ways. For instance SHOT (Serious Hazards of Transfusion), the British hemovigilance system, revisited the TRALI reports from previous years and moved cases which did not properly meet the current definition to the TAD box. Frequently a hemovigilance system may categorise a reaction where dyspnea is prominent as TAD is it doesn't meet the criteria for TRALI or TACO – including cases which are complex or haven't been adequately investigated. So far TRIP has followed the principle that cases may only be registered as TAD if TRALI, TACO and the patient's underlying medical condition have been be reasonably excluded as the cause of the dyspnea. This gives us the highest chances of detecting patterns which can bring us closer to understanding the cause and pathophysiology.

Case: TAD

A 77 year old woman receives a unit of RBCs because of hemorrhage following a vascular operation. After 20 minutes (approximately 125 ml has been infused) the transfusion is halted because of an increase in temperature. 30 minutes after the beginning of the transfusion she also becomes dyspneic: the temperature at that time is 38oC, blood pressure 117/69 (pulse 85) and oxygen saturation 79%. The chest X-ray does not show circulatory overload. She receives nebulisation treatment and is given (5L) oxygen supplementation through a mask. Her dyspnea settles within 30 minutes. Her body temperature first rises to 38.9oC and then goes down so that the patient recovers fully. A culture of the remainder of the unit yields no growth, blood group serology and hemolysis parameters determined in connection with the reaction show no abnormalities.

TRIP report:

TAD, grade 1 severity, possible imputability

Acute hemolytic transfusion reaction (AHTR)

Signs or symptoms of hemolysis occurring within a few minutes of commencement or until 24 hours after a transfusion, such as a drop in systolic and/or diastolic blood pressure of ≥ 20 mmHg, fever/chills, nausea/vomiting, back pain, dark or red urine, no or poor increase of Hb level or an unexpected drop in Hb

Table 18. Acute hemolytic transfusion reactions

	Total AHTR	F	M	AHTR with certain, probable or possible imputability	Severity				
					0	1	2	3	4
2006	19	10	9	18	1	11	5	1	
2007	11	7	4	10		8	2		
2008	18	14	4	17		10	7		
2009	18	13*	4*	17		11	4	1	1
2010	21	8	13	20		14	5	1	
2011	17	10	7	15		6	8		1
2012	7	5	2	7		4	2		1
2013	11	8	3	11		4	7		
2014	17	8	9	12		10	2		
2015	18	12	6	16		9	4	1	2
2016	18	12	6	18	1	10	7		
Totaal	**175**	**107***	**67***	**161**	**2**	**97**	**53**	**4**	**5**

* *1x patient's sex not stated*

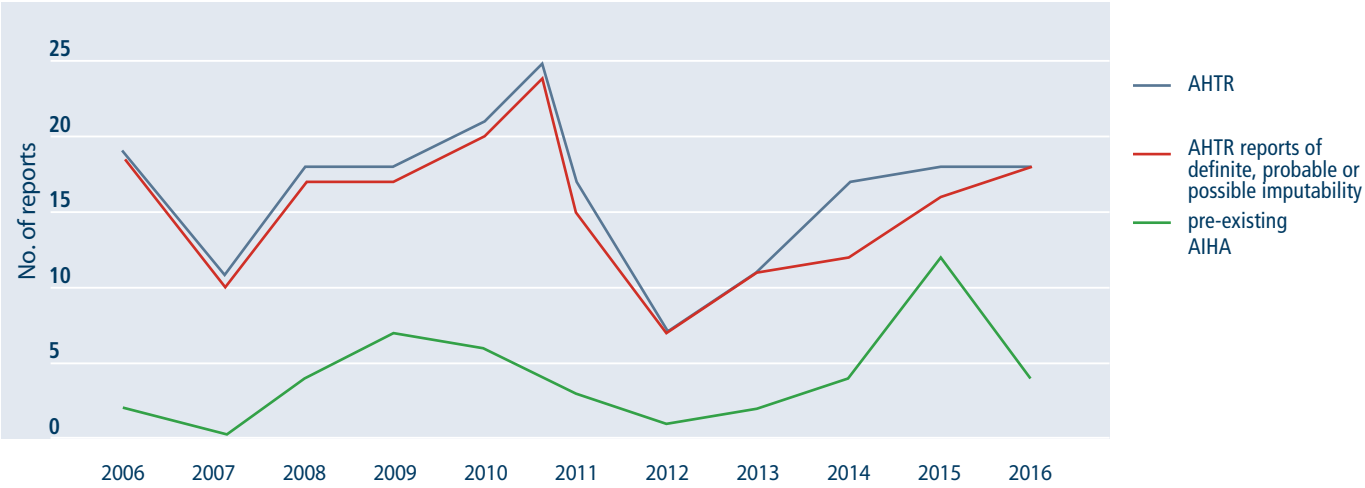


Figure 9. Acute hemolytische transfusionreactions 2006-2016
Abbreviations: AHTR = acute hemolytic transfusionreaction; AIHA = auto-immune hemolytic anemia

- In 2016 there were 18 reports of acute hemolytic transfusion reaction, seven of them serious (grade 2)
- In terms of the mechanism, one reaction was caused by ABO incompatibility (anti-A1), seven AHTR were caused by another irregular antibody (anti-Wra (3x), anti-E, anti-Jkb, complement binding HLA antibodies and nonspecific warm auto-antibodies. In four cases the patient had ongoing auto-immune hemolytic anemia (Figure 9) and in one case AHTR of grade 0 severity was reported in association with extra-corporeal membrane oxygenation (ECMO), as demonstrated by laboratory parameters alone. In five reports the cause of hemolysis was not found.
- In addition a report of incorrect bloood component transfused and a calculated risk situation were associated with acute hemolytic transfusion reactions caused by an irregular antibody (see the relevant paragraphs in chapter 3.1).

AHTR: Conclusion

The number of AHTR reports is consistent with previous years. The increased number of cases of AHTR occurring in patients with underlying auto-immune hemolysis, observed in 2015, has not continued. Anti-Wra caused three AHTR in 2016, including two severe reactions. Wra is not present on the standard screening panel for irregular antibody screening. The likelihood of a hemolytic transfusion reaction from anti-Wra is described as extremely low in the literature. Three cases in one year probably constitutes a once-off peak. Complement binding HLA antibodies caused repeated AHTR in a female patient (Abstract 41, NVB-TRIP symposium 2017), of which one was formally reported to TRIP.

Delayed hemolytic transfusion reaction

Signs or symptoms of hemolysis occurring from 24 hours to a maximum of 28 days after transfusion, such as: unexplained drop in hemoglobin, dark urine, fever or chills, or laboratory findings indicating hemolysis.

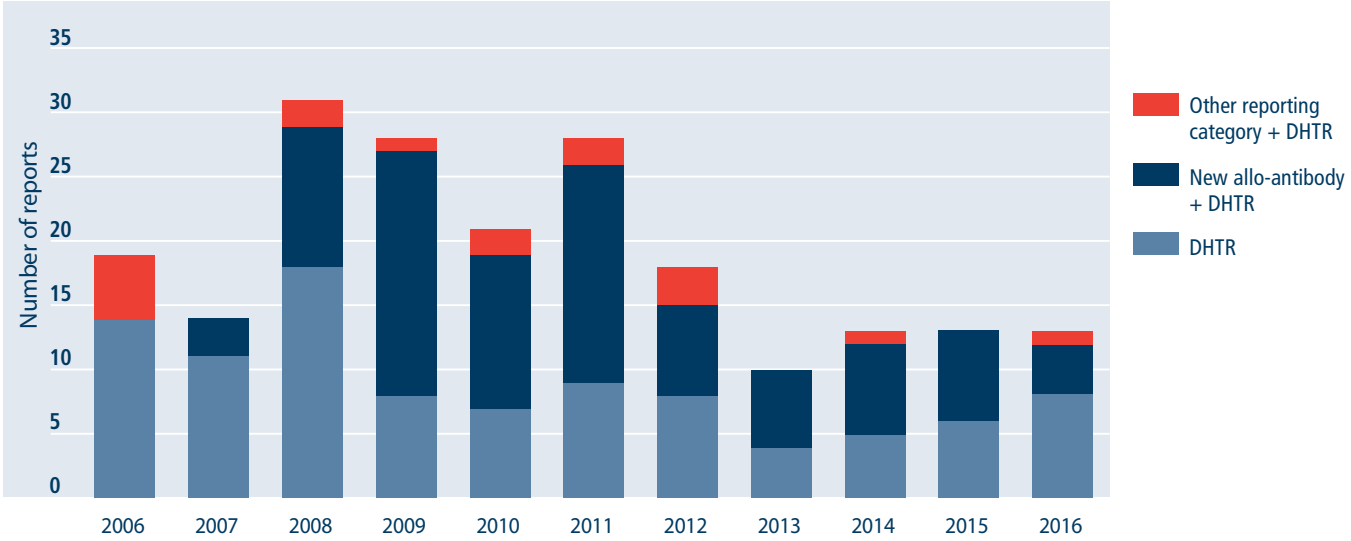


Figure 10. Delayed hemolytic transfusion reaction (reporting category or additional category), 2006-2016

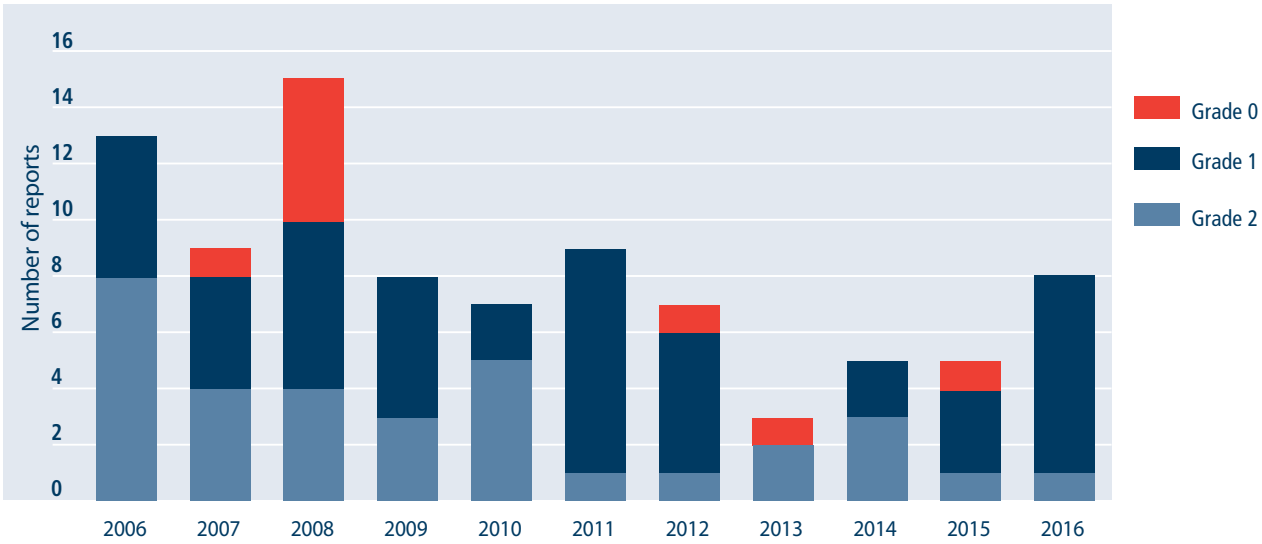


Figure 11. Severity of delayed hemolytic transfusion reactions reports (reporting category DHTR, imputability definite, probable or possible), 2006-2016

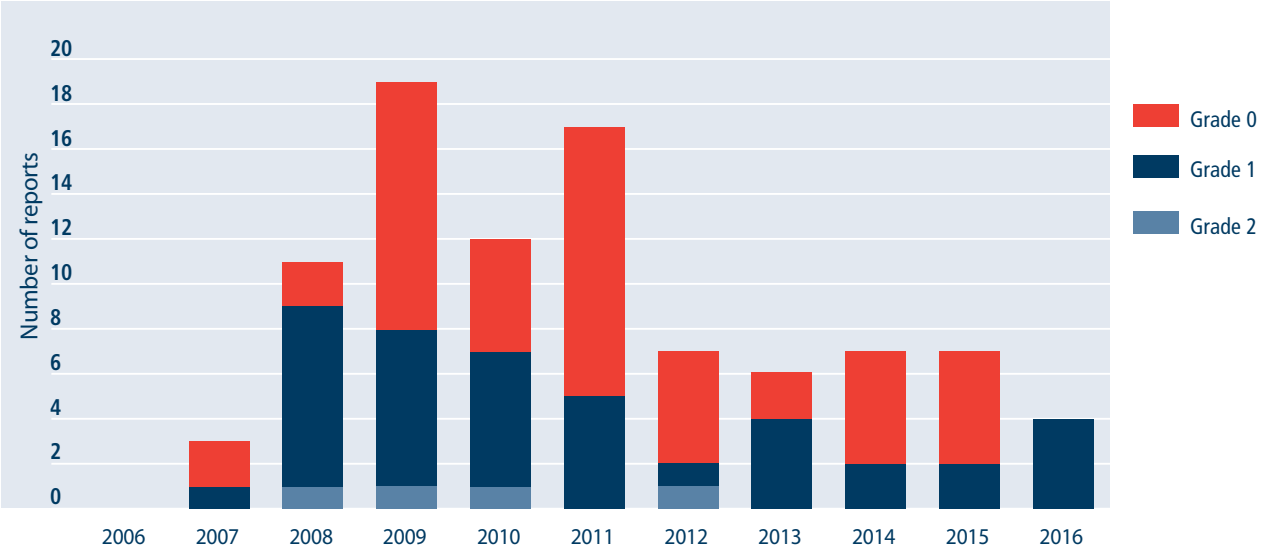


Figure 12. Reports of new allo-antibody formation associated with delayed hemolytic transfusion reaction, subdivided by severity grade, 2006-2016

- A total of 13 delayed hemolytic transfusion reactions were reported.
- 8 cases were reported in the category of DHTR (all of definite, probable or possible imputability), including one case of severity grade 2.
- 4 cases were recorded as an additional category in cases registered as new allo-antibody formation; in one of these cases there had been a transfusion of an incorrect blood component which was not rhesus compatible whereas the patient already had an allo-antibody. There was an urgent need for transfusion and it was said that no unit of the appropriate rhesus phenotype would be available on time. It was not possible to elucidate the exact circumstances at the time of compiling the report.
- 1 report of incorrect blood component transfused with additional category of DHTR (see the relevant paragraph in chapter 3.1). In the past three years there have been no cases of DHTR following IBCT.
- With the exception of one case where a 'private' antibody (antibody against a rare blood group antigen) was suspected, the immunological mechanism involving an allo-antibody was established in all cases. The most frequent was anti-Jka (5x), followed by anti-c (2x) and anti-Jkb, -K, -e, -P1, -M.

For demonstrating or excluding a delayed hemolytic transfusion reaction it is essential to determine the hemolysis parameters at least once and in relevant cases to perform repeated determinations. This is not always performed exhaustively because often the parameters are not requested or no samples are available. In 2016 there were six reports of IBCT where there was a risk of allo-antibody incompatibility and in only one of these cases was delayed hemolysis demonstrated.

Investigations in cases where a delayed hemolytic transfusion reaction is suspected:

- LDH, bilirubin, haptoglobin, Hb course (insufficient increase or unexplained drop?)
- DAT and eluate (even if DAT is negative)
- Auto-control
- Was the cognate antigen present on the transfused RBC? (mixed field?)

If the hemolysis parameters do not show abnormalities, repeat after 24-48 hours.

The "TRIX" (Transfusion Register for Irregular antibodies and crossmatch(X)problems) national database for irregular antibodies is now operational in nearly all Dutch hospitals. The number of DHTR reports in the last four years has run at roughly half the level of the years before this period. The TRIP data cannot

prove that the reduction is a consequence of having the database, but it is plausible that TRIX has made an important contribution, as well as the national recommendations for preventive selection of compatible components for specific groups of at-risk patients. As far as TRIP has been able to establish, one report of delayed hemolysis in 2016 was submitted by a hospital which had not yet implemented TRIX at that time. This does not however mean that the reaction could have been avoided through consulting TRIX. That would only be the case if the particular allo-antibody had previously been demonstrated in another hospital. The IBCT report which led to a DHTR was a case where the laboratory scientist forgot to consult TRIX.

New allo-antibody formation

After receiving a transfusion, demonstration of clinically relevant antibodies against blood cells (irregular antibodies, HLA or HPA antibodies) that were not present previously (as far as is known in that hospital).

- 635 reports (656 including reports with an new allo-antibody as an additional category), 776 antibodies
- 63 hospitals (67%), 1-55 reports per hospital
- 249 male and 404 female patients
- 34 new allo-antibodies in women aged < 45 at the time of transfusion

The specificities of the most frequently detected and reported antibodies in 2016 are listed in Table 19. According to the (2011) national "CBO" transfusion guidelines women younger than 45 should receive RBC units which are Kell and rhesus c and E negative or compatible. Table 20 lists the reports of anti-K, anti-c and anti-E in women of child-bearing age. There were no cases in 2016 where anti-D was detected in a woman less than 45 years of age.

Table 19. New allo-antibodies in 2016: most frequent specificities in women and men

New antibody	F<45y	F total	M	Ratio F/M	Percentage (TRIP 2016)	TRIX top 10*
anti-E	8	130	73	0,6	28%	16,8%
anti-K	6	111	71	0,6	25%	13,8%
anti-C	4	31	11	0,7	6%	5,9%
anti-Fya	2	31	25	0,6	8%	5,3%
anti-Jka	2	29	21	0,6	7%	3,2%
anti-Wra	3	24	8	0,8	4%	5,5%
anti-Jkb	1	11	7	0,6	2%	
anti-S	1	11	6	0,6	2%	
anti-Kpa	1	10	2	0,8	2%	
anti-D	-	9	3	0,8	2%	11,6%
anti-Lua	-	9	17	0,3	4%	
anti-M	2	9	5	0,6	2%	9,5%
anti-Fyb	2	8	-	1,0	1%	
anti-e	-	5	7	0,4	2%	
anti-c	4	4	17	0,2	3%	5,2%
anti-Cw	-	4	10	0,3	2%	
anti-P1	-	4	3	0,6	1%	
anti-Lea	-	3	1	0,8	1%	6%

* *Information presented by TRIX user committee at NVB-TRIP symposium, May 2017*

Table 20. Reports of anti-K, anti-c and anti-E in women <45 years of age in 2016 en 2015

Antibody	2016	2015
Anti-K*	6 1x IBCT 2x Calculated risk situation/emergency 1x platelets 2x Tf 2002 or before	8 Tf in 2003 or before
Anti-c#	4 2x calculated risk situation/emergency 2x Tf 2012 or before	4 1x platelets 1x IBCT 2x Tf in 2011 or before
Anti-E#	8 1x platelets 1x O neg, urgent transfusion, selection error 5x Tf 2011 or before 1x Tf 2014, patient aged 43y, no further details	6 5x (also) platelets 1x Tf in 2006

* *Recommendation re Kell matching was introduced in 2004 guidelines*
\# *Recommendation re rhesus phenotype matching was introduced in 2011 guidelines*

In a presentation by the "TRIX" user committee at the NVB-TRIP symposium in May 2017 it was shown that some 7000 new allo-antibodies are detected and registered in TRIX each year, of which approximately one-fifth are detected in men. This shows that not all newly formed allo-antibodies which are possibly formed as a result of blood transfusion are reported to TRIP. Now that TRIX is operational in nearly all the hospitals, TRIP and TRIX are considering possibilities for an annual summary of information to be provided by TRIX.

In TRIX it is not recorded whether an allo-antibody which has been demonstrated was formed as a result of a blood transfusion. TRIP requests all hospitals to (continue to) report cases of new allo-antibody formation in women of childbearing age (< 45 years of age) and multiply transfused patients, particularly patients with hemoglobinopathy or MDS, for whom preventive component matching is recommended. Sometimes a calculated risk may have been taken in an emergency situation in the past, or an error in component selection in the past may come to light. By continuing to report such cases hospitals will make it possible to monitor the effectiveness and the difficulties with the preventive recommendations.

Other reaction

Transfusion reaction which does not fit into the categories above.

- Just as in the last few years 'other reaction' stands in fourth position as regards total number of reported cases
- Each year since 2010 it has been one of the largest three categories of reports of grade 2 or higher and definite, probable or possible imputability
- 'Dump category' of reactions which do not fit in the standard reaction categories
- In a lot of reports of other reaction it is difficult to distinguish between clinical manifestions which arise or worsen following the transfusion, and features which can be explained by the underlying condition of the patient. The imputability is generally low (unlikely or possible).

Table 21. Types of reactions which are registered as other reaction (broken down as in previous TRIP reports)

Type of reaction	2012	2013	2014	2015	2016	2016 certain, probable	2016 possible	2016 ≥ gr 2*
Reactions with hypotension	42	47	30	42	40	2	34	3
Reactions with dyspnea	30	34	20	38	24	3	18	2
Subgroup: met criteria for TAD	*Not assessed*	*Not assessed*	*3*	*5*	*(See TAD paragraph)*			
Rise in blood pressure	14	6	3	17	9	0	8	0
(Possible) cardiac symptoms	10	9	5	13	14	4	8	3
Did not completely fit TRIP definition for standard category	63	73	77	39	58	11	32	6
Unproven sepsis	Not assessed	2	3	2	2	0	1	0
Other signs								
Overige verschijnselen	57	45	53	48	60	6	34	5
Total	**216**	**216**	**191**	**201**	**207**	**26**	**135**	**19**

** Definite, probable or possible imputability*

3.4 Blood management techniques (BMT)

The number of reports associated with the application of blood management techniques was low in 2016, as before: there were only five reports, all with drain blood (2015: n=3 with drain blood). There were four febrile reactions (3x NHTR, 1x mild non-hemolytic febrile reaction) and one report of an other reaction, with chills, dyspnea and a rise in blood pressure. It is relevant to note that all of the 2016 reports came from one hospital.

The annual number of reports for the different BMT from 2008 is shown in Figure 13. The majority of reports concern the administration of unwashed drain blood. There have been 13 serious reports concerning this technique in the period 2008-2015 (12x grade 2, 1x grade 3). The appplication figures (Figure 14) show a declining trend, just like the number of reports, and consistently the hospital hemovigilance officers and hemovigilance assistants in roughly half of the hospitals are unaware of whether drain blood procedures are applied in their hospital.

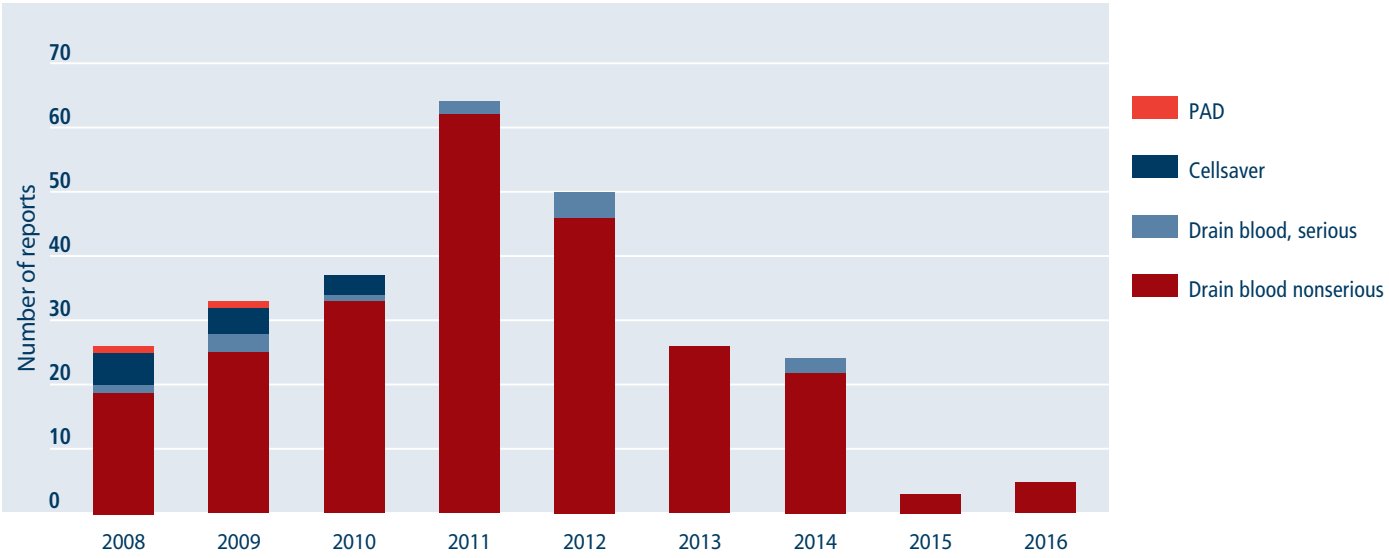


Figure 13. Reports per type of BMT, 2008-2016

Abbreviation: PAD = preoperative autologous donation

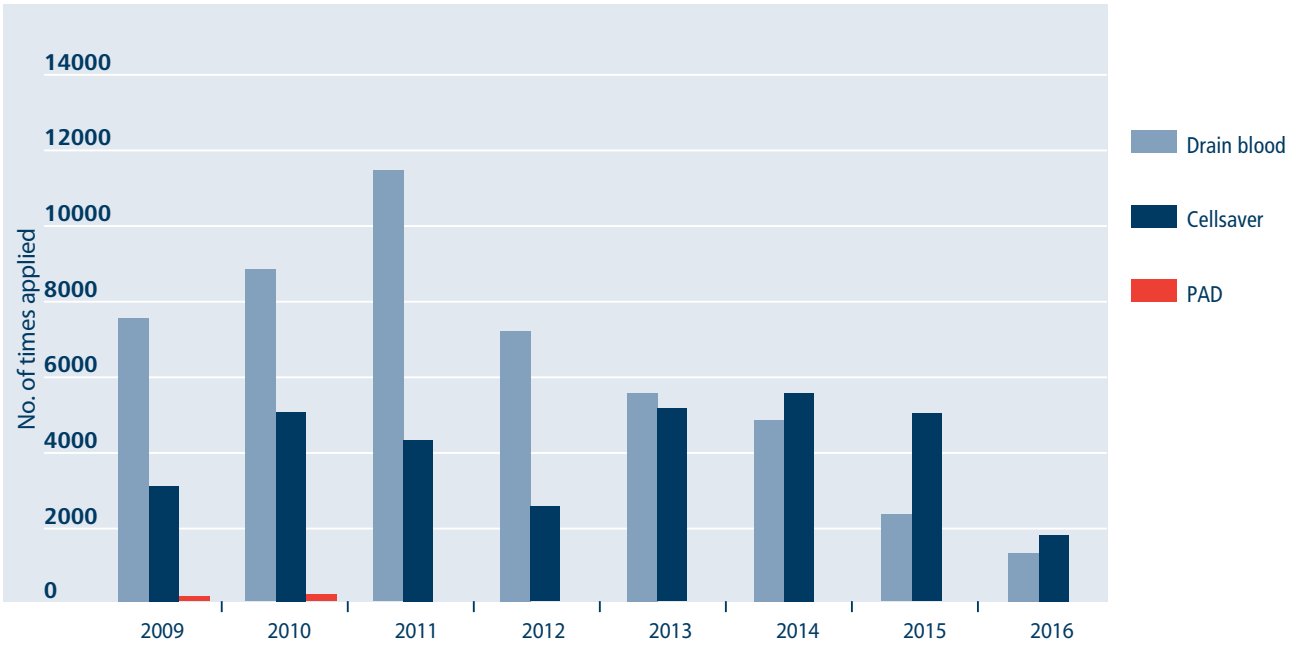


Figure 14. Application data for drain blood procedures, cell saver procedures and patients referred for autologous donation (2016 data from 6, 15 and 2 hospitals respectively, 2015 data from 11, 26 and 6 hospitals)

Abbreviation: PAD = preoperative autologous donation

BMT: conclusion

The numbers of reports associated with BMT and the use of BMT are declining. National collection of this data, as recommended in the national "CBO" blood transfusion guidelines (2011) and incorporated in the NIAZ quality standards, has not produced a consolidated national overview. It no longer seems relevant for TRIP to collect this information annually. In the future in will become possible to extract more accurate data regarding the use of these techniques from electronic patient dossiers. Serious reactions and incidents should continue to be reported to TRIP.

3.5 Reports with SD-plasma (Omniplasma®) in 2016

Under joint authorship with Lareb (Netherlands Pharmacovigilance Centre)

Use of SD-plasma in The Netherlands

SD stands for solvent-detergent, a pharmaceutical virus reduction method which is applied to pools of donor plasma units. Omniplasma®, which is an SD-plasma produced from Dutch plasma donors collected by Sanquin, has been progressively rolled out by Sanquin as the standard plasma product for transfusion since the beginning of 2014.

Because Omniplasma is legally a medicine and is covered by legislation on pharmaceutical products, in each hospital there will be a contract between the hospital pharmacy and the blood transfusion laboratory. In accordance with arrangements made between TRIP and Lareb, the Dutch pharmacovigilance agency, vigilance reporting in relation to Omniplasma follows the same route, using the TRIP online reporting system, as for the labile blood components. This ensures that the TRIP reporting will cover the whole transfusion chain. Further information (in Dutch) about reporting arrangements can be found on www.tripnet.nl.

SD-plasma was in use in 85 of the 94 hospitals in 2016 (no information from two hospitals; in 2015 68 hospitals used SD-plasma, in 2014: 20 hospitals) thus the transition is nearly complete. FFP is still supplied by Sanquin for pediatric transfusions and for other special indications.

A total of 12 reactions and six incidents were reported in association with exclusively SD-plasma in 2016 and a further 19 reactions occurred where red blood cells and/or platelets were also transfused. The incidents (3x other incident, 3x incorrect blood component transfused) are described in chapter 3.1. Tables 3a and 3b (supplemental material with this report) summarise the types of reports with SD-plasma in 2016. Six reactions were of severity grade 2 or higher. The serious anaphylactic reaction is described below. Another serious reation was a case of possible TRALI. The TRALI paragraph in chapter 3.3 explains that the patient (a child) had additional risk factors for acute lung injury. A TRALI case without extra risk factors would have been remarkable because TRALI has not previously been reported in the literature.

Case description: anaphylactic reaction

A man in the 60-80 age group received a unit of blood group O and a unit of blood group AB Omniplasma at the end of a cardiothoracic operation for correcting the coagulation. The units were transfused in 15 minutes; an hour later his oxygen saturation dropped to 76%, he had tachycardia and an unstable blood pressure and had a widespread erythematous rash.

Following administration of adrenaline/noradrenaline, di-adreson F and clemastine he recovered within an hour. Further investigation excluded IgA deficiency. The patient also received fibrinogen/prothrombin complex which could also have caused the reaction.

TRIP report:

anaphylactic reaction, severity grade 2, imputability possible

Conclusion

Few reactions occur with SD-plasma (Omniplasma®); the reported reactions are similar in nature to those with quarantine fresh frozen plasma.

CHAPTER 4

General information

4.1 TRIP working methods and participation in TRIP reporting

A central registration system for blood transfusion reactions and incidents makes it possible to monitor the transfusion chain, detect weak links and make recommendations for improving transfusion safety. The incidence of known side effects of blood transfusions is tracked and previously unknown reactions to transfusion of current or new blood products can be detected in timely fashion.

TRIP foundation (originally: Transfusion Reactions In Patients) was created in 2001 by representatives of the various professional societies involved in blood transfusion. The national TRIP Hemovigilance and Biovigilance Office has operated a registry for transfusion reactions and incidents since 2003 in collaboration with the contact persons in the hospitals and the national blood service, Sanquin. Since August 2006 TRIP has also run a national reporting system for serious adverse reactions and events in the chain of clinical application of human tissues and cells. When the biovigilance activities were structurally assigned to TRIP the foundation's statutes were changed (2012) and its name became Transfusion and Transplantation Reactions in Patients. The tissue and cell vigilance findings are reported in a separate annual biovigilance report which is also available on www.tripnet.nl under publications/reports.

Reporting to TRIP is anonymous. Though voluntary in principle, it is regarded as the professional standard by the Healthcare Inspectorate (Inspectie voor Gezondheidszorg en Jeugd, IGJ) and the national "CBO" transfusion guidelines (2004 and 2011 versions; the guidelines are under revision as of 2017-2018). Reporting to TRIP is separate from the hospitals' responsibility to provide care.

Nearly all reports to TRIP are submitted through the online reporting system: >95% since 2012. Since 2016, when a new secure reporting system was taken in to use, all reports have been submitted online. Reporters of transfusion reactions and incidents are asked to provide results of relevant investigations and grade the clinical severity of the reaction. The imputability, i.e. the likelihood that the reaction can be ascribed to the administered transfusion, is also assessed. If necessary TRIP requests further explanation or details from the reporter. All reports are reviewed by the TRIP physicians, who assess their coherence and verify the reporting category of (potentially) serious reports. Each year TRIP checks for duplicate reports and merges them in consultation with the reporting hospitals.

An Expert Committee (EC), consisting of experts appointed by the TRIP Board, additionally assesses the serious reports by category. Complex or unusual reports are specifically discussed in an annual meeting. Only after this review process are the reports included in the annual report. The EC is composed of representatives of professional societies and of experts who are appointed for their specialised knowledge in a particular domain; the members are also members of TRIP's Hemovigilance Advisory Board.

Under the requirements of European Directive 2002/98/EC it is mandatory to report serious adverse reactions and incidents which could have a relation to quality and/or safety of blood components. TRIP provides the analysis of these serious reports (severity grade 2 or higher) and prepares the annual overview for the competent authority, the Ministry of Health, Welfare and Sports, and the healthcare inspectorate. The hospitals can send the serious reports to the healthcare inspectorate and Sanquin using the TRIP online reporting system.

At the end of each reporting year TRIP receives a copy of Sanquin's annual overview of serious adverse reactions and serious adverse events as reported to the healthcare inspectorate, as well as numbers of

distributed blood components. Each year TRIP and Sanquin match up relevant serious reports which have been reported through different routes using anonymous details (date of transfusion, age, sex, type of blood component and general type of reaction), the intention being to ensure that the information in the TRIP database is as complete as possible. If all reports to Sanquin are sent through the TRIP reporting system (even if this might be a duplicate report of a reaction which has already been reported by telephone) this will ensure that they can be matched and that Sanquin always has access to the final classification (diagnosis) of each reaction in the TRIP system. After completion of the expert review process, TRIP also provides Sanquin with the final TRIP classification of the reports which are registered in both systems. TRIP annually checks for duplicate reports and if any are found, merges them in consultation with the reporting hospital.

The value of reporting and collecting transfusion reactions and incidents at the national level depends on the participation of all the reporting establishments. In 2016 there were 94 contact addresses of hospitals which had administered transfusions. In situations where hospitals merge, TRIP advises the hemovigilance professionals to merge for reporting purposes from the time when work processes have been harmonised and the flow of information has been merged. Out of the 94 hospitals, 86 submitted reports and seven indicated that there had been no reactions or incidents in the TRIP categories. One institution was not able to provide information about reactions before the closing date. At the time of writing this report, 92 hospitals had provided information about numbers of transfused blood components. Besides the hospitals, TRIP is in contact with the four private clinics which have been licensed by the ministry of health to receive and transfuse blood components (these clinics have contracts with Sanquin or other hospitals for the provision of component selection and crossmatching services). One of the four licensed clinics informed TRIP that a transfusion (one unit) had taken place in 2016; no units were transfused in the other three clinics.

List of terms and abbreviations

AHTR	acute hemolytic transfusion reaction
BMT	blood management techniques
Bc	blood component
CBO	CBO quality organisation in healthcare
DHTR	delayed hemolytic transfusion reaction
EC	expert committee
EU	European Union
FFP	fresh frozen plasma
Hosp.	hospital
IBCT	incorrect blood component transfused
IC	intensive care
Irrab	irregular antibodies
Mild NHFR	mild non-hemolytic febrile reaction
New allo-ab	new allo-antibody formation
NAT	nucleic acid amplification test
NHTR	non-hemolytic transfusion reaction
NM	near miss
OI	other incident
PAD	preoperative autologous donation
PAS	platelet additive solution
Pt	patient
Plts	platelets, platelet concentrate
Post-Tf bact/sepsis	post-transfusion bacteremia/sepsis
PTP	post-transfusion purpura
RBC	red blood cell concentrate
Sanquin	Sanquin (Dutch national blood establishment)
SD	solvent detergent (a pathogen reduction method)
TA-GvHD	transfusion-associated graft versus host disease
TACO	transfusion-associated circulatory overload
TAD	transfusion-associated dyspnea
Tf	transfusion
TR	transfusion reaction
TRALI	transfusion-related acute lung injury
TRIP	TRIP Foundation (Transfusion and Transplantation Reactions In Patients)
TRIX	Transfusion Register of irregular antibodies and X(crossmatch) problems
TTBI	transfusion-transmitted bacterial infection
Tx	transplantation

TRIP Hemovigilance
and biovigilance office
Schuttersveld 2
2316 ZA Leiden
Email: info@tripnet.nl
www.tripnet.nl