TRIP REPORT 2017

Hemovigilance

Extended version

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Foreword

A blood transfusion can save a patient's life, but what if a complication occurs? As a hematologist, I see the benefits of blood transfusion in my patients on a daily basis – but every now and then I see a complication or a problem, which leads to questions concerning safety and preventability. In 2017, TRIP received a total of 2131 hemovigilance reports, of which 121 concerned serious cases. Thus a serious reaction only occurs once for every 4000 units distributed. Once again it may be concluded from the reports of transfusion reactions and incidents to TRIP that there is a high level of safety in the Dutch transfusion chain.

Yet, some important concerns should be addressed by professionals in the transfusion chain: the report shows, among other things, the dangers of transfusion-associated circulatory overload (TACO). My fellow clinicians are often inclined not to consider TACO a transfusion reaction. However, scientific research in the domain of hemovigilance is making it increasingly clear that there is more to blood than simply the volume that is administered and that inflammatory and/or immunological processes may play a significant part in the development of TACO. This is where the value of hemovigilance can be seen. TRIP has developed a pocket reference card and an app to support doctors and nurses in recognizing patients who have an increased risk of developing circulatory overload and implementing preventive measures when appropriate.

How can TRIP work with the professionals in the transfusion chain to do more with the hemovigilance findings? Firstly, I encourage you to work on the implementation of our recommendations within your own organisation through the blood transfusion committee. Furthermore, TRIP data may be used for educational purposes. Tables and figures of the data TRIP has collected over the years may be requested in English and/or Dutch. TRIP would also be glad to hear of any regional meetings or meetings of health care professionals, where you or a TRIP hemovigilance physician could raise awareness for the findings of this report. The systematic registration of transfusion reactions may raise scientific research questions which could lead to new pathophysiological insights into blood transfusion complications. Anonymised data may be requested from TRIP for specific research questions. For more information on how to request data, please visit our website.

As in other years, this report could not have been produced without the essential contributions 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 thank you all for your contributions, and wish you all the best in in your professional activities.

Dr Martin R. Schipperus
President, TRIP Foundation

CHAPTER 1

Main 2017 findings

1.1 Hemovigilance trends in 2017

In 2017, TRIP received a total of 2131 hemovigilance reports. The use of red blood cell concentrates fell by 2.5%, whereas the use of platelet concentrates saw little change in comparison to 2016 (Figure 1). The number of reported reactions per type of blood component in 2017 is similar to the number reported in recent years (Figure 2).

Transfusion reactions

The data on transfusion reactions show a notable increase in the number of reports of transfusion associated circulatory overload (TACO). This complication also accounts for the largest number of serious reactions (33 out of 121). In 2017, TACO pocket reference cards for physicians and nurses were developed to support implementation of TACO risk reduction measures in patients requiring transfusion who have an increased risk of developing this complication.

The category of other reactions also shows a steady increase in the number of reports; after TACO, other reactions and anaphylactic reactions account for the largest numbers of serious transfusion reactions. In a relatively large number of cases categorized as other reaction, the reaction may have been at least partly due to the patient's underlying condition. Thus, for a correct understanding of this kind of report, sufficient information about findings of physical examination, the clinical assessment and the patient's response to treatment is needed.

Errors and incidents

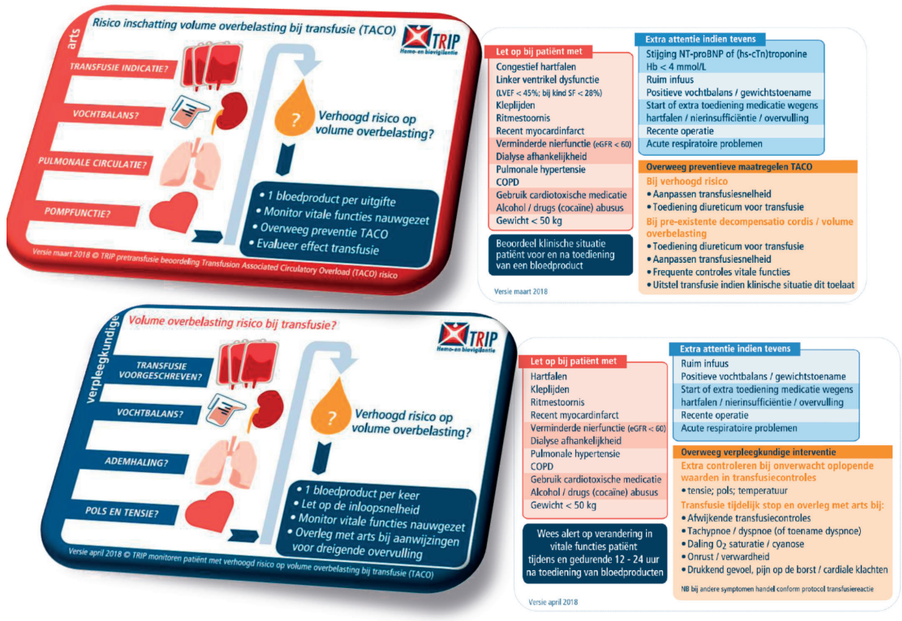
The near miss category shows a downward trend whereas these incidents may provide important insights into the weak points in the transfusion chain. About 75% of these reports concern cases with a potential ABO risk in which a mix-up of, for instance, labels with patient identity details or samples seems probable. The majority of these mistakes was detected in time because a blood group discrepancy was found. The mistakes registered in occurrences of this type of report are similar to the mistakes that lead to cases of incorrect blood component transfused (IBCT). It must be noted that the number of reports of IBCT with a risk of ABO incompatibility has been hovering around 15 per year since 2010. This type of mistake may also lead to incorrect laboratory results, due to which a blood component may be inappropriately requested or conversely not requested. Registration and analysis of this type of near miss may provide more insight into the circumstances that play a part in producing these mistakes and may contribute to a (nation-wide) mapping of high-risk situations.

Infectious transfusion complications

As in 2016, a transmission of hepatitis E was diagnosed and reported in 2017. The implicated blood component was administered in 2016. Since mid-2017, Sanquin has tested all blood donated for transfusion purposes for hepatitis E.

1.2 Recommendations

Recommendation	Who?
Active implementation of TACO pocket reference cards	Hemovigilance professionals in collaboration with the transfusion laboratory, clinicians, nurses
Registering and examining reports of near miss situations concerning blood group discrepancies	Hemovigilance professionals in collaboration with hospital patient safety committee, blood transfusion committee
Serious reactions, especially cases reported as other reaction, should be discussed with the treating physician if necessary, for the optimisation of its classification	Hemovigilance professionals in collaboration with clinicians



TRIP pocket TACO prevention reference cards for doctors and nurses (see discussion in TACO paragraph, page 28)

HOOFDSTUK 2

Overview of 2017 hemovigilance results

2.1 Overview of 2017 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 definitions and in the relevant sections of this report.
The reported data are presented in the following tables and figures:

Table 1 Incidents reported to TRIP, 2010-2017
Table 2 Transfusion reactions per reporting category, 2010-2017
Table 2a Transfusion reactions in small categories, 2010-2017*
Table 3 Reports per type of blood component in 2017
Tabel 3a Types of blood component for each type of reaction or incident in 2017*
Tabel 3b Types of reactions and incidents for each type of blood component in 2017*
Figure 1 Distributed units of blood components, 2008-2017
Figure 2 Transfusion reactions excluding new allo-antibodies per 1000 units, 2008-2017
Figure 3 Severity of the transfusion reactions, 2008-2017
Figure 4 Imputability of the transfusion reactions, 2008-2017
** Supplementary tables available as online annexe*

Table 1. Incidents reported to TRIP, 2010-2017

Incident	2010	2011	2012	2013	2014	2015	2016	2017	No. of hospitals with reports in 2017
Incorrect blood component transfused (IBCT)	58	43	51	43	71	53	43	44	30
Near miss	71	45	50	39	33	40	52	31	11
Other incident	118	138	139	107	120	93	112	71	30
Calculated risk situation*	-	-	-	-	-	-	7	6	5
Hemolysed product	0	2	0	0	1	0	0	0	0
Total	**247**	**228**	**240**	**189**	**225**	**186**	**214**	**152**	**46**

* *Separate category of calculated risk introduced in 2016, see discussion in chapter 3.1*

Table 2. Transfusion reactions per reporting category, 2010-2017

Reaction	2010	2011	2012	2013	2014	2015	2016	2017	Severity grade 2 or higher[#]	No. of hospitals with reports in 2017
Post-transfusion bacteremia/sepsis	41	61	50	47	56	79	64	72	7	35
Post-transfusion viral infection	1	5	2	5	0	2	3	1	1	1
TRALI	17	12	9	9	6	9	6	6	5	6
TACO	47	39	56	69	76	76	87	104	33	47
Transfusion-associated dyspnea (TAD)[+]	-	-	-	-	-	-	8	7	2	7
Anaphylactic reaction	73	67	59	70	53	43	62	64	26	25
Other allergic reaction	184	191	180	193	153	151	126	125	1	39
AHTR	21	17	7	11	17	18	18	16	9	12
DHTR	7	9	8	4	5	6	8	5	2	5
New allo-antibody	814	831	851	849	763	697	649	657	0	66
NHTR	506	504	456	442	419	448	407	353	11	65
Mild non-hemolytic febrile reaction	363	366	383	340	311	336	365	308	7	63
Other reaction	164	218	225	221	191	205	215	249	13	58
Other small categories of TR	4	5	1	5	17	3	4	3	1	1
Total TR	**2242**	**2325**	**2287**	**2265**	**2067**	**2073**	**2022**	**1970**	**118**	**85**
Total grade 2 or higher[#*]	93	101	100	108	96	112	108	121		
Total reports	**2594**	**2630**	**2580**	**2504**	**2318**	**2289**	**2248**	**2131**		

[#] *Imputability certain, probable, possible; for types of reactions not categorized as severe, grade 2 applies when a reaction led to a (prolonged) hospital admission*

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

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

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

Table 2a Transfusion reactions in small categories, 2010-2017

Table 3. Reports per type of blood component in 2017

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	406938	393018	1692	76	4.16	0.19
Platelet concentrate	56045	53696	267	33	4.76	0.59
Fresh frozen plasma	1499	1197	1	1	0.67	0.67
SD-plasma[1]	63945	57980	35	4	0.55	0.06
Fitrix® fibrin glue	70					
Blood management techniques[2]			1	0		
Combinations[3]			63	7		
Not stated			63	0		
Total	**528497**	**505891**	**2131**	**121**	**4.03**	**0.23**

[#] *Imputability definite, probable or possible*

[1] *SD-plasma = solvent-detergent treated plasma; Omniplasma® in the Netherlands*

[2] *See chapter 3.4*

[3] *Including combinations of labile blood components with SD-plasma*

Table 3a Types of blood component for each type of reaction or incident in 2017
Table 3b Types of reactions and incidents for each type of blood component in 2017

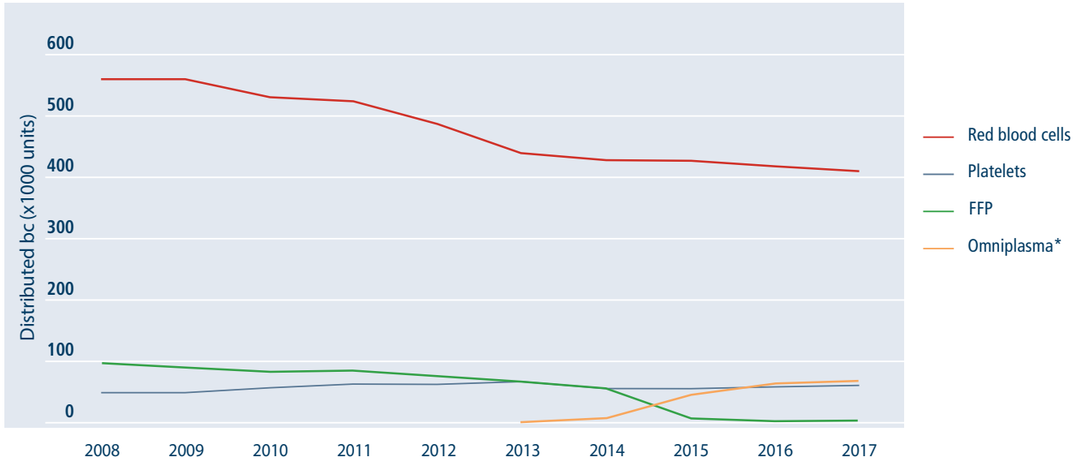


Figure 1. Distributed units of blood components, 2008-2017

[*] *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)*

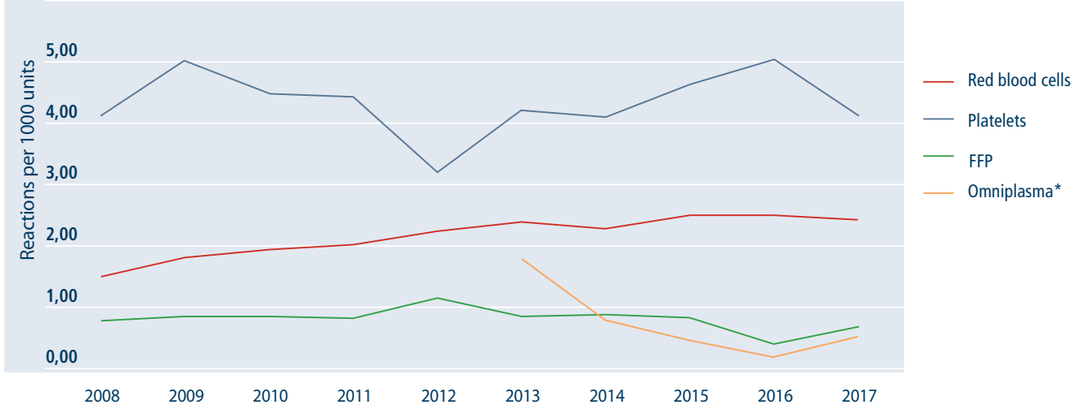


Figure 2. Transfusion reactions excluding new allo-antibodies per 1000 units, 2008-2017

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

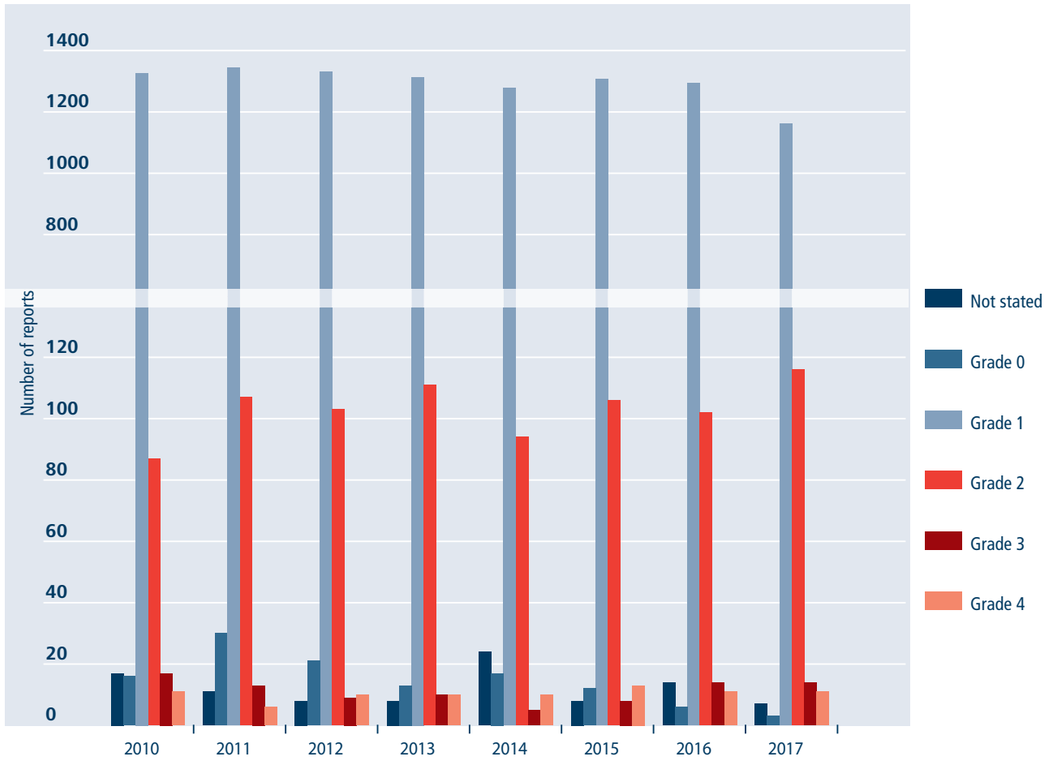


Figure 3. Severity of the transfusion reactions, 2010-2017

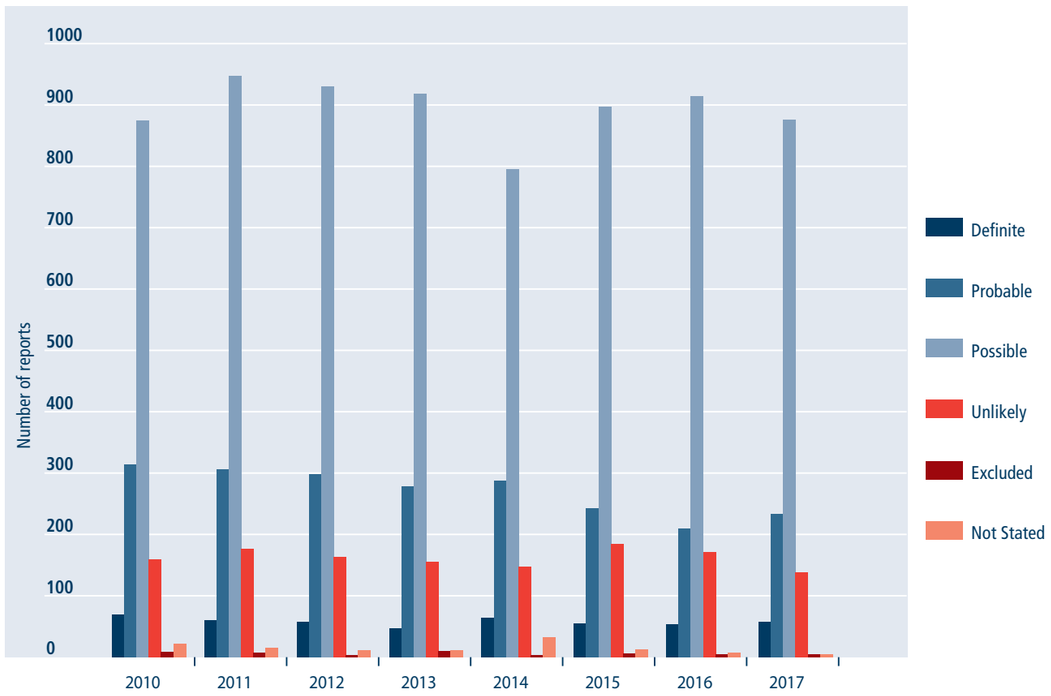


Figure 4. Imputability of the transfusion reactions, 2010-2017

2.2 Overview of mandatory reports of serious transfusion reactions

Every 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, probable and possible imputability are to be reported; late reports from the previous year are to be included
- Reactions following a transfusion of an incorrect blood component and other incidents are included in the appropriate category.
- Hemolytic reactions are subdivided into immunological (ABO), immunological (not ABO) and 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.
- Reports are subdivided in the form according to the type of blood component administered.

The febrile reactions included in the table have been classified as severe due to (prolongation of) hospital admission.

Table 4. Number and imputability of reports of grade 2 and higher in 2017

Severity	2 or 3			4	
Imputability	Definite	Probable	Possible	Probable	Possible
Hemolytic transfusion reaction (ABO)	1	1	0	0	0
Hemolytic transfusion reaction (immunological, not ABO)	1	5	1	0	0
Hemolytic transfusion reaction, (not immunological)	1	1	1	0	0
Allergic reaction	5	10	9	0	0
Febrile reaction	0	4	15	0	0
Other reaction[$]	1	2	13	0	1
TAD	0	0	2	0	0
Transfusion-transmission of bacterial infection	0	0	2	0	0
Post-transfusion viral infection*	1	0	1	0	0
TRALI	0	1	3	0	1
Transfusion-associated circulatory overload	3	7	17	1	5
Total	**13**	**31**	**64**	**1**	**7**

$ Includes three late reports from 2016
** Includes a report that had not been concluded when the 2016 report was published*
Abbreviations: TAD=Transfusion-associated dyspnea; TRALI=transfusion-related acute lung injury

2.3 Transfusion reactions with fatal outcome (Grade 4)

In 2017 a total of 12 transfusion reaction reports were of grade 4 severity. These reports are summarized in Table 5. For eight of the 12 reactions, the relation to the transfusion was assessed as probable or possible.

Table 5. Reports with fatal outcome

Reaction	Gender, age	Blood component/ product	Imputability	Clinical situation
Transfusion-associated circulatory overload (TACO)	M, 75	Red blood cells	Probable	Melena with high INR, respiratory deterioration after 4 RBC, decline despite furosemide pump and CPAP
Transfusion-associated circulatory overload (TACO)	M, 71	Red blood cells	Possible	Disseminated malignancy, Tf for severe anemia, preceded by furosemide; circulatory overload after ½ unit
Transfusion-associated circulatory overload (TACO)	M, 90	Red blood cells	Possible	Admission with anemia and cardiac decompensation; after 2 RBC, despite prior furosemide, worsening of dyspnea and poor result of additional diuretics
Transfusion-associated circulatory overload (TACO)	F, 87	Red blood cells	Possible	Transfusion for symptomatic anemia in patient with cardiovascular history; during 2nd RBC dyspnea and variable BP
Transfusion-associated circulatory overload (TACO)	F, 87	Red blood cells	Possible	Tf-dependent patient, increase of cardiac decompensation, no response to additional diuretics, patient no longer wished to receive treatment
Transfusion-associated circulatory overload (TACO)	F, 76	SD-plasma	Possible	COPD, kidney disease, incipient pneumonia; CXR (also) shows signs of TACO
Transfusion-associated Acute Lung Injury (TRALI) and additional category of transfusion-associated circulatory overload (TACO)	F, 87	Red blood cells	Possible	COPD, vascular disease, alcohol abuse, kidney failure, Hb 2.2 mMol/L; after Tf extensive pulmonary edema, persistence of interstitial shadowing after diuresis
Other reaction	M, 88	Red blood cells	Possible	Weakness, comorbidity, anemia; dyspnea during Tf, rapid decline
Other reaction	M, 81	Red blood cells	Unlikely	Recurrent malignancy, sepsis; during Tf dyspnea+temp, decision to abstain from active treatment
Other reaction	F, 79	Red blood cells	Unlikely	Hematemesis and unresponsive during 3rd RBC
Other reaction	F, 90	Red blood cells	Unlikely	Atrial flutter and anemia, hematemesis after 1 RBC
Post-transfusion bacteremia/sepsis	M, 70	Platelets	Unlikely	Carcinomatous pleurisy, planned pleural tap; progressive dyspnea after platelet concentrates, septic

Abbreviations: BP=Blood pressure; COPD=chronic obstructive pulmonary disease; CPAP=continuous positive airway pressure; CXR=Chest X-ray; Hb=Hemoglobin; INR=International normalized ratio; RBC=Red blood cell unit; Tf=Transfusion

2.4 Late reports from 2016

After the final submission date for reports for 2016, 49 more reports were definitively submitted and these have now been finalised (Table 6). This number of late reports is similar to that in other years. Four of these reports were reports of serious reactions, all of which were categorized as other reactions. These reports are discussed in the relevant section of chapter 3.3. By now, all late reports have been formally assessed and have been included in the relevant figures and tables in this report.

Table 6. Late 2016 reports included in the 2017 report

Reporting category	Severity					No reaction, severity not applicable
	Not stated or 0	1	2	3	4	
Other allergic reaction		2				
Look-back						1
Mild non-hemolytic febrile reaction		5				
Non-hemolytic transfusion reaction		11				
New allo-antibody formation	12					
Other incident						5
Other reaction	1	4	3	1		
Incorrect blood component						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 has 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 would be for the unit to be ABO in-compatible – regardless of what the two patients' blood groups turned out to be. Before 2013, IBCT cases where the patient could have received an ABO incompatible unit constituted the largest subgroup. From 2013 onwards, 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 (risk group: Irrab prevention) (Figure 5).

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

In 2017, a report was received of an ICT issue that occurred when files from different locations of one hospital were combined and which led to important information that the lab needed to select the correct blood component (indication for irradiated blood components) not being shown on the screen. As a result of a single error, a situation arose in which there was a risk of repetition for the same patient or for others.

In six IBCT cases where a mix-up resulted in an IBCT with an ABO risk, the blood components were administered in full before the error was detected. Furthermore, it should be noted that in two of these 10 cases (20%) the report indicated that the error occurred during the busy period just before a shift change/ handing over to colleagues. Likewise, in two cases the report indicated that the transfusion was initiated during the night. It is important to note such information about relevant circumstances in a report to TRIP.

- 42 reports from 30 hospitals (32%), 1 - 5 reports per hospital.
- In 8 cases a reaction was identified and registered in the appropriate additional category (1x AHTR, 1x other reaction, 1x NHTR, 5x new allo-antibody formation), see Table 7.
- 3 reports of reactions in which analysis showed that IBCT preceded the reaction (1x DHTR with additional category IBCT, 2x new allo-antibody formation after a transfusion in a previous year with additional category IBCT in the past), see Table 8.
- In 6 cases, analysis of IBCT showed that the same error or a similar error had occurred in the past and led to the same patient receiving an incorrect blood component, although no report of this had been made yet. These cases are registered with the additional category of IBCT in the past

Table 7. Clinical symptoms after transfusion of an incorrect blood component in 2017

IBCT Risk group	Blood component	Reaction (additional category)	Imputability *	Severity*
ABO	RBC	AHTR	definite	3
	Platelets	Other reaction	probable	1
Prevention Irrab	RBC	NHTR$	unlikely	1
		New allo-antibody:		
	RBC	Anti-c		
	RBC	Anti-c	definite	
	RBC	Anti-c		
	RBC	Anti-c	definite	
	RBC	Anti-K	definite	

* *imputability and severity grade apply to clinical symptoms of a transfusion reaction; new allo-antibody formation is severity grade 0 by definition*
$ *increase in temperature in patient with an infection and a history of sickle cell anemia, up to two months after transfusion no indication of new allo-antibody formation.*
Abbreviations: AHTR = acute hemolytic transfusion reaction; RBC=Red blood cells

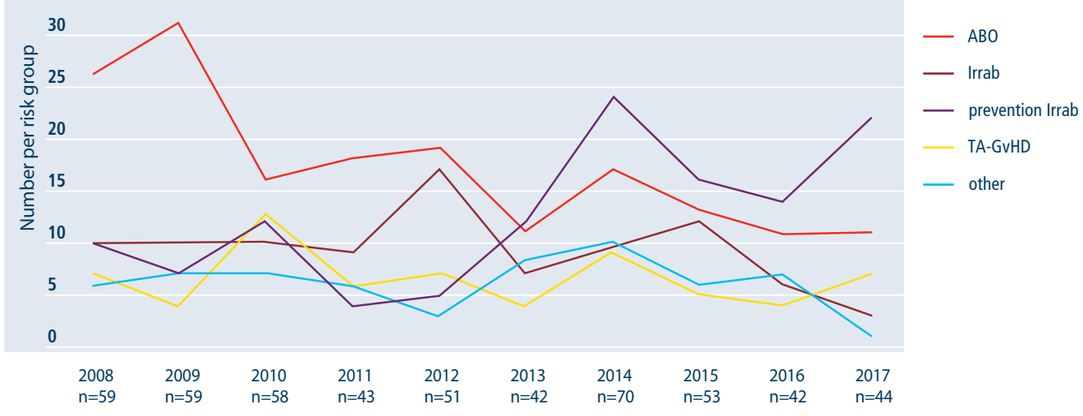


Figure 5. Incorrect blood component transfused broken down according to risk group, 2008-2017
Abbreviations:
ABO = risk of an ABO incompatible blood transfusion
Irrab = risk of an irregular antibody incompatible transfusion
Preventie irrab = guidelines not followed with regard to prevention of irregular antibody formation
TA-GVHD = risk of transfusion-associated graft versus host disease (after transfusion of a non-irradiated blood component)

- Out of the 11 cases in which there was a risk of an ABO incompatible blood transfusion, 10 stemmed from a mix-up of blood bags, patients and/or patient identification and 1 stemmed from ignoring transfusion advice concerning the ABO blood group for platelets for a patient who had undergone allogeneic stem cell transplantation (only administer blood group O). After the administration of 2 units of A platelets, the patient had a temperature increase of ≥ 2 °C and chills, and 24 hours after the platelet transfusion there was no increment.
- In one case, after a mix-up of patient identification details during the request of blood components, two units of ABO incompatible red blood cells were administered in full (A pos RBC and O pos patient) to a patient with cholecystitis and stomach bleeding with extreme INR. The patient was already in the ICU for the gastrointestinal pathology, which caused necrosis, perforation and sepsis during the same period. The mix-up caused AHTR in the patient and was treated chiefly with extensive diuresis. The intended red blood cell apheresis was only partially executed, because the patient developed signs of an acute abdomen which necessitated immediate surgery. Approximately 72 hours after the incident the DAT (IgA, C3d) was negative again and no A positive red blood cells could be found in the patient's blood. LDH and bilirubin peaked initially and then declined. The Hb fluctuated around 5 mMol/L with regular transfusions. Ultimately, the patient died 8 days after this incident.
- In one case, incompatible SD-plasma (O plasma and B pos patient) was transfused to a trauma patient in an acute setting. By mistake, the plasma intended for a different patient was still present in the operating room and was used for a subsequent patient. No transfusion reaction was reported.
- In one case, a small amount of a unit of A positive platelets was administered to an O positive patient. This incident was caused because the wrong blood bag was picked up in a situation where two bags of platelets were present awaiting administration to different patients on the same ward. The wrong blood component was then spiked and the transfusion commenced before the patient identification details were checked.
- In the remaining 7 cases (64%), by coincidence an ABO-compatible blood component was administered, and in all of these cases the component was also rhesus D compatible. However, it should be noted that two cases concerned erroneous administration to a patient who did not need transfusion and for whom, logically, there was no transfusion prescription.
- In the 3 cases with irregular antibody risk, the blood component was incompatible for the known antibody in two cases. In one case the compatibility status of the antigens in the blood component is unknown. In 2017, there were no reports of transfusion reactions after administering an antibody-incompatible RBC. In all cases, the patient screened negative for irregular antibodies at the time of transfusion. Two of these cases arose from errors made when registering the patient's details in the hospital's system. Due to a different spelling of the surname (for instance, van der Burg instead of van der Burgh), information about antibodies demonstrated in the patient's blood elsewhere and registered in the "TRIX" database went unnoticed. In the third case, the antibody demonstrated elsewhere had not been registered in the "TRIX" database.

IBCT case descriptions (in Dutch) can be found in the Report of the Month (Melding van de maand) series on www.tripnet.nl, e.g.:
Report of the Month January 2018: Identification when issuing blood components: some pitfalls
Report of the Month March 2018: A post-transfusion viral infection?
Report of the Month April 2018: failure to provide irradiated blood components
Report of the Month May 2018: 2x 2 RBC → IBCT?

Table 8. Reports in 2017 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 (additonal category)
Delayed hemolytic transfusion reaction	Prevention B19	Assessment error → Failure to comply with B19-safe policy for a patient with hemoglobinopathy. Subsequently it was found that the patient was not subject to this policy because of seropositivity indicating a previous B19-infection.	1
New allo-antibody formation: Anti-K	Prevention Irrab	Selection error → previous failure to comply with preventive Kell Tf advice for a patient with a known antibody.	1
Anti-c and anti-K		Selection error → previous failure to comply with preventive Tf advice for rhesus and Kell for a patient with a known antibody	1
Incorrect blood component transfused	Prevention Irrab	Communication error → Previously not registered as an MDS patient (known since 2011).	83
		Communication error → Previously not registered as an MDS patient (known since 2011).	31
		Type of error unknown → Previous erroneous registration of rhesus typing in the LIS	1
		Administrative error → Tf advice not set to "yes" in the system, resulting in non-activation of the function of automatic selection of antigen-negative RBC components.	2
	Prevention TA-GVHD	Communication error → Physician has recorded in the EHR that patient is to receive irradiated blood components, but this is forgotten in the request for the blood components	1
		Communication error → Failure to indicate history of IUT in a request for blood components for a neonate, nor were irradiated or B19-safe components requested.	1

Abbreviations: EHR = electronic health record; Irrab = irregular antibody; IUT = intrauterine transfusion; LIS = laboratory information system; MDS = myelodysplastic syndrome; TA-GVHD = transfusion-associated graft versus host disease; Tf = transfusion

* *IBCT or IBCT in the past is recorded as an additional category if the error was detected after a reaction or incident; in some cases this affected more than one episode or several patients*

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.

- 31 reports from 11 hospitals (33%), 1-11 reports per hospital
- In 24 cases there was a potential ABO risk and in 15 of these cases this error was detected after detecting a blood group discrepancy. It may be likely that there Is considerable under-reporting of these types of incidents. The reporting of these instances could provide more insight Into the circumstances that can lead to these errors, errors that are of a similar nature as errors that do actually lead to the administration of incorrect blood components. Furthermore, it may be expected that this type of error can lead to erroneous laboratory results that may result in unnecessarily requesting blood components for certain patients and neglecting to request blood components for others.
- In 23 cases, a mix-up of patients or patient identification details (presumably) occurred; for instance a mix-up of labels, blood samples, blood components, testing materials. 3 of these cases concern a situation in which blood group discrepancy with a previously determined blood group was established, in which the newly determined blood group was found to be correct, but in which the errors that occurred previously could not be recovered.
- 4 reports describe a potential TA-GVHD risk due to almost administering a non-irradiated blood component. In 2 of these cases the error was detected by a nurse, after the blood component was distributed by the laboratory, during an inspection before administering the component to the patient. In 1 case, a patient's alertness allowed the error to be detected during the connection of the component. In the 4th case, the laboratory had registered an indication for irradiated blood components in the laboratory system, so a request for "regular" blood components was converted into a request for irradiated components. Whether or not a case like this is reported as a near miss, differs from hospital to hospital. In a number of Dutch hospitals the usual operating procedure does not require an indication for irradiated blood components in a request, because, for patients for whom the indication for irradiated components has been registered in the laboratory system, this indication is automatically supplied by this system. TRIP assumes that hospitals in which it is not necessary to specify an indication for irradiated blood components, because this indication is automatically supplied by the laboratory system, do not register an incident like this one as a near miss, because this is their usual procedure.

TA-GVHD is extremely rare in cases in which leukocyte depletion has been applied (which has been mandatory in the Netherlands for standard blood components since 2001), but not impossible. Furthermore, (nearly) administering an erroneously non-irradiated blood component may also have different further consequences for a patient, for instance because a planned transfusion, or even further treatment must be delayed. In 3 of the 4 cases, the administration of an erroneously non-irradiated blood component was only prevented at the last minute because of the attentiveness of the nurse or even the patient. Furthermore, similar cases have been reported in which the error was not detected in time. In nearly all cases, the reason for the indication for irradiated blood components does appear in the patient's file.
If nurses and patients are sufficiently aware of the requirements that should be met by the blood component that is to be administered, it may be possible for them to play a supplementary role in checking whether components meet the specifications indicated for irradiation and other special requirements.

From 2008 to 2017, just over half of Dutch hospitals reported at least one near miss (n=47 from a total of 93; Table 9). One large hospital reported 24% of the near misses reported to TRIP in this period (n=114). It seems it may justifiably be concluded that near misses are not systematically reported to TRIP by all hospitals. This complicates a fruitful analysis of near misses on a national level. It may however be assumed that the introduction of mandatory safe incident reporting systems (veilig incident melden, VIM) in Dutch hospitals has led to these incidents being reported and analyzed in each hospital.

Table 9. Near miss reports, 2008-2017

	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Total
No. of reports	55	72	71	45	50	39	33	40	52	31	481
No. of reporting hospitals	14	20	21	16	18	15	16	15	17	11	47
Range per hospital	1-24	1-12	1-15	1-8	1-19	1-17	1-5	1-9	1-10	1-11	

Descriptions of Near miss cases (in Dutch) can be found in the Report of the Month series on www.tripnet.nl:
Report of the month January 2018: Identification when issuing of blood components: some pitfalls
Report of the month April 2018: failure to provide irradiated blood components
Report of the month July 2018: Blood group discrepancy

The Hemovigilance advisory board has recommended the thematic collection of certain types of near misses in order to substantiate the importance of introducing certain measures, for instance emphasizing the importance of digital identification when drawing blood samples too by reporting and analyzing all blood group discrepancies.. With this in mind, the digital form for reporting incidents in TRIP's new reporting system includes the possibility of reporting so-called "bulk reports".
As in 2016, only one hospital made use of this possibility to communicate a bulk report, which in this case concerned 9 cases of blood group discrepancy.

In a survey distributed to all hospitals, TRIP asked in which hospitals all cases of blood group discrepancies are registered systematically. Blood group discrepancy may result from an error, but can also result from treatments such as allogeneic hematopoietic stem cell transplantation (HSCT), if a transplant comes from a donor with a different blood group. In patients with certain blood group variants, blood group determination may yield varying results, dependent on the technique used to determine the blood group. It may be assumed that this type of particularity concerning a certain patient is always registered in the lab, but that respondents did not always consider this to be a case of registration of blood group discrepancy. The questions concerning blood group discrepancies were answered by over 50% of Dutch hospitals (n=47). In 34 of these hospitals, all blood group discrepancies are registered,
3 hospitals indicated that some cases of blood group discrepancies are registered. The way in which blood group discrepancies are registered within the hospital is not consistent across the Netherlands. Among other ways, registration takes place by reporting blood group discrepancies in internal incident reporting systems, in the transfusion history of a patient and/or in a laboratory information system (LIS). Out of the 10 hospitals that answered "no" when asked whether they registered blood group discrepancies, two indicated that they did treat this type of occurrence as an incident, by reporting the incident to TRIP, or by investigating its cause. A third hospital indicated that they do report this type of occurrence in the laboratory information system (LIS), but not in a reporting system (Table 10). Out of all responding hospitals, 20 (43%) indicated that they are unable to report or estimate the number of blood group discrepancies that occurred that year, approximately a third (n=16) indicated that they are able to report

the exact number of blood group discrepancies that occurred that year, and nine hospitals indicated they are able to provide an estimate of this number. The numbers that were given varied greatly and ranged from 0 to 15 cases per year or from 0 to 2 or 3 per 1000 blood group determinations (Table 11).

Table 10. Results of TRIP survey 2017: Does registration of blood group discrepancies take place systematically? (n=47 responding hospitals)

Registration blood group discrepancies	Total number	Type of registration			
		incident	LIS	Tf history	Not indicated
Yes	34	8	5	3	18
No	7				
No, but*	3	2	1		
Some	3			1	2

** are treated as incidents or reported in LIS*
Abbreviations: LIS = Laboratory Information System; Tf = transfusion

Table 11. Results of TRIP survey 2017: Is it possible to retrieve a total per year? (n=47 responding hospitals)

Registration blood group discrepancies	Total number	Number of blood group discrepancies known*			
		exact	estimated	not available	not indicated
Yes	34	14	6	12	2
No	10	2	3	5	
Some	3			3	

** may be reported as a number per year and/or per 1000 blood group determinations*

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.

- 71 reports from 30 hospitals (32%), 1-11 reports per hospital
- In 4 cases of OI a reaction was reported (additional category): 4x Other reaction
- 22 reports (9x mild NHFR; 5x TACO; 3x Other allergic reaction; 2x Post-transfusion bacteremia/sepsis; 2x NHTR; 1x Other reaction) have OI as an additional category.

In 2017, one of the larger subcategories of OI is that of cases in which there was a (considerable chance of) delay of transfusion, which caused risks of clinical issues due to lack of transfusion for patients (n=15).

Another subgroup consists of (nearly) unnecessary transfusions (n=17). In one of these cases, an investigation into a transfusion reaction (feeling of tiredness, rise in BP) showed that there was actually no need for a transfusion of two units of red blood cells, as the patient had a Hb of 6,3 mMol/L prior to the transfusion. This patient received extra furosemide and was kept in hospital for one night for observation, see Table 12.

Wastage of (a large part of) a blood component in a case where there has been no unintended delay of transfusion or (nearly) unnecessary transfusion remains the largest subgroup in 2017. In 14 of these cases, the wastage of the blood component is considered avoidable. Most of these cases concern a situation in which a blood component was collected at the lab but returned when it became clear that the transfusion would not take place (yet). In 7 of these cases the component had been spiked before determining whether or not the transfusion could be initiated at that moment. In two of the cases in which wastage was avoidable, the blood component was transferred with a patient to a different ward, which is against the rules. Of the remaining cases, in which the wastage was either judged inevitable or not assessable, 50% concern a situation in which the wastage of (part of) the blood component was caused by an issue with the IV which arose during administration. Further reported reasons for wastage of blood components: cancelling an order for platelets that had already been distributed, puncturing the component during the process of spiking it and initiating a transfusion for a patient who had not yet been assessed by a physician. In one case, blood components were unintentionally left in the emergency department when they should have been transferred along with a bleeding patient who was being transferred by ambulance.

Furthermore, small clusters of reports were received concerning errors and problems during administration of blood components, such as infusion in combination with an unsuitable IV solution or with medication (1x); an infusion time >6 hours, or pace of infusion set too rapidly (5x); issues concerning the investigation or actions following a positive screening result, a discovery in the TRIX database, or a transfusion reaction (5x); and abnormalities detected in blood components after they were delivered at the hospital (2x).

In the majority of cases in which an other incident was reported as an additional category (n=17), this was because a reaction was reported to the laboratory late or not at all. The five reactions which concern a different type of other incident are described in Table 12.

Case descriptions (in Dutch) of Other incident reports in 2017 can be found on www.tripnet.nl in the Report of the month series:
Report of the month October/November 2017: investigation of transfusion reaction?
Report of the month January 2018: Identification when issuing blood components: some pitfalls
Report of the month, May 2018: 2x 2 RBC → IBCT?

Table 12. Symptoms (reactions) in combination with other incidents in 2017

Reporting category	Subgroup of OI	Type of error and brief description	Additional category
Post-tf bacteremia/ sepsis	Test executed using samples from incorrect units	Patient develops TR with dyspnea, fever and chills after administration of multiple units of RBC. Decision is made to culture 4 units, which were sampled. Afterwards, it was established that 2 of these 4 units of RBC had not been administered to this patient, but to a different patient (after returning them to stock).	Other incident
NHTR	Wastage of (large part of) blood component	The blood component infuses subcutaneously. Administration is stopped and a new IV cannula sited. Tf is continued. Subsequently, patient develops fever and arm appears red, swollen and painful. Tf is broken off definitively.	Other incident
TACO	Failure of checks/ monitoring Tf	Furosemide has been prescribed for COPD patient (86 y/o), to be taken after infusion of 1st unit of RBC. Tablet is ready on bedside table, nurse fails to ensure timely ingestion. At end of unit, patient displays raised BP (193/81), mild rise in temperature and respiratory deterioration, thus CXR is ordered. Approximately 45 minutes after Tf, following a restroom visit she deteriorates acutely with dyspnea, decrease in 02 saturation, BP rise to 207/115, and fever. This is diagnosed as circulatory overload. Patient is briefly transferred to ICU for NIV and diuresis with intravenous furosemide, which stimulates abundant UP and quick recovery.	Other incident
Other allergic reaction	Wastage of (large part of) blood component	After administration of platelets, patient displays some urticaria. Dr decides to proceed with transfusion of prescribed RBC anyway. After 20 minutes, administration of RBC is stopped because urticaria have become generalized.	Other incident
Mild NHFR	Wastage of (large part of) blood component	Patient is to receive transfusion of 2 units of RBC. First unit is infused in full by 17:10, second unit is initiated at 18:00. After 5 minutes, a body temperature of 39.0 °C is measured, and no temperature prior to transfusion is known. Tf is stopped and investigation of reaction initiated.	Other incident
Other incident	Unnecessary transfusion	Patient with kidney disease and iron deficiency anemia was sent for Tf by GP. Cross matching and pre-transfusion Hb level determined: Hb 6.3 mMol/L; 2 units of RBC are administered without a physician checking the Hb level. Pt displays raised BP and is kept in the clinic for one night for observation.	Other reaction
	Wastage of (large part of) blood component	Tf broken off after detecting swelling in arm because blood has been infused subcutaneously.	Other reaction
	Wastage of (large part of) blood component	Patient shows rise in temperature after 1st RBC/ before administering 2nd RBC. Erroneously, transfusion of 2nd RBC is initiated nevertheless, but it is stopped and taken down after approximately 10 minutes.	Other reaction
	Wastage of (large part of) blood component	After transfusion of 1 RBC a hematoma across the entire forearm is seen. A large part of the blood has infused subcutaneously.	Other reaction

Abbreviations: BP=blood pressure; COPD=chronic obstructive pulmonary disease; CXR=chest x-ray; GP=general practitioner; Hb=hemoglobin; IV=intravenous; NHTR=non-hemolytic transfusion reaction; NHFR=non-hemolytic febrile reaction; NIV=non-invasive ventilation; RBC=red blood cells; TACO=transfusion-associated circulatory overload; Tf=transfusion; TR=transfusion reaction; UP=urine production; y/o=years old.

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.

- 6 reports from 5 hospitals (6%), 1-2 reports per hospital
- 1 report (new allo-antibody formation) with additional category of calculated risk situation in the past

A noteworthy report of calculated risk describes a situation in which blood group-identical platelets (A pos) were ordered for a different patient from the person requiring platelets. After the platelet units had been delivered to the hospital laboratory, the error was discovered. There was no possibility of storing the platelet concentrates, nor of returning them to Sanquin. In consultation with the Sanquin transfusion physician, a decision was taken to administer the platelets to the O negative patient despite the incompatibility.

The report with an additional category of calculated risk situation the past and three of the six reports from 2017 concern emergency situations in which circumstances make it impossible to take previously detected irregular antibodies (n=1) or preventive matching guidelines for the target group into consideration (n=2). In one case, a bleeding patient with negative antibody screening at the time of the transfusion turns out to have screened positively for anti-Fya previously, in a different hospital. This information was not available in the TRIX database at the time of the (T&S) blood component selection. Finally, one case concerns the administration of non-irradiated blood components in an emergency situation to a patient who had an indication for irradiated blood components because of treatment with fludarabine.

3.2 Infectious transfusion complications

Bacterial problems associated with blood transfusions

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.

Table 13 shows the numbers of reports of bacterial problems associated with blood transfusion in the years 2010-2017. 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 diagram also indicates how the results of the investigations are used to assess whether a report might represent a case of TTBI. Figure 6 illustrates this process of assessment using the numbers of reports in 2017.

Tabel 13. Overview of reports from hospitals relating to bacterial problems, 2010-2017

	2010	2011	2012	2013	2014	2015	2016	2017
Post-transfusion bacteremia/sepsis (cases of TTBI, as assessed by experts)	41 (3)	61 (2)	50 (1)	47 (2)	55 (2)	79 (2)	64 (3)	72 (2)
Post-transfusion bacteremia/sepsis as an additional category (not TTBI)	17	13	14	6	10	4	2	5
Bacterial contamination of blood component (including positive bacterial screening)	44	43	42	25	12	15	10	4
Bacterial contamination of blood component (including reports of positive bacterial screening) as an additional category	17	19	16	10	14	7	16	19

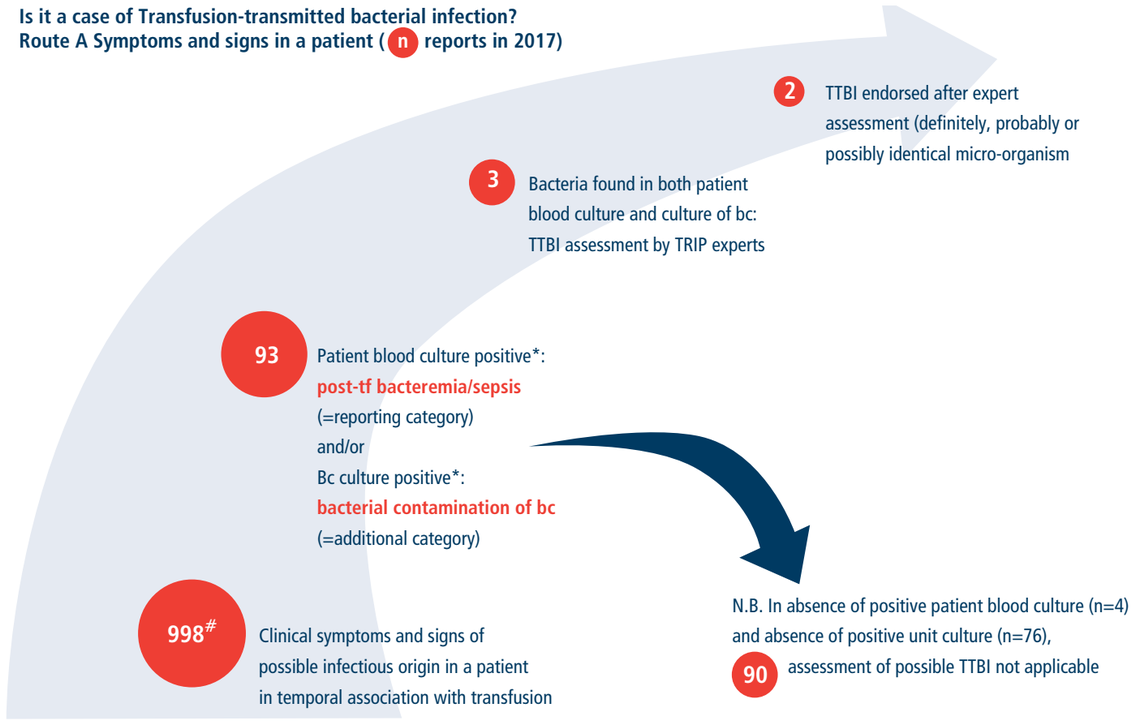


Figure 6. Assessment of TTBI, 2017

Abbreviations: pt=patient; bc=blood component; Tf=transfusion; TTBI=transfusion-transmitted bacterial infection
 # Number of reports in 2017 concerning reactions with rise/drop in temperature and/or chills
** Culture result should be deemed relevant*

For two reports of post-transfusion bacteremia/sepsis in 2017 (2x severity grade 2) the same micro-organism was detected in the patient's post-transfusion blood culture as in the culture of the administered blood component. These reports have been discussed by the Expert Committee. Both cases were judged to be cases in which transfusion-transmitted bacterial infection (TTBI) should be considered possible, see Table 14 (section on post-transfusion bacteremia/sepsis).

Furthermore, four reactions were reported in cases in which a blood component (3x platelets, 1x RBC) was administered that was later recalled by Sanquin because of a positive bacterial screening result on a platelet unit. These reactions could possibly be ascribed to the administration of a contaminated blood component. In three of these cases, Propionibacterium acnes was detected in the culture of the blood component, in one case Staphylococcus saccharolyticus was detected in the culture of the pooled platelet unit produced using the same donation. In two of these cases, the patient's blood was also cultured after a reaction was detected. In one of these cases, no bacterial growth was detected in the culture, and in the other case a micro-organism different from the one in the blood component was detected, see Table 14 (section on post-transfusion bacteremia/sepsis). These reports were categorized as bacterial contamination of blood component and the reactions that were detected have been reported as an additional category (section on bacterial contamination of blood component). Bacterial screening of platelet units is an important safety measure but it cannot completely eliminate the risk of TTBI following transfusions of platelets or associated RBC units.

Post-transfusion bacteremia/sepsis

- 72 reports from 35 hospitals (38%), 1-8 reports per hospital
- 3 reports with bacterial contamination of blood component as an additional category
- 5 reports (1x bacterial contamination of blood component, 1x anaphylactic reaction and 3x TACO) with post-transfusion bacteremia/sepsis as an additional category, see Table 15 as well (section on bacterial contamination of blood component)

Table 14. Summary of TTBI assessment, 2017 (Expert meeting April 2018)

Patient blood culture	Unit (culture result in hospital)	BacTalert / Culture by Sanquin	Reporting category	Severity grade	Imputability of reaction	bc	TTBI
Enterococ. faecium	Enterococ. faecium	Negative*	Post-Tf bact/sepsis*	2	Possible	RBC	Possible
Gram neg E. coli	Gram neg E. coli	Negative	Post-Tf bact/sepsis	2	Possible	Plts	Possible
Staph. hominis	Staph. epidermidis	Not stated	Post-Tf bact/sepsis	1	Possible	Plts	Not applicable
Staph. epidermidis, Staph. haemolyticus	Not performed#	Staph. Sacharolyticus	Bacterial contamination of bc	2	Possible	Plts	Not applicable

Abbreviations: bc=blood component; Enterococ.=Enterococcus; Plts=platelets; Post-Tf bact/sepsis=post-transfusion bacteremia/sepsis; RBC=red blood cells; Staph.=Staphylococcus; TTBI=transfusion-transmitted bacterial infection
** Concerns BacTalert screening result of platelets from same donation*
 # The detected rise in temperature in this patient with pre-existing fever was only classified as a possible transfusion reaction following the notification from Sanquin

Bacterial contamination of blood component

- 4 reports concerning notifications of positive bacterial screening from Sanquin, from 4 reporting hospitals.
- 4 cases with an additional category (2x other reaction, 1x other allergic reaction and 1x post-transfusion bacteremia/sepsis). In two cases the laboratory only received reports of the patient's

symptoms during or shortly after the transfusion after Sanquin had sent a notification about the positive screening results of the blood components.

- 19 reports (11x other reaction, 3x NHR, 1x other allergic reaction, 1x TACO and 3x post-transfusion bacteremia/sepsis) with an additional category of bacterial contamination of blood component (Figure 6, Tables 14 and 15).

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

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

Table 15. Overview of reactions (excluding post-transfusion bacteremia/sepsis) reported with an additional category of bacterial contamination of a blood component

Remarks re TR* and patient#	Blood component culture$ (culture performed in hospital); in none of the cases did the component screen positively at Sanquin	Reporting category	Total	Patient blood culture
Oncology patient without pre-existing infection	Staphylococcus sp (not aureus) (RBC)	Mild NHFR	1	Not performed
	Staphylococcus aureus (Plts)	Other reaction	1	No growth
	2x Paracoccus yeei (2x Plts)	Mild NHFR	1	No growth
		Other reaction	1	No growth
	Micrococcus luteus (Plts)	Other reaction	1	Not performed
Oncology patient with pre-existing infection and/or already receiving AB	Staphylococcus sp (not aureus) (1x Plts, 1x RBC)	Other allergic reaction	1	Not stated
		Other reaction	1	Not performed
	Staphylococcus aureus (2x RBC)	Other reaction	2	No growth
Other patients without pre-existing infection	Staphylococcus sp (not aureus) (2x Plts, 2x RBC)	Other reaction	3	No growth
		Circulatory overload	1	Not stated
	Clostridium (RBC)	Other reaction	1	No growth
Other patients with pre-existing infection	E. coli (RBC)	Other reaction	1	No growth
	Bacillus pumilus (RBC)	NHTR	1	Before and after Tf positive result for different m.o.
	Total		**16**	

* *Concerns a TR with rise in temperature and chills or solely chills in over 80% (n=13) of the cases, with or without further symptoms (remaining cases: 1x generalized redness and itching; 1x dyspnea and transpiration; 1x abdominal pain, rapid pulse and transpiration)*

\# *Concerns an oncology patient (5x hemato-oncology) in 56% (n=9) of the cases*

$ *Blood components: 9x RBC en 7x Platelets*

Abbreviations: AB = antibiotics; NHFR = non-hemolytic febrile reaction; m.o.=micro-organism; NHTR = non-hemolytic transfusion reaction; Plts=platelets; RBC=red blood cells; sp = species; Tf = transfusion; TR = transfusion reaction

Table 16. Overview of bacteriological screening of platelet concentrates by Sanquin

Total numbers (Sanquin)	2010	2011	2012	2013	2014	2015	2016	2017
Platelet concentrates with initial positive result	332	321	238	165	214	190	218	188
Units already transfused (Platelet concentrates and corresponding RBC units)	106	125	90	83	80	82	79	96 *

* *Information provided to Sanquin: 3x mild reaction; 3x hospital did not reply to Sanquin following notification*
Abbreviations: RBC=red blood cells

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 hospitalsn

In 2017, TRIP received one report concerning post-transfusion viral infection. A patient that received chemotherapy and subsequently hematopoietic stem cell transplantation in 2016 developed symptoms in 2017 and was later diagnosed with hepatitis E. Testing of the patient's blood samples that had been stored in the hospital demonstrated (retrospectively) that the infection could be detected in the autumn of 2016. Further investigations by Sanquin confirmed that the infection was transmitted by a pooled platelet concentrate (genetically identical sequences).

Another report concerning hepatitis E had not been finalized at the time of publication of the 2016 report. Further investigations by Sanquin were unable to confirm or rule out that the infection had been transmitted via an administered blood component because of the patient's low-grade viremia (possible imputability). Because hepatitis E can take a serious course in patients with immunosuppression, in consultation with the Dutch Ministry of Health, Welfare and Sport, midway through 2017 Sanquin introduced a screening test for Hepatitis E virus (HEV) for donations which are used for the production of labile blood components (a minipool NAT test). The main source for transmission of HEV is the food chain; in healthy individuals HEV infection gives a viremia which lasts for several weeks but Is generally asymptomatic.

Look-back by the blood establishment

Retrospective notification of a possibly infectious donation, leading to investigation of the recipient for that infection

In 2017, TRIP received five reports from hospitals that were connected to look-back investigations by Sanquin. In one case, the report concerned a unit which turned out to come from a donor that had failed to report use of antibiotics at the time of donation. There was no report of any symptoms in the recipient of the related unit (platelet concentrate). In four cases, the look-back investigations by Sanquin were related to prior donations of a donor in whom a seroconversion was detected or whose donation was HEV positive.

Information from Sanquin

In 2017, seven seroconversions occurred (3x HBV, 2x Syphilis, 2x HIV). As prescribed by the protocol, look-back investigations were performed, but no transmissions were found..

Infectious transfusion complications: conclusion

There were no reports of viral infections transmitted in 2017. Two reported bacterial infections (1x Enterococcus faecium, 1x E. coli; both severity grade 2) were judged to represent TTBI.
This demonstrates again that patients in the Netherlands are at a very low risk of contracting an infection through blood transfusion of 1 infection per 100,000-250,000 units administered.

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.

- 104 reports from 45 reporting hospitals (51%), 1-10 reports per hospital
- In 4 reports, other incident was added as an additional category (1x administration error; 3x reaction not reported to blood transfusion laboratory)

In comparison to previous years, 2017 shows a clear increase in reports of TACO (2015: 76; 2016; 87), both in the total number of reports and in the number of reports with a severity grade of 2 or higher (n=33). In 98% (n=102) of the TACO cases, the imputability was rated possible, probable or definite. As in recent years, the reporting category of TACO encompasses the largest number of reports with a high severity grade. Table 17 shows a breakdown of the reports according to severity grade and imputability.

In 2017, TRIP and the Hemovigilance advisory board developed TACO pocket reference cards for physicians and nurses, in support of implementing preventive measures against TACO for patients who are at an increased risk of developing this complication. From May 2018 onwards, these pocket reference cards will be available to hospitals. At the time of writing this report, a mobile application for the pocket reference cards is in development.

Most reports of TACO concern the administration of one or more RBC concentrates (n=90); a combination of an RBC concentrate with platelets or plasma (n=4); or the administration of a number of different blood components for acute major blood loss (n=2). Some cases are ascribed to the administration of only platelet concentrates (n=6) or plasma (n=2). In four cases TACO occurred in combination within incident classified as other incident. In one case, the prescribed 20 mg of furosemide was not administered. Approximately 45 minutes later the patient developed signs of cardiac asthma, which necessitated a transfer to the ICU. In the other three cases, the reaction was not reported to the blood transfusion laboratory.

Furthermore, in 2017 TRIP received two reports classified as other incident with an additional category of other reaction, in which symptoms were described which could fit circulatory overload. However, the symptoms in these cases did not sufficiently fit the criteria for TACO to be classified and reported as such. In one case, a patient displayed a considerable rise in blood pressure after a transfusion that eventually turned out to be unnecessary. Furosemide was administered and the patient was briefly admitted to hospital for observation. In the other case, a possible transfusion reaction was not reported to the blood transfusion lab. In this case, a patient who was known to suffer from angina pectoris experienced chest pain and a rise in blood pressure during the administration of a red blood cell concentrate.

A number of 2017 TACO cases have been described (in Dutch) in the Report of the Month series on www.tripnet.nl:
Report of the month September 2017: Dyspnea, which reporting category?
Report of the month December 2017: Pneumonia? Or perhaps not
Report of the month February/June 2017: Is it a transfusion reaction?

Table 17. Severity and imputability of TACO cases in 2017

Imputability	Total number of reports	Severity grade			
		1	2	3	4
Definite	10	7	3		
Probable	27	19	7		1
Possible	65	43	12	5	5
Unlikely	2	2			
Total	104	71	22	5	6

Transfusion-related acute lung injury (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.

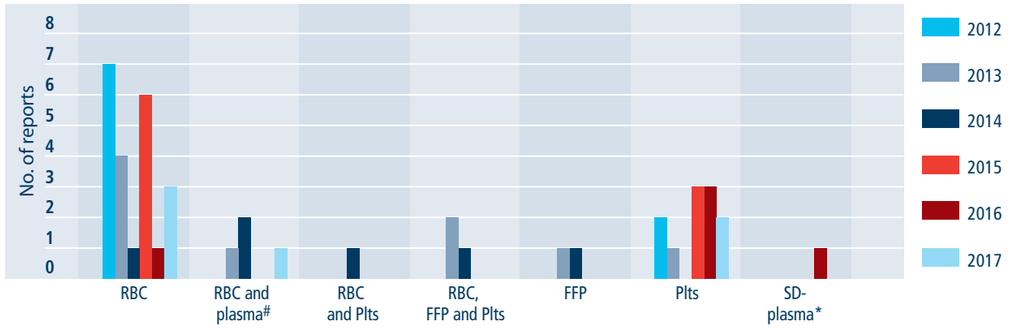


Figure 7. Type of blood component in TRALI reports of certain, probable or possible imputability, 2012-2017

 # concerns red blood cells + FFP in 2013-2014 and red blood cells + SD-plasma in 2017

** report discussed in 2016; patient had multiple TRALI/ARDS risk factors and circulatory overload could not be ruled out*

After review of all reports of TRALI – in most cases the reports were also discussed with the Expert Committee – six reports were registered as TRALI, a number similar to that of previous years. For five reports, the severity grade was 2 or higher and the imputability was assessed as possible, probable or definite. Figure 7 shows the blood components transfused to patients in whom TRALI was reported from 2012 to 2017.

Can a patient have both TRALI and TACO?

Remarkably, in one case TACO was reported as an additional category, and there were features of both TRALI and TACO in the patient. This phenomenon had also been observed previously, for instance in 2016, in TRIP's data. At the time of writing this report, an international group is working on a revision of the definition of TRALI. According to provisional communications from this group, the possibility of a combination of TACO and TRALI will be recognised as a formal reporting category.

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, or 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 exact nature of reactions reported as TAD is unclear. In 2016, 8 reports of TAD were submitted, none of which was categorised as severe. In 2017, however, two of the seven TAD reports were rated as severe (severity grade 2).

Table 18 shows the blood components and patient characteristics in TAD cases in 2016 and 2017. The average age of patients in whom TAD is reported is 53 years old. Last year, based on the reported reactions, it was found that the average age for TAD is more similar to that of TRALI (average of 53 years old) than that of TACO (average of 73 years old). For other reactions with dyspnea, the average age was higher. In 2017, TAD commenced on average 1 hour and 36 minutes after the transfusion was started (median 1:30).

Internationally, work is currently being done on revisions of the definitions of circulatory overload and TRALI. Because a criterion for reporting a reaction as TAD is that circulatory overload and TRALI should be excluded, this revision will also affect the reporting category of TAD. Pending the finalisation of this work, TRIP's practice is to only register reports as TAD if results of investigations show it can reasonably be ruled out that the reported dyspnea was caused by TRALI, TACO, an anaphylactic reaction or the underlying clinical condition of a patient.

Patient characteristics and features of reaction in 2016 and 2017 TAD reports

Type of reaction	2016 (n=8)	2017 (n=7)
Patient		
Age (average; range)	53 (14-77)	53 (30-81)
M/F	3F 5M	4F 3M
Imputability		
Definite	-	-
Probable	2	1
Possible	6	4
Unlikely	-	2
Product		
RBC	7	5
Platelets	1	2
Reaction		
Severity grade (average)	1	1.3
Number of severe cases (definite, probable, possible)	-	2
Interval from initiation of transfusion (average)	1h 05 mins	1h 36 mins
Symptoms (besides dyspnea and/or drop in oxygen saturation)		
Chest heaviness		1
Rise in temperature	3	4
Nausea and/or vomiting	1	3
Drop in blood pressure (≥ 20 mm Hg)	3	1
Tachycardia		4

Conclusion TACO, TRALI and TAD

Among reports of respiratory complications of blood transfusions, the yearly number of reports of TRALI is stable, but TACO is being recognized and reported more and more often. In 2017, most reports of serious transfusion reactions were associated with TACO; TRIP is issuing a tool for physicians and nurses to aid them in applying preventive measures to avoid TACO, such as decreasing the speed at which blood components are infused, and preventively administering loop diuretics (furosemide). A small number of reports is registered in the new category TAD. It is important to investigate reactions and apply the definitions of reactions with respiratory complications consistently, in order to gain a better understanding of such reactions and improve the means of preventing them.

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 mm Hg, fever/chills, nausea/vomiting, back pain, dark or red urine, no or poor increase of Hb level or an unexpected drop in Hb.

2017:

- 16 reports
- All reports involve transfusion of red blood cells; in one case the patient also received platelets.
- One AHTR occurred in a neonate, cause/mechanism unclear (imputability: unlikely): increased icterus was found in the patient one day after the Tf and an exchange transfusion was indicated.
- In 1 case, AHTR was reported as an additional category following the administration of ABO and irregular antibody incompatible red blood cells (AHTR severity grade 3 with a definite imputability). This report was discussed in chapter 3.1 (section on IBCT). AHTR was also reported as an additional category in a case categorized as other reaction and in a case of post-transfusion bacteremia/sepsis.
- Reports of AHTR in relation to the number of red blood cell units distributed are stable from year to year (Figure 8).

The 16 reports of which the imputability has been classified as definite, probable or possible are summarized in Table 19. Figure 8 shows that the number of reports of AHTR is similar to that of other years. Furthermore, as is shown in Figure 9, the symptoms reported align with what is to be expected in AHTR. For approximately half of the reactions, the cause of the reaction was established; this corresponds to reports from previous years (2014; 2015), in which TRIP highlighted that the cause of hemolysis can be established only in a limited number of cases of AHTR.

A case of AHTR is described (in Dutch) on www.tripnet.nl in the Report of the Month series:
Report of the month August 2018: A transfusion reaction with fever, dyspnea and increased blood pressure

Table 19 AHTR (definite, probable or possible) in 2017

AHTR N=16	
Age	Median 70, range 0-87;
Sex	10 M, 6 F
Previous Tf and/or pregnancy	Two male patients (one was the neonate described above) with no previous Tf One female patient had never received a Tf or been pregnant One female patient had a reaction after a post-partum Tf 12/16 had previously received a Tf
Severity grade	9 severe (1x grade 3, 8x grade 2), 7x grade 1
Cause	One patient with underlying autoimmune hemolytic anemia (AIHA) had 3 reactions (2x severe); he was treated with intravenous immunoglobulin therapy. 1x anti-E, 1x anti-Le(a) and anti-Le(b) 1x retrospectively had a positive cross match, presumably from antibody for low frequency blood group antigen 1x AHTR after administering platelets of blood group O to a patient with blood group A In the remaining (9) cases, it was not possible to establish the cause
Hemolysis-parameters and/or Hb course	In all cases consistent with hemolysis
Interval	Median 2h 45 mins after the start of Tf, in 6/16 cases the transfusion was broken off

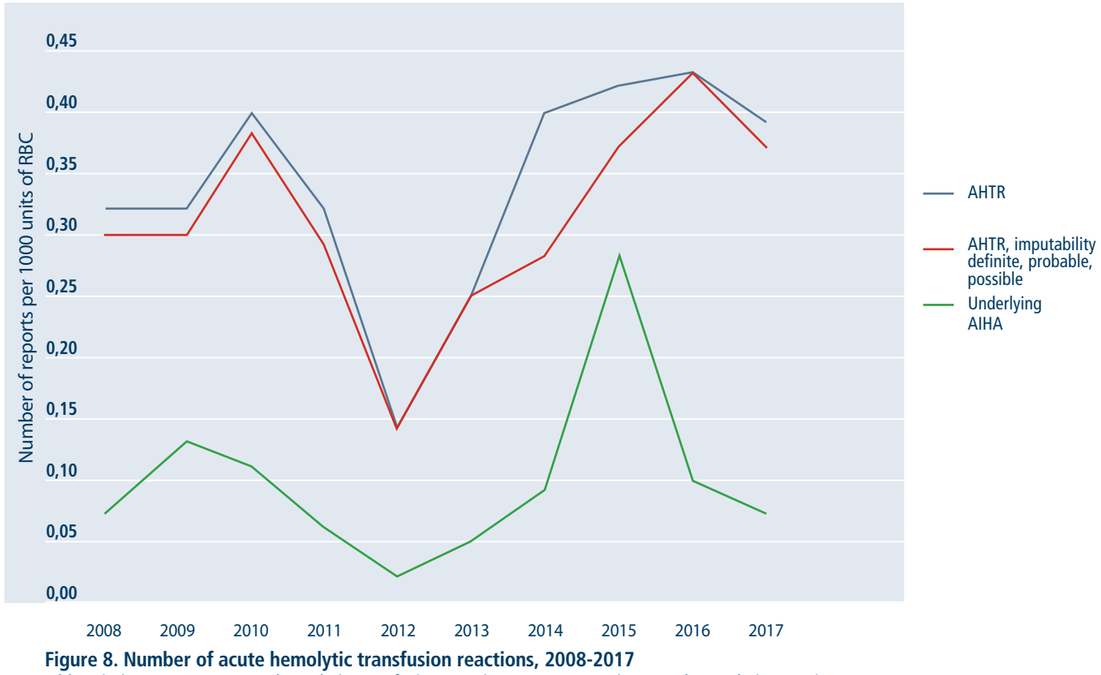


Figure 8. Number of acute hemolytic transfusion reactions, 2008-2017
Abbreviations: AHTR = acute hemolytic transfusion reaction; AIHA = autoimmune haemolytic anemia

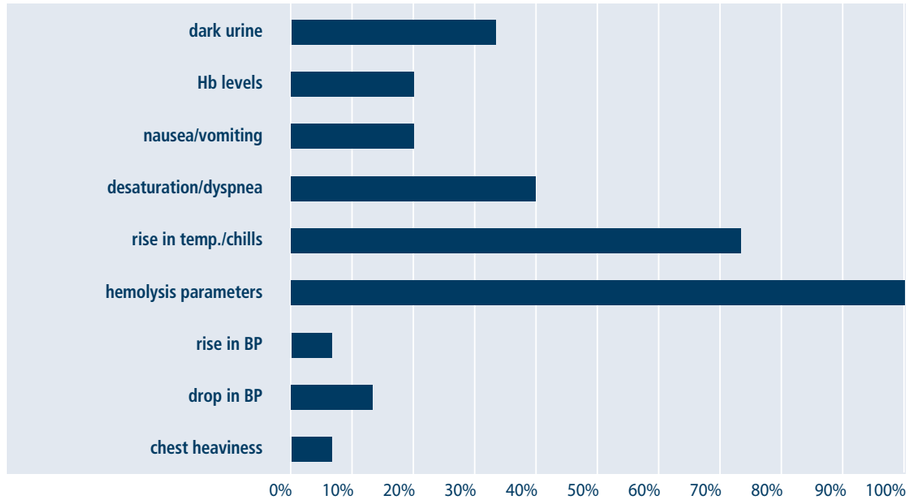


Figure 9. Signs and symptoms reported with acute hemolytic transfusion reactions in 2017 (n=16)
Abbreviations: AHTR = acute hemolytic transfusion reaction; BP= blood pressure

Delayed hemolytic transfusion reaction (DHTR)

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.

- In 2017, TRIP received a total of eight reports of delayed hemolytic transfusion reactions, the imputability of all reactions being definite, probable, or possible
- In all cases the reaction occurred in a female patient receiving red blood cells
- In three out of eight reports, the DHTR was discovered after a new antibody was detected, and therefore the DHTR was registered as an additional category.
- One report concerns a case in which a Parvovirus B19-safe blood component should have been selected but was not. In this case, the transfusion of an incorrect blood component was registered as an additional category. The error was judged not to be related to the DHTR. The report is discussed in chapter 3.1 (chapter on IBCT).
- Table 20 summarizes the reports of DHTR in 2017. Figures 10 and 11 display the number and severity of cases of DHTR since 2008.
- As has been noted in previous years, the number of cases of a DHTR in relation to the number of red blood cell units distributed shows a downward trend. Recommendations for preventive matching may have contributed to this trend. Additionally, the nation-wide implementation of TRIX (Transfusion Register for Irregular antibodies and crossmatch(X)-problems) may have had a positive influence. However, because entry of historically demonstrated antibodies into the TRIX database is only performed on a limited scale, the database's potential benefits are not yet being reaped to their full potential.

A 2017 DHTR case is described (in Dutch) onwww.tripnet.nl in the Report of the Month series:
Report of the month march 2018: post-transfusion viral infection?

Table 20. DHTR* in 2017

DHTR	(imputability: definite, probable, possible) N=8
Age (years)	Median 49, range 20-64;
Sex, component	8 F, all receiving red blood cell concentrates
Previous Tf and/or pregnancy	In one case, no previous Tf was recorded, nor was any information on possible previous pregnancies reported. In seven cases, the patient had previously received a transfusion, and two reports also note a previous pregnancy.
Severity grade	2x severe (grade 2) 4x grade 1 and 2x grade 0 (i.e. changes in laboratory parameters only)
Cause	4x anti-Jk(a) and potentially a fifth report (anti-Jk(a) detected but eluate was negative; DHTR reported as additional category) 1x anti-Fy(a) 1x anti-Fy(a); anti-Fy3; anti-S 1x patient with thalassemia, no serologic explanation found
Hemolysis parameters and/or Hb course	In all cases laboratory determinations yielded abnormalities were consistent with hemolysis and showed Hb decrease
Clinical symptoms	Three reports note the following symptoms respectively: back pain and jaundice; red urine; symptoms of anemia (dizziness, shortness of breath/dyspnea; chest heaviness; chest pain)
Interval	Median 10.5 days, range 3-26 days

** DHTR as reporting category or as an additional category in reports of new allo-antibody formation*

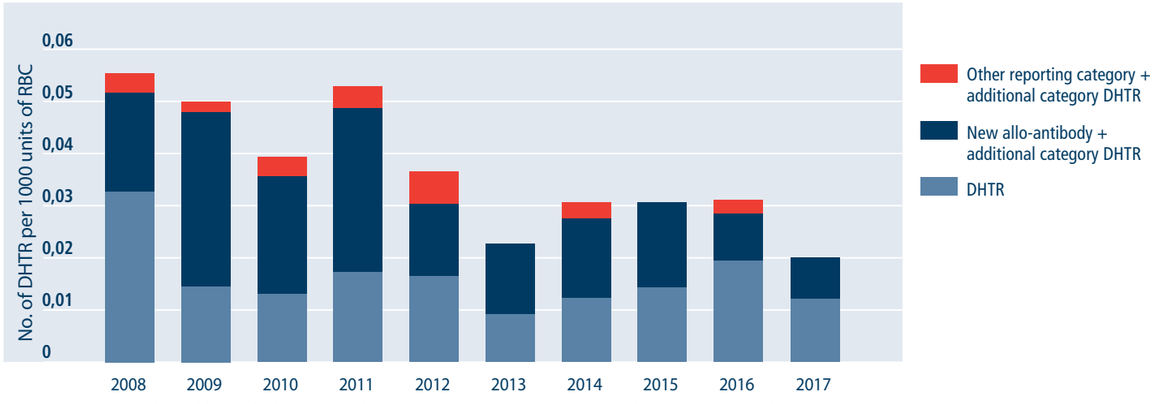


Figure 10. Delayed hemolytic transfusion reactions, 2008-2017, reporting category and additional category

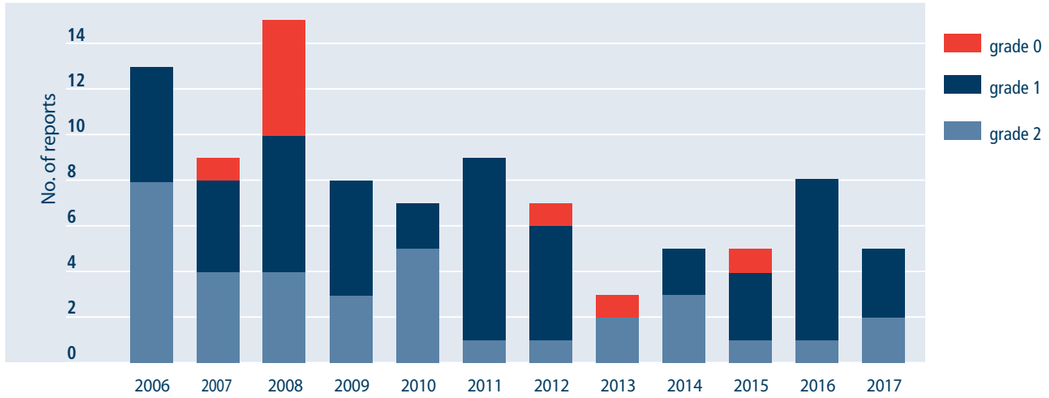


Figure 11. Severity of reports of delayed hemolytic transfusion reactions (reporting category; imputability definite, probable, possible), 2006-2017

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).

- 657 reports (674 including reports with new allo-antibody formation as an additional category), 802 new allo-antibodies.
- 66 reporting hospitals, range of 1-40 reports per hospital.
- 256 M and 418 F.
- 27 new allo-antibodies in women < 45 years old at the time of transfusion
  *specificities shown in Table 21.
  *formation of anti-D, anti-c, anti-E, or anti-K in 8 women <45 years old (Table 22).

Table 21. New allo-antibodies 2017: most frequent specificities in women and men.

New antibody	F < 45 year	F total	M	Ratio F/M	Percentage (TRIP 2017)	TRIX top 10*
anti-E	3	139	94	1.5	28%	16.8%
anti-K	5	98	56	1.8	18.5%	13.8%
anti-Fya	6	49	25	2.0	8.9%	5.3%
anti-Lua	1	20	27	0.7	5.7%	
anti-Jka	3	30	16	1.9	5.5%	3.2%
anti-Wra	-	28	17	1.6	5.4%	5.5%
anti-c	-	33	10	3.3	5.2%	5.2%
anti-C	-	32	10	3.2	5.1%	5.9%
anti-Kpa	2	18	13	1.4	3.7%	
anti-Jkb	-	11	9	1.2	2.4%	
anti-Cw	3	12	9	1.7	2.3%	3.3%
anti-S	1	11	6	1.8	2.0%	
anti-M	-	11	5	2.2	1.9%	9.5%
anti-D	1	8	6	1.3	1.7%	11.6%
anti-e	1	6	6	1.0	1.4%	
anti-Lea	1	3	3	1.0	0.7%	6.0%

** Information presented by the TRIX users' board at the 2017 NVB-TRIP symposium*

Tabel 22. Reports of formation of anti-K and anti-c in women <45 years old in 2017

Antibody	2016	2017
Anti-K	6 1x IBCT 2x Calculated risk situation/emergency 1x platelets 2x Tf 2002 or before	5 5x Tf 2002 or before
Anti-c	4 2x calculated risk situation/emergency 2x Tf 2012 or before	
Anti-E	8 1x platelets 1x O neg emergency situation, selection error 5x Tf 2011 or before 1x Tf 2014, patient aged 43 y/o, no further details	3 1x Tf 2014 (at that time K negative policy only in the hospital) 1x calculated risk in emergency situation 1x Tf in 2002

Other reaction

Transfusion reaction which does not fit into the categories above.

- As in previous years, the category of other reaction represents the fourth largest number of reported reactions (249)
- Since 2010, other reactions are one of the three categories with most reports of transfusion reactions of severity grade 2 or higher with a definite, probable or possible imputability.
- Imputability is low for reports in which the symptoms that occur or worsen during or after the transfusion may (partly) be explained by the patient's underlying medical condition.
- Increase in the number of reports (n=58) in which hypotension occurred, sometimes combined with other symptoms (Table 23)

Table 23. Types of reactions that are registered as other reaction (broken down as in previous reports))

Type of reaction	2016	2017	2017 D,P	2017 P	2017 ≥ gr 2*
Reactions with hypotension	40	52	10	38	1
Reactions with dyspnea	24	37	6	23	-
Rise in blood pressure	9	13	0	11	-
(Possible) cardiac symptoms	14	12	1	8	-
Did not completely fit TRIP definition for standard category	58	45	11	25	3
Unproven sepsis	2	5	0	5	3
Other signs	60	78	14	50	6
Total	**207**	**249**	**42**	**160**	**13**

Abbreviations: D,P = Definite, Probable; P = Possible
** Imputability definite, probable or possible*

Reports of other reaction with hypotension

This subgroup of reports is summarized in Table 24. Some of these reactions consisted merely of a drop in blood pressure, at times into the hypotensive range. Other reports described a reaction in which a drop in blood pressure occurred with other symptoms. Internationally, some hemovigilance systems recognise hypotensive reactions as a specific type of transfusion reaction. Within the subgroup of reports of other reactions that TRIP received in 2017, six reports meet the (international ISBT) criteria of a hypotensive reaction which include a drop in systolic blood pressure to ≤ 80 mm Hg. In 2013, the TRIP Hemovigilance advisory board decided it would not be useful to create a separate reporting category for hypotensive reactions. On the one hand because proper patient monitoring should ensure that action is taken before a patient's blood pressure gets to be so low, and on the other hand to restrict the total number of possible reporting categories. However, due to the large number of reports of a reaction with hypotension in 2017, TRIP will flag reports that fit the international definition for future analyses.

Hypotensive transfusion reaction

Among cases of hypotensive transfusion reactions that have been described in the scientific literature, some have been attributed to the use of a bedside leukocyte filter, but cases of such reactions in which such a filter was not used have been reported as well, e.g. in countries where a switch to universal pre-storage leukodepletion has been made. In a small number of cases, an association with the use of angiotensin converting enzyme (ACE) inhibitors has been described; a possible explanation is the fact that this type of medication slows the breaking down of bradykinin (Chapter on Hypotensive Transfusion Reactions, Robillard P. et al., in Popovsky et al., Transfusion Reactions, 4th edition).

The ISBT definition for hypotensive reactions is as follows:
"This reaction is characterized by hypotension defined as a drop in systolic blood pressure of ≥ 30 mm Hg occurring during or within one hour of completing transfusion and a systolic blood pressure ≤ 80 mm Hg.

Most reactions do occur very rapidly after the start of the transfusion (within minutes).
This reaction responds rapidly to cessation of transfusion and supportive treatment.
This type of reaction appears to occur more frequently in patients on ACE inhibitors.
Hypotension is usually the sole manifestation but facial flushing and gastrointestinal symptoms may occur.

All other categories of adverse reactions presenting with hypotension, especially allergic reactions, must have been excluded. The underlying condition of the patient must also have been excluded as a possible explanation for the hypotension."

Table 24. Characteristics of reactions in the subgroup of other reactions with hypotension

Type of reaction	2017 (n=52)
Patient	
Age (average (years); range)	68 (3-101)
M/F	26F 26 M
Imputability	
Definite	0
Probable	10
Possible	38
Unlikely	4
Product	
RBC	47
Platelets	3
SD-plasma	2
Reaction	
Number of severe reactions (definite, probable, or possible)	1
Interval from initiating transfusion (average h:min)	1:04
Symptoms (besides drop in blood pressure)	
Chest heaviness	1
Rise in temperature	16
Nausea and/or vomiting	3
Bradycardia	1
Tachycardia	4

An other reaction case with hypotension is described (in Dutch) in the Report of the Month series on www.tripnet.nl:
Report of the month September 2018: transfusion reaction with hypotension

Reports of other reactions lacking in information

By submitting a reaction as other reaction (not including the more specific subgroups within the category), a reporter actually indicates that the cause of the observed symptoms is unclear. In some cases, this is inevitable, for instance when something unusual occurs during a transfusion, after which the transfusion is broken off and, according to the transfusion reaction protocol, hemolysis is ruled out as a cause through standard tests. The symptoms clear without any need for further action and it is unlikely that the reaction will recur. However, in some cases, the observed symptoms are pronounced, sometimes to the point that they are reported as severe. For these severe other reactions it is important to compile the report in collaboration with the treating physician and to supply sufficient information (for instance through providing an anonymized discharge letter as an attachment in the reporting system), to increase the value of the report and make it possible for lessons to be learned from the case on a national level.

Conclusion other reaction

In 2017 the number of reports classified as other reaction increased again, most notably in the subgroups of reactions with dyspnea and of reactions with hypotension. In the subgroup of reactions with hypotension, six reports describe a drop in systolic blood pressure to ≤ 80 mmHg. TRIP will flag these reports, which fit the international definition of a hypotensive transfusion reaction, in the database.

The analysis of all reports of other reactions showed (as has been the case before) that some reports of other reactions lack proper investigation into the reaction and/or proper substantiation. TRIP recommends to prepare (at least) reports of severe other reactions in collaboration with the treating physician.

3.4 Blood management techniques (BMT)

In 2017, TRIP received one report of a reaction from the use of autologous blood management techniques: a mild non-hemolytic febrile reaction after drain blood was reinfused after orthopedic surgery. Due to the decrease in application of BMT, in addition to the limited information available on how often these techniques are applied, TRIP has stopped collecting yearly data on the application of BMT. However, it remains important to recognize, treat, and report reactions in patients.

3.5 Reports with SD-plasma (Omniplasma®) in 2017

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. In 2014-2016, Omniplasma®, which is an SD-plasma produced from Dutch plasma donations collected by Sanquin, was progressively introduced as the standard plasma product for transfusion. Sanquin does still distribute FFP for pediatric use and other special indications.

Because SD-plasma is prepared under legislation on pharmaceutical products, the process of reporting reactions to SD-plasma falls under pharmacovigilance. However, in accordance with arrangements made between TRIP and Lareb, the Dutch pharmacovigilance agency, reports of transfusion reactions and/or transfusion incidents are made in the TRIP system, because of the similarities in using the different plasma products and the relevance of Omniplasma® for the transfusion chain. In 2018 the arrangements between TRIP and Lareb were updated. TRIP ensures that anonymised reports associated with the administration of Omniplasma® are entered into the Lareb reporting database (including cases in which labile blood components were also administered). After the reports have been coded according to pharmacovigilance practices, the reports are transferred to the European database Eudravigilance.
At the same time, the TRIP annual hemovigilance reports continue to provide a complete picture of the transfusion chain.

Figure 1 shows the course of the use of SD-plasma and Figure 2 shows the occurrence of all types of reactions per 1000 units of SD-plasma per year. The reactions associated with SD-plasma in 2016 and 2017 are broken down in Table 25. The categories which represent the largest numbers of reactions are the allergic reactions (anaphylactic and other allergic reactions), as was previously the case for FFP.

Table 25. Reports associated with SD-plasma in 2016 and 2017

	2016		2017	
Units distributed	64,124		63,945	
Units administered	58,800		57,980	
(number of hospitals)	(85)		(86)	
No. of reactions with SD-plasma (total)	29		46	
No. of reactions with SD-plasma only	12		32	
Severe reactions[#]	2		4	
Type of reaction	**SD only**	**SD in combination**	**SD only**	**SD in combination**
Anaphylactic reaction	2	2	6	2
Other allergic reaction	6	0	14	0
Mild NHFR	0	1	1	1
Non-hemolytic TR	1	5	4	6
New allo-antibody formation	0	4	0	1
Other reaction	2	2	5	1
Post-Tf bacteremia/sepsis	0	0	0	1
TRALI[$]	1	0	0	0
Transfusion-associated circulatory overload	0	3	2	2

[#] Cases where SD-plasma only was administered, with imputability definite, probable or possible
[$] See discussion in 2016 report

Conclusion SD-plasma

The side effects of the use of SD-plasma (Omniplasma®) reported in 2017 are similar to those reported in 2016 and are of a similar nature to the side effects that used to be reported for the use of 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 into 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 (MoH), 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.

The value of reporting and collecting transfusion reactions and incidents at the national level depends on the participation of all the reporting establishments. In 2017, TRIP received reports from 84 hospitals. Seven hospitals indicated that there had been no reports of incidents or reactions in the TRIP reporting categories. Two hospitals had not provided any information about reports or administered transfusions to TRIP at the time of compiling this report. Besides the hospitals, TRIP is in contact with 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). Three of the four licensed clinics informed TRIP that a transfusion no units were transfused that year. The fourth has indicated that reports, if necessary, will be made through the hospital to which they are contracted for component selection. Altogether, this makes the level of participation among hospitals 91/93=98%.

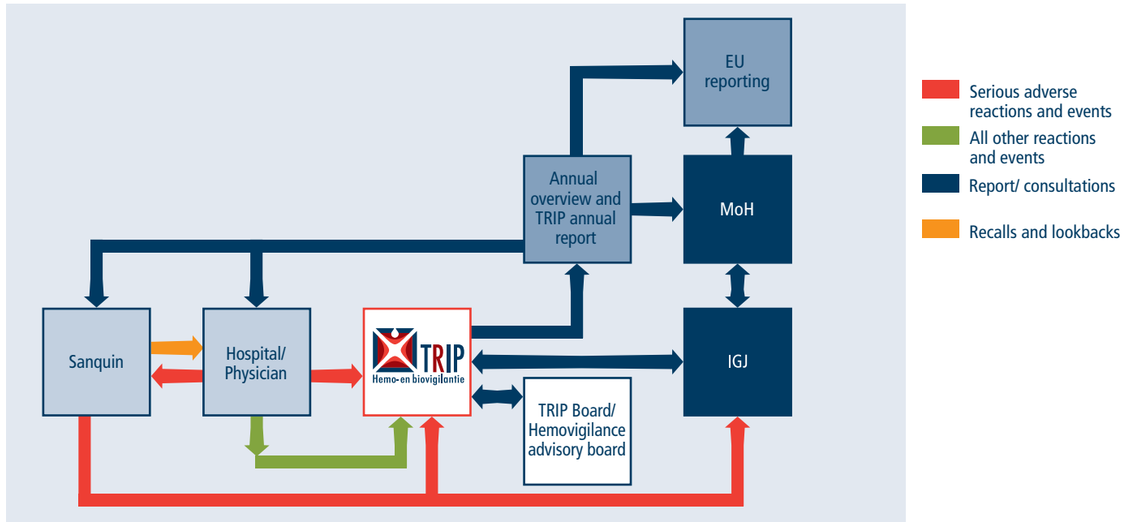


Figure 9. Flow of hemovigilance information and outputs in The Netherlands

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

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